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# Bismuth (III) triflate: An Economical and Environmentally Friendly Catalyst for the Nazarov Reaction

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# Abstract

We describe the use of bismuth (III) triflate as an efficient and environmentally friendly catalyst for the Nazarov reaction of aryl vinyl ketones, leading to the synthesis of 3-aryl-2-carboethoxy-1-indanones and 3-aryl-1-indanones. By changing the temperature and reaction time, it was possible to modulate the reactivity, allowing the synthesis of two different products in good to excellent yields (3-aryl-2-carboethoxy-1-indanones and 3-aryl-2-carbethoxy-1-indanones). The reaction does not need additives and is insensitive to both air and moisture. The preliminary biological evaluation of some indanones show a promissory profile against some human cancer line cells



# Keywords

Indanones; Heterocycles; Nazarov reaction; Bismuth; Catalysis


# Introduction

Natural products are the source of inspiration for several research groups that develop new synthetic methodologies. The chemistry of five-membered rings plays an important role within organic chemistry, both because of its wide occurrence in nature,[1] and its broad spectrum of biological activities. Within the class of five-membered rings, we find indanones (**1**). In this class, we can highlight some interesting compounds. Nakaterpiosinne (**2**), which inhibits the growth of P388 mouse leukemia cells with an average inhibitory concentration ($IC_{50}$) of 10 ng/mL, lepistatin A (**3**), along with two other new chlorinated analogs, that were isolated from Basidiomycete *Lepista sordida* culture, pauciflorol F (**4**), isolated from *Vatica pauciflora*, which is an important building block for the biosynthesis of bioactive polyphenols, in addition to having

antiviral activity, indacrinone (**5**), which is related to ethacrinic acid, and usually stimulates the reversible short-circuit current and the influx of sodium when applied to the epithelial surface of amphibian skin, and donepezil (**6**), a drug used to treat Alzheimer's disease.[2]

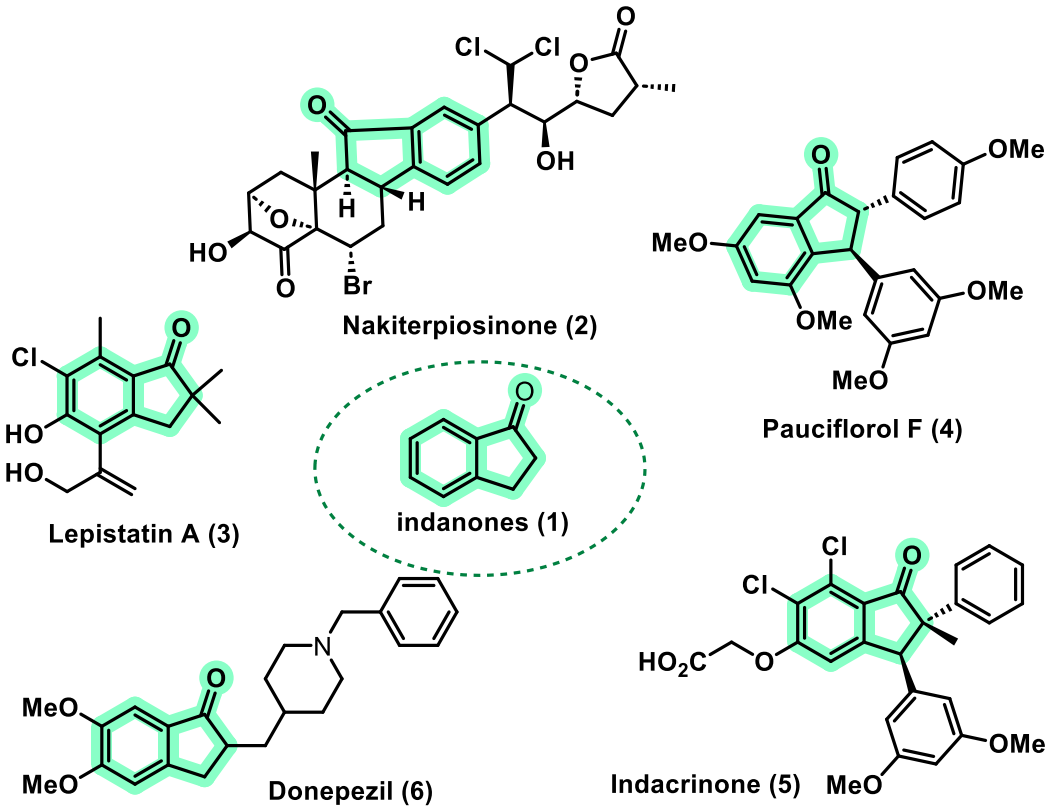



**Figure 1.** Example of different compounds containing the indanone moiety.

The interest in the preparation of functionalized indanone derivatives has increased enormously, and many synthetic methods have been developed, including Friedel-Crafts cyclization reactions,[3] cyclization of acetylenic derivatives,[4] ring contractions and ring expansions,[5] and the Nazarov reaction.[6]

The Nazarov cyclization is one of the most versatile and simple methods for preparing indanones from aryl vinyl ketone derivatives (**Scheme 1**).[6] The Nazarov reaction is classically formulated as a 4π electron conrotatory electrocyclization of a pentadienyl cation.[1[,[2] Until the past decade, the conditions used for the Nazarov reaction

involved the use of stoichiometric amounts of strong Lewis acids (e.g. $BF_3$, $TiCl_4$, $SnCl_4$, $AlCl_3$) in relation to the divinyl ketone derivative. [7]

In this context, some research groups developed methodologies that allowed the use of catalytic amounts of Lewis acids. By using more reactive divinyl ketone derivatives, the electrocyclization reaction could be mediated by weaker Lewis´s acids, and consequently catalytic amounts of them could be used. The first example of a catalytic version of the Nazarov cyclization was reported by Denmark and Jones.[8] They found that sub-stoichiometric amounts of $FeCl_3$ (40-50 mol%) promoted the cyclization of silylated derivatives efficiently, however when 10 mol% was used the conversion was poor. Denmark and Jones' pioneering work was use as inspiration for the development of catalytic methodologies for this reaction. In 2004, Lang and Trauner described the first report on an asymmetric catalytic Nazarov reaction.[9] In recent years, several strategies were reported employing different Lewis acid, such as, $AuCl_3/AgSbF_6$, Cu(II), $In(OTf)_3$, Ir(III), Al(III), $Sc(OTf)_3/LiClO_4$, $In(OTf)_3$/diphenylphosphoric acid (DPP), $Fe(OTf)_3/(CF_3)_2PhB(OH)_2$, iodine,[10] and other strategies.[11]

Although methodologies catalyzed by different Lewis acids are very efficient, including in asymmetric versions of the Nazarov reaction, the experimental protocols, in most cases, are quite laborious, requiring low-temperature conditions, the use of inert gas atmospheres, or the use of Lewis acids sensitive to moisture. [1b],[8c], [8d],[8g-f], [10a-b], [10d], [10h-10k], [12]

Despite the innumerous reports of protocols for the catalytic version of the Nazarov reaction, few of them describe the use of bismuth salts as catalysts for Nazarov-type reaction [13] and none for the classical Nazarov reaction. In this article, we describe a simple and direct protocol for the preparation of indanones through a classical Nazarov reaction catalyzed by Bismuth(III) triflate. In addition to its simplicity,

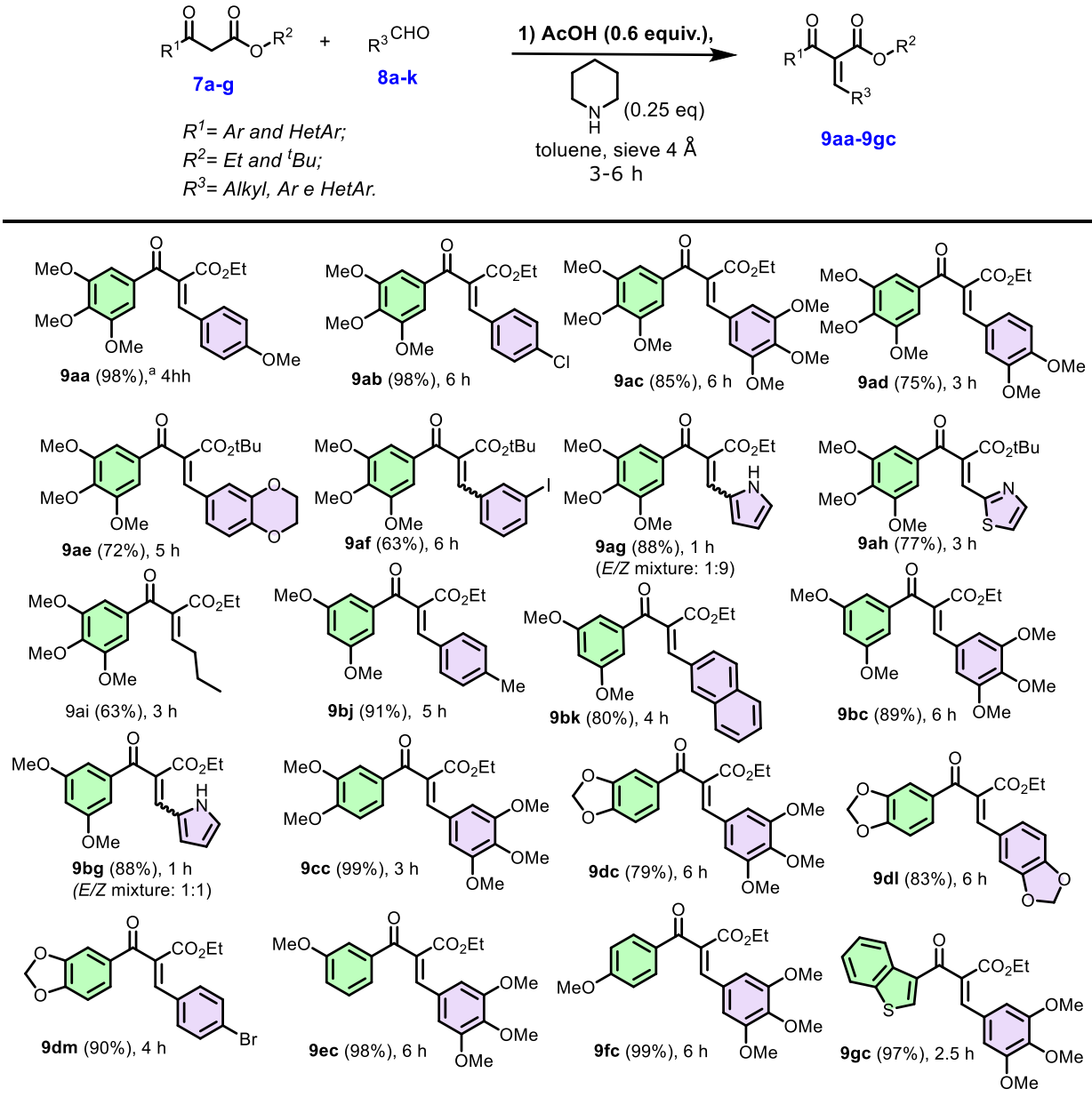
the moisture stability of bismuth triflate allows the protocol to be carried out under ambient atmospheric conditions.

# Results and Discussion

## Preparation of β-keto esters

We initiated our studies with the preparation of the β–ketoesters, that were synthesized according well-established protocols.[14],[15] The β–ketoesters were obtained employing a sequence of two reactions, the formation of the benzylic alcohol derivative, through a Reformatsky reaction using In(0), followed by a pyridinium chlorochromate (PCC) oxidation, giving the β–ketoesters **7a-g** in moderate to good yields.[14],[15] With the β–ketoesters prepared, we began the synthesis of the Knoevenagel derivatives. To do so, we employed an adapted protocol from the literature. Using 1.00 equivalent of the β–ketoester, 1.50 equivalents of aldehyde, 0.60 equivalents of acetic acid, and 0.25 equivalents of piperidine, the desired products were obtained in good to excellent yields and selectivities (*E*) (**Table 1**).[14],[15] Various substrates (**9aa-9gc**), containing electron donating, withdrawing and neutral groups, as well as heteroaryls (2-thiophene and 3-benzothiophene) were obtained in good to excellent yields. For derivatives **9af**, **9ag** and **9bq** we observed the formation of an *E/Z* mixture of products, inseparable by column chromatography.

**Table 1:** Synthesis of unsaturated β-ketoesters (Knoevenagel derivatives)



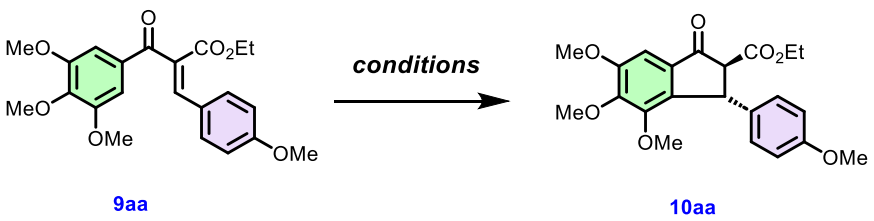

[a] Isolated yields after purification using silica gel column chromatography.

## Synthesis of 3-aryl-2-carboethoxy-1-indanones and 3-aryl-2-carbethoxy-1-indanones

With the starting materials prepared, we began evaluating the use of bismuth salts to promote the Nazarov reaction, using models already studied in the literature.[10] We investigated several conditions, such as type of catalyst, temperature, solvent, and the

amount of catalyst (**Table 2**). Our optimization studies began with the reaction of substrate **9aa** with $Bi(OTf)_3$ (10 mol%) in acetonitrile at room temperature (Entry 1, **Table 2**). The desired product was obtained in 72% after 12 hours. When the reaction was carried out at 40 °C for 8 hours, the yield increased slightly to 76% (Entry 2, **Table 2**). When the reaction was carried out at 60 °C, the yield increase to 93%, in addition to a marked decrease in reaction time (Entry 3, **Table 2**). Despite this excellent result, we continued to evaluate other catalysts to improve the yield and reaction time further. For this purpose, a series of Lewis acid such as $Bi(NO)_3$, $BiBr_3$, $BiCl_3$, $Yt(OTf)_3$, $Dy(OTf)_3$, $ZrCl_4$, $In(OTf)_3$, $InCl_3$, and $AlCl_3$ were selected as catalysts (Entries 5-13, **Table 2**), and even after this screening, the best result still remained the one obtained with $Bi(OTf)_3$. The Brønsted acids TFA and TsOH were also tested for the transformation, but gave worse results (Entries 14 and 15, **Table 2**). Once the catalyst was chosen, we investigated the influence of the solvent. For this purpose, we evaluated dichloroethane (DCE), dichloromethane (DCM), toluene, and tetrahydrofuran (THF) as solvents for the transformation (Entries 16-19, **Table 2**), but acetonitrile remained the best solvent. Finally, we evaluated the amount of catalyst, using two other catalyst loadings (5 and 20 mol%), but these variations also did not provide an improvement in the yield (Entries 20 and 21, **Table 2**). After this screening, the optimum condition employed 10 mol% of bismuth triflate ($Bi(OTf)_3$) in acetonitrile at 60 °C (Entry 3, **Table 2**).

**Table 2:** Optimization of the reaction conditions.




**9aa** **10aa**

| Entry | Catalyst (mol%) | Solvent | Temp. (ºC) | Time (h) | Yield (%)[a] |
|---|---|---|---|---|---|
| **1** | $Bi(OTf)_3$ (10) | acetonitrile | 25 | 12 | 72 |
| **2** | $Bi(OTf)_3$ (10) | acetonitrile | 40 | 8 | 76 |
| **3** | **$Bi(OTf)_3$ (10)** | **acetonitrile** | **60** | **2** | **93** |
| **4** | $Bi(OTf)_3$ (10) | acetonitrile | 70 | 2 | 88 |
| **5** | $Bi(NO)_3$ (10) | acetonitrile | 60 | 24 | 15[b] |
| **6** | $BiBr_3$ (10) | acetonitrile | 60 | 24 | 26[b] |
| **7** | $BiCl_3$ (10) | acetonitrile | 60 | 12 | 24[b] |
| **8** | $Yt(OTf)_3$(10) | acetonitrile | 60 | 24 | 15 [b] |
| **9** | $Dy(OTf)_3$ (10) | acetonitrile | 60 | 12 | 45 |
| **10** | $ZrCl_4$ (10) | acetonitrile | 60 | 12 | 58 |
| **11** | $In(OTf)_3$ (10) | acetonitrile | 60 | 2 | 71 |
| **12** | $InCl_3$ (10) | acetonitrile | 60 | 12 | 30 |
| **13** | $AlCl_3$ (10) | acetonitrile | 60 | 24 | 5 [b] |
| **14** | TFA (10) | acetonitrile | 60 | 6 | 58 |
| **15** | TsOH (10) | acetonitrile | 60 | 2 | 65 |
| **16** | $Bi(OTf)_3$ (10) | DCE | 60 | 1 | 65 |
| **17** | $Bi(OTf)_3$ (10) | DCM | 60 | 1 | 73 |
| **18** | $Bi(OTf)_3$ (10) | toluene | 60 | 1.5 | 67 |
| **19** | $Bi(OTf)_3$ (10) | THF | 60 | 3 | 53 |
| **20** | $Bi(OTf)_3$ (5) | acetonitrile | 60 | 2 | 87 |
| **21** | $Bi(OTf)_3$ (20) | acetonitrile | 60 | 1.5 | 91 |

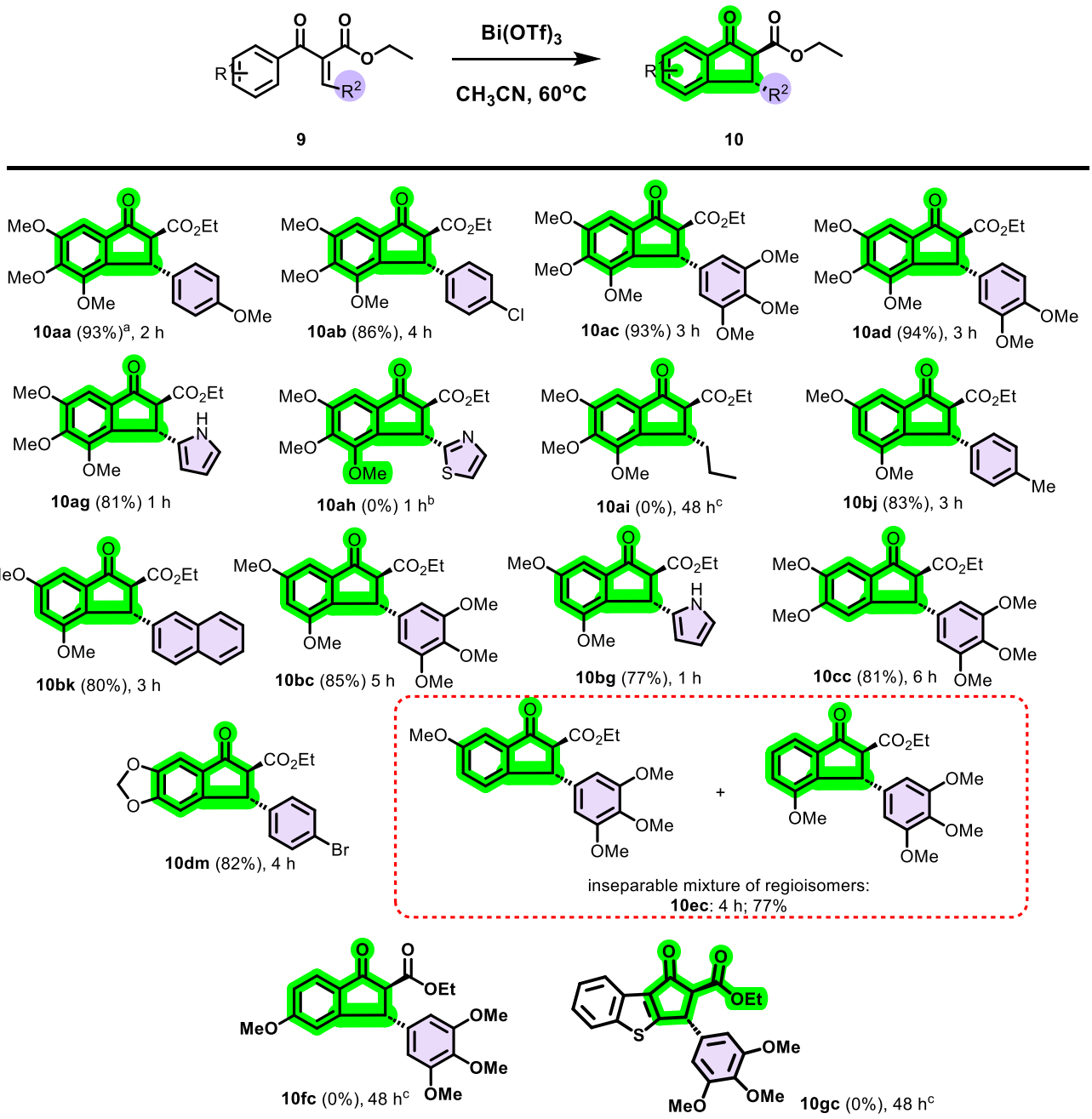
[a] Isolated yields after purification using silica gel column chromatography. [b] recovery of the starting material

With the growing environmental concern, and the need to use green reagents, the interest in the use of bismuth in organic synthesis has increased significantly as can be seen - which reflects the large number of works dedicated to this topic.[16],[17] In addition to the use of bismuth compounds to replace methodologies that use toxic heavy metals, methods that use bismuth compounds to promote reactions have the

following advantages: low cost, they are tolerant to the presence of water and air, thus not requiring special experimental techniques, such as inert atmosphere and anhydrous solvents.[18] The use of bismuth salts in organic synthesis has been reported in several transformations, such as epoxide opening,[19] ketal formation and deprotection,[20] Mannich reaction,[21] intramolecular Sakurai cyclization,[22] alcohol oxidation,[23] aromatic hydrocarbon nitration,[24] imine allylation,[25] Knoevenagel condensation,[26] Reformatsky reaction,[27] azalactone synthesis,[28] nitro reduction,[29] epoxide rearrangement, thiourea guanylation, among others.[30]

With the optimized conditions in hand, we explored the scope of the substrates. In general, substrates with electron donor groups provide better yields when compared to those obtained with neutral or electron-withdrawing groups. Particularly, for substrates **9ai**, **9fc** and 9gc, there was no formation of the corresponding indanones, even though the reaction remained under 60 °C for a longer period (48h), but the starting materials could be recovered. For substrate **9ah**, there was complete decomposition of the starting material, with the formation of several byproducts.

**Table 3**: Synthesis of 3-aryl-2-carboethoxy-1-indanones and 3-aryl-2-carbethoxy-1-indanones mediated by bismuth triflate.

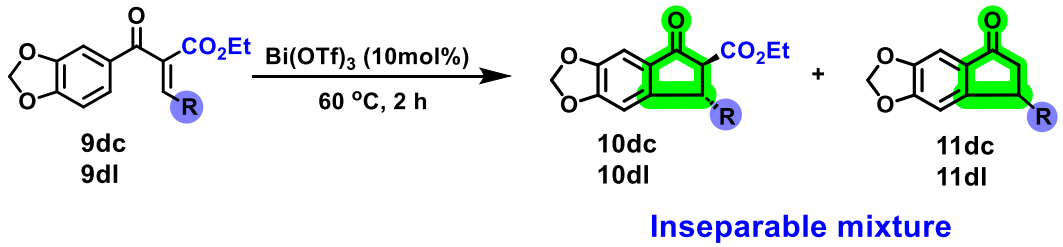



[a] Isolated yields after purification using silica gel column chromatography. b Extensive degradation. [c] The starting material was recovered. **Basic protocol**: In a sealed tube was added the Knoevenagel product (0.5 mmol), dry acetonitrile (2 mL), and $Bi(OTf)_3$ (0.05 mmol). The reaction mixture was stirred at 60 °C and monitored by TLC.

Surprisingly, when using the optimized condition for substrates **9dc** and **9dl**, we found that in addition to the products of interest, they also formed the decarboxylated

products, in an inseparable mixture. Given this result, we investigated another milder condition to avoid decarboxylation. For this, we proceeded the reaction for substrate **9dc** at room temperature for 24 hours. Despite this long period, we still observed the formation of the decarboxylated derivative, in addition to the partial recovery of the starting material (Table 4).

**Table 4**: Evaluation of the reactivity of **9dc** and **9dl** derivatives.

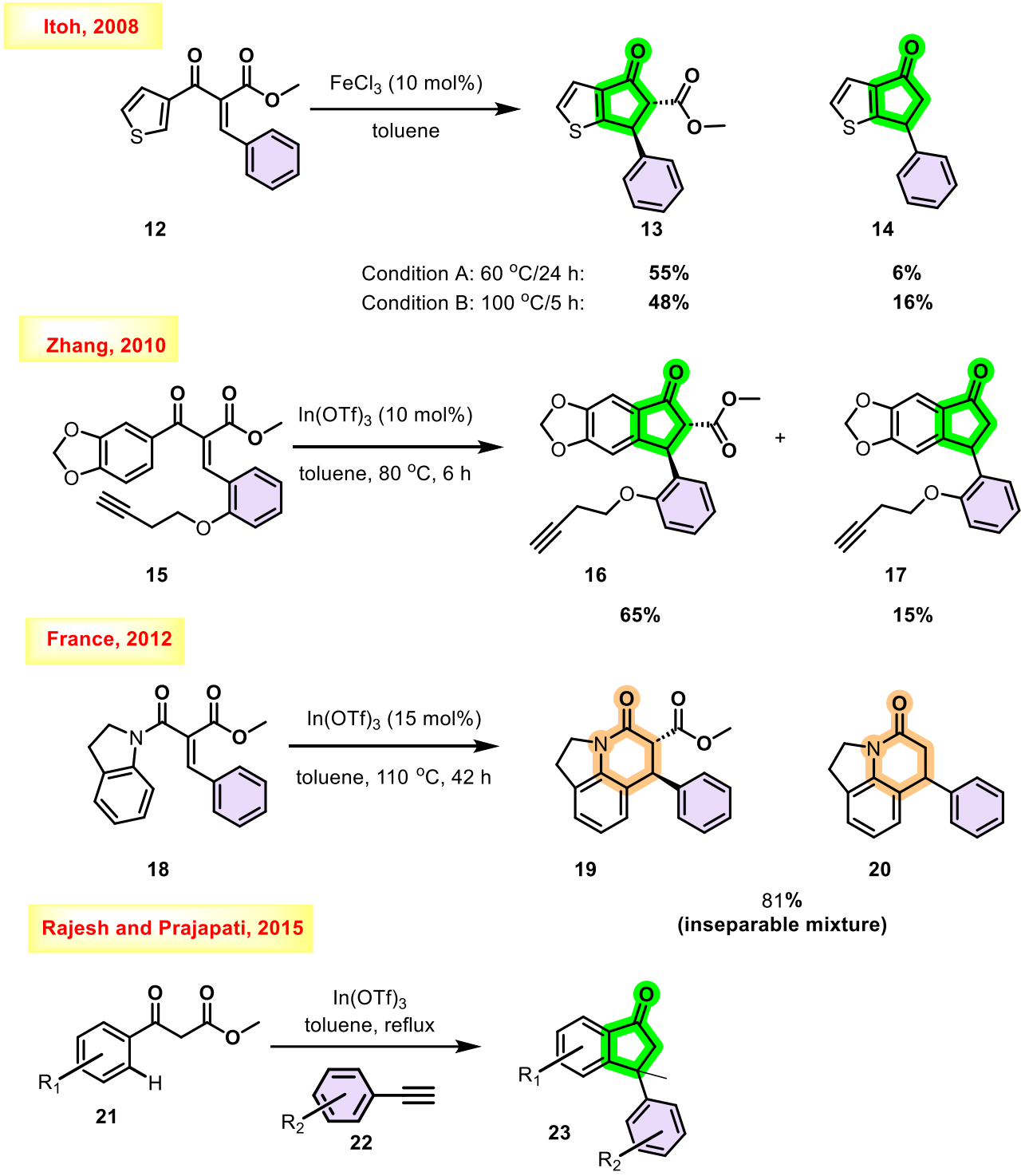



| R | Yield (%)[a] | Ratio 10:11[b] |
|---|---|---|
| 3,4,5-($CH_3O$)$C_6H_2$ (**9dc**) | 77 | 8:2 |
| Piperonyl (**9dl**) | 75 | 7:3 |

[a] Yield determined by $^1$H NMR using dimethyl terephthalate as internal standard. [b]

The decarboxylation reactions of indanones have been previously described in the literature. In 2008, Itoh et al., when evaluating the Nazarov cyclization catalyzed by $FeCl_3$ of 3-substituted thiophene derivatives, carried out at 60 °C for 24 hours led to the formation of a mixture of **13:14** (9:1) products, in 61% combined yield (**Scheme 1**).[31] Under a more drastic condition (100 °C for 5 hours), there was a slight increase in the yield of decarboxylated product **14**. In 2010, Zhang *et al.*[32] developed a methodology catalyzed by $In(OTf)_3$ for the synthesis of bicycles and, they also verified the decarboxylation occurred when the reaction remained at 80 °C for 6 hours (**Scheme 1**). This same behavior was observed by France during the synthesis of the lilolidone nucleus [33a] and by Jung in the stereoselective synthesis of podophyllotoxin derivatives (**Scheme 1**).[33b] Although the decarboxylation reaction of indanones has been observed and described in the literature, there are few reports of extensive studies aimed at exploring this transformation. The only exception was described by Rajesh and Prajapati,[34] in 2015. In this work, the authors aimed to obtain substituted

β,β-indanones, and the decarboxylation step was a mandatory part of the methodology, with no interest in controlling the process.

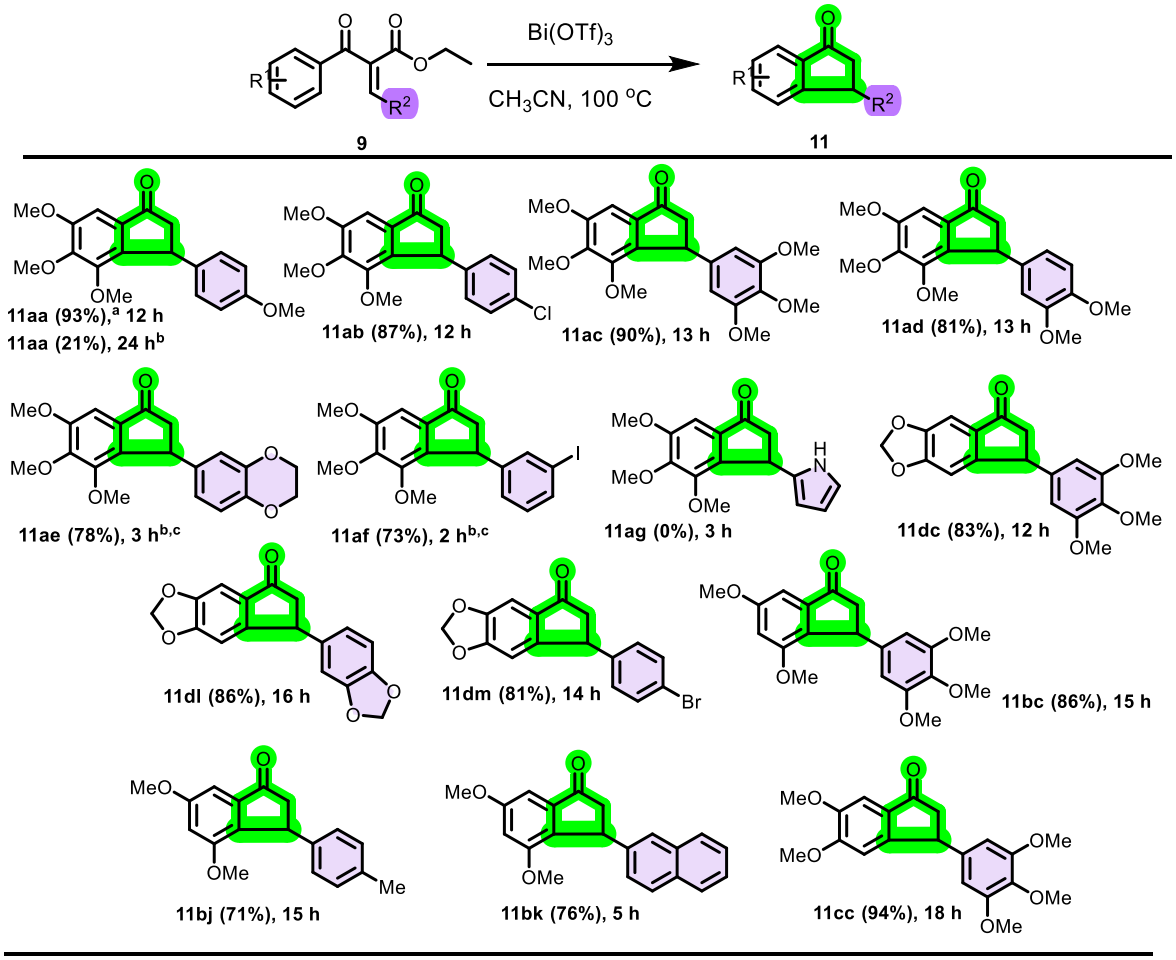



**Scheme 1:** Previous methods describing decarboxylation reactions of indanones and xanthenones.

The indanone core is a privileged structure, as it is often found in a series of natural products and synthetic molecules with different biological activities. [35] In particular, 1-indanones substituted in position 3 are important synthons to synthesize some drugs and natural products.[36] A bibliographic survey revealed some methods were developed for the synthesis of 3-aryl-1-indanones. In this context, due to the formation of the **11dc** and **11dl** derivatives, shown previously, we decided to explore the reaction sequence of the Nazarov reaction/decarboxylation catalyzed by $Bi(OTf)_3$, to prepare other patterns of 3-aryl-1-indanones, from substrate **9**.

We initially investigated the behavior of substrate **9aa** in the conditions established for the Nazarov cyclization (60 °C), however, despite the reaction remaining under these conditions for a long period (24 hours), only partial decarboxylation of the Nazarov product was observed. Thus, we decided to increase the temperature to 100 °C, and the reaction was maintained in these conditions in a sealed tube for 12 hours. To our delight, we obtained only the decarboxylated indanone in an excellent yield (93%). This condition was chosen as the optimal condition and the scope for the synthesis of 3-aryl-1-indanones derivatives is summarized in Table 5.

**Table 5:** Controlled decarboxylation directed by bismuth triflate at 100 °C. Synthesis of 3-aryl-indanones.




[a] Isolated yields after purification using silica gel column chromatography. [b] the reaction was performed at 60 °C. [c] from *tert*-butyl Knoevenagel derivative. Basically, in a sealed tube was added the Knoevenagel product (0.5 mmol), dry acetonitrile (2 mL), and $Bi(OTf)_3$ (0.05 mmol). The reaction mixture was stirred at 100 °C and monitored by TLC.

Simply by controlling the reaction temperature, it is possible to obtain indanones with different substitution patterns. At the lower temperature (60 °C), 2,3-substituted indanones could be obtained, while at higher temperatures (100 °C), 3-substituted indanones were achievable. Under both conditions, virtually no product mixtures were observed.

## Preliminary Biological Evaluation

To investigate the cytotoxic potential of indanones derivates, a total of 20 compounds were tested at concentrations of 5 and 50 µg/mL for 72 hours in a panel of four histologically unrelated tumor lines, HCT116 (colon adenocarcinoma), MCF7 (breast adenocarcinoma), SK-MEL-28 (melanoma), and NB4 (acute leukemia) by methylthiazol tetrazolium (MTT) assay, as previously described.37 Among the tested cells, NB4 cells were the most sensitive one, with 7 compounds (**10aa**, **10bk**, **11aa**, **11ad**, **11ae**, **11dc**, and **11bj**) being active at 5 µg/mL, using a cut off 75%, inhibition at both concentrations. On the other hand, MCF-7 and SK-MEL-28 cells were the most resistant ones, with no active compound at the lowest concentration (Figure 2). This evidence of selective cytotoxic effects for a specific histological subtype of a tumor may drive further studies of the structure-activity relationship to identify molecular targets of indanones derivates with pharmacological interest.

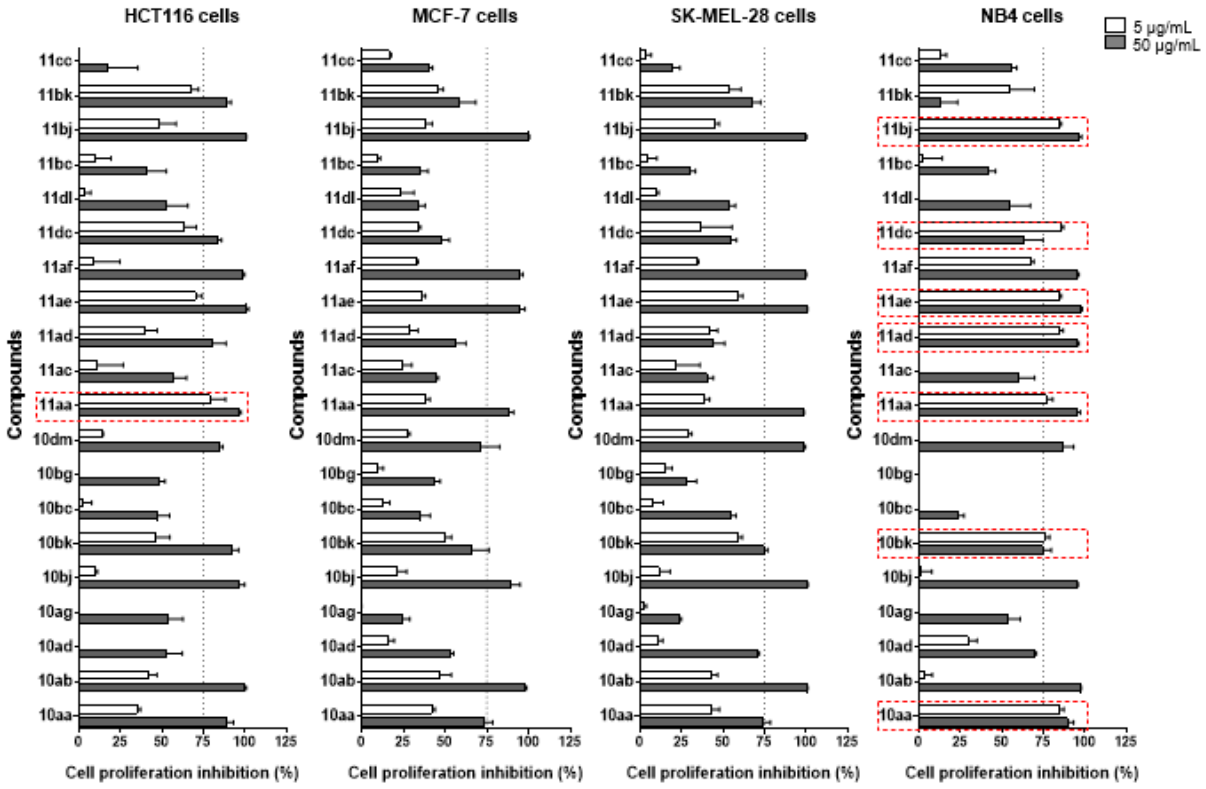


**Figure 2:** Impact of indanones derivatives on cell viability of tumor cells. Cell viability was determined by MTT assay (72h) for a total of 20 compounds (tested at concentrations of 5 and 50 µg/ml) in HCT116 cells (colon adenocarcinoma), MCF7 cells (breast adenocarcinoma), SK-MEL-28 cells (melanoma), and NB4 cells (acute leukemia). Data were expressed as a reduction in viability in relation to the vehicle and the dotted line indicates a 75% reduction in cell viability. Compounds that reduced at least 75% cell viability at the concentration of 5 µg/ml are highlighted in the graph.

# Conclusion

In summary, we developed a simple and efficient methodology for the Nazarov reaction of aryl vinyl ketones, leading to the synthesis of 3-aryl-2-carboethoxy-1-indanones and 3-aryl-1-indanones, catalyzed by bismuth triflate, an environmentally friendly metal. By simply changing the temperature and reaction time, it was possible to modulate the reactivity. In this methodology, no additives were used, and the reaction is insensitive to both air and moisture. As far as we know, the uniqueness of this manuscript lies in the fact that there are no precedents reporting the use of bismuth triflate as a catalyst for a classic Nazarov reaction, as well as no precedent describing the preparation of indanones with different substitution patterns through the simple control of the reaction temperature.

The initial biological profile of 20 indanones was assessed, revealing promising activity against certain human cancer cell lines in some cases. To enhance the anticancer potential of these compounds, it is imperative to carry out additional comprehensive studies.

# Experimental

General Information

All chemicals and solvents were of analytical grade, purchased from commercial sources and used without further purification unless otherwise stipulated. Unless otherwise noted, all reactions were performed under ambient atmosphere in oven-dried open-flask glassware with magnetic stirring. Reaction progress was monitored by analytical thin-layer chromatography (TLC) performed on Merck precoated silica gel 60 F254 (5-40 μm thickness) plates. The TLC plates were visualized with UV light (254 nm) and/or phosphomolybdic acid or sulfuric vanillin followed by heating. The reaction products were purified by flash column chromatography using silica gel (230-400 Mesh).

Nuclear magnetic resonance spectra were recorded in CDCl3 solutions at room temperature, unless noted otherwise. 1H NMR and proton-decoupled 13C NMR spectra were acquired on a Bruker DPX250 (250 MHz for 1H NMR and 63 MHz for 13C NMR), Bruker Avance 400 (400 MHz for 1H NMR and 101 MHz for 13C NMR), Bruker Avance 500 (500 MHz for 1H and 126 MHz for 13C NMR), or Bruker Avance 600 (600 MHz for 1H and 150 MHz for 13C NMR). Chemical shifts (δ) were reported in ppm and the coupling constants (J) in Hertz (Hz). Signal multiplicity was assigned as singlet (s), doublet (d), double doublet (dd), double double doublet (ddd), triplet (t), quartet (qt), dq (double quartet), multiplet (m) and broad singlet (bs). High resolution mass spectrometry (HRMS) was performed using electrospray ionization (ESI) on a Thermo Scientific Q Exactive mass spectrometer. Melting points were obtained using a Gehaka equipment model PF 1500 FARMA and were corrected. The compounds were named according to IUPAC rules using the program MarvinSketch 15.9.21.0.

**General Procedure and Characterization Data for Compounds 9aa – 9gc, 10aa – 10dm and 11aa – 11af.**

A solution of β-ketoester (1 mmol), aldehyde (1.5 mmol), acetic acid (0.6 mmol), piperidine (0.25 mmol), molecular sieve (100 mg) in anhydrous toluene was refluxed. The reaction was monitored by TLC. After this period, the solvent was removed under reduced pressure. The crude reaction mixture was purified by column chromatography using a mobile phase of hexane/ethyl acetate (9:1-7:3 v/v).

**Ethyl (2*Z*)-3-(4-methoxyphenyl)-2-[(*Z*)-3,4,5-trimethoxybenzoyl]prop-2-enoate** (**9aa**). Purified by column chromatography (hexane/EtOAc 95:5 to 9:1), to give **9aa** (392 mg, 0.98 mmol, 98%) as a yellow solid. Mp 103-104 °C. $^{1}$H NMR (250 MHz, $CDCl_3$) δ 7.88 (s, 1H), 7.29 (d, *J* = 8.8 Hz, 2H), 7.20 (s, 2H), 6.75 (d, *J* = 8.9 Hz, 2H), 4.22 (q, *J* = 7.1 Hz, 2H), 3.89 (s, 3H), 3.81 (s, 6H), 3,74 (s, 3H), 1.19 (t, *J* = 7.1 Hz, 3H). $^{13}$C NMR (63 MHz, $CDCl_3$) δ 194.98, 165.50, 161.54, 153.40, 143.42, 142.40, 132.35, 131.50, 128.55, 125.63, 114.47, 106.65, 61.52, 61.04, 56.38, 55.43, 14.30. IR (ATR, νmax) 3403, 2918, 1589, 1455, 1321, 835, 747, 728 cm$^{-1}$. HRMS (ESI) *m/z* calcd for $C_{22}H_{25}O_7^+$ $[M + H]^+$ 401.1595, found 401.1601.

**Ethyl (2*Z*)-3-(4-chlorophenyl)-2-[(*Z*)-3,4,5-trimethoxybenzoyl]prop-2-enoate** (**9ab**). Purified by column chromatography (hexane/EtOAc 95:5 to 9:1), to give **9ab** (396 mg, 0.98 mmol, 98%) as a yellow solid. Mp 87-89 °C (Lit. 97-98 °C). $^{1}$H NMR (400 MHz, Acetone) δ 8.00 (s, 1H), 7.92 (s, 1H), 7.44 (d, *J* = 8.6 Hz, 2H), 7.38 – 7.30 (m, 2H), 7.24 (s, 2H), 4.24 (p, *J* = 7.0 Hz, 2H), 3.82 (s, 6H), 3.79 (s, 3H), 1.20 (t, *J* = 7.0 Hz, 3H). $^{13}$C NMR (101 MHz, Acetone) 193.25, 164.40, 153.62, 143.67, 140.25, 135.68, 132.57, 132.16, 131.48, 131.29, 128.94, 106.52, 61.19, 59.88, 55.75, 13.59. IR (ATR, νmax) 3403, 2918, 1589, 1455, 1321, 835, 747, 728 cm$^{-1}$. HRMS (ESI) *m/z* calcd for $C_{21}H_{22}ClO_6^+$ $[M + H]$+ 405.1099, found 405.1105.

**Ethyl 2-[(*Z*)-3,4,5-trimethoxybenzoyl]-3- (3,4,5-trimethoxyphenyl)prop-2-enoate** (**9ac**).

Purified by column chromatography (hexane/EtOAc 95:5 to 9:1), to give **9ac** (391 mg, 0.85 mmol, 85%) as a white solid. Mp 77-78 °C. $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.82 (s, 1H), 7.19 (s, 2H), 6.55 (s, 2H), 4.35 – 4.09 (m, 2H), 3.86 (s, 3H), 3.79 (s, 6H), 3.76 (s, 3H), 3.62 (s, 6H), 1.19 (t, *J* = 7.1 Hz, 3H). $^{13}$C NMR (126 MHz, CDCl3) δ 194.46, 165.04, 153.35, 153.06, 143.44, 142.41, 140.02, 131.39, 130.23, 128.14, 107.70, 106.41, 61.58, 60.95, 60.85, 56.31, 55.89, 14.18. HRMS (ESI) *m/z* calcd for $C_{24}H_{29}O_9^+$ $[M + H]^+$ 461.1806, found 461.1823.

**Ethyl 2-[(*Z*)-3,4-dimethoxybenzoyl]-3-(3,4,5-trimethoxyphenyl)prop-2-enoate** (**9ad**). Purified by column chromatography (hexane/EtOAc 95:5 to 9:1), to give **9ad** (322 mg, 0.75 mmol, 75%) as a yellow oil. $^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.85 (s, 1H), 7.19 (s, 2H), 6.96 (dd, *J* = 8.4, 2.0 Hz, 1H), 6.80 (d, *J* = 2.0 Hz, 1H), 6.75 – 6.69 (m, 1H), 4.27 – 4.13 (m, 2H), 3.87 (s, 3H), 3.80 (s, 3H), 3.78 (s, 6H), 3,59 (s, 3H), 1.19 (t, *J* = 7.1 Hz, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 195.01, 165.46, 153.46, 151.24, 148.92, 143.51, 142.62, 131.56, 128.73, 125.84, 125.12, 112.58, 111.12, 106.60, 61.60, 61.10, 56.43, 56.02, 55.73, 14.34. HRMS (ESI) *m/z* calcd for $C_{23}H_{27}O_8^+$ $[M + H]^+$ 431.1700, found 431.1708.

***Tert*-butyl (2*Z*)-3-(2,3-dihydro-1,4-benzodioxin-6-yl)-2-[(*Z*)-3,4,5-trimethoxybenzoyl]prop-2-enoate** (**9ae**). Purified by column chromatography (hexane/EtOAc 95:5 to 9:1), to give **9ae** (327 mg, 0.72 mmol, 72%) as a yellow oil. $^{1}$H NMR (500 MHz, $CDCl_3$) δ7.72 (s, 1H), 7.21 (s, 2H), 6.93 – 6.86 (m, 2H), 6.75 (d, *J* = 8.3 Hz, 1H), 4.29 – 4.16 (m, 4H), 3.93 (s, 3H), 3.86 (s, 6H), 1.39 (s, 9H). $^{13}$C NMR (126

MHz, $CDCl_3$) δ 194.99, 164.56, 153.37, 145.84, 143.61, 143.14, 141.58, 132.09, 130.95, 126.66, 124.51, 119.32, 117.82, 106.41, 82.19, 64.69, 64.24, 61.13, 56.43, 28.10. HRMS (ESI) *m/z* calcd for $C_{25}H_{29}O_8^+$ $[M + H]^+$ 457.1857, found 457.1862.

***Tert*-butyl (2)-3-(3-iodophenyl)-2-[-3,4,5-trimethoxybenzoyl]prop-2-enoate** (**9af**). Purified by column chromatography (hexane/EtOAc 95:5 to 8:2), to give **9af** (330 mg, 0.63 mmol, 63%) as a brown oil. *E/Z* ratio ≅ 1:3. $^1$H NMR (500 MHz, $CDCl_3$) δ 7.73 (s, 1H), 7.71 (t, *J* = 1.5 Hz, 1H), 7.62 (d, J = 8.0 Hz, 1H), 7.32 (s, 1H), 7.30 (s, 1H), 7.28 (s, 1H), 7.17 (s, 2H), 6.99 (t, *J* = 7.9 Hz, 1H), 3.92 (s, 3H), 3.87 (s, 6H), 1.43 (s, 9H). $^{13}$C NMR (126 MHz, $CDCl_3$) δ194.07, 163.94, 153.44, 153.13, 143.43, 139.89, 139.14, 139.05, 135.39, 134.62, 131.71, 130.55, 128.72, 125.34, 106.99, 106.46, 94.57, 82.79, 61.17, 61.11, 56.49, 56.42, 52.42, 28.09. HRMS (ESI) *m/z* calcd for $C_{23}H_{25}INaO_6$+ $[M + Na]^+$ 547.0594, found 547.0602.

**Ethyl (2*Z*)-3-(1H-pyrrol-2-yl)-2-[(*Z*)-3,4,5-trimethoxybenzoyl]prop-2-enoate** (**9ag**). Purified by column chromatography (hexane/EtOAc 95:5 to 8:2), to give **9ag** (316 mg, 0.88 mmol, 88%) as a brown solid. *E/Z* ratio ≅ 1:10. Mp 105-108 °C. $^1$H NMR (500 MHz, $CDCl_3$) δ 11.90 (s, 1H), 7.34 (s, 1H), 7.28 (s, 1H), 7.09 (d, *J* = 7.6 Hz, 2H), 6.80 – 6.74 (m, 1H), 6.39 (d, *J* = 3.7 Hz, 1H), 4.17 (q, *J* = 7.1 Hz, 2H), 3.94 (s, 3H), 3.90 (s, 6H), 1.07 (t, *J* = 7.1 Hz, 3H). $^{13}$C NMR (126 MHz, $CDCl_3$) δ193.92, 167.5, 152.98, 141.98, 136.92, 134.09, 127.54, 125.95, 123.30, 120.42, 111.58, 106.30, 61.20, 61.01, 56.33, 13.76. HRMS (ESI) **m/z** calcd for $C_{19}H_{22}NO_6^+$ $[M + H]^+$ 360.1442, found 360.1449.

***Tert*-butyl (2*Z*)-3-(1,3-thiazol-2-yl)-2-[(*Z*)-3,4,5-trimethoxybenzoyl]prop-2-enoat**e (**9ah**). Purified by column chromatography (hexane/EtOAc 95:5 to 8:2), to give **9ah** (310 mg, 0.77 mmol, 77%) as a brown oil. $^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.94 (s, 1H), 7.83 (d, *J* = 3.2 Hz, 1H), 7.40 (d, *J* = 3.1 Hz, 1H), 7.20 (s, 2H), 3.91 (s, 3H), 3.85 (s, 6H), 1.41 (s, 9H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 193.11, 163.44, 160.37, 153.32, 145.08, 143.29, 135.64, 132.00, 131.47, 123.13, 106.32, 61.06, 56.37, 27.99. HRMS (ESI) *m/z* calcd for $C_{20}H_{24}NO_6S^+$ $[M + H]^+$ 406.1319, found 406.1326.

**Ethyl (2*Z*)-2-[(*Z*)-3,4,5-trimethoxybenzoyl]hex-2-enoate** (**9ai**). Purified by column chromatography (hexane/EtOAc 95:5 to 9:1), to give **9ai** (210 mg, 0.63 mmol, 63%) as a yellow oil. $^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.28 (s, 1H), 7.18 (s, 2H), 4.25 – 4.18 (m, 2H), 3.96 (s, 3H), 3.91 (s, 6H), 2.12 (dd, *J* = 15.0, 7.6 Hz, 2H), 1.51 (dq, *J* = 14.6, 7.4 Hz, 2H), 1.21 (t, *J* = 7.1 Hz, 3H), 0.92 (t, *J* = 7.4 Hz, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 193.33, 164.62, 153.21, 148.04, 143.19, 133.65, 131.93, 106.49, 61.20, 60.97, 56.29, 31.59, 29.70, 21.79, 14.11, 13.81. HRMS (ESI) *m/z* calcd for $C_{18}H_{25}O_6^+$ $[M + H]^+$ 337.1646, found 337.1640.

**Ethyl (2*Z*)-2-[(*Z*)-3,5-dimethoxybenzoyl]-3-(4-methylphenyl)prop-2-enoate** (**9bj**). Purified by column chromatography (hexane/EtOAc 95:5 to 9:1), to give **9bj** (322 mg, 0,91 mmol, 91%) as a yellow solid. Mp 80-83 °C $^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.90 (s, 1H), 7.60 (d, *J* = 1.9 Hz, 1H), 7.48 (dd, *J* = 8.4, 1.9 Hz, 1H), 7.25 (d, *J* = 8.2 Hz, 2H), 7.03 (d, *J* = 8.1 Hz, 2H), 6.79 (d, *J* = 8.4 Hz, 1H), 4.22 (q, *J* = 7.1 Hz, 2H), 3.91 (s, 3H), 3.89 (s, 3H), 2.26 (s, 3H), 1.20 (t, *J* = 7.1 Hz, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 194.52, 165.43, 154.11, 149.41, 142.29, 140.93, 130.38, 130.32, 130.29, 129.63, 129.59, 125.00, 110.35, 110.30, 61.51, 56.13, 56.07, 21.48, 14.22. HRMS (ESI) *m/z* calcd for $C_{21}H_{23}O_5^+$ $[M + H]_+$ 355.1540, found 355.1541.

**Ethyl (2*Z*)-2-[(*Z*)-3,5-dimethoxybenzoyl]-3-(naphthalen-1-yl)prop-2-enoate** (**9bk**). Purified by column chromatography (hexane/EtOAc 95:5 to 8:2), to give **9bk** (312 mg, 0.80 mmol, 80%) as a yellow oil. $^{1}$H NMR (500 MHz, CDCl3) δ 8.13 (s, 1H), 7.92 (s, 1H), 7.81 – 7.72 (m, 2H), 7.68 (d, *J* = 8.7 Hz, 1H), 7.52 – 7.44 (m, 2H), 7.41 (dd, *J* = 8.6, 1.6 Hz, 1H), 7.18 (d, *J* = 2.3 Hz, 2H), 6.65 (t, *J* = 2.3 Hz, 1H), 4.29 (q, *J* = 7.1 Hz, 2H), 3.79 (s, 6H), 1.25 (t, *J* = 7.1 Hz, 3H). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 195.57, 142.74, 138.35, 134.02, 133.12, 131.95, 131.36, 130.58, 128.87, 128.72, 127.76, 126.80, 126.02, 106.98, 106.53, 61.74, 55.69, 14.27. HRMS (ESI) *m/z* calcd for $C_{24}H_{23}O_5$+ $[M + H]^+$ 391.1540, found 391.1547.

**Ethyl (2*Z*)-2-[(*Z*)-3,5-dimethoxybenzoyl]-3-(4-methylphenyl)prop-2-enoate** (**9bc**). Purified by column chromatography (hexane/EtOAc 95:5 to 9:1), to give **9bc** (383 mg, 0.89 mmol, 89%) as a yellow solid. Mp 126-128 °C. $^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.83 (s, 1H), 7.11 (d, *J* = 2.3 Hz, 2H), 6.64 (s, 1H), 6.57 (s, 2H), 4.23 (q, *J* = 7.1 Hz, 2H), 3.80 (s, 3H), 3.78 (s, 6H), 3.65 (s, 6H), 1.21 (t, *J* = 7.1 Hz, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 195.54, 165.03, 161.25, 153.13, 142.53, 140.08, 138.28, 130.46, 128.22, 107.82, 106.85, 106.39, 61.65, 60.94, 55.99, 55.70, 14.21. HRMS (ESI) *m/z* calcd for $C_{23}H_{27}O_8^+$ $[M + H]^+$ 431.1700, found 431.1707.

**(*E/Z*)-Ethyl -2-[3,5-dimethoxybenzoyl]-3-(1H-pyrrol-2-yl)prop-2-enoate** (**9bg**). Purified by column chromatography (hexane/EtOAc 95:5 to 8:2), to give **9bg** (389 mg, 0.88 mmol, 88%) as a yellow oil. *E/Z* ratio ≅ 1:1. $^{1}$H NMR (500 MHz, $CDCl_3$) δ 11.84 (s, 1H), 10.39 (s, 1H), 9.47 (d, *J* = 1.2 Hz, 0H), 7.13 – 7.02 (m, 1H), 7.00 – 6.92 (m, 1H), 6.90 (dd, *J* = 3.9, 2.3 Hz, 2H), 6.70 (dq, *J* = 3.8, 1.7 Hz, 1H), 6.59 (td, *J* = 2.3, 1.1 Hz, 1H), 6.38 – 6.24 (m, 1H), 4.19 – 3.99 (m, 2H), 3.76 (d, *J* = 6.2 Hz, 6H), 0.98 (dt, *J*

= 14.4, 7.2 Hz, 3H). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 196.83, 179.45, 167.52, 160.81, 160.77, 141.42, 141.19, 137.31, 136.33, 127.70, 127.65, 126.71, 126.25, 125.92, 123.65, 122.52, 120.93, 111.91, 111.70, 111.39, 106.53, 106.11, 105.58, 104.97, 61.26, 61.09, 55.70, 55.66, 14.02, 13.76. HRMS (ESI) *m/z* calcd for $C_{18}H_{20}NO_5^+$ [M + H]$^+$ 330.1336, found 330.1340.

**Ethyl (2*Z*)-2-[(*Z*)-3,4-dimethoxybenzoyl]-3-(4-methylphenyl)prop-2-enoate** (**9cc**). Purified by column chromatography (hexane/EtOAc 95:5 to 8:2), to give **9cc** (426 mg, 0.99 mmol, 99%) as a yellow oil. $^1$H NMR (400 MHz, $CDCl_3$) δ 7.82 (s, 1H), 7.60 (d, *J* = 1.8 Hz, 1H), 7.50 (dd, *J* = 8.4, 1.8 Hz, 1H), 6.82 (d, *J* = 8.4 Hz, 1H), 6.59 (s, 2H), 4.23 (q, *J* = 7.1 Hz, 2H), 3.90 (d, *J* = 1.7 Hz, 6H), 3.78 (s, 3H), 3.64 (s, 6H), 1.20 (t, *J* = 7.1 Hz, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 194.43, 165.29, 154.24, 153.10, 149.52, 142.18, 139.99, 130.57, 129.68, 128.32, 125.05, 110.49, 110.03, 107.81, 61.61, 60.94, 56.20, 56.16, 55.98, 14.24. HRMS (ESI) m/z calcd for $C_{23}H_{27}O_8^+$ [M + H]$^+$ 431.1700, found 431.1708.

**Ethyl (2*Z*)-2-[(*Z*)-2H-1,3-benzodioxole-5-carbonyl]-3-(3,4,5-trimethoxyphenyl)prop-2-enoate** (**9dc**). Purified by column chromatography (hexane/EtOAc 95:5 to 9:1), to give **9dc** (327 mg, 0.79 mmol, 79%) as a brown solid. mp 70-72 °C (lit. 97-98 °C). $^1$H NMR (400 MHz, $CDCl_3$) δ 7.82 (s, 1H), 7.54 (dd, J = 8.2, 1.7 Hz, 1H), 7.48 (d, *J* = 1.6 Hz, 1H), 6.81 (d, *J* = 8.2 Hz, 1H), 6.61 (s, 2H), 6.06 (s, 2H), 4.25 (q, *J* = 7.1 Hz, 2H), 3.82 (s, 3H), 3.69 (s, 6H), 1.23 (t, J = 7.1 Hz, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 194.04, 165.23, 153.20, 152.83, 148.71, 108.48, 108.23, 107.83, 102.25, 61.70, 61.03, 56.09, 14.30. HRMS (ESI) *m/z* calcd for $C_{22}H_{23}O_8^+$ [M + H]$^+$ 415.1387, found 415.1405.

**Ethyl (2*Z*)-3-(2H-1,3-benzodioxol-5-yl)-2-[(*Z*)-2H-1,3-benzodioxole-5-carbonyl]prop-2-enoate** (**9dl**). Purified by column chromatography (hexane/EtOAc 95:5 to 9:1), to give **9dl** (305 mg, 0.83 mmol, 83%) as a brown solid. Mp 103-105 °C. $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.80 (s, 1H), 7.57 – 7.47 (m, 2H), 6.94 (dd, *J* = 8.2, 1.7 Hz, 1H), 6.80 (t, *J* = 4.9 Hz, 2H), 6.72 (d, *J* = 8.1 Hz, 1H), 6.05 (s, 2H), 5.93 (s, 2H), 4.22 (q, *J* = 7.1 Hz, 2H), 1.21 (t, *J* = 7.1 Hz, 3H). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 194.12, 165.40, 152.80, 149.77, 148.67, 148.24, 142.04, 131.41, 129.32, 127.26, 126.90, 126.56, 109.32, 108.73, 108.41, 108.37, 102.20, 101.75, 61.59, 14.27. HRMS (ESI) *m/z* calcd for $C_{20}H_{17}O_7^+$ $[M + H]^+$ 369.0969, found 369.0972.

**Ethyl (2*Z*)-2-[(*Z*)-2H-1,3-benzodioxole-5-carbonyl]-3-(4-bromophenyl)prop-2-enoate** (**9dm**). Purified by column chromatography (hexane/EtOAc 95:5 to 9:1), to give **9dm** (462 mg, 0.90 mmol, 90%) as a brown oil. $^{1}$H NMR (400 MHz, $CDCl^3$) δ 7.83 (s, 1H), 7.50 – 7.44 (m, 2H), 7.40 – 7.35 (m, 2H), 7.26 – 7.20 (m, 2H), 6.78 (d, *J* = 8.1 Hz, 1H), 6.04 (s, 2H), 4.24 (q, *J* = 7.1 Hz, 2H), 1.21 (t, *J* = 7.1 Hz, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 193.41, 164.95, 152.94, 148.71, 140.77, 132.24, 132.19, 131.95, 131.61, 131.03, 126.56, 124.97, 108.37, 108.25, 102.24, 61.82, 14.21. HRMS (ESI) *m/z* calcd for $C_{19}H_{16}BrO_5^+$ $[M + H]^+$ 403.0176, found 403.0185.

**Ethyl (2*Z*)-2-[(*Z*)-3-methoxybenzoyl]-3-(3,4,5-trimethoxyphenyl)prop-2-enoate** (**9ec**). Purified by column chromatography (hexane/EtOAc 95:5 to 9:1), to give **9ec** (393 mg, 0.98 mmol, 98%) as a yellow oil. $^{1}$H NMR (400 MHz, CDCl3) δ 7.83 (s, 1H), 7.50 (d, *J* = 7.4 Hz, 2H), 7.35 – 7.25 (m, 1H), 7.08 (d, *J* = 8.0 Hz, 1H), 6.56 (s, 2H), 4.21 (q, *J* = 7.0 Hz, 2H), 3.79 (s, 3H), 3,77 (s, 3H), 3.61 (s, 6H), 1.17 (t, *J* = 7.0 Hz, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 195.58, 164.97, 160.12, 153.06, 142.40, 140.01,

137.66, 130.53, 130.05, 128.15, 122.08, 120.51, 112.84, 107.75, 61.53, 60.83, 55.88, 55.47, 14.11. HRMS (ESI) *m/z* calcd for $C_{22}H_{25}O_7^+$ $[M + H]^+$ 401.1595, found 401.1602.

**Ethyl (2*Z*)-2-[(*Z*)-4-methoxybenzoyl]-3-(3,4,5-trimethoxyphenyl)prop-2-enoate** (**9fc**). Purified by column chromatography (hexane/EtOAc 95:5 to 9:1), to give **9fc** (395 mg, 0.99 mmol, 99%) as a yellow oil. $^1$H NMR (250 MHz, $CDCl_3$) δ 7.92 (d, *J* = 8.8 Hz, 2H), 7.79 (s, 1H), 6.88 (d, *J* = 8.8 Hz, 2H), 6.58 (s, 2H), 4.21 (q, *J* = 7.1 Hz, 2H), 3.82 (s, 3H), 3.77 (s, 3H), 3.62 (s, 6H), 1.18 (t, *J* = 7.1 Hz, 3H). $^{13}$C NMR (63 MHz, $CDCl_3$) δ 194.36, 165.28, 164.38, 153.12, 142.01, 139.98, 131.58, 130.77, 129.61, 128.34, 114.29, 107.83, 61.57, 60.93, 55.99, 55.62, 14.22. HRMS (ESI) *m/z* calcd for $C_{22}H_{25}O_7^+$ $[M + H]^+$ 401.1595, found 401.1600.

**Ethyl (2*Z*)-2-[(*Z*)-1-benzothiophene-3-carbonyl]-3-(3,4,5-trimethoxyphenyl)prop-2-enoate** (**9gc**). Purified by column chromatography (hexane/EtOAc 95:5 to 8:2), to give **9gc** (414 mg, 0.97 mmol, 97%) as a brown solid. Mp 119-122 °C. $^1$H NMR (400 MHz, $CDCl_3$) δ 8.92 (d, *J* = 8.1 Hz, 1H), 8.21 (s, 1H), 7.85 (d, *J* = 8.8 Hz, 2H), 7.54 (dd, *J* = 11.2, 3.9 Hz, 1H), 7.45 (dd, *J* = 11.2, 3.8 Hz, 1H), 6.65 (s, 2H), 4.33 – 4.23 (m, 2H), 3.77 (s, 3H), 3.54 (s, 6H), 1.23 (t, *J* = 7.1 Hz, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 189.95, 165.13, 153.03, 142.04, 140.89, 140.22, 139.96, 136.12, 134.88, 131.21, 128.11, 126.19, 125.89, 125.28, 122.47, 107.65, 61.61, 60.79, 55.80, 14.17. HRMS (ESI) *m/z* calcd for $C_{23}H_{23}O_6S^+$ $[M + H]^+$ 427.1210, found 427.1215.

In a sealed tube was added the Knoevenagel product (12) (0.5 mmol), dry acetonitrile (2 mL), and Bi(OTf)3 (0.05 mmol). The reaction mixture was stirred at 60 °C and monitored by TLC. After confirming the completion of the reaction, the reaction mixture was concentrated under reduced pressure. The resulting crude reaction mixture was

purified by column chromatography using a mobile phase of hexane/ethyl acetate (9:1 - 8:2 v/v).

**Ethyl 4,5,6-trimethoxy-3-(4-methoxyphenyl)-1-oxo-2,3-dihydro-1H-indene-2-carboxylate** (**10aa**)

Purified by column chromatography (hexane/EtOAc 95:5 to 9:1), to give **10aa** (112 mg, 0.28 mmol, 93%) as a yellow oil. $^{1}$H NMR (250 MHz, $CDCl_3$) δ 7.09 – 7.00 (m, 3H), 6.82 (d, *J* = 8.6 Hz, 2H), 4.89 (d, *J* = 3.1 Hz, 1H), 4.23 (q, *J* = 7.1 Hz, 2H), 3.90 (s, 6H), 3.76 (s, 3H), 3.56 (d, *J* = 3.1 Hz, 1H), 3.38 (s, 3H), 1.28 (t, *J* = 7.2 Hz, 3H). $^{13}$C NMR (63 MHz, $CDCl_3$) δ 198.25, 168.65, 158.81, 155.33, 150.49, 149.62, 143.82, 134.97, 130.66, 128.57, 114.28, 101.14, 64.12, 61.94, 61.08, 60.28, 56.44, 55.41, 45.70, 14.36. HRMS (ESI) *m/z* calcd for $C_{22}H_{25}O_7^+$ $[M + H]^+$ 401.1595, found 401.1565.

**Ethyl 4,5,6-trimethoxy-3-(4-chlorophenyl)-1-oxo-2,3-dihydro-1H-indene-2-carboxylate** (10ab). Purified by column chromatography (hexane/EtOAc 95:5 to 9:1), to give **10ab** (104 mg, 0.26 mmol, 86%) as a brown oil. $^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.29 (d, *J* = 8.2 Hz, 2H), 7.10 (s, 1H), 7.08 (d, *J* = 8.3 Hz, 2H), 4.93 (d, *J* = 3.2 Hz, 1H), 4.26 (q, *J* = 7.0 Hz, 2H), 3.93 (d, *J* = 2.3 Hz, 6H), 3.56 (d, *J* = 3.3 Hz, 1H), 3.45 (s, 3H), 1.32 (t, *J* = 7.1 Hz, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 197.47, 168.19, 155.42, 150.19, 149.37, 142.67, 141.31, 132.88, 130.51, 128.92, 128.76, 101.03, 63.61, 61.96, 60.96, 60.13, 56.31, 45.51, 14.20. HRMS (ESI) *m/z* calcd for $C_{21}H_{22}ClO_6^+$ $[M + H]^+$ 405.1099, found 405.1107.

**Ethyl 4,5,6-trimethoxy-1-oxo-3-(3,4,5-trimethoxyphenyl)-2,3-dihydro-1H-indene-2-carboxylate** (**10ac**). Purified by column chromatography (hexane/EtOAc 95:5 to 8:2), to give 10ac (127 mg, 0.28 mmol, 93%) as a brown oil. $^{1}$H NMR (500 MHz, $CDCl_3$)

δ7.09 (s, 1H), 6.32 (s, 2H), 4.88 (d, *J* = 3.3 Hz, 1H), 4.26 (qd, *J* = 7.1, 2.2 Hz, 2H), 3.92 (d, *J* = 1.3 Hz, 6H), 3.82 (s, 3H), 3.78 (s, 6H), 3.62 (d, *J* = 3.2 Hz, 1H), 3.45 (s, 3H), 1.31 (t, *J* = 7.1 Hz, 3H). $^{13}$C NMR (126 MHz, $CDCl_3$) δ197.97, 168.51, 155.43, 153.59, 150.50, 149.57, 143.19, 138.61, 137.23, 130.64, 104.56, 101.18, 63.83, 62.06, 61.10, 61.04, 60.35, 56.43, 56.33, 46.57, 14.37. HRMS (ESI) *m/z* calcd for $C_{24}H_{29}O_9^+$ $[M + H]^+$ 461.1806, found 461.1817.

**Ethyl 3-(3,4-dimethoxyphenyl)-4,5,6-trimethoxy-1-oxo-2,3-dihydro-1H-indene-2-carboxylate** (**10ad**). Purified by column chromatography (hexane/EtOAc 95:5 to 8:2), to give **10ad** (120 mg, 0.28 mmol, 94%) as a yellow oil. $^1$H NMR (400 MHz, $CDCl_3$) δ 7.05 (s, 1H), 6.75 (d, *J* = 8.1 Hz, 1H), 6.64 – 6.59 (m, 2H), 4.86 (d, *J* = 3.1 Hz, 1H), 4.21 (q, *J* = 6.9 Hz, 2H), 3.88 (s, 6H), 3.82 (s, 3H), 3.78 (s, 3H), 3.57 (d, *J* = 3.1 Hz, 1H), 3.38 (s, 3H), 1.27 (t, *J* = 7.1 Hz, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 198.21, 168.63, 155.37, 150.52, 149.63, 149.31, 148.27, 143.61, 135.48, 130.65, 119.62, 111.51, 110.83, 101.17, 64.08, 62.02, 61.11, 60.36, 56.45, 56.13, 56.07, 46.06, 14.39. HRMS (ESI) *m/z* calcd for $C_{23}H_{27}O_8^+$ $[M + H]^+$ 431.1700, found 431.1708.

**Ethyl 4,5,6-trimethoxy-1-oxo-3-(1H-pyrrol-2-yl)-2,3-dihydro-1H-indene-2-carboxylate** (10ag). Purified by column chromatography (hexane/EtOAc 95:5 to 8:2), to give **10ag** (87 mg, 0.24 mmol, 81%) as a yellow oil. $^1$H NMR (400 MHz, $CDCl_3$) δ 8.83 (s, 1H), 7.28 (s, 1H), 7.07 (s, 1H), 6.73 (d, J = 1.4 Hz, 1H), 6.13 (d, *J* = 3.0 Hz, 1H), 5.96 (s, 1H), 5.06 (d, *J* = 2.9 Hz, 1H), 4.27 (q, *J* = 7.1 Hz, 2H), 3.98 (s, 3H), 3.93 – 3.89 (m, 1H), 3.91 (s, 3H), 3.76 (s, 3H), 1.33 (t, *J* = 7.1 Hz, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 197.23, 168.41, 155.13, 149.90, 149.24, 141.85, 131.50, 129.95, 117.45, 108.43, 105.18, 101.78, 62.01, 61.26, 61.07, 60.94, 56.32, 39.14, 14.19. HRMS (ESI) *m/z* calcd for $C_{19}H_{22}NO_6^+$ $[M + H]^+$ 360.1442, found 360.1433.

**Ethyl 4,6-dimethoxy-3-(4-methylphenyl)-1-oxo-2,3-dihydro-1H-indene-2-carboxylate** (**10bj**). Purified by column chromatography (hexane/EtOAc 95:5 to 9:1), to give **10bj** (88 mg, 0.25 mmol, 83%) as a yellow oil. $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.23 (s, 1H), 7.18 (d, *J* = 3.7 Hz, 1H), 7.10 (d, *J* = 8.0 Hz, 2H), 6.99 (dd, *J* = 11.5, 8.0 Hz, 2H), 6.61 (d, *J* = 2.5 Hz, 1H), 4.82 (d, *J* = 4.0 Hz, 1H), 4.22 (dd, *J* = 7.1, 5.2 Hz, 2H), 3.90 (s, 3H), 3.81 (s, 3H), 3.56 (d, *J* = 4.1 Hz, 1H), 2.31 (s, 3H), 1.27 (t, *J* = 7.1 Hz, 3H). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 197.46, 168.99, 156.49, 152.24, 150.29, 139.20, 137.32, 129.90, 129.76, 128.20, 127.91, 127.61, 107.46, 104.42, 64.11, 61.91, 56.56, 56.38, 48.25, 21.26, 14.42. HRMS (ESI) *m/z* calcd for $C_{21}H_{23}O_5$+ $[M + H]^+$ 355.1540, found 355.1545.

**Ethyl 4,6-dimethoxy-3-(naphthalen-2-yl)-1-oxo-2,3-dihydro-1H-indene-2-carboxylate** (**10bk**). Purified by column chromatography (hexane/EtOAc 95:5 to 8:2), to give **10bk** (94 mg, 0.24 mmol, 80%) as an orange solid. Mp 130-131 °C. $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.91 – 7.72 (m, 3H), 7.58 (d, *J* = 1.8 Hz, 1H), 7.54 – 7.41 (m, 3H), 7.18 (dd, *J* = 8.5, 1.9 Hz, 1H), 6.93 (d, *J* = 2.1 Hz, 1H), 6.70 (d, *J* = 2.2 Hz, 1H), 5.13 (d, *J* = 3.1 Hz, 1H), 4.29 (q, *J* = 7.1 Hz, 2H), 3.90 (s, 3H), 3,70 (d, *J* = 3,0 Hz, 2H), 3.61 (s, 3H), 1.33 (t, *J* = 7.1 Hz, 3H). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 199.05, 168.37, 162.14, 157.88, 139.80, 138.13, 137.76, 133.47, 132.49, 128.49, 127.75, 127.66, 126.17, 125.88, 125.70, 125.31, 106.92, 96.61, 64.19, 61.90, 55.86, 55.62, 46.09, 14.23. HRMS (ESI) *m/z* calcd for $C_{24}H_{23}O_5^+$ $[M + H]^+$ 391.1540, found 391.1544.

**Ethyl 4,6-dimethoxy-1-oxo-3-(3,4,5-trimethoxyphenyl)-2,3-dihydro-1H-indene-2-carboxylate** (**10bc**). Purified by column chromatography (hexane/EtOAc 95:5 to 9:1), to give **10bc** (110 mg, 0.26 mmol, 85%) as a yellow solid. Mp 144-145 °C. $^{1}$H NMR

(400 MHz, $CDCl_3$) δ 6.87 (d, *J* = 2.1 Hz, 1H), 6.69 (d, *J* = 2.1 Hz, 1H), 6.27 (s, 2H), 4.86 (d, *J* = 2.9 Hz, 2H), 4.31 – 4.23 (q, *J* = 7.1 Hz, 2H), 3.88 (s, 3H), 3.85 – 3.82 (m, 3H), 3.77 (s, 6H), 3.70 (s, 3H), 3.62 (d, *J* = 3.0 Hz, 1H), 1.32 (t, *J* = 7.1 Hz, 3H). $^{13}C$ NMR (101 MHz, $CDCl_3$) δ199.11, 168.49, 162.24, 158.01, 153.46, 138.28, 138.05, 137.77, 137.01, 107.05, 104.34, 96.76, 64.29, 62.04, 61.00, 56.29, 55.98, 55.85, 46.29, 14.40. HRMS (ESI) *m/z* calcd for $C_{23}H_{27}O_8^+$ $[M + H]^+$ 431.1700, found 431.1708.

**Ethyl 4,6-dimethoxy-1-oxo-3-(1H-pyrrol-2-yl)-2,3-dihydro-1H-indene-2-carboxylate** (**10bg**). Purified by column chromatography (hexane/EtOAc 95:5 to 8:2), to give 10bg (76 mg, 0.23 mmol, 77%) as a yellow solid. Mp 100-102 °C. $^1H$ NMR (500 MHz, $CDCl_3$) δ 8.57 (s, 1H), 6.72 (d, *J* = 2.1 Hz, 1H), 6.62 (d, *J* = 2.1 Hz, 1H), 6.60 (m, 1H), 5.99 (q, *J* = 2.9 Hz, 1H), 5.79 (m, 1H), 4.91 (d, *J* = 2.7 Hz, 1H), 4.14 (q, *J* = 7.1 Hz, 2H), 3.84 (s, 3H), 3.77 (s, 3H), 3.73 (s, 3H), 1.21 (t, *J* = 7.2 Hz, 3H). $^{13}C$ NMR (125 MHz, $CDCl_3$) δ 13C NMR (126 MHz, CDCl3) δ 198.52, 168.50, 162.11, 157.50, 137.26, 137.22, 131.77, 117.51, 108.44, 107.29, 104.96, 97.58, 62.21, 61.62, 56.24, 56.06, 39.14, 14.40. HRMS (ESI) *m/z* calcd for $C_{18}H_{19}NNaO_5^+$ [M + Na]+ 352.1155, found 352.1165.

**Ethyl 5,6-dimethoxy-1-oxo-3-(3,4,5-trimethoxyphenyl)-2,3-dihydro-1H-indene-2-carboxylate** (**10cc**). Purified by column chromatography (hexane/EtOAc 95:5 to 8:2), to give **10cc** (104 mg, 0.24 mmol, 81%) as a brown oil. $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.23 (s, 1H), 6.69 (s, 1H), 6.34 (s, 2H), 4.84 (d, *J* = 4.1 Hz, 1H), 4.29 (dd, *J* = 7.1, 4.3 Hz, 2H), 3.95 (s, 3H), 3.90 (s, 3H), 3.85 (s, 3H), 3.80 (s, 6H), 3.63 (d, *J* = 4.1 Hz, 1H), 1.33 (t, *J* = 7.1 Hz, 3H). $^{13}C$ NMR (101 MHz, $CDCl_3$) δ197.15, 168.91, 156.57, 153.84, 151.69, 150.44, 137.85, 137.46, 128.17, 107.47, 104.94, 104.48, 63.95, 61.99, 61.01,

56.65, 56.35, 48.82, 14.43. HRMS (ESI) *m/z* calcd for $C_{23}H_{27}O_8^+$ $[M + H]^+$ 431.1700, found 431.1706.

**Ethyl 5-(4-bromophenyl)-7-oxo-2H,5H,6H,7H-indeno[5,6-d][1,3]dioxole-6-carboxylate** (**10dm**). Purified by column chromatography (hexane/EtOAc 95:5 to 9:1), to give **10dm** (99 mg, 0.25 mmol, 82%) as a yellow oil. $^1$H NMR (500 MHz, $CDCl_3$) δ 7.84 (s, 1H), 7.50 – 7.45 (m, 2H), 7.39 (d, *J* = 8.6 Hz, 2H), 7.26 – 7.19 (m, 2H), 6.79 (d, *J* = 8.1 Hz, 1H), 6.05 (s, 2H), 4.25 (q, *J* = 7.1 Hz, 2H), 1.22 (t, *J* = 7.1 Hz, 3H). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 193.39, 164.91, 152.90, 148.66, 140.74, 132.30, 132.15, 131.89, 131.57, 130.97, 129.66, 126.53, 124.94, 108.34, 108.21, 102.20, 61.79, 14.18. HRMS (ESI) *m/z* calcd for $C_{19}H_{16}BrO_5^+$ $[M + H]^+$ 403.0176, found 403.0183.

In a sealed tube was added the Knoevenagel product (**12**) (0.5 mmol), dry acetonitrile (2 mL), and $Bi(OTf)_3$ (0.05 mmol). The reaction mixture was stirred at 100 °C and monitored by TLC. After confirming the completion of the reaction, the reaction mixture was concentrated under reduced pressure. The resulting crude reaction mixture was purified by column chromatography using a mobile phase of hexane/ethyl acetate (9:1 - 8:2 v/v).

**4,5,6-Trimethoxy-3-(4-methoxyphenyl)-2,3-dihydro-1H-inden-1-one** (**11aa**). Purified by column chromatography (hexane/EtOAc 95:5 to 9:1), to give **11aa** (91 mg, 0.28 mmol, 93%) as a yellow solid. Mp 60-62 °C. $_1$H NMR (400 MHz, $CDCl_3$) δ 7.10 (s, 1H), 7.06 – 7.02 (m, 2H), 6.86 – 6.80 (m, 2H), 4.56 (dd, *J* = 8.0, 2.5 Hz, 1H), 3.93 (s, 3H), 3.92 (s, 3H), 3.79 (s, 3H), 3.38 (s, 3H), 3.19 (dd, *J* = 19.3, 8.0 Hz, 1H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 205.69, 158.47, 155.04, 150.59, 149.01, 145.05, 136.61, 132.33,

128.40, 114.16, 100.45, 61.06, 60.28, 56.42, 55.43, 47.52, 41.03. HRMS (ESI) *m/z* calcd for $C_{19}H_{21}O_5$+ $[M + H]^+$ 329.1384, found 190.1391.

**4,5,6-Trimethoxy-3-(4-chlorophenyl)-2,3-dihydro-1H-inden-1-one** (**11ab**). Purified by column chromatography (hexane/EtOAc 95:5 to 9:1), to give **11ab** (87 mg, 0.26 mmol, 87%) as a yellow oil. $^1$H NMR (400 MHz, $CDCl_3$) δ 7.32 – 7.22 (m, 2H), 7.09 (s, 1H), 7.05 (d, *J* = 8.4 Hz, 2H), 4.56 (dd, *J* = 8.0, 2.5 Hz, 1H), 3.93 (s, 3H), 3.91 (s, 3H), 3.42 (s, 3H), 3.19 (dd, *J* = 19.2, 8.0 Hz, 1H), 2.56 (dd, *J* = 19.2, 2.6 Hz, 1H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 204.94, 155.29, 150.45, 148.89, 144.09, 143.12, 132.49, 132.35, 128.91, 128.78, 100.49, 61.06, 60.25, 56.42, 47.16, 41.14. HRMS (ESI) *m/z* calcd for $C_{18}H_{18}ClO_4^+$ $[M + H]^+$ 333.0888, found 333.0894.

**4,5,6-Trimethoxy-3-(3,4,5-trimethoxyphenyl)-2,3-dihydro-1H-inden-1-one** (**11ac**). Purified by column chromatography (hexane/EtOAc 95:5 to 8:2), to give **11ac** (105 mg, 0.27 mmol, 90%) as a yellow oil. $^1$H NMR (400 MHz, $CDCl_3$) δ 7.06 (s, 1H), 6.28 (s, 2H), 4.49 (dd, *J* = 8.0, 2.5 Hz, 1H), 3.90 (s, 3H), 3.88 (s, 3H), 3.78 (s, 3H), 3.75 (s, 6H), 3.40 (s, 3H), 3.14 (dd, *J* = 19.3, 8.0 Hz, 1H), 2.59 (dd, *J* = 19.3, 2.5 Hz, 1H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 205.34, 155.11, 153.47, 150.56, 148.91, 144.35, 140.27, 136.85, 132.34, 104.38, 100.46, 61.02, 60.30, 56.36, 56.28, 47.23, 42.07. HRMS (ESI) *m/z* calcd for $C_{21}H_{25}O_7^+$ $[M + H]^+$ 389.1595, found 389.1596.

**4,5,6-Trimethoxy-3-(3,4-dimethoxyphenyl)-2,3-dihydro-1H-inden-1-one** (**11ad**). Purified by column chromatography (hexane/EtOAc 95:5 to 9:1), to give **11ad** (87 mg, 0.24 mmol, 81%) as a yellow oil. $^1$H NMR (500 MHz, $CDCl_3$) δ 7.10 (s, 1H), 6.79 (d, *J* = 8.2 Hz, 1H), 6.68 – 6.57 (m, 2H), 4.55 (dd, *J* = 7.9, 2.5 Hz, 1H), 3.94 (s, 3H), 3.92 (s, 3H), 3.86 (s, 3H), 3.82 (s, 3H), 3.40 (s, 3H), 3.19 (dd, *J* = 19.2, 8.0 Hz, 1H), 2.61 (dd,

*J* = 19.3, 2.5 Hz, 1H). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 205.47, 154.89, 150.43, 149.04, 148.83, 147.73, 144.65, 136.96, 132.17, 119.25, 111.25, 110.50, 100.30, 60.89, 60.17, 56.24, 55.93, 55.89, 47.30, 41.29. HRMS (ESI) *m/z* calcd for $C_{20}H_{23}O_6^+$ $[M + H]^+$ 359.1489, found 359.1493.

4**,6-Dimethoxy-3-(4-methylphenyl)-2,3-dihydro-1H-inden-1-one** (**11bj)**. Purified by column chromatography (hexane/EtOAc 95:5 to 9:1), to give **11bj** (60 mg, 0.21 mmol, 71%) as a brown oil. $^1$H NMR (400 MHz, $CDCl_3$) δ 7.24 (s, 1H), 7.14 (d, *J* = 7.9 Hz, 2H), 7.03 (d, *J* = 8.0 Hz, 2H), 6.66 (s, 1H), 4.47 (dd, *J* = 7.7, 3.3 Hz, 1H), 3.95 (s, 3H), 3.86 (s, 3H), 3.21 (dd, *J* = 19.0, 7.7 Hz, 1H), 2.62 (dd, *J* = 19.0, 3.4 Hz, 1H), 2.35 (s, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 204.91, 155.96, 153.52, 150.01, 141.03, 136.77, 129.78, 127.62, 107.65, 103.86, 56.46, 56.34, 47.52, 44.04, 21.22. HRMS (ESI) *m/z* calcd for $C_{18}H_{19}O_3$+ $[M + H]^+$ 283.1329, found 283.1337.

**4,6-Dimethoxy-3-(naphthalen-2-yl)-2,3-dihydro-1H-inden-1-one** (**11bk**). Purified by column chromatography (hexane/EtOAc 95:5 to 8:2), to give **11bk** (72 mg, 0.23 mmol, 76%) as a yellow solid. Mp 138-139 °C. 1H NMR (400 MHz, CDCl3) δ 7.90 – 7.70 (m, 3H), 7.55 (d, *J* = 1.8 Hz, 1H), 7.52 – 7.36 (m, 2H), 7.18 (dd, *J* = 8.4, 1.9 Hz, 1H), 6.93 (d, *J* = 2.1 Hz, 1H), 6.67 (d, *J* = 2.1 Hz, 1H), 4.76 (dd, *J* = 8.0, 2.3 Hz, 1H), 3.91 (s, 3H), 3.62 (s, 3H), 3.30 (dd, *J* = 19.3, 7.9 Hz, 1H), 2.70 (dd, *J* = 19.3, 2.3 Hz, 1H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 206.50, 162.02, 158.15, 141.56, 139.54, 139.44, 133.69, 132.48, 128.44, 127.84, 127.81, 126.21, 125.71, 125.66, 125.63, 106.33, 96.12, 55.99, 55.76, 47.77, 41.63. HRMS (ESI) *m/z* calcd for $C_{21}H19O_3^+$ $[M + H]^+$ 319.1329, found 319.1335.

**4,6-Dimethoxy-3-(3,4,5-trimethoxyphenyl)-2,3-dihydro-1H-inden-1-one** (**11bc**). Purified by column chromatography (hexane/EtOAc 95:5 to 8:2), to give **11bc** (92 mg, 0.26 mmol, 86%) as a yellow solid. Mp 142-143 °C. $^{1}$H NMR (400 MHz, $CDCl_3$) δ 6.87 (d, *J* = 1.9 Hz, 1H), 6.67 (d, *J* = 1.9 Hz, 1H), 6.27 (s, 2H), 4.52 (dd, *J* = 7.9, 2.0 Hz, 1H), 3.88 (s, 3H), 3.83 (s, 3H), 3.78 (s, 6H), 3.71 (s, 3H), 3.21 (dd, *J* = 19.2, 7.9 Hz, 1H), 2.63 (dd, *J* = 19.2, 2.1 Hz, 1H). $^{13}$C NMR (101 MHz, CDCl3) δ 206.43, 161.97, 158.11, 153.36, 139.89, 139.30, 139.26, 136.69, 106.31, 104.27, 96.12, 61.01, 56.28, 55.96, 55.82, 47.73, 41.76. HRMS (ESI) *m/z* calcd for $C_{20}H_{23}O_6^+$ [M + H]+ 359.1489, found 359.1492.

**7-(3,4,5-Trimethoxyphenyl)-2H,5H,6H,7H-indeno[5,6-d][1,3]dioxol-5-one** (**11dc**). Purified by column chromatography (hexane/EtOAc 95:5 to 9:1), to give **11dc** (85 mg, 0.25 mmol, 83%) as a yellow solid. Mp 176-178 ˚C. $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.15 (s, 1H), 6.66 (s, 1H), 6.32 (s, 2H), 6.09 (d, *J* = 1.1 Hz, 2H), 4.37 (dd, *J* = 7.7, 3.4 Hz, 1H), 3.84 (s, 3H), 3.82 (s, 6H), 3.21 (dd, *J* = 19.0, 7.8 Hz, 1H), 2.68 (dd, *J* = 19.1, 3.5 Hz, 1H). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 203.74, 155.35, 154.56, 153.58, 148.80, 139.22, 136.99, 131.50, 105.81, 104.47, 102.40, 101.78, 60.86, 56.19, 47.14, 44.66. HRMS (ESI) *m/z* calcd for $C_{19}H_{19}O_6^+$ $[M + H]^+$ 343.1176, found 343.1183.

**7-(2H-1,3-Benzodioxol-5-yl)-2H,5H,6H,7H-indeno[5,6-d][1,3]dioxol-5-one** (**11dl**). Purified by column chromatography (hexane/EtOAc 95:5 to 9:1), to give **11dl** (76 mg, 0.26 mmol, 86%) as a brown solid. Mp 193-195 °C. $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.14 (s, 1H), 6.76 (d, *J* = 7.9 Hz, 1H), 6.69 – 6.61 (m, 2H), 6.53 (d, *J* = 1.8 Hz, 1H), 6.10 – 6.04 (m, 2H), 5.95 (d, *J* = 1.7 Hz, 1H), 4.38 (dd, *J* = 7.7, 3.4 Hz, 1H), 3.19 (dd, *J* = 19.1, 7.8 Hz, 1H), 2.62 (dd, *J* = 19.0, 3.5 Hz, 1H). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 203.70, 155.54, 154.52, 148.73, 148.19, 146.60, 137.46, 131.51, 120.82, 108.38, 107.58,

105.81, 102.35, 101.75, 101.11, 47.30, 44.01. HRMS (ESI) *m/z* calcd for $C_{17}H_{13}O_5^+$ [M + H]$^+$ 297.0757, found 297.0762.

**7-(4-Bromophenyl)-2H,5H,6H,7H-indeno[5,6-d][1,3]dioxol-5-one** (**11dm**). Purified by column chromatography (hexane/EtOAc 95:5 to 9:1), to give **11dm** (80 mg, 0.24 mmol, 81%) as a brown solid. Mp 167-169 °C. $^1$H NMR (500 MHz, $CDCl_3$) δ 7.45 (d, *J* = 8.4 Hz, 2H), 7.15 (s, 1H), 7.01 (d, *J* = 8.4 Hz, 2H), 6.58 (s, 1H), 6.08 (d, *J* = 3.0 Hz, 2H), 4.42 (dd, *J* = 7.8, 3.3 Hz, 1H), 3.22 (dd, *J* = 19.0, 7.8 Hz, 1H), 2.61 (dd, *J* = 19.0, 3.4 Hz, 1H). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 203.42, 154.99, 154.80, 149.06, 142.85, 132.23, 131.79, 129.44, 121.07, 105.92, 102.62, 102.08, 47.22, 43.90. HRMS (ESI) *m/z* calcd for $C_{16}H_{12}BrO_3^+$ [M + H]+ 330.9964, found 330.9973.

**5,6-Dimethoxy-3-(3,4,5-trimethoxyphenyl)-2,3-dihydro-1H-inden-1-one** (**11cc**). Purified by column chromatography (hexane/EtOAc 95:5 to 8:2), to give **11cc** (101 mg, 0.28 mmol, 94%) as a yellow solid. Mp 137-139 °C. $^1$H NMR (400 MHz, $CDCl_3$) δ 7.25 (s, 1H), 6.69 (s, 1H), 6.32 (s, 2H), 4.43 (dd, *J* = 7.6, 3.3 Hz, 1H), 3.96 (s, 3H), 3.89 (s, 3H), 3.85 (s, 3H), 3.81 (s, 6H), 3.21 (dd, *J* = 19.0, 7.7 Hz, 1H), 2.64 (dd, *J* = 19.0, 3.4 Hz, 1H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 204.73, 156.02, 153.76, 153.03, 150.13, 144.79, 139.71, 137.13, 130.08, 107.64, 104.73, 103.90, 61.04, 56.55, 56.35, 47.40, 44.77, 29.77. HRMS (ESI) *m/z* calcd for $C_{20}H_{23}O_6^+$ [M + H]$^+$ 359.1489, found 359.1494.

**3-(2,3-Dihydro-1,4-benzodioxin-6-yl)-4-ethyl-5,6-dimethoxy-2,3-dihydro-1H-inden-1-one** (**11ae**). Purified by column chromatography (hexane/EtOAc 95:5 to 9:1), to give **11ae** (83 mg, 0.23 mmol, 78%) as a brown oil. $^1$H NMR (500 MHz, $CDCl_3$) δ 7.09 (s, 1H), 6.79 (d, *J* = 8.2 Hz, 1H), 6.60 (d, *J* = 7.3 Hz, 2H), 4.50 (d, *J* = 6.8 Hz, 1H), 4.24 (s, 3H), 3.93 (s, 6H), 3.47 (s, 3H), 3.16 (dd, *J* = 19.2, 7.9 Hz, 1H), 2.58 (d, *J* =

19.3 Hz, 1H). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 205.40, 154.89, 150.40, 148.79, 144.53, 143.51, 142.19, 137.72, 132.18, 120.17, 117.26, 115.87, 100.29, 64.38, 64.31, 60.92, 60.17, 56.26, 47.29, 40.95. HRMS (ESI) *m/z* calcd for $C_{20}H_{21}O_6^+$ $[M + H]^+$ 357.1333, found 357.1335.

**4-Ethyl-3-(3-iodophenyl)-5,6-dimethoxy-2,3-dihydro-1H-inden-1-one** (**11af**). Purified by column chromatography (hexane/EtOAc 95:5 to 9:1), to give **11af** (93 mg, 0.22 mmol, 73%) as a yellow oil. $^1$H NMR (500 MHz, $CDCl_3$) δ 7.57 (d, *J* = 7.5 Hz, 1H), 7.50 (s, 1H), 7.15 – 6.99 (m, 3H), 4.52 (d, *J* = 6.2 Hz, 1H), 3.95 (s, 3H), 3.93 (s, 3H), 3.43 (s, 3H), 3.19 (dd, *J* = 19.2, 8.0 Hz, 1H), 2.60 (d, *J* = 19.3 Hz, 1H). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 155.37, 150.48, 148.94, 146.98, 143.89, 136.57, 135.97, 132.39, 130.57, 126.73, 100.58, 94.67, 61.10, 60.30, 56.47, 47.02, 41.31. HRMS (ESI) *m/z* calcd for $C_{18}H_{18}IO_4^+$ $[M + H]^+$ 425.0244, found 425.0253.

# Supporting Information

Experimental section and copies of 1H and 13C NMR spectra of all new compounds.

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