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Synthesis of Enantioenriched Phthalide and Isoindolinone Derivatives from 2-Formylbenzoic Acid

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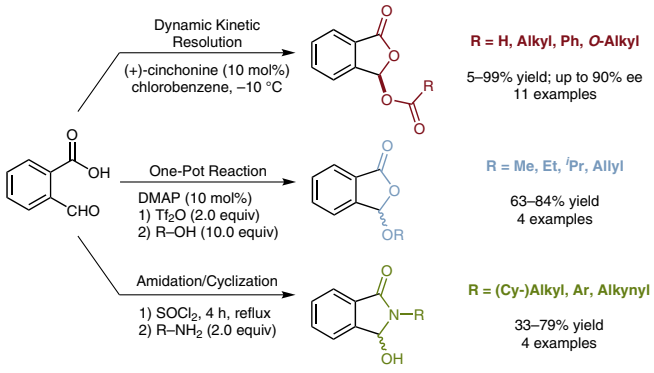
This manuscript is dedicated to Prof. Dieter Enders on the occasion of his 70th birthday and for his seminal contributions to organic chemistry.



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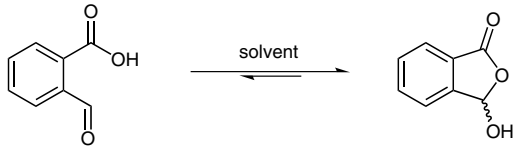
Abstract Transformations of 2-formylbenzoic acid provide direct access to a series of heterocyclic organic compounds such as phthalides and isoindolinones. Here, we use (+)-cinchonine as a catalyst in conjunction with nonafluoro-*tert*-butanol as a hydrogen-bond donor to afford enantiomerically enriched acylated 3-hydroxyphthalides with up to 99% yield and 90% *ee* through dynamic kinetic resolution. Moreover, various 3-alkoxyphthalides as well as 2-alkyl-3-hydroxy-1-isoindolinones were synthesized from 2-formylbenzoic acid.

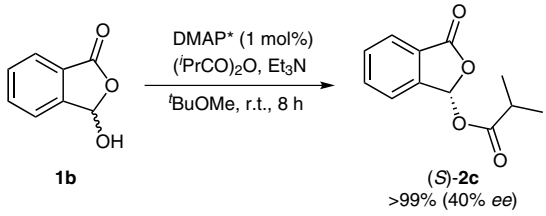
Keywords acylation, chiral auxiliary, cinchona alkaloids, dynamic kinetic resolution, organocatalysis

Since its discovery in 1886,[1] 2-formylbenzoic acid **1a** (FBA) or its tautomeric form 3-hydroxyphthalide **1b** (Scheme 1) (ring-chain tautomerism) was often described as a useful precursor in organic synthesis.[2] The atypical chemical behavior that fits neither to an aldehyde nor to a carboxylic acid, and especially the unexpected high reactivity of this compound toward nucleophiles as well as electrophiles, are probably the main reasons for the great attention it has received.[2,3] The cyclized tautomeric form **1b** of 2-formylbenzoic acid is considerably favored in almost all solvents. The only exception is pure sulfuric acid, in which the open-chain aldehyde is preferred.[3] The reactivity of **1** was previously described to be comparable to that of an acyl chloride. Thus, under appropriate conditions **1a**/**1b** reacts with a series of nucleophiles, such as alcohols, thiols, primary as well as secondary amines, amides, ureas, carbamates, but also with electrophilic carboxylic anhydrides affording 3-substituted phthalides.[2,4,5] The synthesis of the phthalide core in general and 3-substituted derivatives in particular have been comprehensively reported[6–15] because of their important role in the synthesis of biologically active compounds, natural products, and pharmaceuticals.[16–26] 3-Phthalideyl alkanoates, which can be obtained from FBA through reaction with carboxylic anhydrides under reflux,[2,5] were employed as precursors of arylspiroketals,[27] building blocks for polyaromatics,[28] as reagents for the phthalidation of heteroarenes,[11] and also as building blocks for antitumor agents,[29] β-lactam antibiotics,[30] and orally active opioid peptides.[31] In case of the enantiopure compound, the phthalide core could act as an auxiliary for further functionalization of the carbonyl group of the ester to generate, for example, enantiomerically enriched tertiary alcohols. Furthermore, these compounds may be applied as chiral acylating reagents.[32–35]



Scheme 1 Equilibrium of 2-formylbenzoic acid **1a** and its tautomeric form 3-hydroxyphthalide **1b**

There are some transition-metal-catalyzed approaches to prepare 3-phthalideyl alkanoates.[6–7,36] However, the desired products are generally obtained as racemic mixtures. To our knowledge, there is only one example of a dynamic kinetic resolution (DKR) employing a chiral 4-(*N*,*N*-dimethylamino)pyridine (DMAP) derived catalyst and isobutyric anhydride. By using **1b**, the acylated product (*S*)-**2c** formed



Scheme 2 Dynamic kinetic resolution of FBA using a chiral DMAP-derived catalyst (labeled DMAP*)

in quantitative yield with moderate selectivity (40% *ee*; Scheme 2).[37,38]

Besides the phthalides, 3-substituted isoindolinones are also important building blocks in organic synthesis.[39,40] There are several applications described, for example, in the synthesis of pharmaceutically active agents or natural products.[41–45] Especially the synthesis of 2-alkyl-3-hydroxy-1-isoindolinones starting from *N*-alkylphthalimides is described in detail.[46–50] Again, to our knowledge, no strategy starting from readily available FBA and the desired amine to perform an amidation/cyclization process has been reported. This strategy is advantageous compared with the reduction of *N*-alkylphthalimides. Amines and FBA are readily available starting materials and the substrate scope could be appreciably improved. Moreover, the reaction can be performed in one pot and with much better atom economy.

We first observed the unexpected reactivity and behavior of the formyl group of the FBA while trying to convert its aldehyde functionality into a trifluoromethyl ketone with the Ruppert–Prakash reagent by following a known protocol.[51] After work-up and purification, we isolated a small amount of a single cyclic product that was identified as 3-ethoxyphthalide (**3b**; see Figure 3 below).

Inspired by the previously reported DKR,[37] we envisaged the development of an enantioselective synthesis of 3-substituted phthalides employing a chiral catalyst. We chose (–)-cinchonidine **4b** as catalyst, acetic anhydride as an inexpensive and readily available electrophile and, referring to our established π–methylhistidine based acylation concept,[52–56] toluene as solvent. Under these conditions at 0 °C, product **2a** formed in 83% yield with 28% *ee* (Table 1, entry 1). Based on this promising result, we optimized the reaction conditions and tested the pseudoenantiomer of **4b** (+)-cinchonine (**4a**), (+)-quinidine (**5a**), (–)-quinine (**5b**), (+)-dihydroquinidine (**6a**), and (–)-dihydroquinine (**6b**) as well as some chiral thioureas developed by Soós (**7**),[57] Takemoto (**8**),[58] and Nagasawa (**9**) (Figure 1) as further catalysts.[59]

The best results were obtained with a catalytic amount of (+)-cinchonine (**4a**; Table 1, entry 9); a stoichiometric amount of catalyst **4a** led to lower yields and selectivities (entries 8 and 9). Consequently, we selected 10 mol% **4a** and 2.0 equiv Ac_2O for further investigations. To improve

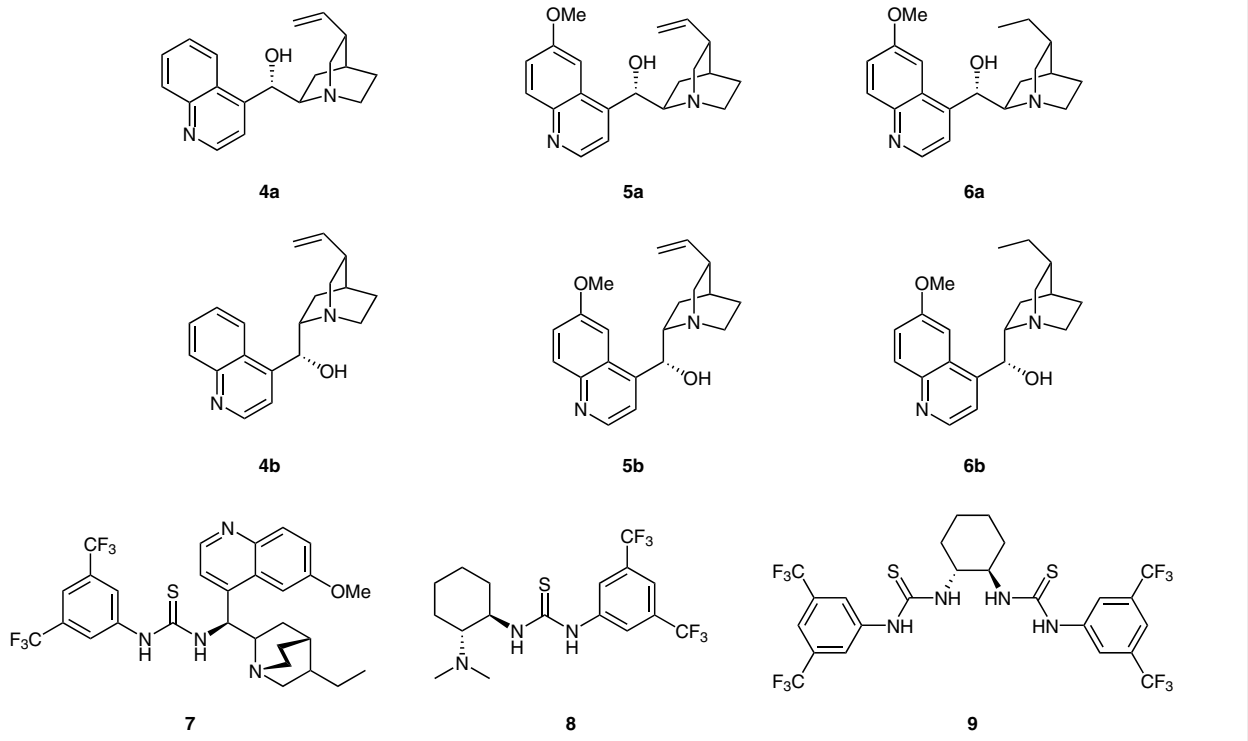
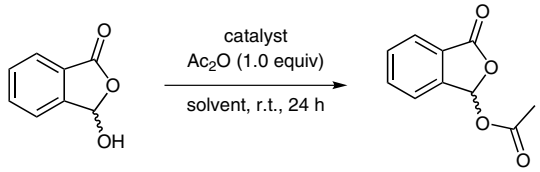


Figure 1 Employed chiral catalysts

Table 1 Catalyst Screening

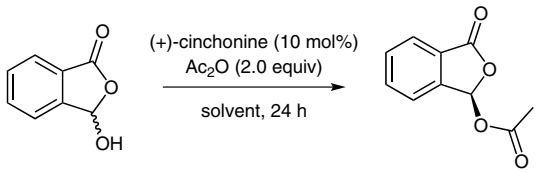


1b **2a**

Entry	Catalyst	Yield (%)	*ee* (%)[e]
1[a]	**4b**	83	28 (*S*)
2[b]	**4a**	67	28 (*R*)
3[b]	**4b**	n.d.	28 (*S*)
4[b]	**5a**	53	20 (*R*)
5[b]	**5b**	41	18 (*S*)
6[b]	**6a**	55	20 (*R*)
7[b]	**6b**	59	20 (*S*)
8[b,d]	**4a**	83	28 (*R*)
9[c,d]	**4a**	89	36 (*R*)
10[c,d]	**7**	74	24 (*S*)
11[c,d]	**8**	77	20 (*R*)
12[c,d]	**9**	96	2 (*R*)

[a] Reaction conditions: FBA (1.0 mmol), toluene (15 mL), **4b** (1.0 equiv).
[b] Reaction conditions: FBA (0.3 mmol), anhydrous toluene (4.0 mL), cinchona alkaloid (1.0 equiv).
[c] Reaction conditions: FBA (0.3 mmol), anhydrous $CHCl_3$ (4.0 mL), catalyst (10 mol%).
[d] Ac_2O (2.0 equiv).
[e] Enantiomeric excess determined based on chiral GC analysis without internal standard.

Table 2 Influence of Solvent and Temperature on the Selectivity[a]



1b (*R*)-**2a**

Entry	Solvent	Temp (°C)	*ee* (%)[b]
1	cyclohexane	r.t.	26
2	benzene	r.t.	33
3	hexafluorobenzene[c]	r.t.	40
4	toluene	r.t.	36
5	CH_2Cl_2	0	43
6	chlorobenzene	0	54
7	toluene	0	48
8	*n*-hexane[c]	0	67
9	acetone[c]	−10	14
10	1,2-DCE	−10	50
11	chlorobenzene	−10	60
12	xylene	−10	53
13	perfluorohexane[c]	−10	17
14	*n*-hexane[c]	−10	71
15	chlorobenzene	−30	66
16	xylene	−30	58
17	*n*-hexane[c]	−30	59

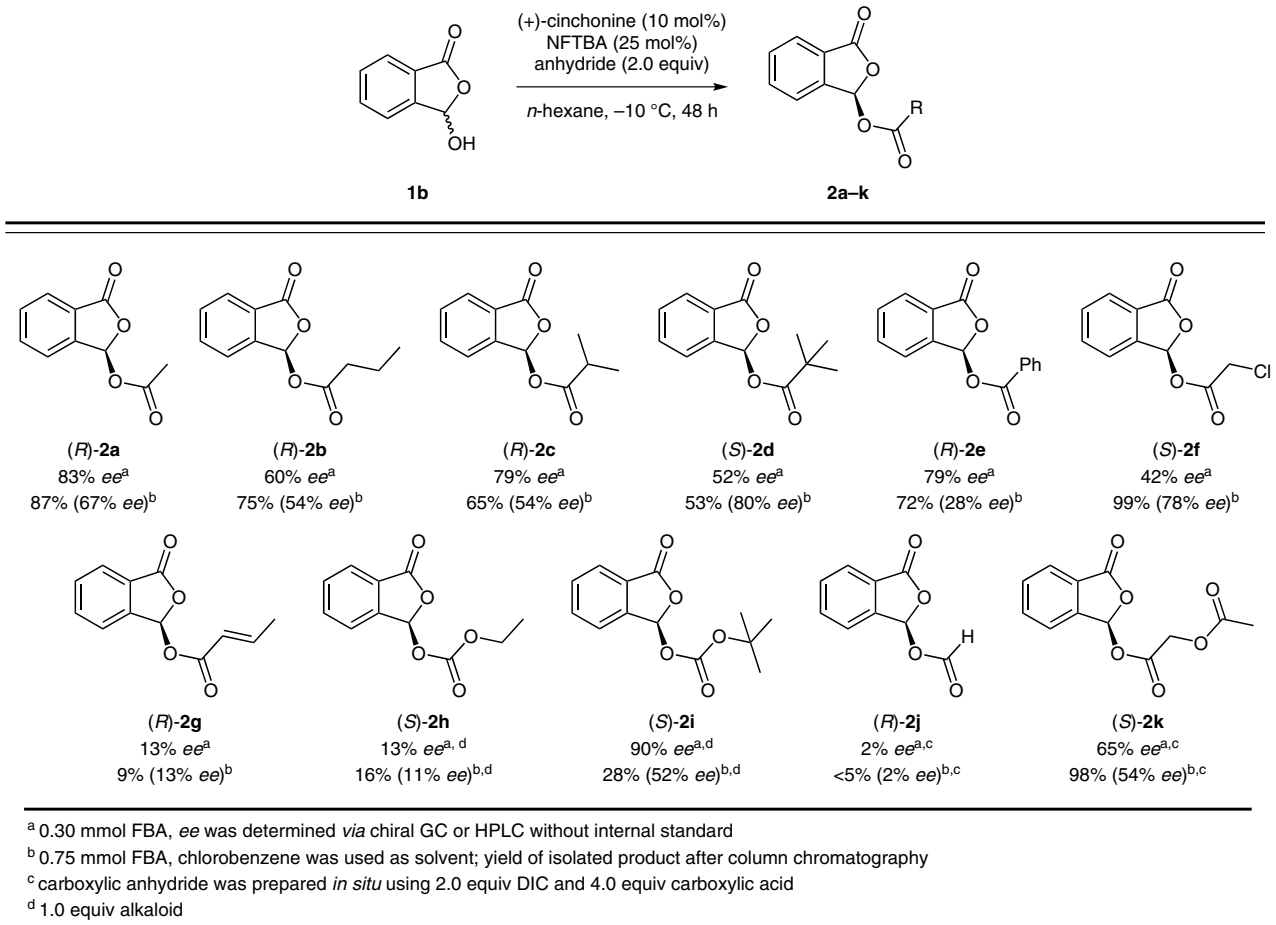
[a] Reaction conditions: FBA (0.3 mmol), **4a** (10 mol%), anhydrous solvent (2.0 mL).
[b] Enantiomeric excess determined based on chiral GC analysis without internal standard.
[c] Distilled solvent used.

the selectivity, we performed a solvent screening and investigated the influence of the temperature on the selectivity (Table 2).

The best results were obtained in nonpolar aprotic solvents at low temperatures (Table 2, entries 6, 8, 11, 14, and 15). Given that non-anhydrous *n*-hexane afforded the highest selectivity, we assumed a polar transition state that necessitates the presence of a hydrogen-bonding donor (HBD). To support this postulate, the reaction was performed in extra anhydrous *n*-hexane and defined amounts of strong HBDs, such as hexafluoroisopropanol (HFIP), trifluoroethanol (TFEA), nonafluoro-*tert*-butanol (NFTBA), or pentafluorophenol (PFP) were added (Table 3). To our delight, we found an appreciable influence of the hydrogen donor strength on the selectivity. With increasing acidity of the additive, the selectivity also increased. The only exception was PFP, because of its low solubility in *n*-hexane. Interestingly, water also delivered comparable results. Addition of 25 mol% NFTBA was found to be ideal for our system.

With the optimized reaction conditions in hand, we started a substrate screening using various electrophiles; the results are summarized in Figure 2. For the preparative-scale experiments chlorobenzene was used as solvent, because of better solubility of the reagents and much shorter reaction times. The reactions were monitored by TLC in each case and quenched with methanol upon complete consumption of the starting material. In cases where the solubility of the carboxylic anhydrides was low in *n*-hexane, the selectivities were higher in chlorobenzene (compare **2d** and **2f**); compounds **2b** and **2c** quickly racemized upon heating.

We also developed a Steglich esterification protocol[60,61] for the formation of the carboxylic anhydride *in situ* using a carbodiimide (in this case *N*,*N*′-diisopropyl carbodiimide; DIC) and the desired carboxylic acid. This provides access to products for which the corresponding carboxylic anhydrides are either not readily available or expensive. Thus, products **2j** and **2k** were obtained in moderate yields, but with rather low selectivity, which is probably due to the basic character of DIC. For comparison we also used acetic acid and obtained **2a** in 55% yield with 56% *ee*.



[a] 0.30 mmol FBA, *ee* was determined *via* chiral GC or HPLC without internal standard
[b] 0.75 mmol FBA, chlorobenzene was used as solvent; yield of isolated product after column chromatography
[c] carboxylic anhydride was prepared *in situ* using 2.0 equiv DIC and 4.0 equiv carboxylic acid
[d] 1.0 equiv alkaloid

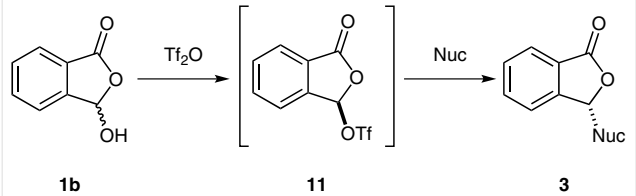
Figure 2 Substrate scope of the DKR of 2-formylbenzoic acid

We also investigated other electrophiles including benzyl bromide, benzyl isocyanate, and benzyl isothiocyanate under our optimized conditions. Unfortunately, we only isolated (±)-3-phthalideyl (benzyl)carbamate (**10**; see experimental section and the Supporting Information) resulting from benzyl isocyanate as a racemate. In case of isothiocyanate, the reactivity was too low and starting materials were re-isolated.

We then employed the protocol detailed above in conjunction with triflic anhydride to introduce a good leaving group on phthalide **11**. This would allow the installation of a broad variety of substituents on the phthalide core (Scheme 3).

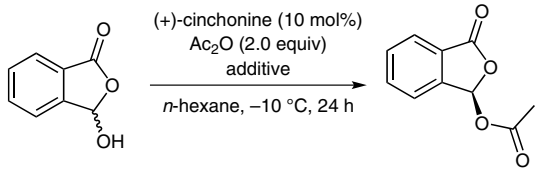
As we were not able to isolate triflate **11**, the nucleophile was added directly after complete consumption of the starting material (monitored by TLC) without intermittent purification. To gain deeper insight on the reactivity, we selected primary, secondary, tertiary, and allylic alcohols as nucleophiles (Figure 3). The desired products **3a–d** were obtained in good yields but as racemic mixtures. By using *tert*-butanol the desired product either did not form or was not stable upon purification.

The lack of selectivity could be caused by rapid uncatalyzed formation of **11**, which outperforms the DKR by the catalyst. On the other hand, the nucleophilic substitution itself may lead to racemization if S_N1 character prevails because the substitution must exclusively proceed through an S_N2 mechanism to preserve the enantiomeric excess. To avoid the S_N1 reaction, we added only a small excess of the desired alcohol instead of using the alcohol itself also as solvent and used polar aprotic dichloromethane, without success. Nevertheless, the use of FBA, alcohol and DMAP instead of the chiral alkaloid enabled the formation of (±)-3-



Scheme 3 One-pot reaction sequence to yield 3-substituted phthalides

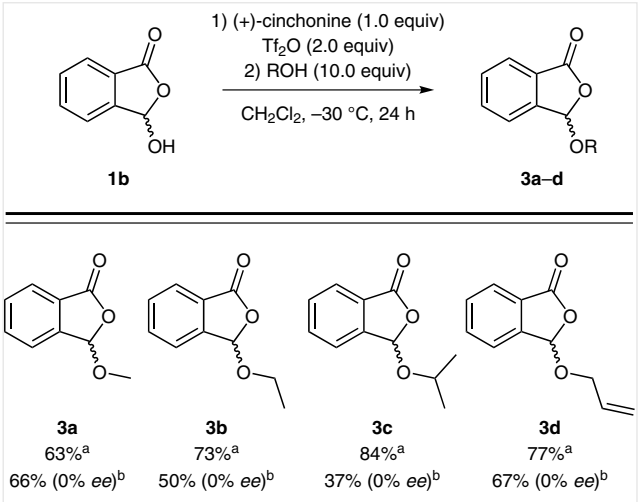
Table 3 Improvement of the Selectivity by Addition of a Hydrogen-Bond Donor[a]



1b (*R*)-**2a**

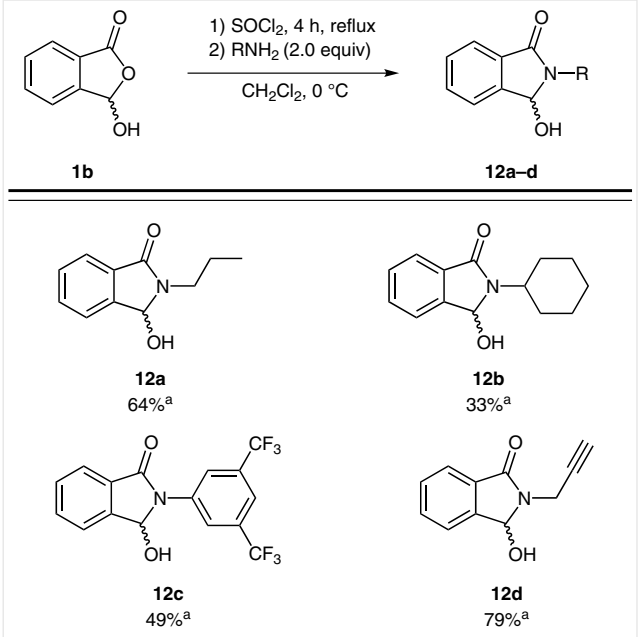
Entry	Additive	Amount (equiv)	*ee* (%)[b]
1	HFIP	31.7	4
2	HFIP	15.8	7
3	HFIP	2.02	40
4	HFIP	1.01	45
5	HFIP	0.51	63
6	HFIP	0.25	78
7	HFIP	0.13	78
8	HFIP	0.06	45
9	TFEA	0.25	74
10	NFTBA	0.25	83
11	PFP	0.25	72
12	H_2O	0.25	70
13	–	–	35

[a] Reaction conditions: FBA (0.3 mmol), **4a** (10 mol%), –10 °C, 24 h, solvent (2.00 mL in total).
[b] Enantiomeric excess determined based on chiral GC analysis without internal standard



[a] 10 mol% DMAP instead of alkaloid, yield of isolated product after column chromatography
[b] 0.30 mmol FBA, yield of isolated product after column chromatography, *ee* was determined *via* chiral GC without internal standard.

Figure 3 Screening of alcohols



[a] yield of isolated product after column chromatography

Figure 4 Amidation/cyclization of **1b** in one pot

alkoxyphthalides in good yields up to 84% under much milder conditions compared with previously reported protocols.[9,10,62]

3-Alkoxyphthalides are building blocks for the synthesis of, for example 2-alkyl-3-hydroxy-1-isoindolinones **12** (Figure 4).[4,19,63] Notably, their synthesis is also possible directly from **1b** as starting material. After heating **1b** to reflux in $SOCl_2$, the addition of primary amines directly led to substrates **12a–d** in moderate yields.

The DKR using **12a–d** was not possible as a result of the very slow isomerization of the stereogenic center. Desired products **13a–d** were obtained as racemic mixtures (see experimental section and the Supporting Information). Addition of DBU to accelerate isomerization[64,65] also did not enable the desired DKR. Note that kinetic resolution of **12a–d** was not observed while monitoring product formation by chiral GC. Moreover, DKR of **14** yielding acetylated compound **15** was also not successful, which was already reported;[37,38] hence, under our catalytic conditions, the isomerization of such isoindolinones seems to be too slow compared with the acylation (see experimental section and the Supporting Information).

In summary, we have demonstrated the synthesis of a series of compounds related to different chemical classes starting from 2-formylbenzoic acid (**1a**). We describe an optimized protocol for the dynamic kinetic resolution of **1b**, using readily available cinchona alkaloids and anhydrides, thus yielding the corresponding products in excellent yields

(up to 99%) and good enantioselectivities (up to 90% *ee*). The products are potential substrates for further syntheses of complex cyclic core structures.

Chemicals were purchased from commercial suppliers and were used without further purification. Solvents for column chromatography, extractions, filtrations, and recrystallizations were distilled prior to use. Solvents were dried by using standard procedures and they were stored under Ar and over activated molecular sieves (3 Å or 4 Å) or sodium. Column chromatography was carried out with silica gel 60 M (Macherey–Nagel; 0.040–0.063 mm, 230–400 mesh ASTM). TLC was performed using precoated Macherey–Nagel plastic sheets Polygram® SIL G/UV_{254} (Macherey–Nagel; 0.2 mm silica gel layer with fluorescent indicator). For visualization, UV light (254 nm) or staining solutions ($KMnO_4$: 2.5 g $KMnO_4$, 8.3 g K_2CO_3, 250 mL H_2O; phosphomolybdic acid: 9.86 g in 250 mL ethanol) were utilized.

All NMR spectra were recorded with Bruker AV 400 spectrometers. Chemical shifts (δ) are reported in parts per million (ppm) using either tetramethylsilane (TMS) or the corresponding residual solvent signal as internal standard.[66] IR spectra were measured with a Bruker IFS25 spectrometer. HRMS were recorded with a Bruker Micro TOF LC. Reaction progress and product formation were monitored by GC-MS with a Hewlett Packard 5890 gas chromatograph equipped with flame-ionization detector (FID), a Quadrupole-MS Hewlett Packard MSD 5971 detector (EI, 70 eV) and a DB-5 MS column (30 m × 0.250 mm). Enantioselectivities were determined either by chiral stationary phase GC analyses with Hewlett Packard 5890 or 6890 gas chromatographs, respectively, or by chiral stationary phase HPLC with a Dionex system (Dionex P680 HPLC pump, Shodex RI-101 detector). For measurement of melting points, a Krüss KSP1N capillary melting-point apparatus was utilized using a heating rate of 1 °C min^{-1}. All melting points were determined at least twice and are uncorrected. Absolute stereochemistry was determined by VCD with a Bruker PMA 50 spectrometer (see the Supporting Information).

Synthesis of 2a–i through Acylation of (±)-3-Hydroxyphthalides; General Procedure A

2-Formylbenzoic acid (**1a**; 1.0 equiv) and DMAP (0.1 equiv) were dissolved in CH_2Cl_2 (0.15 M), producing a colorless clear solution. The desired carboxylic anhydride (2.0 equiv) and triethylamine (1.0 equiv) were subsequently added and the reaction mixture was stirred at r.t. until complete conversion of the starting material was achieved (monitored by TLC). The solvent was removed under reduced pressure and the crude products were purified by column chromatography (*n*-hexane/EtOAc, 2:1).

Synthesis of 2j,k through Acylation of (±)-3-Hydroxyphthalides; General Procedure B

2-Formylbenzoic acid (**1a**; 1.0 equiv) and DMAP (0.1 equiv) were dissolved in CH_2Cl_2 (0.15 M), producing a colorless clear solution. The desired carboxylic anhydride was formed *in situ* by adding carboxylic acid (4.0 equiv) and carbodiimide (2.0 equiv). The reaction mixture was stirred at r.t. for 18 h, while the corresponding urea was formed as a pale-yellow precipitate. The reaction was monitored by TLC. Upon complete conversion of the starting material, the precipitated urea was filtered off and the solvent was removed under reduced pressure. The crude products were purified by column chromatography (*n*-hexane/EtOAc, 2:1).

Synthesis of 2a–i through DKR of 1b; General Procedure C

2-Formylbenzoic acid (**1a**; 1.0 equiv) and (+)-cinchonine (**4a**; 0.1 equiv) were dissolved either in *n*-hexane or chlorobenzene (0.15 M) and cooled to –10 °C. Carboxylic anhydride (2.0 equiv) was then added and the mixture was stirred at –10 °C until the starting material was consumed, which was monitored by TLC. The reaction was quenched by addition of an excess of MeOH. The resulting mixture was stirred for 15–30 min at –10 °C, then the solvent was removed under reduced pressure and the products were purified by column chromatography.

Synthesis of 2j–k through DKR of 1b; General Procedure D

Carboxylic acid (4.0 equiv) and DIC (2.0 equiv) were dissolved either in *n*-hexane or chlorobenzene (0.15 M) and cooled to –10 °C. After stirring for 12 h at –10 °C, 2-formylbenzoic acid (**1a**; 1.0 equiv) and (+)-cinchonine (**4a**; 0.1 equiv) were added and the mixture was stirred at –10 °C until the starting material was consumed, which was monitored by TLC (up to 48 h). The reaction was quenched by addition of an excess of MeOH. The resulting mixture was stirred for 15–30 min at –10 °C, then the solvent was removed under reduced pressure and the products were purified by column chromatography.

Synthesis of (±)-3-Alkoxyphthalides (3a–d); General Procedure E

2-Formylbenzoic acid (**1a**; 0.045 g (0.30 mmol, 1.0 equiv) and DMAP (0.004 g, 0.03 mmol, 0.1 equiv) were dissolved in anhydrous CH_2Cl_2 (2.0 mL; 0.15 M) and cooled to –30 °C. Triflic anhydride (0.172 g, 0.102 mL, 0.60 mmol, 2.0 equiv) was carefully added in one portion and the mixture was stirred at –30 °C for 5 h. To the resulting clear yellow solution an excess of the desired alcohol (10 equiv) was added and the mixture was stirred for 24 h at –30 °C. The colorless clear solution was allowed to warm to r.t. and the solvent was removed under reduced pressure. The crude products were purified by column chromatography (*n*-hexane/EtOAc, 2:1).

Synthesis of 3a–d through DKR of 1b; General Procedure F

2-Formylbenzoic acid (**1a**; 1.0 equiv) and (+)-cinchonine (**4a**; 1.0 equiv) were dissolved in CH_2Cl_2 (0.15 M) and cooled to –30 °C. Triflic anhydride (2.0 equiv) was subsequently added in one portion and the reaction mixture was stirred for 8 h at –30 °C until the starting material was consumed, which was monitored by TLC. At this point the desired alcohol (10.0 equiv) was added and stirring at –30 °C was continued overnight. The solvent was removed under reduced pressure and the products were purified by column chromatography.

Synthesis of (±)-Isoindolinones 12a–d; General Procedure G

2-Formylbenzoic acid (**1a**; 1.0 equiv) was heated at reflux in $SOCl_2$ (5–10 equiv) for 4 h at 100 °C. The remaining $SOCl_2$ was removed in vacuum and the obtained solid was dissolved in CH_2Cl_2 (10 mL). The mixture was cooled to 0 °C and the desired primary amine (2.0 equiv) was slowly added. The solution was stirred for 24 h at r.t. then the reaction mixture was diluted with EtOAc (70 mL), washed with citric acid (0.5 M), sat. aq Na_2CO_3 solution, and brine. The organic layer was dried over $MgSO_4$ and the solvent was removed under reduced pressure. The obtained products were used without further purification.

Acylation of (±)-Isoindolinones 12a–d to give 13a–d; General Procedure H

The corresponding (±)-isoindolinone (1.0 equiv) and DMAP (0.1 equiv) were dissolved in CH_2Cl_2 (0.15 M), followed by the addition of acetic anhydride (2.0 equiv) and triethylamine (1.0 equiv). The reac-

tion mixture was stirred at r.t. for 24 h. At this point the solvent was removed under reduced pressure and the crude products were purified by column chromatography (*n*-hexane/EtOAc, 2:1).

(±)-3-Phthalideyl Acetate (2a)

Obtained from 2-formylbenzoic acid (0.045 g, 0.30 mmol) and acetic anhydride (0.061 g, 0.057 mL, 0.60 mmol) by following General Procedure A.

Yield: 0.050 g (87%, 0.26 mmol); colorless solid; mp 68–69 °C; R_f = 0.39 (*n*-hexane/EtOAc, 2:1).

IR (ATR): 2972, 1794, 1767, 1361, 1207, 1043, 960, 940, 880, 857, 751, 717, 687, 543 cm^{-1}.

^1H NMR (400.13 MHz, $CDCl_3$): δ = 7.91 (d, $^3J_{H-H}$ = 7.6 Hz, 1 H, CH_{Ar}), 7.74 (dt, $^3J_{H-H}$ = 7.5 Hz, $^4J_{H-H}$ = 1.0 Hz, 1 H, CH_{Ar}), 7.64 (t, $^3J_{H-H}$ = 7.3 Hz, 1 H, CH_{Ar}), 7.59 (d, $^3J_{H-H}$ = 7.6 Hz, 1 H, CH_{Ar}), 7.41 (s, 1 H, CH), 2.18 (s, 3 H, CH_3).

^{13}C NMR (100.62 MHz, $CDCl_3$): δ = 169.5 (Cq, C=O), 167.9 (Cq, C=O), 144.3 (Cq, C_{Ar}), 134.9 (CH_{Ar}), 131.4 (CH_{Ar}), 126.5 (Cq, C_{Ar}), 125.8 (CH_{Ar}), 123.6 (CH_{Ar}), 92.7 (CH), 20.9 (CH_3).

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{10}H_8O_4Na$: 215.0321; found: 215.0325.

Analytic data are identical to those reported in the literature.[11]

(±)-3-Phthalideyl Butyrate (2b)

Obtained from 2-formylbenzoic acid (0.045 g, 0.30 mmol) and butyric anhydride (0.094 g, 0.098 mL, 0.60 mmol) by following General Procedure A.

Yield: 0.055 g (83%, 0.25 mmol); colorless solid; mp 53–54 °C; R_f = 0.47 (*n*-hexane/EtOAc, 2:1).

IR (ATR): 2969, 2878, 1768, 1758, 1356, 1285, 1148, 1052, 960, 750, 717, 686 cm^{-1}.

^1H NMR (400.13 MHz, $CDCl_3$): δ = 7.91 (d, $^3J_{H-H}$ = 7.6 Hz, 1 H, CH_{Ar}), 7.74 (dt, $^3J_{H-H}$ = 7.5 Hz, $^4J_{H-H}$ = 1.1 Hz, 1 H, CH_{Ar}), 7.64 (t, $^3J_{H-H}$ = 7.5 Hz, 1 H, CH_{Ar}), 7.58 (d, $^3J_{H-H}$ = 7.6 Hz, 1 H, CH_{Ar}), 7.44 (s, 1 H, CH), 2.40 (t, $^3J_{H-H}$ = 7.4 Hz, 2 H, CH_2), 1.69 (sext, $^3J_{H-H}$ = 7.4 Hz, 2 H, CH_2), 0.97 (t, $^3J_{H-H}$ = 7.4 Hz, 3 H, CH_3).

^{13}C NMR (100.61 MHz, $CDCl_3$): δ = 172.2 (Cq, C=O), 168.0 (Cq, C=O), 144.5 (Cq, C_{Ar}), 134.9 (CH_{Ar}), 131.3 (CH_{Ar}), 126.6 (Cq, C_{Ar}), 125.8 (CH_{Ar}), 123.6 (CH_{Ar}), 92.7 (CH), 35.9 (CH_2), 18.2 (CH_2), 13.6 (CH_3).

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{12}H_{12}O_4Na$: 243.0634; found: 243.0636.

Analytic data are identical to those reported in the literature.[6]

(±)-3-Phthalideyl 2-Methylpropionate (2c)

Obtained from 2-formylbenzoic acid (0.045 g (0.30 mmol) and isobutyric anhydride (0.094 g, 0.099 mL, 0.60 mmol) by following General Procedure A.

Yield: 0.053 g (0.24 mmol, 81%); colorless solid; mp 64–65 °C; R_f = 0.52 (*n*-hexane/EtOAc, 2:1).

IR (ATR): 2973, 2936, 2876, 1758, 1468, 1285, 1122, 1050, 1031, 961, 938, 751, 715, 688 cm^{-1}.

^1H NMR (400.13 MHz, $CDCl_3$): δ = 7.91 (d, $^3J_{H-H}$ = 7.6 Hz, 1 H, CH_{Ar}), 7.74 (t, $^3J_{H-H}$ = 7.5 Hz, 1 H, CH_{Ar}), 7.64 (t, $^3J_{H-H}$ = 7.5 Hz, 1 H, CH_{Ar}), 7.57 (d, $^3J_{H-H}$ = 7.6 Hz, 1 H, CH_{Ar}), 7.42 (s, 1 H, CH), 2.63 (m, 1 H, CH), 1.20 (d, $^3J_{H-H}$ = 7.1 Hz, 6 H, CH_3).

^{13}C NMR (100.62 MHz, $CDCl_3$): δ = 175.6 (Cq, C=O), 168.0 (Cq, C=O), 144.6 (Cq, C_{Ar}), 134.9 (CH_{Ar}), 131.3 (CH_{Ar}), 126.6 (Cq, C_{Ar}), 125.8 (CH_{Ar}), 123.5 (CH_{Ar}), 92.7 (CH), 34.0 (CH), 18.7 (CH_3), 18.7 (CH_3).

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{12}H_{12}O_4Na$: 243.0634; found: 243.0632.

(±)-3-Phthalideyl 2,2-Dimethylpropionate (2d)

Obtained from 2-formylbenzoic acid (0.045 g, 0.30 mmol) and pivalic anhydride (0.112 g, 0.122 mL, 0.60 mmol) by following General Procedure A.

Yield: 0.048 g (0.20 mmol, 68%); colorless solid; mp 57–59 °C; R_f = 0.56 (*n*-hexane/EtOAc, 2:1).

IR (ATR): 2976, 2936, 1780, 1747, 1467, 1276, 1122, 1047, 968, 937, 766, 752, 715, 688 cm^{-1}.

^1H NMR (400.13 MHz, $CDCl_3$): δ = 7.92 (td, $^3J_{H-H}$ = 7.6 Hz, $^4J_{H-H}$ = 1.0 Hz, 1 H, CH_{Ar}), 7.74 (dt, $^3J_{H-H}$ = 7.5 Hz, $^4J_{H-H}$ = 1.1 Hz, 1 H, CH_{Ar}), 7.64 (dt, $^3J_{H-H}$ = 7.5 Hz, $^4J_{H-H}$ = 1.0 Hz, 1 H, CH_{Ar}), 7.55 (qd, $^3J_{H-H}$ = 7.6 Hz, $^4J_{H-H}$ = 0.8 Hz, 1 H, CH_{Ar}), 7.41 (s, 1 H, CH), 1.23 (s, 9 H, CH_3).

^{13}C NMR (100.61 MHz, $CDCl_3$): δ = 177.1 (Cq, C=O), 168.1 (Cq, C=O), 144.7 (Cq, C_{Ar}), 134.9 (CH_{Ar}), 131.3 (CH_{Ar}), 126.7 (Cq, C_{Ar}), 125.9 (CH_{Ar}), 123.5 (CH_{Ar}), 92.9 (CH), 39.1 (Cq), 26.9 (CH_3).

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{13}H_{14}O_4Na$: 257.0790; found: 257.0786.

Analytic data are identical to those reported in the literature.[11]

(±)-3-Phthalideyl Benzoate (2e)

Obtained from 2-formylbenzoic acid (0.150 g, 1.00 mmol) and benzoic anhydride (0.452 g, 2.00 mmol) by following General Procedure A.

Yield: 0.171 g (0.67 mmol, 67%); colorless solid; mp 135–136 °C; R_f = 0.47 (*n*-hexane/EtOAc, 2:1+1% TEA).

IR (ATR): 3010, 1773, 1740, 1360, 1248, 1213, 1081, 1053, 970, 930, 751, 702, 687, 590 cm^{-1}.

^1H NMR (400.13 MHz, $CDCl_3$): δ = 8.08–8.03 (m, 2 H, CH_{Ar}), 8.00–8.03 (m, 1 H, CH_{Ar}), 7.77 (dt, $^3J_{H-H}$ = 7.4 Hz, $^4J_{H-H}$ = 1.2 Hz, 1 H, CH_{Ar}), 7.72–7.65 (m, 3 H, CH_{Ar}), 7.61 (tt, $^3J_{H-H}$ = 7.5 Hz, $^4J_{H-H}$ = 1.2 Hz, 1 H, CH_{Ar}), 7.49–7.42 (m, 2 H, CH_{Ar}/CH).

^{13}C NMR (100.62 MHz, $CDCl_3$): δ = 168.0 (Cq, C=O), 165.2 (Cq, C=O), 144.6 (Cq, C_{Ar}), 135.0 (CH_{Ar}), 134.2 (CH_{Ar}), 131.5 (CH_{Ar}), 130.3 (CH_{Ar}), 128.7 (CH_{Ar}), 128.5 (Cq, C_{Ar}), 126.7 (Cq, C_{Ar}), 126.0 (CH_{Ar}), 123.9 (CH_{Ar}), 93.4 (CH).

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{15}H_{10}O_4Na$: 277.0477; found: 277.0467.

Analytic data are identical to those reported in the literature.[6]

(±)-3-Phthalideyl Chloroacetate (2f)

Obtained from 2-formylbenzoic acid (0.150 g, 1.00 mmol) and chloroacetic anhydride (0.342 g, 2.00 mmol) by following General Procedure A.

Yield: 0.216 g (0.95 mmol, 95%); colorless solid; mp 86–87 °C; R_f = 0.38 (*n*-hexane/EtOAc, 2:1).

IR (ATR): 3002, 2959, 1770, 1607, 1397, 1284, 1147, 1050, 1034, 984, 963, 949, 922, 885, 870, 789, 748, 715, 688 cm^{-1}.

^1H NMR (400.13 MHz): δ = 7.91 (td, $^3J_{H-H}$ = 7.6 Hz, $^4J_{H-H}$ = 1.0 Hz, 1 H, CH_{Ar}), 7.77 (dt, $^3J_{H-H}$ = 7.5 Hz, $^4J_{H-H}$ = 1.1 Hz, 1 H, CH_{Ar}), 7.69–7.61 (m, 2 H, CH_{Ar}), 7.44 (s, 1 H, CH), 4.17 (s, 2 H, CH_2Cl).

^{13}C NMR (100.62 MHz): δ = 167.5 (Cq, C=O), 166.3 (Cq, C=O), 143.5 (Cq, C_{Ar}), 135.2 (CH_{Ar}), 131.7 (CH_{Ar}), 126.3 (Cq, C_{Ar}), 126.0 (CH_{Ar}), 123.8 (CH_{Ar}), 93.5 (CH), 40.5 (CH_2Cl).

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{10}H_7ClO_4Na$: 248.9931; found: 248.9932.

(±)-(*E*)-3-Phthalideyl Crotonate (2g)

Obtained from 2-formylbenzoic acid (0.150 g, 1.00 mmol) and *trans*-crotonic anhydride (0.308 g, 0.296 mL, 1.20 mmol) by following General Procedure A.

Yield: 0.172 g (0.79 mmol, 79%); colorless solid; mp 52–53 °C; R_f = 0.42 (*n*-hexane/EtOAc, 2:1).

IR (ATR): 3062, 3030, 2985, 1774, 1736, 1642, 1468, 1234, 1207, 1047, 966, 928, 858, 842, 748, 713, 685 cm^{-1}.

^{1}H NMR (400.13 MHz): δ = 7.85 (td, $^3J_{H-H}$ = 7.6 Hz, $^4J_{H-H}$ = 1.0 Hz, 1 H, CH_{Ar}), 7.71 (dt, $^3J_{H-H}$ = 7.6 Hz, $^4J_{H-H}$ = 1.2 Hz, 1 H, CH_{Ar}), 7.64–7.55 (m, 2 H, CH_{Ar}), 7.43 (s, 1 H, C*H*), 7.06 (dq, $^3J_{H-H}$ = 15.6 Hz, $^3J_{H-H}$ = 6.9 Hz, 1 H, CH_{Alkene}), 5.82 (qd, $^3J_{H-H}$ = 15.6 Hz, $^4J_{H-H}$ = 1.7 Hz, 1 H, CH_{Alkene}), 1.85 (dd, $^3J_{H-H}$ = 6.9 Hz, $^4J_{H-H}$ = 1.8 Hz, 3 H, CH_3).

^{13}C NMR (100.62 MHz): δ = 167.9 (Cq, C=O), 164.5 (Cq, C=O), 148.4 (CH_{Alkene}), 144.5 (Cq, C_{Ar}), 134.8 (CH_{Ar}), 131.2 (CH_{Ar}), 126.4 (Cq, C_{Ar}), 125.6 (CH_{Ar}), 123.7 (CH_{Ar}), 121.0 (CH_{Alkene}), 92.7 (CH), 18.2 (CH_3).

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{12}H_{10}O_4Na$: 241.0477; found: 241.0479.

Analytic data are identical to those reported in the literature.[7]

(±)-Ethyl 3-Phthalideyl Carbonate (2h)

Obtained from 2-formylbenzoic acid (0.150 g, 1.00 mmol) and diethyl dicarbonate (0.324 g, 0.295 mL, 2.00 mmol) by following General Procedure A.

Yield: 0.086 g (0.39 mmol, 39%); colorless oil; R_f = 0.40 (*n*-hexane/EtOAc, 2:1).

IR (ATR): 2986, 1785, 1756, 1608, 1469, 1363, 1239, 1212, 959, 858, 751, 685 cm^{-1}.

^{1}H NMR (400.13 MHz, $CDCl_3$): δ = 8.13–8.09 (m, 1 H, CH_{Ar}), 7.96 (dt, $^3J_{H-H}$ = 7.5 Hz, $^4J_{H-H}$ = 1.1 Hz, 1 H, CH_{Ar}), 7.89–7.82 (m, 2 H, CH_{Ar}), 7.49 (s, 1 H, C*H*), 4.60–4.46 (m, 2 H, CH_2), 1.55 (t, $^3J_{H-H}$ = 7.2 Hz, 3 H, CH_3).

^{13}C NMR (100.62 MHz, $CDCl_3$): δ = 167.6 (Cq, C=O), 153.5 (Cq, C=O), 143.4 (Cq, C_{Ar}), 134.9 (CH_{Ar}), 131.5 (CH_{Ar}), 126.4 (Cq, C_{Ar}), 125.8 (CH_{Ar}), 123.7 (CH_{Ar}), 95.3 (CH), 65.4 (CH_2), 14.1 (CH_3).

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{11}H_{10}O_5Na$: 245.0426; found: 245.0424.

(±)-*tert*-Butyl 3-Phthalideyl Carbonate (2i)

Obtained from 2-formylbenzoic acid (0.150 g, 1.00 mmol) and di-*tert*-butyldicarbonate (0.437 g, 0.428 mL, 2.00 mmol) by following General Procedure A.

Yield: 0.152 g (0.61 mmol, 61%); colorless solid; mp 72–73 °C; R_f = 0.48 (*n*-hexane/EtOAc, 2:1).

IR (ATR): 2983, 1785, 1754, 1370, 1249, 1155, 1085, 1052, 961, 843, 783, 745, 685 cm^{-1}.

^{1}H NMR (400.13 MHz, $CDCl_3$): δ = 7.93–7.89 (m, 1 H, CH_{Ar}), 7.74 (dt, $^3J_{H-H}$ = 7.3 Hz, $^4J_{H-H}$ = 1.1 Hz, 1 H, CH_{Ar}), 7.67–7.61 (m, 2 H, CH_{Ar}), 7.26 (s, 1 H, C*H*), 1.55 (s, 9 H, CH_3).

^{13}C NMR (100.62 MHz, $CDCl_3$): δ = 167.9 (Cq, C=O), 151.6 (Cq, C=O), 143.8 (Cq, C_{Ar}), 134.9 (CH_{Ar}), 131.5 (CH_{Ar}), 126.7 (Cq, C_{Ar}), 125.9 (CH_{Ar}), 123.8 (CH_{Ar}), 94.9 (CH), 84.8 (Cq), 27.8 (CH_3).

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{13}H_{14}O_5Na$: 273.0739; found: 273.0737.

(±)-3-Phthalideyl Formate (2j)

Obtained from 2-formylbenzoic acid (0.074 g, 0.50 mmol), formic acid (0.092 g, 0.075 mL, 2.00 mmol) and diisopropylcarbodiimide (0.126 g, 0.155 mL, 1.00 mmol) by following General Procedure B.

Yield: 0.037 g (0.21 mmol, 42%); colorless solid; mp 82–84 °C; R_f = 0.33 (*n*-hexane/EtOAc, 2:1).

IR (ATR): 2992, 2920, 1772, 1733, 1607, 1467, 1359, 1282, 1213, 1120, 1046, 986, 962, 919, 743, 714, 686 cm^{-1}.

^{1}H NMR (400.13 MHz, $CDCl_3$): δ = 8.22 (d, $^4J_{H-H}$ = 1.0 Hz, 1 H, C*H*O), 7.95 (d, $^3J_{H-H}$ = 7.5 Hz, 1 H, CH_{Ar}), 7.77 (dt, $^3J_{H-H}$ = 7.5 Hz, $^4J_{H-H}$ = 1.1 Hz, 1 H, CH_{Ar}), 7.68 (dt, $^3J_{H-H}$ = 7.6 Hz, $^4J_{H-H}$ = 1.0 Hz, 1 H, CH_{Ar}), 7.62 (d, $^3J_{H-H}$ = 7.6 Hz, 1 H, CH_{Ar}), 7.51 (s, 1 H, C*H*).

^{13}C NMR (100.62 MHz, $CDCl_3$): δ = 167.6 (Cq, C=O), 159.2 (Cq, C=O), 143.9 (Cq, C_{Ar}), 135.1 (CH_{Ar}), 131.7 (CH_{Ar}), 126.5 (Cq, C_{Ar}), 126.1 (CH_{Ar}), 123.8 (CH_{Ar}), 92.2 (CH).

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_9H_6O_4Na$: 201.0164; found: 201.0169.

(±)-3-Phthalideyl Acetoxyacetate (2k)

Obtained from 2-formylbenzoic acid (0.074 g, 0.50 mmol), acetoxyacetic acid (0.237 g, 2.00 mmol) and dicyclohexylcarbodiimide (1.0 M in CH_2Cl_2, 0.206 g, 1.0 mL, 1.00 mmol) by following General Procedure B.

Yield: 0.050 g (0.20 mmol, 40%); colorless oil; R_f = 0.59 (*n*-hexane/EtOAc, 1:1).

IR (ATR): 3307, 2932, 2856, 1789, 1751, 1703, 1664, 1522, 1258, 1217, 1162, 1080, 1053, 1013, 976, 800, 754, 732, 687 cm^{-1}.

^{1}H NMR (400.25 MHz, $CDCl_3$): δ = 7.94 (td, $^3J_{H-H}$ = 7.5 Hz, $^4J_{H-H}$ = 1.0 Hz, 1 H, CH_{Ar}), 7.76 (dt, $^3J_{H-H}$ = 7.5 Hz, $^4J_{H-H}$ = 1.1 Hz, 1 H, CH_{Ar}), 7.67 (dt, $^3J_{H-H}$ = 7.6 Hz, $^4J_{H-H}$ = 1.0 Hz, 1 H, CH_{Ar}), 7.61 (qd, $^3J_{H-H}$ = 7.6 Hz, $^4J_{H-H}$ = 0.8 Hz, 1 H, CH_{Ar}), 7.46 (s, 1 H, C*H*), 4.74 (d, $^3J_{H-H}$ = 16.4 Hz, 1 H, CH_2), 4.64 (d, $^3J_{H-H}$ = 16.4 Hz, 1 H, CH_2), 2.17 (s, 3 H, CH_3).

^{13}C NMR (100.65 MHz, $CDCl_3$): δ = 170.3 (Cq, C=O), 167.6 (Cq, C=O), 166.8 (Cq, C=O), 143.8 (Cq, C_{Ar}), 135.1 (CH_{Ar}), 131.7 (CH_{Ar}), 126.4 (Cq, C_{Ar}), 126.0 (CH_{Ar}), 123.8 (CH_{Ar}), 93.1 (CH), 60.4 (CH_2), 20.5 (CH_3).

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{12}H_{10}O_6Na$: 273.0375; found: 273.0382.

(±)-3-Methoxyphthalide (3a)

Obtained by following General Procedure E.

Yield: 0.031 g (0.19 mmol, 63%); colorless solid; mp 44–45 °C; R_f = 0.47 (*n*-hexane/EtOAc, 2:1).

IR (ATR): 2941, 2843, 1763, 1378, 1285, 1212, 1122, 1090, 1056, 920, 897, 744, 713, 687 cm^{-1}.

^{1}H NMR (400.13 MHz, $CDCl_3$): δ = 7.89 (d, $^3J_{H-H}$ = 7.6 Hz, 1 H, CH_{Ar}), 7.71 (dt, $^3J_{H-H}$ = 7.4 Hz, $^4J_{H-H}$ = 1.1 Hz, 1 H, CH_{Ar}), 7.64–7.53 (m, 2 H, CH_{Ar}), 6.30 (s, 1 H, C*H*), 3.63 (s, 3 H, CH_3).

^{13}C NMR (100.62 MHz, $CDCl_3$): δ = 168.7 (Cq, C=O), 144.8 (Cq, C_{Ar}), 134.5 (CH_{Ar}), 131.0 (CH_{Ar}), 127.4 (Cq, C_{Ar}), 125.6 (CH_{Ar}), 123.5 (CH_{Ar}), 103.2 (CH), 56.9 (CH_3).

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_9H_8O_3Na$: 187.0371; found: 187.0377.

Analytic data are identical to those reported in the literature.[67]

(±)-3-Ethoxyphthalide (3b)

Obtained by following General Procedure E.

Yield: 0.039 g (0.22 mmol, 73%); colorless solid; mp 70–71 °C; R_f = 0.49 (*n*-hexane/EtOAc, 2:1).

IR (ATR): 3067, 2974, 2906, 1770, 1605, 1360, 1288, 1203, 1138, 1088, 1048, 932, 865, 745, 712, 687, 637 cm^{-1}.

^1H NMR (400.13 MHz, $CDCl_3$): δ = 7.87 (d, $^3J_{H-H}$ = 7.5 Hz, 1 H, CH_{Ar}), 7.73–7.64 (m, 1 H, CH_{Ar}), 7.62–7.50 (m, 2 H, CH_{Ar}), 6.36 (s, 1 H, CH), 3.75 (m, 2 H, CH_2), 1.31 (t, $^3J_{H-H}$ = 7.1 Hz, 3 H, CH_3).

^{13}C NMR (100.62 MHz, $CDCl_3$): δ = 168.8 (Cq, C=O), 145.2 (Cq, C_{Ar}), 134.5 (CH_{Ar}), 130.9 (CH_{Ar}), 127.3 (Cq, C_{Ar}), 125.5 (CH_{Ar}), 123.5 (CH_{Ar}), 102.4 (CH), 66.0 (CH_2), 15.2 (CH_3).

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{10}H_{10}O_3Na$: 201.0528; found: 201.0533.

Analytic data are identical to those reported in the literature.[15]

(±)-3-Isopropoxyphthalide (3c)

Obtained by following General Procedure E.

Yield: 0.049 g (0.25 mmol, 84%); colorless solid; mp 66–67 °C; R_f = 0.54 (*n*-hexane/EtOAc, 2:1).

IR (ATR): 3064, 2977, 2903, 1756, 1347, 1287, 1212, 1108, 1091, 1063, 916, 898, 829, 780, 752, 714, 689 cm^{-1}.

^1H NMR (400.13 MHz, $CDCl_3$): δ = 7.86 (td, $^3J_{H-H}$ = 7.5 Hz, $^4J_{H-H}$ = 0.9 Hz, 1 H, CH_{Ar}), 7.69 (dt, $^3J_{H-H}$ = 7.5 Hz, $^4J_{H-H}$ = 1.1 Hz, 1 H, CH_{Ar}), 7.60–7.52 (m, 2 H, CH_{Ar}), 6.42 (s, 1 H, CH), 4.23 (hept, $^3J_{H-H}$ = 6.2 Hz, 1 H, CH), 1.36 (d, $^3J_{H-H}$ = 6.2 Hz, 3 H, CH_3), 1.32 (d, $^3J_{H-H}$ = 6.2 Hz, 3 H, CH_3).

^{13}C NMR (100.62 MHz, $CDCl_3$): δ = 169.0 (Cq, C=O), 145.6 (Cq, C_{Ar}), 134.4 (CH_{Ar}), 130.8 (CH_{Ar}), 127.3 (Cq, C_{Ar}), 125.4 (CH_{Ar}), 123.5 (CH_{Ar}), 101.5 (CH), 73.8 (CH), 23.4 (CH_3), 22.3 (CH_3).

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{11}H_{12}O_3Na$: 215.0684; found: 215.0692.

Analytic data are identical to those reported in the literature.[62]

(±)-3-(3-Phthalideyloxy)-1-propene (3d)

Obtained by following General Procedure E.

Yield: 0.044 g (0.23 mmol, 77%); yellow oil; R_f = 0.50 (*n*-hexane/EtOAc, 2:1).

IR (ATR): 2925, 1765, 1355, 1285, 1056, 922, 891, 748, 714, 689 cm^{-1}.

^1H NMR (400.13 MHz, $CDCl_3$): δ = 7.91–7.83 (m, 1 H, CH_{Ar}), 7.73–7.66 (m, 1 H, CH_{Ar}), 7.63–7.54 (m, 2 H, CH_{Ar}), 6.40 (s, 1 H, CH), 6.05–5.92 (m, 1 H, CH_{Alkene}), 5.38 (qd, $^3J_{H-H}$ = 17.2 Hz, $^4J_{H-H}$ = 1.4 Hz, 1 H, CH_2), 5.28 (qd, $^3J_{H-H}$ = 10.4 Hz, $^4J_{H-H}$ = 1.3 Hz, 1 H, CH_2), 4.42 (tdd, $^3J_{H-H}$ = 12.5 Hz, $^3J_{H-H}$ = 5.4 Hz, $^4J_{H-H}$ = 1.5 Hz, 1 H, $CH_{2,\ Alkene}$), 4.32 (tdd, $^3J_{H-H}$ = 12.5 Hz, $^3J_{H-H}$ = 5.4 Hz, $^4J_{H-H}$ = 1.3 Hz, 1 H, $CH_{2,Alkene}$).

^{13}C NMR (100.62 MHz, $CDCl_3$): δ = 168.7 (Cq, C=O), 145.1 (Cq, C_{Ar}), 134.5 (CH_{Ar}), 133.0 (CH_{Alkene}), 130.9 (CH_{Ar}), 127.3 (Cq, C_{Ar}), 125.5 (CH_{Ar}), 123.6 (CH_{Ar}), 119.9 ($CH_{2,Alkene}$), 101.4 (CH), 70.8 (CH_2).

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{11}H_{10}O_3Na$: 213.0522; found: 213.0527.

(±)-3-Phthalideyl (Benzyl)carbamate (10)

Obtained from 2-formylbenzoic acid (0.045 g, 1.00 mmol) and benzylisocyanate (0.045 g, 0.040 mL, 0.30 mmol) by following General Procedure A.

Yield: 0.016 g (0.06 mmol, 19%); colorless solid; mp 154–157 °C; R_f = 0.30 (*n*-hexane/EtOAc, 2:1).

IR (ATR): 3294, 3064, 1777, 1717, 1540, 1244, 1126, 1041, 957, 749, 700, 687 cm^{-1}.

^1H NMR (400.13 MHz, $CDCl_3$): δ = 7.89 (td, $^3J_{H-H}$ = 7.6 Hz, $^4J_{H-H}$ = 0.9 Hz, 1 H, CH_{Ar}), 7.72 (dt, $^3J_{H-H}$ = 7.5 Hz, $^4J_{H-H}$ = 1.1 Hz, 1 H, CH_{Ar}), 7.65–7.57 (m, 2 H, CH_{Ar}), 7.44 (s, 1 H, CH), 7.39–7.27 (m, 5 H, CH_{Ar}), 5.29 (br. s, 1 H, NH), 4.45 (d, $^3J_{H-H}$ = 6.0 Hz, 2 H, CH_2).

^{13}C NMR (100.62 MHz, $CDCl_3$): δ = 168.1 (Cq, C=O), 154.2 (Cq, C=O), 144.4 (Cq, C_{Ar}), 137.5 (Cq, C_{Ar}), 134.8 (CH_{Ar}), 131.1 (CH_{Ar}), 128.9 (CH_{Ar}), 128.0 (CH_{Ar}), 127.8 (CH_{Ar}), 126.8 (Cq, C_{Ar}), 125.8 (CH_{Ar}), 123.6 (CH_{Ar}), 93.9 (CH), 45.4 (CH_2).

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{16}H_{13}NO_4Na$: 306.0743; found: 306.0742.

(±)-3-Hydroxy-2-Propyl-1-isoindolinone (12a)

Obtained from 2-formylbenzoic acid (0.751 g, 5.00 mmol), $SOCl_2$ (3.28 g, 2.00 mL, 27.6 mmol), and propylamine (0.591 g, 0.821 mL, 10.0 mmol) by following General Procedure G.

Yield: 0.610 g (3.19 mmol, 64%); colorless solid; mp 90–92 °C; R_f = 0.17 (*n*-hexane/EtOAc, 2:1).

IR (ATR): 2992, 1771, 1733, 1467, 1357, 1282, 1213, 1120, 1045, 962, 918, 743, 714, 686, 515 cm^{-1}.

^1H NMR (400.25 MHz, acetone-d_6): δ = 7.65 (td, $^3J_{H-H}$ = 7.4 Hz, $^4J_{H-H}$ = 1.1 Hz, 1 H, CH_{Ar}), 7.62–7.59 (m, 2 H, CH_{Ar}), 7.55–7.48 (m, 1 H, CH_{Ar}), 5.90 (d, $^3J_{H-H}$ = 9.4 Hz, 1 H, CH), 5.39 (d, $^3J_{H-H}$ = 9.5 Hz, 1 H, OH), 3.68–3.54 (m, 1 H, CH_2), 3.45–3.28 (m, 1 H, CH_2), 1.83–1.57 (m, 2 H, CH_2), 0.93 (t, $^3J_{H-H}$ = 7.4 Hz, 3 H, CH_3).

^{13}C NMR (100.65 MHz, acetone-d_6): δ = 167.1 (Cq, C=O), 145.8 (Cq, C_{Ar}), 133.3 (Cq, C_{Ar}), 132.5 (CH_{Ar}), 130.1 (CH_{Ar}), 124.3 (CH_{Ar}), 123.2 (CH_{Ar}), 82.2 (CH), 41.6 (CH_2), 23.3 (CH_2), 11.8 (CH_3).

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{11}H_{13}NO_2Na$: 214.0844; found: 214.0855.

Analytic data are identical to those reported in the literature.[68]

(±)-2-Cyclohexyl-3-hydroxy-1-isoindolinone (12b)

Obtained from 2-formylbenzoic acid (0.300 g, 2.00 mmol), $SOCl_2$ (2.46 g, 1.50 mL, 20.7 mmol), and cyclohexylamine (0.298 g, 0.343 mL, 4.00 mmol) by following General Procedure G.

Yield: 0.154 g (0.98 mmol, 33%); colorless solid; mp 130–132 °C; R_f = 0.25 (*n*-hexane/EtOAc, 2:1).

IR (ATR): 3338, 3257, 2924, 2856, 1656, 1406, 1042, 804, 747, 700, 603, 535 cm^{-1}.

^1H NMR (400.13 MHz, acetone-d_6): δ = 7.67–7.42 (m, 4 H, CH_{Ar}), 5.98 (d, $^3J_{H-H}$ = 10.1 Hz, 1 H, CH), 5.23 (d, $^3J_{H-H}$ = 10.2 Hz, 1 H, OH), 3.99–3.81 (m, 1 H, CH), 2.03–1.76 (m, 6 H, CH_2), 1.74–1.62 (m, 1 H, CH_2), 1.50–1.12 (m, 3 H, CH_2).

^{13}C NMR (100.62 MHz, acetone-d_6): δ = 168.8 (Cq, C=O), 146.0 (Cq, C_{Ar}), 133.4 (Cq, C_{Ar}), 132.4 (CH_{Ar}), 130.0 (CH_{Ar}), 124.1 (CH_{Ar}), 123.1 (CH_{Ar}), 81.9 (CH), 52.7 (CH_2), 32.8 (CH_2), 31.1 (CH_2), 26.9 (CH_2), 26.8 (CH_2), 26.4 (CH_2).

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{14}H_{17}NO_2Na$: 254.1157; found: 254.1153.

(±)-2-[3,5-Bis(trifluoromethyl)phenyl]-3-hydroxy-1-isoindolinone (12c)

Obtained from 2-formylbenzoic acid (0.300 g, 2.00 mmol), $SOCl_2$ (2.460 g, 1.50 mL, 20.7 mmol), and 3,5-bis(trifluoromethyl)aniline (0.458 g, 0.312 mL, 4.00 mmol) by following General Procedure G.

Yield: 0.353 g (0.98 mmol, 49%); colorless solid; mp 127–129 °C; R_f = 0.50 (*n*-hexane/EtOAc, 2:1).

IR (ATR): 3400, 3062, 1786, 1745, 1530, 1469, 1388, 1279, 1187, 1162, 1148, 1119, 1093, 1076, 870, 701, 683 cm^{-1}.

^1H NMR (400.13 MHz, acetone-d_6): δ = 7.99–7.68 (m, 6 H, CH_{Ar}), 7.63 (s, 1 H, CH_{Ar}), 7.48 (d, $^3J_{H-H}$ = 11.0 Hz, 1 H, *CH*), 7.28–7.21 (m, 1 H, O*H*).

^{13}C NMR (100.62 MHz, acetone-d_6): δ = 169.2 (Cq, C=O), 167.9 (Cq, C=O), 149.9 (Cq, C_{Ar}), 148.1 (CH_{Ar}), 146.1 (CH_{Ar}), 136.4 (CH_{Ar}), 135.4 (CH_{Ar}), 133.1 (q, $^2J_{C-F}$ = 34.1 Hz, Cq, $C_{Ar}CF_3$), 132.2 (CH_{Ar}), 131.7 (CH_{Ar}), 128.5 (Cq, C_{Ar}), 126.2 (CH_{Ar}), 125.9 (CH_{Ar}), 124.8 (CH_{Ar}), 124.7 (CH_{Ar}), 115.2. (CH), 113.1 (CH_{Ar}), 87.0 (CF_3), 86.5 (CF_3) (both tautomeric forms).

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{16}H_9F_6NO_2Na$: 384.0435; found: 384.0430.

(±)-3-Hydroxy-2-(2-propynyl)-1-isoindolinone (12d)

Obtained from 2-formylbenzoic acid (0.300 g, 2.00 mmol), $SOCl_2$ (2.46 g, 1.50 mL, 20.7 mmol), and propargylamine (0.166 g, 0.193 mL, 3.00 mmol) by following General Procedure G.

Yield: 0.294 g (1.57 mmol, 79%); colorless solid; mp 154–155 °C; R_f = 0.15 (*n*-hexane/EtOAc, 2:1).

IR (ATR): 3267, 2914, 2122, 1680, 1614, 1422, 1268, 1044, 752, 699, 651, 594 cm^{-1}.

^1H NMR (400.13 MHz, $CDCl_3$/MeOH-d_4): δ = 8.00–7.41 (m, 5 H, *CH*/CH_{Ar}), 5.94 (br. s, 1 H, O*H*), 4.60 (dd, $^2J_{H-H}$ = 17.6 Hz, $^4J_{H-H}$ = 2.6 Hz, 1 H, CH_2), 4.02 (dd, $^2J_{H-H}$ = 17.6 Hz, $^4J_{H-H}$ = 2.6 Hz, 1 H, CH_2), 2.26–2.19 (m, 1 H, *CH*).

^{13}C NMR (100.62 MHz, $CDCl_3$/MeOH-d_4): δ = 166.9 (Cq, C=O), 144.1 (Cq, C_{Ar}), 135.1 (Cq, C_{Ar}), 132.6 (CH_{Ar}), 131.2 (CH_{Ar}), 129.9 (CH_{Ar}), 123.5 (CH_{Ar}), 98.5 (CH), 81.0 (Cq), 71.9 (CH), 28.6 (CH_2).

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{11}H_9NO_2Na$: 210.0531; found: 210.0536.

(±)-3-Oxo-2-propyl-1-isoindolinyl Acetate (13a)

Obtained from **12a** (0.050 g, 0.26 mmol) and acetic anhydride (0.053 g, 0.049 mL, 0.52 mmol) by following General Procedure H.

Yield: 0.015 g (0.06 mmol, 24%); colorless solid; mp 92–93 °C; R_f = 0.35 (*n*-hexane/EtOAc, 2:1).

IR (ATR): 3258, 2971, 2927, 2875, 1664, 1600, 1459, 1408, 1317, 1056, 797, 742, 691, 591 cm^{-1}.

^1H NMR (400.25 MHz, $CDCl_3$): δ = 7.83–7.79 (m, 1 H, CH_{Ar}), 7.59–7.48 (m, 3 H, CH_{Ar}), 7.01 (s, 1 H, *CH*), 3.71 (ddd, $^3J_{H-H}$ = 13.9 Hz, $^3J_{H-H}$ = 8.6 Hz, $^2J_{H-H}$ = 7.0 Hz, 1 H, CH_2), 3.24 (ddd, $^3J_{H-H}$ = 14.0 Hz, $^3J_{H-H}$ = 8.5 Hz, $^2J_{H-H}$ = 5.5 Hz, 1 H, CH_2), 2.17 (s, CH_3), 1.76–1.57 (m, 2 H, CH_2), 0.94 (t, $^3J_{H-H}$ = 7.4 Hz, 3 H, CH_3).

^{13}C NMR (100.65 MHz, $CDCl_3$): δ = 171.3 (Cq, C=O), 168.0 (Cq, C=O), 141.1 (Cq, C_{Ar}), 132.4 (Cq, C_{Ar}), 132.3 (CH_{Ar}), 130.4 (CH_{Ar}), 123.9 (CH_{Ar}), 123.7 (CH_{Ar}), 81.3 (CH), 42.1 (CH_2), 21.7 (CH_3), 21.2 (CH_2), 11.5 (CH_3).

HRMS (ESI): *m*/*z* [M–Ac+Na]$^+$ calcd for $C_{11}H_{13}NO_2Na$: 214.0838; found: 214.0839.

(±)-2-Cyclohexyl-3-oxo-1-isoindolinyl Acetate (13b)

Obtained from **12b** (0.048 g, 0.20 mmol) and acetic anhydride (0.042 g, 0.039 mL, 0.40 mmol) by following General Procedure H.

Yield: 0.020 g (0.07 mmol, 36%); colorless oil; R_f = 0.51 (*n*-hexane/EtOAc, 2:1).

IR (ATR): 3401, 2932, 2856, 1739, 1707, 1400, 1372, 1231, 1207, 1182, 1167, 1125, 1009, 937, 803, 753, 697 cm^{-1}.

^1H NMR (400.13 MHz, $CDCl_3$): δ = 7.81–7.75 (m, 1 H, CH_{Ar}), 7.56–7.48 (m, 3 H, CH_{Ar}), 7.11 (s, 1 H, *CH*), 4.02 (tt, $^3J_{H-H}$ = 12.1 Hz, $^3J_{H-H}$ = 3.7 Hz, 1 H, *CH*), 2.14 (s, 3 H, CH_3), 2.06–1.96 (m, 1 H, CH_2), 1.90–1.77 (m, 3 H, CH_2), 1.75–1.32 (m, 5 H, CH_2), 1.28–1.08 (m, 1 H, CH_2).

^{13}C NMR (100.65 MHz, $CDCl_3$): δ = 171.1 (Cq, C=O), 167.9 (Cq, C=O), 141.5 (Cq, C_{Ar}), 132.4 (Cq, C_{Ar}), 132.3 (CH_{Ar}), 130.3 (CH_{Ar}), 123.8 (CH_{Ar}), 123.6 (CH_{Ar}), 81.9 (CH), 52.1 (CH_2), 32.0 (CH_2), 30.9 (CH_2), 26.0 (CH_2), 25.6 (CH_2), 21.5 (CH_3).

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{16}H_{19}NO_3Na$: 296.1268; found: 296.1270.

(±)-2-[3,5-Bis(trifluoromethyl)phenyl]-3-oxo-1-isoindolinyl Acetate (13c)

Obtained from **12c** (0.073 g, 0.20 mmol) and acetic anhydride (0.042 g, 0.039 mL, 0.40 mmol) by following General Procedure H.

Yield: 0.016 g (0.04 mmol, 20%); colorless solid; mp 126–127 °C; R_f = 0.61 (*n*-hexane/EtOAc, 2:1).

IR (ATR): 3314, 3124, 1744, 1728, 1708, 1620, 1564, 1475, 1388, 1274, 1123, 1107, 1084, 1017, 885, 758, 700, 681, 664 cm^{-1}.

^1H NMR (400.13 MHz, $CDCl_3$): δ = 8.22–8.15 (m, 2 H, CH_{Ar}), 7.94 (dt, $^3J_{H-H}$ = 7.4 Hz, $^4J_{H-H}$ = 1.2 Hz, 1 H, CH_{Ar}), 7.78–7.59 (m, 5 H, CH_{Ar}/*CH*), 2.11 (s, 3 H, CH_3).

^{13}C NMR (100.65 MHz, $CDCl_3$): δ = 170.8 (Cq, C=O), 166.8 (Cq, C=O), 140.1 (Cq, C_{Ar}), 138.3 (Cq, C_{Ar}), 134.1 (CH_{Ar}), 132.8 (q, $^2J_{C-F}$ = 33.0 Hz, Cq, $C_{Ar}CF_3$), 131.2 (CH_{Ar}), 131.1 (Cq, C_{Ar}), 124.6 (CH_{Ar}), 124.3 (CH_{Ar}), 123.1 (q, $^1J_{H-H}$ = 291.9 Hz, CF_3), 118.9 (CH_{Ar}), 80.8 (CH), 20.8 (CH_3).

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{18}H_{11}F_6NO_3Na$: 426.0535; found: 426.0537.

(±)-3-Oxo-2-(2-propynyl)-1-isoindolinyl Acetate (13d)

Obtained from **12d** (0.105 g, 0.56 mmol) and acetic anhydride (0.042 g, 0.039 mL, 1.12 mmol) by following General Procedure H.

Yield: 0.046 g (0.20 mmol, 36%); colorless solid; mp 97–98 °C; R_f = 0.42 (*n*-hexane/EtOAc, 2:1).

IR (ATR): 3259, 2963, 2927, 2120, 1737, 1714, 1619, 1422, 1232, 1142, 1013, 750, 690, 670, 595, 527 cm^{-1}.

^1H NMR (400.13 MHz, $CDCl_3$): δ = 7.89–7.78 (m, 1 H, CH_{Ar}), 7.63–7.47 (m, 3 H, CH_{Ar}), 7.15 (s, 1 H, *CH*), 4.63 (dd, $^2J_{H-H}$ = 17.7 Hz, $^4J_{H-H}$ = 2.5 Hz, 1 H, CH_2), 4.09 (dd, $^2J_{H-H}$ = 17.7 Hz, $^4J_{H-H}$ = 2.5 Hz, 1 H, CH_2), 2.26 (t, 1 H, $^4J_{H-H}$ = 2.5 Hz, *CH*), 2.17 (s, 3 H, CH_3).

^{13}C NMR (100.62 MHz, $CDCl_3$): δ = 171.1 (Cq, C=O), 167.1 (Cq, C=O), 141.1 (Cq, C_{Ar}), 132.9 (Cq, C_{Ar}), 131.5 (CH_{Ar}), 130.5 (CH_{Ar}), 124.3 (CH_{Ar}), 124.0 (CH_{Ar}), 80.9 (CH), 77.8 (Cq), 72.4 (CH), 30.0 (CH_2), 28.6 (CH_3).

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{13}H_{11}NO_3Na$: 252.0638; found: 252.0638.

(±)-2-Acetyl-3-hydroxy-1-isoindolinone (14)

o-Phthalaldehyde (2.68 g, 20.0 mmol, 1.0 equiv) and acetamide (1.18 g, 20.0 mmol, 1.0 equiv) were suspended in distilled water (150 mL), then NaOH (0.112 g, 2.80 mmol, 0.14 equiv) dissolved in distilled wa-

ter (5 mL) was slowly added by using a syringe. The resulting clear solution was stirred at r.t. for 12 h. The precipitate was filtered off, washed with distilled water and recrystallized from acetonitrile to give 1-(1,3-dihydroxy-2-isoindolinyl)-1-ethanone (**16**).

Yield: 0.809 g (4.19 mmol, 21%); colorless solid.

^{1}H NMR (400.25 MHz, DMSO-d_6): δ = 7.49–7.35 (m, 4 H, CH_{Ar}), 6.34 (d, $^3J_{H-H}$ = 9.5 Hz, 1 H, CH_{Ar}), 6.19 (d, $^3J_{H-H}$ = 7.4 Hz, 1 H, CH_{Ar}), 6.14 (d, $^3J_{H-H}$ = 9.5 Hz, 1 H, CH_{Ar}), 6.09 (d, $^3J_{H-H}$ = 7.5 Hz, 1 H, CH_{Ar}), 2.20 (s, 3 H, CH_3).

^{13}C NMR (100.65 MHz, DMSO-d_6): δ = 170.3 (Cq, C=O), 140.0 (Cq, C_{Ar}), 139.5 (Cq, C_{Ar}), 129.1 (CH_{Ar}), 129.0 (CH_{Ar}), 123.8 (CH_{Ar}), 123.7 (CH_{Ar}), 82.6 (CH), 80.6 (*C*H), 22.4 (CH_3).

Analytic data are identical to those reported in the literature.[69–71]

Compound **16** (0.600 g, 3.10 mmol, 1.0 equiv) was dissolved in boiling distilled water (25.0 mL), then $Na_2Cr_2O_7{\cdot}2\,H_2O$ (0.600 g, 2.01 mmol, 0.65 equiv) and some drops of concentrated H_2SO_4 were added. After heating under vigorous stirring to 110 °C, the resulting dark mixture was slowly cooled to r.t. and allowed to stand for 12 h to give **14** after filtration, washing with cold water, and drying in vacuum.

Yield: 0.260 g (1.36 mmol, 44%); colorless fine needles; mp 150–152 °C (Lit.[70] 163.0–164.5 °C).

IR (ATR): 1721, 1690, 1604, 1466, 1424, 1357, 1271, 1053, 963, 791, 748, 695, 642, 582 cm^{-1}.

^{1}H NMR (400.25 MHz, DMSO-d_6): δ = 11.31 (s, 1 H, C*H*O), 7.86–7.75 (m, 5 H, CH_{Ar}), 7.67–7.59 (m, 2 H, CH_{Ar}), 7.02 (d, $^3J_{H-H}$ = 7.7 Hz, 1 H, C*H*), 7.46 (d, $^3J_{H-H}$ = 7.7 Hz, 1 H, O*H*), 2.52 (s, 3 H, CH_3) (both tautomeric forms).

^{13}C NMR (100.65 MHz, DMSO-d_6): δ = 169.8 (Cq, C=O), 169.2 (Cq, C=O), 166.4 (Cq, C=O), 144.4 (Cq, C_{Ar}), 134.6 (CH_{Ar}), 134.3 (CH_{Ar}), 132.6 (Cq, C_{Ar}), 130.0 (CH_{Ar}), 129.5 (Cq, C_{Ar}), 124.3 (CH_{Ar}), 123.9 (CH_{Ar}), 122.9 (CH_{Ar}), 79.7 (CH), 25.1 (CH_3) (both tautomeric forms).

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{10}H_9NO_3Na$: 214.0480; found: 214.0481.

(±)-2-Acetyl-3-oxo-1-isoindolinyl Acetate (15)

Compound **14** (0.050 g, 0.26 mmol, 1.0 equiv) and DMAP (0.003 g, 0.03 mmol, 0.1 equiv) were dissolved in CH_2Cl_2 (2.0 mL) followed by the addition of acetic anhydride (0.053 g, 0.049 mL, 0.52 mmol, 2.0 equiv) and triethylamine (0.026 g, 0.036 mL, 1.0 equiv). The mixture was stirred at r.t. for 24 h, then the solvent was removed under reduced pressure to give **15** after column chromatography (*n*-hexane/EtOAc, 2:1).

Yield: 0.036 g (0.15 mmol, 59%); colorless solid; mp 123–124 °C; R_f = 0.44 (*n*-hexane/EtOAc, 2:1).

IR (ATR): 2922, 1732, 1702, 1474, 1434, 1375, 1358, 1275, 1227, 1213, 1024, 970, 763, 695, 598 cm^{-1}.

^{1}H NMR (400.13 MHz, $CDCl_3$): δ = 7.88 (td, $^3J_{H-H}$ = 7.7 Hz, $^4J_{H-H}$ = 1.0 Hz, 1 H, CH_{Ar}), 7.72–7.67 (m, 4 H, CH_{Ar}), 2.65 (s, 3 H, CH_3), 2.11 (s, 3 H, CH_3).

^{13}C NMR (100.62 MHz, $CDCl_3$): δ = 170.2 (Cq, C=O), 170.0 (Cq, C=O), 166.5 (Cq, C=O), 140.9 (Cq, C_{Ar}), 135.1 (CH_{Ar}), 131.0 (CH_{Ar}), 130.3 (Cq, C_{Ar}), 125.1 (CH_{Ar}), 124.8 (CH_{Ar}), 78.9 (CH), 25.2 (CH_3), 20.9 (CH_3).

HRMS (ESI): *m*/*z* [M]$^+$ calcd for $C_{12}H_{11}NO_4$: 233.0688; found: 233.0699.

Analytic data are identical to those reported in the literature.[72]

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Supporting Information

Supporting information for this article is available online at http://dx.doi.org/10.1055/s-0036-1589404.

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