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Catalytic Nazarov Reaction of Aryl Vinyl Ketones via Binary Acid Strategy

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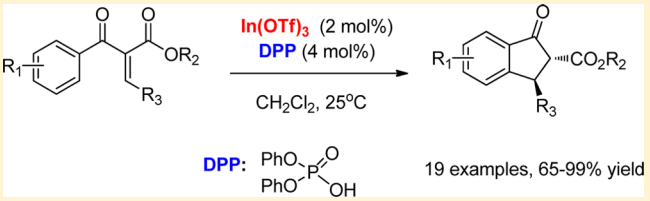
Supporting Information

ABSTRACT: We describe herein a viable binary acid strategy for the catalytic Nazarov reaction of aryl vinyl ketones. Simply combining a Lewis acid and a Brønsted acid led to a dramatic enhancement of the catalytic activity in the Nazarov reaction of aryl vinyl β-ketoesters. The obtained optimal binary acid catalyst $In(OTf)_3$/diphenyl phosphoric acid (DPP) can be applied to a range of aryl vinyl ketones with good activity. A trend of reactivity has also been summarized on the basis of mapping of the substituents.



INTRODUCTION

Natural products have been and continue to serve as inspiration for developing synthetic methodology. Indane-containing natural products as illustrated in Scheme 1 have recently become a prevalent type of natural products with promising pharmaceutical profiles, and the total synthesis of these natural products and their analogues is hence of significant synthetic interest.[1] One of the easily conceived and also the most straightforward strategies for the construction of these indane skeletons is the Nazarov cyclization of aryl vinyl ketones. As a versatile C−C formation reaction, the Nazarov cyclization reaction has demonstrated fascinating power in building cyclopentenone-containing natural or unnatural products.[2] Despite the extensive exploration of Nazarov-type chemistry, aryl vinyl ketones remain difficult substrates with notoriously sluggish reactivity, not to mention the unaddressed issues in controlling enantioselectivity in this type of reactions.[3] Usually, stoichiometric or superstoichiometric amounts of Brønsted or Lewis acids are required to promote the Nazarov cyclization of aryl vinyl ketones.[1c,4] Based on a "polarizing strategy", the Frontier group has developed catalysts such as Cu(II),[5] Pd(II),[6] Ir(III),[7] and $Sc(OTf)_3$/stoichiometric $LiClO_4$[8] for Nazarov cyclization reactions, and these catalysts have also been examined in the Nazarov reactions of several aryl vinyl ketones. The Sarpong group and the Yamamoto group also found $AlCl_3$ and $AuCl_3/AgSbF_6$ as efficient catalysts for aryl vinyl ketones, respectively.[9] Though initial successes have been achieved, those catalytic systems are still suffering from low activity and consequently of narrow scopes. A simple, general, and effective catalyst for cyclization of aryl vinyl ketones remains to be further exploited in Nazarov chemistry.

Building upon the known combined acid principles,[10] we have recently been developing binary acid catalysis as a combinatorial approach for strong acid/electrophilic catalysis.[11] In this binary acid catalysis, the synergistic integration of a Brønsted acid and a metal catalyst would lead to mutually enhanced acidity/electrophilicity and meanwhile provide multiple sites for substrate binding and activation as a result of weak coordinating behaviors between the acid moiety and the metal center. These features inspire us to explore its application in the Nazarov reaction wherein an acid-initialized 4π-electrocyclization and a sequence of proton transfers are key mechanistic steps. Herein, we reported a remarkably active binary acid catalyst $In(OTf)_3$/phosphoric acid for the Nazarov cyclization reaction of aryl vinyl ketones.

RESULTS AND DISCUSSION

Screening and Optimization. Our studies commenced with a model reaction of aryl vinyl ketone **1a**, which has been previously studied.[5−7] A range of Lewis acids have been first examined. The previously reported Lewis acids such as $Cu(OTf)_2$ and $Sc(OTf)_3$ were indeed viable catalysts for the reaction, albeit with rather low activity at room temperature (Table 1, entries 2 and 4). Indium Lewis acids also worked very well in this reaction, and $In(OTf)_3$ was eventually identified as a more active Lewis acid delivering quantitative conversion in 72 h at ambient temperature (Table 1, entries 6−11). To our delight, the combined use of a Brønsted acid such as diphenyl phosphoric acid diester (DPP) led to a dramatic rate enhancement in the reactions (Table 1, entries 3, 5, and 7 vs 2, 4, and 6, respectively). For example, when $In(OTf)_3$ was used together with DPP, the reaction time for complete conversion was sharply reduced from 72 h to 10 min, corresponding to an over 400 times rate increase compared to that using only $In(OTf)_3$! Similar rate enhancement has also

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Scheme 1. Nazarov Strategy in the Synthesis of Indane-Containing Natural Products

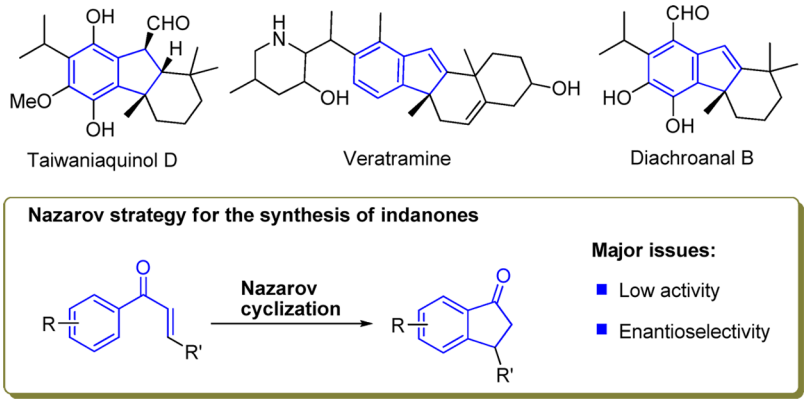
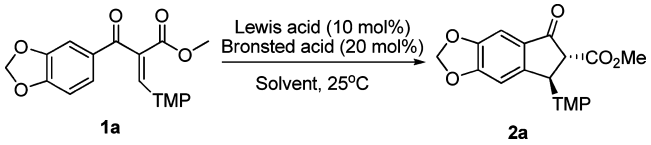


Table 1. Screening of Lewis Acids[a]



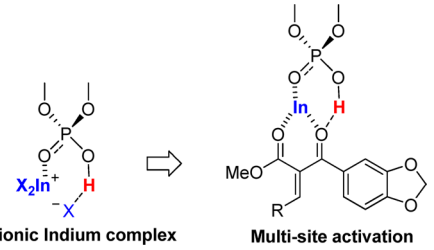
entry	Lewis acid	Brønsted acid	time (h)	conv[b] (%)
1	no	DPP	24	NR
2	$Cu(OTf)_2$	no	72	trace
3	$Cu(OTf)_2$	DPP	24	92
4	$Sc(OTf)_3$	no	72	70
5	$Sc(OTf)_3$	DPP	1	>99
6	$In(OTf)_3$	no	72	>99
7	$In(OTf)_3$	DPP	10 min	>99
8	InF_3	DPP	1	trace
9	$InCl_3$	DPP	0.5	83
10	$InBr_3$	DPP	10 min	>99
11	InI_3	DPP	10 min	>99
12	none	TfOH	30 min	80

[a]Reactions were carried out on a 0.05 mmol scale (substrate **1a**) in 0.5 mL of DCM at 25 °C; only *trans*-diastereoisomer product was observed. [b]Reaction conversion was determined by ^1H NMR. NR: no reaction.

been clearly noted in the cases with $Cu(OTf)_2$ and $Sc(OTf)_3$. The impressive reactivity enhancement highlights the synergistic combination of the Lewis acid and the Brønsted acid in the catalysis of the Nazarov reaction; note that Brønsted acid DPP only was virtually inactive for the reaction (Table 1, entry 1).

In a control reaction, the use of only TfOH (20 mol %), which may be in situ generated from metal triflate and DPP, as the possible active catalytic species has been examined. Though TfOH only with 20 mol % loading is quite active in the reaction, the activity is considerably inferior to that of the metal/weak acid combination (Table 1, entry 12 vs 7). This result together with the observations that $InBr_3$ and InI_3 performed equally well when combined with DPP (Table 1, entries 10 and 11) suggests that both metal and proton play roles in the catalysis, and the contribution from in situ generated strong Brønsted acid, if present, is minor. Mechanistically, this synergistic binary acid effect likely stems from the enhanced electrophilicity as a result of complexation of the metal center with the Brønsted acid ligand, leading to a cationic Indium(III) complex (Scheme 2).[10] Similar ligand enhanced Lewis acidity is well-known[12] and a recent theoretical

Scheme 2. Possible Catalytic Mode of Binary Acid Catalyst



study also suggests a cationic indium complex as the catalytic species in indium halides catalyzed reactions.[13] In addition, the resulted multi acidic centers may also contribute in effective activation of the substrate (Scheme 2).[11f]

With $In(OTf)_3$ as the optimal Lewis acid, the reaction was further optimized. Other Brønsted acids including carboxylic acid (Table 2, entries 1, 3, and 4) and sulfonic acid (Table 2, entry 2) have been first examined, and phosphoric acid turned out to be the optimal Brønsted acid in terms of catalytic activity. The binary acid catalyst $In(OTf)_3$/DPP generally worked well in chlorinated solvents such as dichloromethane and 1,2-dichloroethane (Table 2, entries 5 and 6), while the reactions in MeCN and toluene (Table 2, entries 7 and 8) were slightly slower. In contrast, the reaction did not occur in ethyl ether and THF (Table 2, entries 9 and 10). The catalyst loading can be decreased to 2 mol % with only slight loss of activity (1 h, quantitative conversion, Table 2, entry 11). At 2 mol % loading of the Lewis acid, the possible impact of Lewis acid/Brønsted acid ratio has also been examined. Variations of the ratio from 1:1 to 1:4 indicated that the 1:2 molar ratio of $In(OTf)_3$ and DPP is optimal and the reaction exhibited inferior performance under an either lower or higher molar ratio (Table 2, entry 13 vs 12, 14, and 15). Last but not least, the use of chiral phosphoric acid has also been examined with a hope of attaining enantioselective control.[3] Unfortunately, our initial attempt with chiral phosphoric acids did not lead to any chiral inductions, though the catalytic activity was still maintained (Table 2, entries 16 and 17). At this point, we chose to focus on exploring the synthetic potential of this binary acid catalysis in this paper, and a catalytic asymmetric version is pursued further in separated studies.

Substrate Scope. With the optimized conditions in hand, we embarked on testing the substrate scope of this methodology (Table 3). The bulkiness of the α-substituted ester group demonstrates no obvious impact on the reactivity. Both

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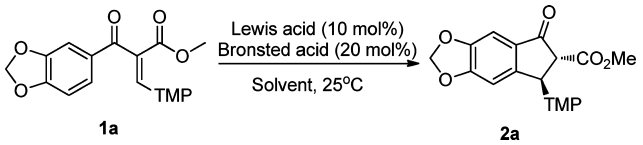
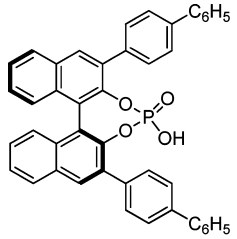
Table 2. Optimization of Reaction Parameters[a]



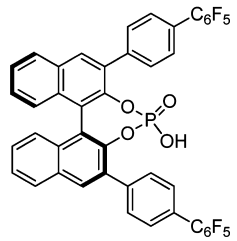
1a 2a

entry	Lewis acid	Brønsted acid	solvent	time (h)	conv[b] (%)
1	$In(OTf)_3$	L-proline	DCM	6	NR
2	$In(OTf)_3$	camphorsulfonic acid	DCM	1	>99[c]
3	$In(OTf)_3$	mandelic acid	DCM	1	95
4	$In(OTf)_3$	benzoic acid	DCM	5.5	75
5	$In(OTf)_3$	DPP	DCM	10 min	>99
6	$In(OTf)_3$	DPP	DCE	10 min	>99
7	$In(OTf)_3$	DPP	MeCN	10 min	65
8	$In(OTf)_3$	DPP	toluene	10 min	92
9	$In(OTf)_3$	DPP	ethyl ether	10 min	NR
10	$In(OTf)_3$	DPP	THF	10 min	NR
11	$In(OTf)_3$ (2 mol %)	DPP (4 mol %)	DCM	1	>99
12	$In(OTf)_3$ (2 mol %)	DPP (2 mol %)	DCM	0.5	23
13	$In(OTf)_3$ (2 mol %)	DPP (4 mol %)	DCM	0.5	64
14	$In(OTf)_3$ (2 mol %)	DPP (6 mol %)	DCM	0.5	31
15	$In(OTf)_3$ (2 mol %)	DPP (8 mol %)	DCM	0.5	30
16	$In(OTf)_3$	(*S*)-BPPA	DCM	10 min	>99[c]
17	$In(OTf)_3$	(*S*)-PFPA	DCM	10 min	>99[c]

[a]Reactions were carried out on a 0.05 mmol scale (substrate **1a**) in 0.5 mL of DCM at 25 °C; when 2 mol % of Lewis acid was loaded, reactions were carried out on a 0.1 mmol scale (substrate **1a**). Only *trans*-product was observed. [b]Reaction conversion was determined by ^{1}H NMR; [c]<5% ee. Enantiomeric excess was determined by Chiral HPLC (Column: chiral AD, elute: iPrOH/hexane = 30/70, rate: 1 mL/min).



(S)-BPPA



(S)-PFPA

reactions of **1b** and **1c** proceeded smoothly to give the desired products with high yields (Table 3, entries 1 and 2). After a prolonged reaction time, decarboxylation of the Nazarov products **2b** and **2c** was observed. This provides a convenient pathway for the synthesis of decarboxylated Nazarov adduct, since the expected Nazarov cyclization with substrates lacking the ester group did not occur under the present conditions.

Previously, it has been shown that *β*-aryl substituents on the enone part influence the reactivity significantly.[3e,5−8] In our work, a similar trend of reactivity, i.e., more electron-rich *β*-aryl substituent reacts faster, was also observed. The electron-rich *β*-aryl-substituted aryl vinyl ketoesters underwent the Nazarov reaction at room temperature smoothly to give excellent yields (Table 3, entries 3 and 5−7). As for the electron-deficient *β*-aryl-substituted aryl vinyl ketoesters such as **1i**−**l**, the Nazarov reaction proceeded very slowly at room temperature. This is not quite unexpected since there have been no reports on the successful cyclizations of electron-deficient *β*-aryl substituted aryl vinyl ketoesters so far. Delightfully, when the temperature was elevated to 40 °C, the Nazarov reaction of these challenging substrates proceeded smoothly to give good to excellent yields under our binary acid catalysis (Table 3, entries 8−12). The reaction of *β*-furan- and *β*-vinyl-substituted **1e** and **1n** worked very well to deliver the desired adducts in high yields (Table 3, entries 4 and 13). The cyclization of a *β*-alkyl-substituted **1o** has also been examined in the catalysis of $In(OTf)_3$/DPP (10 mol %), and the reaction proceeded quite well at 40 °C to give the desired adduct **2o** in 85% yield (Table 3, entry 14). In all cases, the Nazarov products were isolated as dominant *trans*-diastereoisomers, and no *cis*-isomer was observed.[5] The *trans*-adducts mainly exist in their ketoester form, and in several cases particularly with substrates bearing *β*-electron-deficient aryl group on the enone moieties, e.g., **1i**−**l**, the Nazarov adducts in their enol ester form were observed in varied ratios by ^{1}H NMR.

In the Nazarov reaction with aryl vinyl ketones, the general reactivity pattern regarding variations on the aryl part remains obscure. For the first time, we have surveyed the substituent effect of the aryl group. Interestingly, it was found that the electron-donating group on the *meta*-position of the aryl group is vital for the substrates to undergo Nazarov cyclization effectively. For example, while the reaction with *meta*-methoxyl group substituted **1p** reacted smoothly at room temperature to furnish the desired product as a regioisomeric mixture (85:15 favoring the adduct *para* to the methoxyl group as illustrated), those bearing an *o*- or *p*-methoxyl group such as **1q** and **1r** are inert even at elevated temperature for 72 h (Table 3, entry 15 vs entries 16 and 17). This observation is clearly in line with the typical electrophilic aromatic substitution pattern that reaction preferentially occurs *para*- or *ortho*- to the electron-donating group. In further explorations, we could extend our binary acids strategy to Nazarov substrates **1s** and **1t** bearing a naphthyl moiety (Table 3, entries 18 and 19). Interestingly, the Nazarov product **2t** mainly exists in its enol form. When the aryl moiety was replaced by an *N*-methyl-protected indolyl ring, our binary acid system was still applicable, albeit demanding elevated temperature and relatively longer reaction time (Table 3, entry 20).

■ CONCLUSION

In conclusion, we have developed a simple and effective binary acid catalytic strategy for the Nazarov reactions of aryl vinyl ketones. The identified optimal binary acid catalyst $In(OTf)_3$/DPP demonstrates good performance in a broad range of substrates, with activity comparable to the so far best catalyst Ir^{III} complex.[5] One advantage is that our catalytic system is insensitive to air or moisture and is operationally simple and flexible, and hence, it is of practical interest. Besides its wide substrate scope, this method also offers a new opportunity to bring about a catalytic asymmetric variant for the Nazarov reaction of aryl vinyl ketones by judicious selection of active (chiral) Lewis acid, chiral Brønsted acid, and their combinations.

■ EXPERIMENTAL SECTION

The Nazarov substrates were synthesized following a published procedure of Knoevenagel condensation between *β*-ketoesters with corresponding aldehydes.[5b,14] **1a**[5a] and **1b**[15] are known compounds.

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Table 3. Substrate Scope[a]

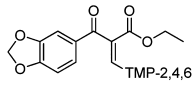
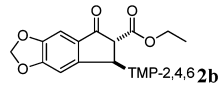
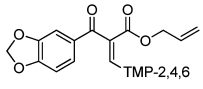
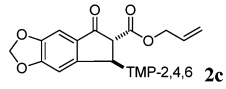
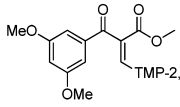
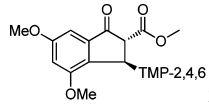
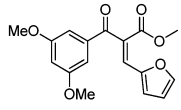
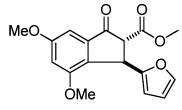
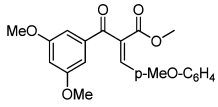
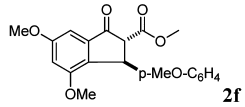
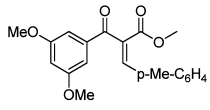
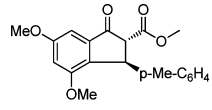
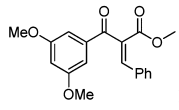
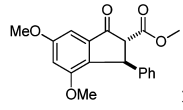
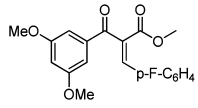
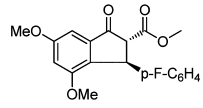
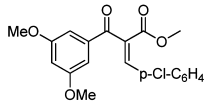
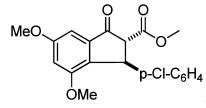
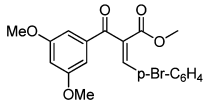
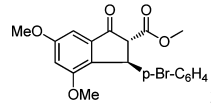
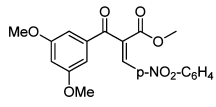
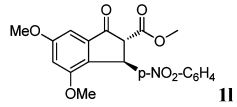
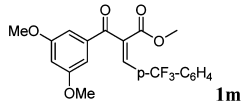
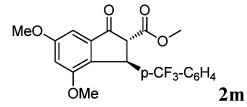
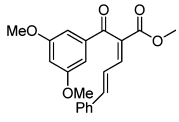
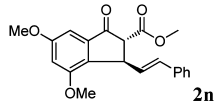
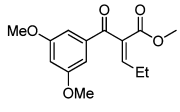
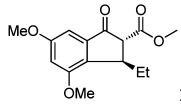
Entry	Substrate [b]	Product	T (°C)	Time (h)	Yield [c] (%)
1	 **1b**	 **2b**	25	1	96
2	 **1c**	 **2c**	25	1	92
3	 **1d**	 **2d**	25	1	99
4	 **1e**	 **2e**	25	1	94 (97: 3)
5	 **1f**	 **2f**	25	6	98 (94: 6)
6	 **1g**	 **2g**	25	10	99 (86:14)
7	 **1h**	 **2h**	25	13	89 (94:6)
8	 **1i**	 **2i**	40	5	95 (83:17)
9	 **1j**	 **2j**	40	5	96 (88:12)
10	 **1k**	 **2k**	40	5	94 (86:14)
11	 **1l**	 **1l**	40	16	80 (77:23)
12	 **1m**	 **2m**	40	6	85 (85:15)
13	 **1n**	 **2n**	25	13	92
14	 **1o**	 **2o**	40	8	85

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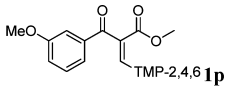
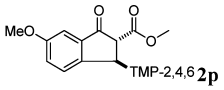
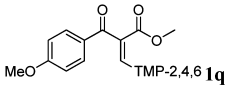
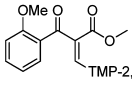
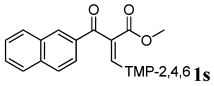
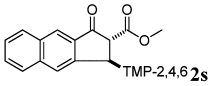
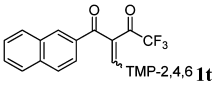
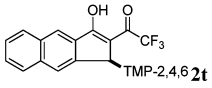
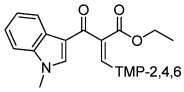
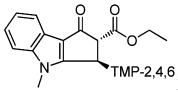
Table 3. continued

Entry	Substrate [b]	Product	T (°C)	Time (h)	Yield [c] (%)
15	 TMP-2,4,6 **1p**	 TMP-2,4,6 **2p**	25	1	94 (85:15)[d]
16	 TMP-2,4,6 **1q**	--	80 (DCE)	72	N.R.
17	 TMP-2,4,6 **1r**	--	80 (DCE)	72	N.R.
18	 TMP-2,4,6 **1s**	 TMP-2,4,6 **2s**	25	1	95
19	 TMP-2,4,6 **1t**	 TMP-2,4,6 **2t**	40	20	65 (7:93)
20	 TMP-2,4,6 **1u**	 TMP-2,4,6 **2u**	40	48	81

[a]Reactions were carried out on a 0.1 mmol scale (substrate **1**) with $In(OTf)_3$/2 DPP (2 mol %) in 0.5 mL of DCM at 25 °C; 10 mol % of catalyst loading in entries 7−12, 14, 16, 17, and 19. [b]TMP-2,4,6 = 2,4,6-trimethoxylphenyl. [c]Isolated yield. Only trans products were obtained. Data in parentheses refers to the keto/enol ratio determined by ^{1}H NMR. [d]Ratio of regioisomers, major isomer is shown.

1c: 1.75 g, 82% yield; yellow solid; mp 126−128 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.14 (s, 1H), 7.46 (dd, J = 8.10, 1.62 Hz, 1H), 7.42 (d, J = 1.56 Hz, 1H), 6.77 (d, J = 8.10 Hz, 1H), 6.00 (s, 2H), 5.95 (s, 2H), 5.86−5.73 (m, 1H), 5.18−5.08 (m, 2H), 4.63- 4.60 (m, 2H), 3.76 (s, 3H), 3.50 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 192.0, 166.5, 163.7, 159.8, 151.1, 147.8, 135.9, 132.8, 132.1, 128.2, 125.3, 117.6, 108.4, 107.7, 105.1, 101.7, 90.3, 65.4, 55.4, 54.8; IR (KBr, cm^{-1}) 1710, 1663, 1604,1440, 1251, 1209, 1129, 1034, 417; HRMS (SIMS-FT-ICRMS) m/z $[M + H]^+$ calcd for $C_{23}H_{23}O_8$ 427.1393, found 427.1385.

1d: 1.23 g, 58% yield; yellow solid; mp 144−146 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.13 (s,1 H), 7.07 (d, J = 2.28 Hz, 2H), 6.58 (t, J= 2.28 Hz, 1H), 5.95 (s, 2H), 3.77 (s, 6H), 3.76 (s, 3H), 3.70 (s, 3H), 3.50 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 193.2, 167.3, 163.8 160.7, 159.8, 139.7, 136.0, 128.1, 106.5, 105.5, 105.3, 90.4, 55.6, 55.5, 54.8, 52.3; IR (KBr, cm^{-1}) 1715, 1672, 1600, 1459, 1339, 1254, 1207, 1157, 1129, 1060, 815, 442, 412; HRMS (SIMS-FT-ICRMS) m/z $[M + H]^+$ calcd for $C_{22}H_{25}O_8$ 417.1549, found 417.1537.

1e: 1.08 g, 69%yield; white solid; mp 104−106 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.67 (s,1 H), 7.31 (d, J = 1.50 Hz, 1H), 7.09 (d, J= 2.40 Hz, 2H), 6.65 (d, J = 2.40 Hz, 2H), 6.37 (q, J = 1.80 Hz, 1H), 3.80 (s, 6H), 3.73 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 194.2, 165.5, 161.1, 149.3, 146.4, 138.4, 128.4, 126.8, 118.0, 112.6, 106.9, 106.2, 55.7, 52.7; IR (KBr, cm^{-1}) 1720, 1677, 1626, 1592, 1551, 1457, 1247, 1206, 1155, 1063, 750; HRMS (ESI) m/z $[M + Na]^+$ calcd for $C_{17}H_{16}O_6Na$ 339.0845, found 339.0840.

1f: 1.24g, 66% yield; white solid; mp 115−117 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.90 (s, 1H), 7.30 (d, J = 8.79 Hz, 2H), 7.12 (d, J = 2.28 Hz, 2H), 6.76 (d, J = 8.82 Hz, 2H), 6.65 (t, J = 2.25 Hz, 1H), 3.79 (s, 6H), 3.75 (s, 3H), 3.74 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 195.8, 165.8, 161.5, 161.2, 142.7, 138.1, 132.4, 128.2, 125.5, 114.4, 107.0, 106.6, 55.7, 55.4, 52.6; IR (KBr, cm^{-1}) 1668, 1601, 1512, 1256, 1172, 1155, 829, 523, 497, 453; HRMS (ESI) m/z $[M + Na]^+$ calcd for $C_{20}H_{20}O_6Na$ 379.1158, found 379.1151.

1g: 980 mg, 58% yield; light yellow solid; mp 80−82 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.92 (s, 1H), 7.24 (d, J = 8.16 Hz, 2H), 7.11 (d, J = 2.31 Hz, 2H), 7.05 (d, J = 8.07 Hz, 2H), 6.64 (t, J = 2.31 Hz, 1H), 3.78 (s, 6H), 3.75 (s, 3H), 2.27 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 195.5, 165.7, 161.2, 143.0, 141.2, 138.0, 130.4, 130.1, 129.7, 129.7, 107.0, 106.6, 55.6, 52.6, 21.5; IR (KBr, cm^{-1}) 2925, 2360, 2342, 1716, 1672, 1592, 1456, 1431, 1256, 1204, 1155, 1064; HRMS (EI-TOF) m/z M^+ calcd for $C_{20}H_{20}O_5$ 340.1311, found 340.1311.

1h: 920 mg, 56% yield; white solid; mp 68−70 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.96 (s, 1H), 7.34−7.23 (m, 2H), 7.30−7.18 (m, 3H), 7.10 (d, J = 2.28 Hz, 2H), 6.64 (t, J = 2.28 Hz, 1H), 3.77 (s, 6H), 3.75 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 195.2, 165.5, 161.2, 142.9, 137.9, 132.9, 130.9, 130.5, 130.3, 128.9, 106.9, 106.6, 55.6, 52.7; IR (KBr, cm^{-1}) 1632, 1456, 1426, 1254, 1203, 1155, 543, 445; HRMS (ESI) m/z $[M + Na]^+$ calcd for $C_{19}H_{18}O_5Na$ 349.1052, found 349.1045.

1i: 830 mg, 48% yield; light yellow solid; mp 70−72 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.89 (s, 1H), 7.36−7.31 (m, 2H), 7.07 (d, J = 2.34 Hz, 2H), 6.96−6.89 (m, 2H), 6.63 (t, J = 2.28 Hz, 1H), 3.77 (s, 6H), 3.74 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 195.2, 165.5, 165.4, 162.1, 161.2, 141.5, 137.8, 132.4, 132.3, 130.7, 130.6, 129.2, 129.1, 116.3, 116.0, 106.9, 106.6, 55.6, 52.7; IR (KBr, cm^{-1}) 2953, 2842, 1721, 1674, 1602, 1509, 1429, 1298, 1259, 1064, 1009, 927, 839, 736, 517; HRMS (EI-TOF) m/z M^+ calcd for $C_{19}H_{17}O_5F$ 344.1060, found 344.1061.

1j: 912 mg, 51% yield; yellow solid; mp 124−126 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.89 (s, 1H), 7.25 (q, J = 8.67 Hz, 4H), 7.08 (d, J = 2.31 Hz, 2H), 6.65 (t, J = 2.25 Hz, 1H), 3.79 (s, 6H), 3.76 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 195.0, 165.3, 161.3, 141.4, 137.7, 136.7, 131.5, 131.5, 131.4, 129.3, 107.0, 106.7, 55.7, 52.8; IR (KBr, cm^{-1}) 1721, 1670, 1591, 1428, 1254, 1203, 1157; HRMS (ESI) m/z $[M + Na]^+$ calcd for $C_{19}H_{17}O_5ClNa$ 383.0662, found 383.0653.

1k: 1.12g, 55% yield; white solid; mp 122−124 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.86 (s, 1H), 7.37 (d, J = 8.55 Hz, 2H), 7.19 (d, J = 8.52 Hz, 2H), 7.06 (d, J = 2.31 Hz, 2H), 6.64 (t, J = 2.28 Hz, 2H), 3.78(s, 6H), 3.75 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 195.0, 165.3, 161.3, 141.4, 137.7, 132.2, 131.8, 131.6, 125.1, 107.0, 106.7, 55.7, 52.8; IR (KBr, cm^{-1}) 2953, 2360, 1712, 1612, 1484, 1306, 1205, 1147, 1010, 833, 737, 554; HRMS (EI-TOF) m/z M^+ calcd for $C_{19}H_{17}O_5Br$ 404.0259, found 404.0257.

1l: 1.32g, 71% yield; white solid; mp 145−147 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.10 (d, J = 8.79 Hz, 2H), 7.96 (s, 1H), 7.50 (d, J = 8.79 Hz, 2H), 7.04 (d, J = 2.22 Hz, 2H), 6.66 (t, J = 2.22 Hz, 1H), 3.80 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 194.1, 164.7, 161.3, 148.4, 139.7, 139.1, 137.4, 134.9, 130.7, 124.1, 107.0, 106.8, 55.7, 53.1; IR (KBr, cm^{-1}) 2923, 2850, 2360, 1721, 1669, 1593, 1523, 1462, 1347,

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1255, 1205, 1158, 1064, 1009, 853, 816; HRMS (EI-TOF) m/z M^+ calcd for $C_{19}H_{17}O_7N$ 371.1005, found 371.1006.

1m: 810 mg, 41% yield; white solid; mp 78−80 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.94 (s, 1H), 7.47 (dd, J = 18.06, 8.49 Hz, 4H), 7.07 (d, J = 2.28 Hz, 2H), 6.65 (t, J = 2.28 Hz, 1H), 3.78 (s, 6H), 3.77 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 194.5, 165.1, 161.3, 140.9, 137.7, 136.3, 133.5, 132.1, 131.6, 130.3, 125.9 (q, J = 3.8 Hz), 107.0, 106.7, 106.4, 55.7, 52.9; IR (KBr, cm^{-1}) 2954, 2841, 1722, 1673, 1593, 1462, 1429, 1356, 1325, 1262, 1205, 1156, 1125, 1068, 1015, 927, 847, 736, 705, 595; HRMS (EI-TOF) m/z M^+ calcd for $C_{20}H_{17}O_5F_3$ 394.1028, found 394.1025.

1n: 650 mg, 45% yield; yellow solid; mp 100−102 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.69 (d, J = 11.76 Hz, 1H), 7.39−7.35 (m, 2H), 7.33−7.27 (m, 3H), 7.07 (d, J = 2.10 Hz, 2H), 7.03 (d, J = 15.51 Hz, 1H), 6.82−6.64 (m, 2H), 3.82 (s, 6H), 3.73 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 194.2, 165.6, 161.1, 144.1, 144.0, 138.9, 135.6, 130.9, 129.8, 128.9, 127.8, 122.9, 107.1, 106.4, 55.7, 52.5; IR (KBr, cm^{-1}) 2360, 2341, 1717, 1669, 1592, 1235, 1204, 1156, 669, 421; HRMS (EI-TOF) m/z M^+ calcd for $C_{21}H_{20}O_5$ 352.1311, found 352.1312.

1o: 1.62g, 83% yield; colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.10 (t, J = 7.92 Hz, 1H), 7.00 (d, J = 2.22 Hz, 2H), 6.64 (t, J = 2.19 Hz, 1H), 3.78 (s, 6H), 3.66 (s, 3H), 2.07 (p, J = 7.62 Hz, 2H), 0.99 (t, J = 7.50 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 194.2, 165.0, 161.1, 149.5, 138.5, 132.7, 106.8, 106.3, 55.6, 52.3, 23.2, 12.9; IR (KBr, cm^{-1}) 2968, 2936, 2874, 2839, 2359, 2340, 1728, 1675, 1593, 1457, 1432, 1362, 1317, 1294, 1242, 1206, 1157, 1065, 773, 675; HRMS (EI-TOF) m/z M^+ calcd for $C_{15}H_{18}O_5$ 278.1154, found 278.1155.

1p: 450 mg, 38% yield; yellow solid; mp 171−173 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.15 (s, 1H), 7.50−7.47 (m, 2H), 7.33−7.27 (m, 1H), 7.06−7.02 (m, 1H), 5.95 (s, 2H), 3.82 (s, 3H), 3.77 (s, 3H), 3.69 (s, 3H) 3.48 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 193.4, 167.3, 163.7, 159.8, 159.6, 139.0, 136.0, 129.2, 128.2, 121.9, 119.2, 112.6, 105.1, 90.3, 55.5, 55.4, 54.8, 52.2; IR (KBr, cm^{-1}) 1712, 1674, 1601, 1467, 1435, 1337, 1260, 1209, 1159, 1129, 814, 734, 403; HRMS (SIMS-FT-ICRMS) m/z $[M + H]^+$ calcd for $C_{21}H_{23}O_7$ 387.1444, found 387.1441.

1q: 600 mg, 50% yield; yellow solid; mp 132−134 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.13 (s, 1H), 7.86 (d, J = 8.85 Hz, 2H), 6.86 (d, J = 8.88 Hz, 2H), 5.93 (s, 2H), 3.83 (s, 3H), 3.75 (s, 3H), 3.68 (s, 3H), 3.47 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 192.5, 167.5, 163.6, 162.9, 159.7, 135.7, 131.0, 130.8, 128.4, 113.4, 105.2, 90.2, 55.5, 55.4, 54.7, 52.2; IR (KBr, cm^{-1}) 1712, 1680, 1603, 1264, 1159, 1128, 741; HRMS (SIMS-FT-ICRMS) m/z $[M + H]^+$ calcd for $C_{21}H_{23}O_7$ 387.1444, found 387.1441.

1r: 540 mg, 45% yield; yellow solid; mp 126−128 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.06 (dd, J = 1.68 Hz, 1H), 7.77 (s, 1H), 7.50−7.43 (m 1H), 7.05−6.95 (m, 2H), 5.98 (s, 2H), 3.81 (s, 3H), 3.75 (s, 3H), 3.66 (s, 3H), 3.42 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 190.6, 167.2, 162.9, 159.7, 159.3, 133.9, 133.8, 131.9, 131.1, 127.1, 120.7, 112.4, 105.6, 90.5, 55.9, 55.4, 54.9, 51.8; IR (KBr, cm^{-1}) 1719, 1654, 1603, 1459, 1254, 1207, 1157, 1129, 1023, 760, 422; HRMS (SIMS-FT-ICRMS) m/z $[M + H]^+$ calcd for $C_{21}H_{23}O_7$ 387.1444, found 387.1439.

1s: 1.23 g, 61% yield; yellow solid; mp 146−148 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.41(s,1 H), 8.25(s,1 H), 8.04 (dd, J = 8.55, 1.50 Hz, 1H), 7.92−7.85 (m, 3H), 7.59−7.48 (m, 2H), 5.93 (s, 2H), 3.74 (s, 3H), 3.67 (s, 3H), 3.44 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 193.8, 167.5, 163.7, 159.8, 136.3, 135.5, 135.2, 132.7, 130.5, 129.8, 128.3, 128.2, 128.0, 127.9, 126.6, 124.8, 105.2, 90.4, 55.5, 54.9, 52.3; IR (KBr, cm^{-1}) 1666, 1604, 1466, 1211, 1157, 1126, 406; HRMS (SIMS-FT-ICRMS) m/z $[M + H]^+$ calcd for $C_{24}H_{23}O_6$ 407.1495, found 407.1488.

1t: 1.32 g, 72% yield; a mixture of E/Z isomers ($E/Z \approx$ 1:4, determined by ^{1}H NMR); yellow solid; mp 57−59 °C; ^{1}H NMR (300 MHz, $CDCl_3$) 8.40 (s, 1H), 8.34 (s, 1.20H), 8.04−7.81 (m, 5H), 7.70 (s, 0.32H), 7.62−7.44 (m, 2.5H), 6.11 (s, 0.40H), 5.92 (s, 2H), 3.84 (s, 0.59H), 3.75 (s, 1.12H), 3.74 (s, 3H), 3.49 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) for the Z isomer: 192.9, 181.2, 165.7, 160.6, 141.5, 135.6, 134.4, 132.6, 130.6, 130.2, 129.7, 128.4, 128.3, 127.9, 126.7, 124.5, 105.3, 90.5, 55.6, 55.0; for the E isomer: 194.8, 180.7, 164.9, 159.7, 141.2, 134.7, 132.4, 131.7, 129.6, 128.6, 128.5, 128.0, 127.0, 125.7, 118.8, 115.0, 104.7, 90.9, 55.8, 55.6; IR (KBr, cm^{-1}) 2942, 2843, 2360, 1667, 1588, 1471, 1417, 1335, 1274, 1207, 1151, 1126, 1059, 1025, 1001, 955, 818, 738, 703, 479, 442, 418, 404; HRMS (EI-TOF) m/z M^+ calcd for $C_{24}H_{19}F_3O_5$ 444.1185, found 444.1183.

1u: 400 mg, 42% yield; light yellow solid; mp 141−143 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.48−8.37 (m, 1H), 8.06 (s, 1H), 7.36 (s, 1H), 7.25 (d, J = 3.33 Hz, 3H), 5.90 (s, 2H), 4.22 (q, J = 7.10 Hz, 2H), 3.71 (s, 3H), 3.65 (s, 3H), 3.56 (s, 6H), 1.21 (t, J = 7.10 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 188.0, 167.3, 163.1, 159.7, 137.6, 136.9, 134.1, 130.9, 126.6, 123.0, 122.6, 122.2, 116.7, 109.5, 105.8, 90.2, 61.0, 55.3, 55.1, 33.3, 14.3; IR (KBr, cm^{-1}) 1708, 1603, 1527, 1464, 1334, 1249, 1207, 1157, 1127, 1034, 750, 458, 409; HRMS (SIMS-FT-ICRMS) m/z $[M + H]^+$ calcd for $C_{24}H_{26}NO_6$ 424.1760, found 424.1750.

General Procedure for the Nazarov Reaction. To a mixture of $In(OTf)_3$ (1.12 mg, 0.002 mmol) and diphenyl phosphate (DPP) (1.00 mg, 0.004 mmol) was added andydrous DCM (0.2 mL). After the mixture was stirred for 0.5 h at room tempreture, a solution of Nazarov substrates (0.1 mmol) in DCM (0.3 mL) was added to the catalyst solution. The reaction was carried out at room temperature and monitored by TLC. After the indicated reaction time, the reaction mixture was directly purified by column chromatography on silica gel with petroleum/ethyl acetate (2:1 to 10:1) to give the Nazarov products. Nazarov product **2a**[5a] is a known compound.

2b: 39.8 mg, 96% yield; colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.08 (s, 1H), 6.52 (s, 1H), 6.19 (s, 1H), 6.00 (broad, 3H), 5.39 (d, J = 3.69 Hz, 1H), 4.3−4.10 (m, 2H), 3.93 (d, J = 3.78 Hz, 1H), 3.86 (s, 3H), 3.80 (s, 3H), 3.44 (s, 3H), 1.27 (t, J = 7.08 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 198.3, 170.0, 160.8, 159.6, 159.1, 156.5, 154.6, 148.1, 129.5, 109.4, 104.7, 102.3, 102.2, 91.5, 90.9, 61.4, 60.4, 56.3, 55.6, 38.0, 14.3; IR (KBr, cm^{-1}) 1733, 1701, 1607, 1469, 1294, 1205, 1149, 1118, 1035, 413; HRMS (ESI) m/z $[M + Na]^+$ calcd for $C_{22}H_{22}O_8Na$ 437.1212, found 437.1205.

2c: 39.2 mg, 92% yield; colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.08 (s, 1H), 6.52 (s, 1H), 6.18 (s, 1H), 6.00 (s, 3H), 5.97−5.84 (m, 1H), 5.40 (d, J = 3.69 Hz, 1H), 5.32 (dd, J = 17.22, 1.44 Hz, 1H), 5.20 (dd, J = 10.47, 1.23 Hz, 1H), 4.75−4.56 (m, 2H), 3.98 (d, J = 3.78 Hz, 1H), 3.85 (s, 3H), 3.79 (s, 3H), 3.44 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 198.0, 169.7, 160.9, 159.5, 159.1, 156.5, 154.6, 148.1, 132.1, 129.4, 118.1, 109.3, 104.7, 102.3, 91.4, 90.8, 60.2, 56.3, 55.5, 55.4, 38.0; IR (KBr, cm^{-1}) 1737, 1698, 1607, 1470, 1456, 1294, 1118, 1035, 938, 816; HRMS (ESI) m/z $[M + Na]^+$ calcd for $C_{23}H_{22}O_8Na$ 449.1212, found 449.1206.

2d: 41.3 mg, 99% yield; colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.80 (d, J = 2.04 Hz, 1H), 6.54 (d, J = 2.04 Hz, 1H), 6.17 (d, J = 2.16 Hz, 1H), 5.96 (d, J = 2.13 Hz, 1H), 5.42 (d, J = 2.76 Hz, 1H), 3.88 (s, 3H), 3.81−3.79 (m, 4H), 3.77 (s, 3H), 3.73 (s, 3H), 3.60 (s, 3H), 3.38 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 200.6, 170.2, 161.0, 160.2, 159.3, 159.0, 157.5, 139.8, 137.7, 110.1, 106.2, 96.5, 91.4, 91.3, 60.9, 56.6, 55.9, 55.8, 55.4, 52.6, 35.6; IR (KBr, cm^{-1}) 1739, 1711, 1607, 1454, 1360, 1308, 1149, 1118, 1035,814, 736, 634, 502; HRMS (ESI) m/z $[M + Na]^+$ calcd for $C_{22}H_{24}O_8Na$ 439.1369, found 439.1357.

2e: 29.8 mg, 94% yield; colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.82 (d, J = 2.0 Hz, 1H), 6.68 (d, J = 2.0 Hz, 1H), 6.25 (dd, J = 3.0, 1.9 Hz, 1H), 6.01 (d, J = 3.1 Hz, 1H), 5.02 (d, J = 2.85 Hz, 1H), 3.83 (s, 3H), 3.80 (d, J = 2.91 Hz, 1H), 3.78 (s, 3H), 3.74 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 198.1, 168.6, 162.3, 157.9, 153.7, 141.8, 137.4, 135.6, 110.4, 107.0, 106.4, 97.0, 60.7, 56.0, 55.9, 53.1, 39.4; IR (KBr, cm^{-1}) 2954, 2842, 1722, 1612, 1495, 1437, 1357, 1309, 1205, 1152, 1037, 1012, 934, 848, 736, 601; HRMS (ESI) m/z $[M + Na]^+$ calcd for $C_{17}H_{16}O_6Na$ 339.0845, found 339.0837.

2f: 35.1 mg, 98% yield; colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$) 7.00−6.92 (m, 2H), 6.84 (d, J = 2.04 Hz, 1H), 6.82−6.75 (m, 2H), 6.66 (d, J = 2.07 Hz, 1H), 4.88 (d, J = 2.88 Hz, 1H), 3.85 (s, 3H), 3.77 (s, 3H), 3.76 (s, 3H), 3.64 (s, 3H), 3.58 (d, J = 2.88 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 199.2, 169.0, 162.1, 158.5, 157.9, 138.7, 137.6, 134.5, 128.2, 114.1, 107.1, 96.6, 64.3, 55.9, 55.8, 55.3, 52.9, 45.3; IR (KBr, cm^{-1}) 1648, 1636, 1559, 1541, 1507, 1456, 467, 417; HRMS

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(ESI) m/z [M + Na]$^+$ calcd for $C_{20}H_{20}O_6Na$ 379.1158, found 379.1155.

2g: 33.7 mg, 99% yield; white solid, containing a inseparable enol isomer (keto/enol = 86:14); data for the keto isomer ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.06 (d, J = 8.04 Hz, 2H), 6.94 (d, J = 8.04 Hz, 2H), 6.85 (d, J = 2.01 Hz, 1H), 6.66 (d, J = 2.04 Hz, 1H), 4.89 (d, J = 2.82 Hz, 1H), 3.85 (s, 3H), 3.78 (s, 3H), 3.65 (s, 3H), 3.59 (d, J = 2.85 Hz, 1H), 2.30 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 199.2, 169.0, 162.1, 157.9, 139.4, 138.6, 137.6, 136.5, 129.4, 127.1, 107.1, 96.67 (s), 64.3, 55.9, 55.8, 52.9, 45.7, 21.2; IR (KBr, cm^{-1}) 2955, 2925, 1740, 1714, 1613, 1495, 1310, 1206, 1151, 934, 834, 420; HRMS (EI-TOF) m/z M$^+$ calcd for $C_{20}H_{20}O_5$ 340.1311, found 340.1313.

2h: 29.1 mg, 89% yield; pink solid, containing a inseparable enol isomer (keto/enol =94:6); data for the keto isomer: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.30−7.14 (m, 3H), 7.07−7.04 (m, 2H), 6.86 (d, J = 2.04 Hz, 1H), 6.66 (d, J = 2.07 Hz, 1H), 4.93 (d, J = 2.91 Hz, 1H), 3.85 (s, 3H), 3.78 (s, 3H), 3.63 (s, 3H), 3.61 (d, J = 2.94 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 199.0, 168.9, 162.2, 157.9, 142.4, 138.4, 137.7, 128.7, 127.3, 127.0, 107.1, 96.7, 64.2, 55.9, 55.7, 53.0, 46.0; IR (KBr, cm^{-1}) 1647, 1636, 560; HRMS (ESI) m/z [M + Na]$^+$ calcd for $C_{19}H_{18}O_5Na$ 349.1052, found 349.1041.

2i: 32.8 mg, 95% yield; light yellow oil, containing a inseparable enol isomer (keto/enol = 83:17); data for the keto isomer ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.05−6.90 (m, 5H), 6.85 (d, J = 1.89 Hz, 1H), 6.66 (d, J = 1.95 Hz, 1H), 4.91 (d, J = 3.00 Hz, 1H), 3.85 (s, 3H), 3.78 (s, 3H), 3.64 (s, 3H), 3.56 (d, J = 3.00 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 198.7, 168.8, 162.3, 157.8, 138.2, 138.0, 137.6, 128.8, 128.7, 115.7, 115.47, 107.17, 96.8, 64.1, 56.0, 55.7, 53.0, 45.3; IR (KBr, cm^{-1}) 2954, 2842, 2360, 1711, 1619, 1510, 1360, 1309, 1231, 1152, 1029, 934, 842, 794, 738, 564; HRMS (EI-TOF) m/z M$^+$ calcd for $C_{19}H_{17}O_5F$ 344.1060, found 344.1059.

2j: 34.6 mg, 96% yield; pink solid, containing an inseparable enol isomer (keto/enol = 88:12); data for the keto isomer ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.24−7.21 (m, 2H), 7.01−6.98 (m, 2H), 6.85 (d, J = 1.78 Hz, 1H), 6.67 (d, J = 1.95 Hz, 1H), 4.90 (d, J = 3.0 Hz, 1H), 3.86 (s, 3H), 3.79 (s, 3H), 3.65 (s, 3H), 3.55 (d, J = 3.30 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 198.5, 168.7, 162.4, 157.8, 141.0, 137.7, 137.6, 132.7, 128.9, 128.7, 128.6, 128.5, 107.1, 96.8, 63.9, 56.0, 55.7, 53.0, 45.3; IR (KBr, cm^{-1}) 1650, 1636, 429; HRMS (ESI) m/z [M + Na]$^+$ calcd for $C_{19}H_{17}O_5ClNa$ 383.0662, found 383.0652.

2k: 38.1 mg, 94% yield; pink solid, containing a inseparable enol isomer (keto/enol = 86:14); data for the keto isomer ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38 (d, J = 1.74 Hz, 1H), 7.36 (d, J = 1.77 Hz, 1H), 6.96−6.92 (m, 2H), 6.84 (d, J = 2.04 Hz, 1H), 6.66 (d, J = 2.04 Hz, 1H), 4.88 (d, J = 3.03 Hz, 1H), 3.85 (s, 3H), 3.78 (s, 3H), 3.64 (s, 3H), 3.54 (d, J = 3.09 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 198.5, 168.7, 162.4, 157.8, 141.5, 137.7, 137.6, 131.8, 131.0, 129.8, 129.0, 120.8, 107.1, 96.8, 63.9, 56.0, 55.7, 53.0, 45.4; IR (KBr, cm^{-1}) 2953, 2360, 1713, 1612, 1484, 1307, 1205, 1147, 1010, 833, 737, 554; HRMS (EI-TOF) m/z M$^+$ calcd for $C_{19}H_{17}O_5Br$ 404.0259, found 404.0253.

2l: 30.0 mg, 80% yield; light yellow oil, containing a inseparable enol isomer (keto/enol = 77:23); data for the keto isomer ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.15 (s, 1H), 8.12 (s, 1H), 7.27 (d, J = 1.23 Hz, 1H), 7.24 (d, J = 1.95 Hz, 1H), 6.88 (d, J = 2.01 Hz, 1H), 6.69 (d, J = 2.04 Hz, 1H), 5.04 (d, J = 3.30 Hz, 1H), 3.87 (s, 3H), 3.82 (s, 3H), 3.65 (s, 3H), 3.57 (d, J = 3.33 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 197.7, 168.3, 162.7, 157.6, 149.9, 147.1, 137.7, 136.4, 128.8, 128.2, 124.1, 123.4, 107.1, 97.1, 63.4, 56.0, 55.7, 53.2, 45.5; IR (KBr, cm^{-1}) 2956, 2360, 1721, 1612, 1519, 1452, 1347, 1311, 1150, 1014, 845, 738, 701, 559; HRMS (EI-TOF) m/z M$^+$ calcd for $C_{19}H_{17}O_7N$ 371.1005, found 371.1021.

2m: 33.4 mg, 85% yield; pink solid, containing an inseparable enol isomer (keto/enol = 85:15); data for the keto isomer: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.52 (d, J = 8.13 Hz, 2H), 7.18 (d, J = 8.10 Hz, 2H), 6.87 (d, J = 2.07 Hz, 1H), 6.67 (d, J = 2.07 Hz, 1H), 4.98 (d, J = 3.12 Hz, 1H), 3.86 (s, 3H), 3.80 (s, 3H), 3.64 (s, 3H), 3.56 (d, J = 3.15 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 198.2, 168.6, 162.5, 157.8, 146.5, 137.7, 137.2, 129.6, 128.3, 127.7, 125.8, 125.7, 107.1, 96.9, 63.7, 56.0, 55.7, 53.1, 45.7; IR (KBr, cm^{-1}) 2955, 2842, 1722, 1656, 1620, 1461, 1325, 1067, 1018, 935, 837, 794, 738, 683, 602, 554; HRMS (EI-TOF) m/z M$^+$ calcd for $C_{20}H_{17}O_5F_3$ 394.1028, found 394.1028.

2n: 32 mg, 92% yield; yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40−7.16 (m, 5H), 6.82 (d, J = 2.04 Hz, 1H), 6.69 (d, J = 2.07 Hz, 1H), 6.50 (d, J = 15.72 Hz, 1H), 6.25 (dd, J = 15.79, 7.81 Hz, 1H), 4.53 (dd, J = 7.81, 2.39 Hz, 1H), 3.84 (s, 3H), 3.81 (s, 3H), 3.79 (s, 3H), 3.62 (d, J = 2.94 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 198.6, 169.0, 162.1, 158.2, 137.6, 137.3, 137.1, 131.3, 129.2, 128.7, 127.6, 126.4, 106.8, 96.9, 61.1, 55.9, 55.8, 52.9, 43.6; IR (KBr, cm^{-1}) 2955, 2839, 2359, 2340, 1715, 1614, 1496, 1308, 797, 749, 694, 472, 457, 444, 423; HRMS (EI-TOF) m/z M$^+$ calcd for $C_{21}H_{20}O_5$ 352.1311, found 352.1311.

2o: 23.7 mg, 85% yield; light yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.74 (d, J = 1.74 Hz, 1H), 6.65 (d, J = 1.71 Hz, 1H), 3.83 (s, 3H), 3.79 (s, 3H), 3.73 (s, 3H), 3.65 (dt, J = 9.15 Hz, 2.85 Hz, 1H), 3.37 (d, J = 2.67 Hz, 1H), 2.20−2.12 (m, 1H), 1.52−1.47 (m, 1H), 0.87 (t, J = 7.41 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 199.5, 169.9, 161.6, 157.9, 139.5, 137.6, 106.5, 96.6, 59.7, 55.8, 55.6, 52.7, 42.6, 26.2, 11.3; IR (KBr, cm^{-1}) 2962, 2360, 2340, 1744, 1713, 1614, 1495, 1456, 1435, 1362, 1323, 1293, 1205, 1151, 1038, 847, 666, 419, 405; HRMS (EI-TOF) m/z M$^+$ calcd for $C_{15}H_{18}O_5$ 278.1154, found 278.1153.

2p: 36.4 mg, 94% yield; white solid (containing an inseparable regioisomer); data for the major isomer: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.18 (d, J = 1.20 Hz, 1H), 7.07 (d, J = 2.25 Hz, 2H), 6.19 (d, J = 2.25 Hz, 1H), 6.01 (s, 1H), 5.46 (d, J = 3.72 Hz, 1H), 4.01 (d, J = 3.72 Hz, 1H), 3.88 (s, 3H), 3.82 (s, 3H), 3.79 (s, 3H), 3.75 (s, 3H), 3.39 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 200.3, 170.3, 160.6, 159.2, 151.4, 136.0, 128.80, 126.1, 124.5, 116.4, 115.6, 109.8, 104.9, 91.6, 91.3, 90.8, 60.4, 55.6, 55.4, 55.3, 52.6 37.5; IR (KBr, cm^{-1}) 2942, 2839, 1714, 1591, 1455, 1267, 1024, 985, 952, 813, 737, 583; HRMS (ESI) m/z [M + Na]$^+$ calcd for $C_{21}H_{22}O_7Na$ 409.1263, found 409.1258.

2s: 36.7 mg, 95% yield; corlorless oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.87 (t, J = 8.45 Hz, 2H), 7.77 (s, 2H), 7.59−7.47 (m, 1H), 7.46−7.31 (m, 1H), 6.27 (d, J = 2.19 Hz, 1H), 5.92−5.89 (m, 2H), 4.02 (s, 3H), 3.91 (d, J = 2.79 Hz, 1H), 3.76 (s, 6H), 3.21 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 200.1, 170.3, 160.7, 159.7, 158.7, 158.1, 137.4, 133.3, 130.2, 128.9, 128.7, 126.8, 125.5, 119.5, 110.2, 91.6, 91.1, 61.1, 56.4, 55.4, 55.1, 52.7, 37.8; IR (KBr, cm^{-1}) 1737, 1704, 1608, 1457, 1334, 1204, 1149, 1118, 816, 752, 737; HRMS (ESI) m/z [M + Na]$^+$ calcd for $C_{24}H_{22}O_6Na$ 429.1314, found 429.1302.

2t: 29 mg, 65% yield; a mixture of enol/keto esters with the enol form as the major product (enol/keto = 93:7); yellow solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 13.79 (s, 1H), 8.06 (d, J = 8.31 Hz, 1H), 7.88 (d, J = 8.04 Hz, 1H), 7.85 (s, 2H), 7.56 (t, J = 7.08 Hz, 1H), 7.44 (t, J = 7.59 Hz, 1H), 6.27 (d, J = 2.25 Hz, 1H), 6.13 (d, J = 1.50 Hz, 1H), 5.85 (d, J = 2.28 Hz, 1H), 4.08 (s, 3H), 3.75 (s, 3H), 3.25 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 199.4, 160.7, 159.6, 158.2, 154.9, 137.3, 134.4, 129.7, 129.1, 129.0, 128.9, 127.2, 125.8, 118.8, 117.7, 109.4, 91.9, 91.2, 56.3, 55.7, 55.3, 36.5, 29.9; IR (KBr, cm^{-1}) 1673, 1606, 1469, 1285, 1203, 1118, 799, 757, 536, 502, 473, 443, 417; HRMS (EI-TOF) m/z M$^+$ calcd for $C_{24}H_{19}F_3O_5$ 444.1185, found 444.1187.

2u: 34.2 mg, 81% yield; yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.98−7.90 (m, 1H), 7.29−7.22 (m, 3H), 6.20 (d, J = 2.22 Hz, 1H), 6.04 (d, J = 2.19 Hz, 1H), 5.56 (d, J = 3.00 Hz, 1H), 4.33−4.17 (m, 2H), 4.08 (d, J = 3.00 Hz, 1H), 3.89 (s, 3H), 3.81 (s, 3H), 3.44 (s, 3H), 3.40 (s, 3H), 1.31 (t, J = 7.11 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 188.3, 170.5, 170.2, 161.2, 160.0, 158.8, 143.4, 123.2, 122.4, 121.9, 121.3, 117.4, 109.9, 105.9, 91.2, 90.9, 65.7, 61.4, 56.3, 55.8, 55.5, 33.8, 30.2, 14.5; IR (KBr, cm^{-1}) 2360, 2341, 1731, 1684, 1457, 1119, 727, 668; HRMS (ESI) m/z [M + Na]$^+$ calcd for $C_{24}H_{25}NNaO_6$ 446.1580, found 446.1578.

■ ASSOCIATED CONTENT

Supporting Information

^{1}H and ^{13}C NMR spectra for all new compounds reported. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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