

Synthesis of 2-(Cyanomethyl)benzoic Esters via Carbon–Carbon Bond Cleavage of Indanones

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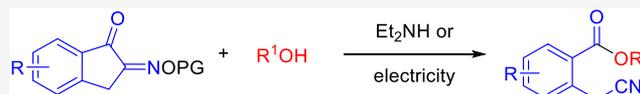


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ABSTRACT: A novel synthesis of 2-(cyanomethyl)benzoic esters from indanone derivatives has been established. This reaction proceeds via a deprotonation of alcohols with a chemical base, followed by a nucleophilic addition to indanones and Beckmann fragmentation. In addition, this reaction could also work under electrochemical conditions, and no external chemical bases were needed. This mild method offers a novel strategy for the late-stage functionalization of various natural alcohols.



2-(Cyanomethyl)benzoic esters have become an important class of building blocks in synthetic chemistry. As shown in Figure 1, their synthetic applications were highlighted in the

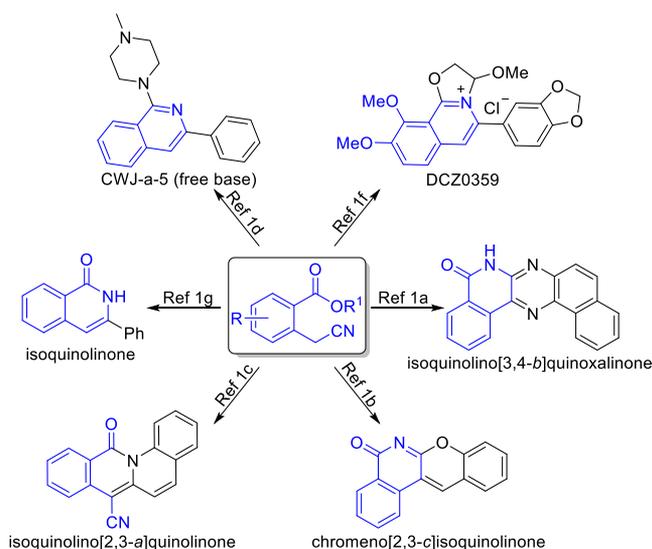
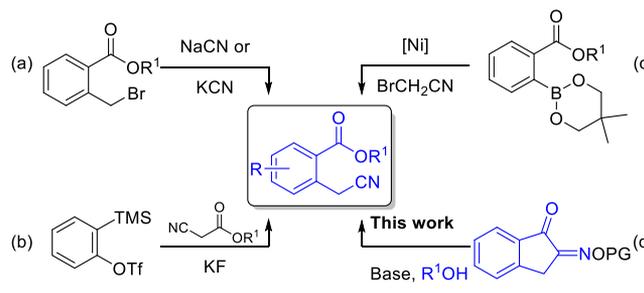


Figure 1. Synthetic utility of 2-(cyanomethyl)benzoic esters.

construction of various bioactive heterocycles¹ including drug candidates CWJ-a-5 and DCZ0359. A classical method for the synthesis of 2-(cyanomethyl)benzoic esters is the S_N2 nucleophilic substitution of benzyl halides with highly toxic metal cyanides (Scheme 1a).² In 2005, Kunai and co-workers reported an alternative approach taking advantage of aryl insertion into α -cyano esters (Scheme 1b).³ Lei developed an efficient Ni-catalyzed coupling reaction of arylboronic esters with α -bromonitriles in 2011 (Scheme 1c).⁴ Nevertheless, the synthetic approaches to 2-(cyanomethyl)benzoic esters are still underdeveloped.

Indanones are widely available feedstocks, as they are found in various natural products⁵ and can be also be accessed via a

Scheme 1. Synthesis of 2-(Cyanomethyl)benzoic Esters



variety of convenient methods.⁶ We envisaged to construct the 2-(cyanomethyl)benzoic esters from readily available indanone oxime ester⁷ via a Beckmann fragmentation⁸ (Scheme 1d). This working hypothesis could be potentially used for late-stage functionalization of natural alcohols and indanones. Herein, we report a novel synthesis of 2-(cyanomethyl)benzoic esters via the fragmentation of indanone oxime esters either in the presence of a chemical base or under electrochemical conditions.

At the outset, we examined our hypothesis with ketoxime ester **1a** as the model substrate (Table 1). A range of experiments identified the optimal reaction conditions (entry 1), which employed Et_2NH as the base in ethanol at room temperature. The use of other bases could also form the desired product **3aa**, albeit in lower yields (entries 2–7). Raising the reaction temperature did not affect the reaction efficiency (entry 8). The shorter reaction time delivered ethyl 2-(cyanomethyl)benzoate with a diminished yield (entry 9).

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Table 1. Optimization of Reaction Conditions^a

entry	deviation from standard conditions	yield (%) ^b
1	none	94
2	<i>t</i> -BuOK as base	11
3	KOH as base	10
4	NaOAc as base	75
5	K ₂ CO ₃ as base	83
6	NaHCO ₃ as base	78
7	DBU as base	90
8	at 50 °C	93
9	reaction time 12 h	75
10	0.5 equiv Et ₂ NH	40
11	EtOH/DCM (0.5 mL/0.5 mL)	82
12	EtOH/MeCN (0.5 mL/0.5 mL)	88

^aReaction conditions: **1a** (0.1 mmol), base (0.2 mmol, 2 equiv), and EtOH (0.1 M). ^bYields were determined by HPLC analysis.

Two equivalents of Et₂NH were found to be required to reach full conversion (entry 10). The amount of ethanol could be reduced when DCM or MeCN was used as the cosolvent (entries 11 and 12), which would be beneficial to the evaluation of alcohol scope.

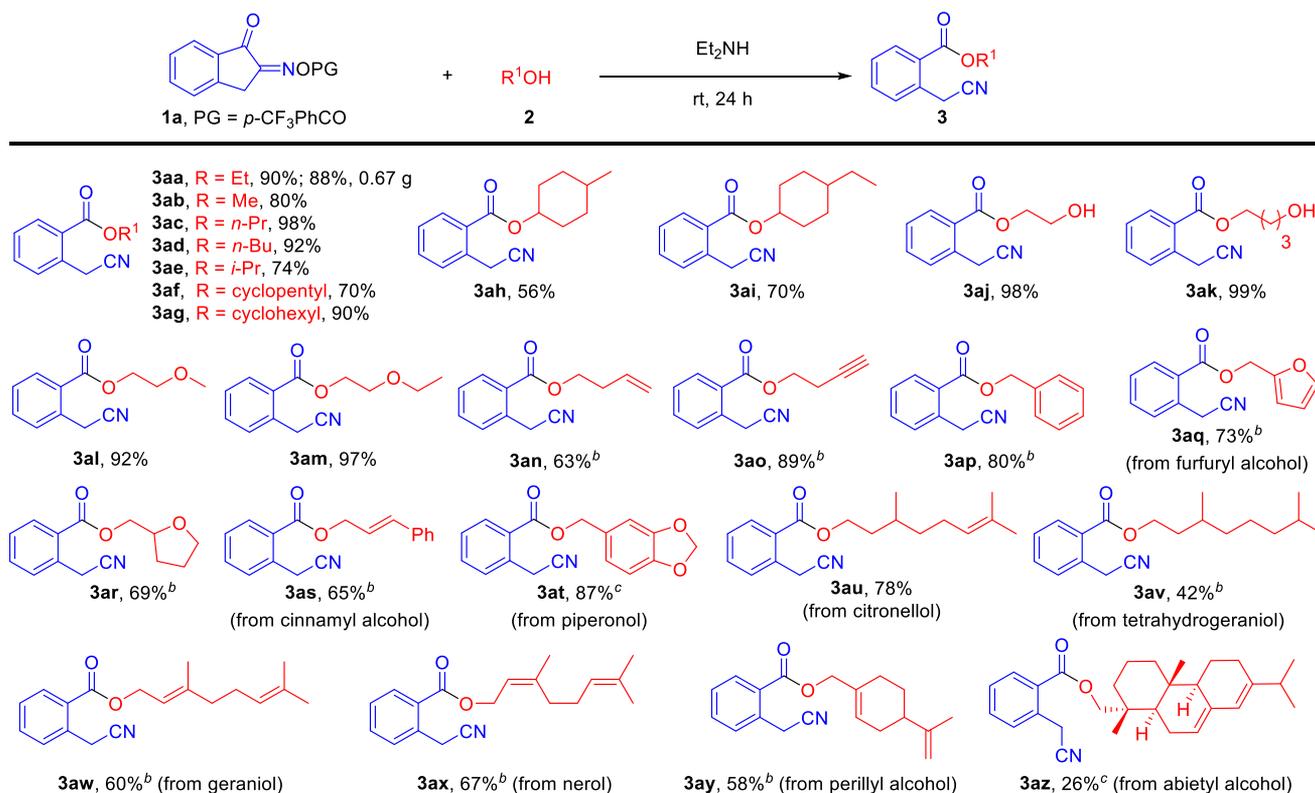
With the optimized conditions in hand, we evaluated the generality of this fragmentation for a range of alcohols (Scheme 2). Simple linear alcohols, such as methanol, ethanol,

propanol, and butanol, were found to be suitable substrates for this transformation, affording products **3aa–3ad** in high yields. Gratifyingly, the reaction is scalable. On 4 mmol scale, **3aa** could be obtained in 88% yield after 28 h. Both acyclic and cyclic secondary alcohols, such as isopropanol, cyclopentanol, and cyclohexanols, were proven to be effective reaction partners as well, giving the desired products **3ae–3ai**. Notably, diols could be selectively converted to the corresponding monoesters **3aj** and **3ak** in excellent yields. Alcohols possessing ether (**3al** and **3am**), alkene (**3an**), alkyne (**3ao**), benzyl (**3ap**), furan (**3aq**), and tetrahydrofuran (**3ar**) groups all worked very well.

To further demonstrate the applicability of this protocol, a series of natural alcohols were subjected to the reaction conditions. Cinnamyl alcohol and piperonol underwent the fragmentation smoothly to deliver **3as** and **3at** in 65% and 87% yield, respectively. Alcohols from plant essential oil, such as citronellol (**3au**), tetrahydrogeraniol (**3av**), geraniol (**3aw**), nerol (**3ax**), and perillyl alcohol (**3ay**), posed no problem either. Abietyl alcohol (**3az**), from natural rosin, was compatible with this fragmentation.

Next, we evaluated different protecting groups of oxime esters. As shown in Figure 2, benzoate **1a'** worked even better than *p*-trifluoromethylbenzoate **1a**. Moreover, *O*-acetyl oxime **1a''** reacted efficiently with ethanol, leading to **3aa** in comparable yield (93%). Therefore, *O*-acetyl oximes were used for the further studies.

The indanone substrate scope was also probed (Scheme 3). Indanones bearing either one or two electron donating groups (**3ba–3da**) all gave good yields. Besides, indanones containing

Scheme 2. Scope of Alcohols^{a,d}

^aReaction conditions: **1** (0.1 mmol), alcohol (1.0 mL, 0.1 M), and Et₂NH (0.2 mmol, 2.0 equiv). ^b**1** (0.1 mmol), alcohol (0.1 mL), CH₃CN (0.9 mL), and Et₂NH (0.4 mmol, 4.0 equiv). ^c**1** (0.1 mmol), alcohol (10.0 equiv), DCM (1.0 mL), and Et₂NH (0.4 mmol, 4.0 equiv). ^dIsolated yield.

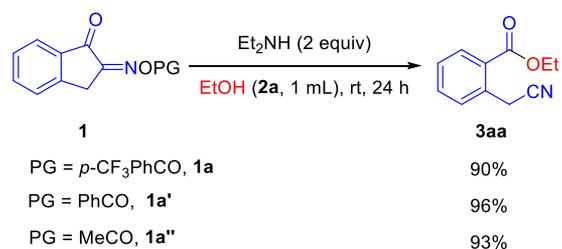
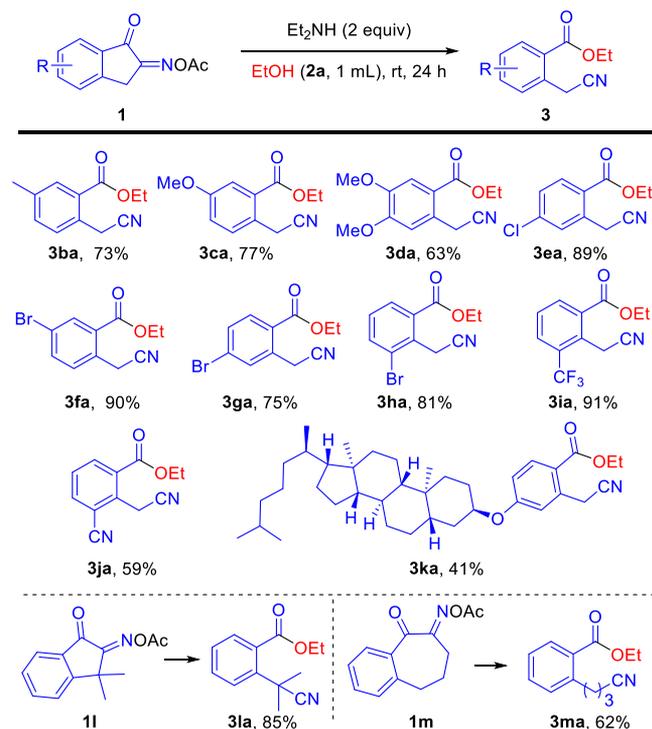


Figure 2. Evaluation of protecting groups.

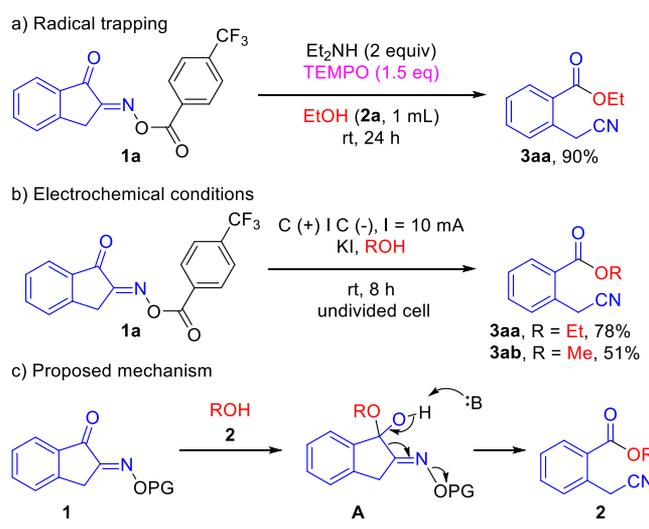
Scheme 3. Scope of Indanones^{a,b}

^aReaction conditions: **1** (0.1 mmol), EtOH (1.0 mL, 0.1 M), and Et₂NH (0.2 mmol, 2.0 equiv). ^bIsolated yield.

halide substituents, which provide opportunities for further functionalization, still provided the desired 2-(cyanomethyl)-benzoic esters **3ea–3ha** in high yields. In addition, indanones bearing electron-withdrawing groups CF₃ (**3ia**) and CN (**3ja**) proved to be competent substrates. Moreover, complex β -cholestanol derivative afforded the desired ester in 41% yield. Substituents at the aliphatic position of indanone derivatives were also explored. For example, *O*-acetyl oxime **1l** exhibited high reactivity, yielding the corresponding 2-(cyanomethyl)-benzoic ester **3la** in 85% yield. Finally, benzosuberone derivative **1m** smoothly participated in this fragmentation, producing **3ma** in 62% yield.

To investigate the pathway for this transformation, we conducted several control experiments (Scheme 4). First, the addition of common free radical scavengers such as TEMPO, BHT, and 1,1-diphenylethylene (see the Supporting Information) had little effect on the reaction (Scheme 4a), which ruled out the well-known radical pathway of oxime esters.⁹ As organic electrochemistry has become one of the highly sustainable techniques in recent years,¹⁰ we also tested the possibility to generate nucleophilic reagents (alkoxide anions) under electrochemical conditions,¹¹ avoiding the use of

Scheme 4. Mechanistic Considerations



stoichiometric amounts of the chemical base Et₂NH. In an undivided electrolytic cell, the electrochemically initiated fragmentation of **1a** occurred efficiently under electrolysis at room temperature for 8 h, when ethanol or methanol were used as the solvent, two graphite plates as the electrodes, and KI as the electrolyte (Scheme 4b). Thus, a plausible reaction mechanism is proposed (Scheme 4c). Initially, intermediate **A** was produced by the addition of alcohol **2** to the activated ketone **1**. Subsequently, a Beckmann fragmentation was promoted by either Et₂NH or electrogenerated base RO⁻, furnishing the final product **3**. In the electrochemical process, ketone **1** could be also attacked by alkoxide anion RO⁻, which was generated by cathodic reduction of alcohol **2**.

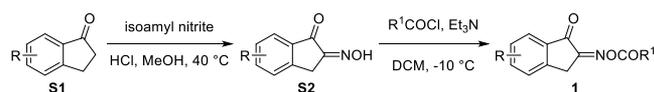
In conclusion, we have developed a facile synthesis of 2-(cyanomethyl)benzoic esters from readily available indanones. This reaction is initiated by the generation of alkoxide anion via deprotonation or cathodic reduction, followed by nucleophilic addition and Beckmann fragmentation. Moreover, this transformation not only unlocks the new reactivity of indanones but also offers a novel method for the late-stage functionalization of various natural alcohols.

EXPERIMENTAL SECTION

General Information. Unless otherwise stated, all glassware was oven-dried. All solvents were distilled from appropriate drying agents prior to use. All reagents were used as received from commercial suppliers unless otherwise indicated. The instrument for electrolysis is a domestic dual display DC stabilized power supply (UTP1303/UTP3305). Both anode electrode and cathode electrode are graphite plates (1.0 cm × 1.0 cm × 0.2 cm). Reactions were monitored using thin layer chromatography (TLC) carried out on Merck silica gel plates (60F-254) using UV light as the visualizing agent and high performance liquid chromatography (HPLC) with UV detection at 254 nm. For HPLC yields, UV response factors relative to an internal standard (1-nitronaphthalene). Flash column chromatography was performed using silica gel 60 (200–300 mesh). HRMS data were recorded on ThermoFisher LTQ Orbitrap XL or Agilent 6500 QTOFMS-ESI. All ¹H NMR, ¹³C NMR spectra were recorded on Bruker DRX600 and AMX-400 instruments. Chemical shifts were given in parts per million (ppm, δ), referenced to the solvent peak of CDCl₃, defined at $\delta = 7.26$ (¹H NMR), defined at $\delta = 77.16$ (¹³C NMR). Coupling constants were quoted in Hz (*J*). ¹H NMR spectroscopy splitting patterns were designated as singlet (s), doublet (d), triplet (t), quartet (q). Splitting patterns that could not be interpreted or easily visualized were designated as multiplet (m) or

broad (br). The diastereomeric ratios were determined by ^1H NMR analysis.

General Procedure for Preparation of Oxime Esters. A solution of 1-indanone¹² **S1** (5 mmol) in MeOH (5 mL) was slowly added to isoamyl nitrite (1.06 mL, 7.5 mmol) at room temperature. The reaction mixture was heated to 40 °C (in an oil bath). Then, concentrated HCl (0.25 mL) was slowly added to the mixture and the mixture was stirred for 2 h. The reaction mixture was cooled to room temperature and a white precipitate formed. Half of methanol was removed by rotary evaporation before filtration. The crude solid was washed with dichloromethane three times, and dried under a vacuum to afford oxime **S2**.



In the second step, oxime **S2** was acylated by dissolving in dried CH_2Cl_2 (4.5 mL, 4.5 mmol, 1.0 mL per mmol), followed by the addition of triethylamine (0.943 mL, 6.75 mmol, 1.5 equiv) and acyl chlorides (6.75 mmol, 1.5 equiv) at -10 °C. After 4 h, the reaction was quenched with saturated aqueous solution of NaHCO_3 and extracted with CH_2Cl_2 (3×10 mL), and the combined organic layers were dried over Na_2SO_4 . The combined organic layers were concentrated in vacuo and the residue was purified by recrystallization with petroleum ether and ethyl acetate to afford the desired product **1**.

2-(((4-(Trifluoromethyl)benzoyl)oxy)imino)-2,3-dihydro-1H-inden-1-one (1a). **1a** was prepared from the corresponding 1-indanone (5.0 mmol) as white solid (1416.3 mg, 85%). ($R_f = 0.2$, petroleum ether/ethyl acetate = 8/2). ^1H NMR (600 MHz, CDCl_3) δ 8.23 (d, $J = 8.1$ Hz, 2H), 7.91 (d, $J = 7.7$ Hz, 1H), 7.77 (d, $J = 8.2$ Hz, 2H), 7.73 (t, $J = 7.4$ Hz, 1H), 7.58 (d, $J = 7.7$ Hz, 1H), 7.49 (t, $J = 7.5$ Hz, 1H), 4.13 (s, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3) δ 187.5, 161.8, 161.0, 145.9, 137.4, 137.1, 135.3 (q, $J = 33.0$ Hz), 131.4, 130.3, 128.8, 126.8, 125.8 (q, $J = 3.7$ Hz), 125.2, 123.4 (q, $J = 272.9$ Hz), 29.9. HRMS-ESI (m/z) [$\text{M} + \text{Na}$] $^+$ calculated for $\text{C}_{17}\text{H}_{10}\text{F}_3\text{NNaO}_3$, 356.0505, found 356.0510.

2-((Benzoyloxy)imino)-2,3-dihydro-1H-inden-1-one (1a'). **1a'** was prepared from the corresponding 1-indanone (5.0 mmol) as white solid (1206.6 mg, 90%). ($R_f = 0.2$, petroleum ether/ethyl acetate = 8/2). ^1H NMR (600 MHz, CDCl_3) δ 8.11 (d, $J = 7.4$ Hz, 2H), 7.90 (d, $J = 7.7$ Hz, 1H), 7.71 (t, $J = 7.4$ Hz, 1H), 7.63 (t, $J = 7.4$ Hz, 1H), 7.56 (d, $J = 7.6$ Hz, 1H), 7.52–7.48 (m, 2H), 7.47 (d, $J = 7.4$ Hz, 1H), 4.10 (s, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3) δ 187.7, 162.9, 160.5, 146.1, 137.5, 136.9, 134.0, 129.9, 128.8, 128.7, 128.1, 126.8, 125.1, 29.9. HRMS-ESI (m/z) [$\text{M} + \text{Na}$] $^+$ calculated for $\text{C}_{16}\text{H}_{11}\text{NNaO}_3$, 288.0631, found 288.0637.

2-(Acetoxyimino)-2,3-dihydro-1H-inden-1-one (1a''). **1a''** was prepared from the corresponding 1-indanone (5.0 mmol) as white solid (843.2 mg, 81%). ($R_f = 0.2$, petroleum ether/ethyl acetate = 8/2). ^1H NMR (600 MHz, CDCl_3) δ 7.88 (d, $J = 7.7$ Hz, 1H), 7.71 (t, $J = 7.5$ Hz, 1H), 7.54 (d, $J = 7.7$ Hz, 1H), 7.47 (t, $J = 7.5$ Hz, 1H), 3.96 (s, 2H), 2.34 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3) δ 188.0, 168.7, 159.3, 146.3, 137.3, 136.9, 128.6, 126.9, 15.0, 29.8, 19.6. HRMS-ESI (m/z) [$\text{M} + \text{Na}$] $^+$ calculated for $\text{C}_{11}\text{H}_9\text{NNaO}_3$, 226.0474, found 226.0475.

2-(Acetoxyimino)-6-methyl-2,3-dihydro-1H-inden-1-one (1b). **1b** was prepared from the corresponding 1-indanone (5.0 mmol) as white solid (694 mg, 32%). ($R_f = 0.2$, petroleum ether/ethyl acetate = 8/2). ^1H NMR (600 MHz, CDCl_3) δ 7.62 (s, 1H), 7.48 (d, $J = 7.8$ Hz, 1H), 7.38 (d, $J = 7.8$ Hz, 1H), 3.86 (s, 2H), 2.38 (s, 3H), 2.30 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3) δ 188.0, 168.7, 159.8, 143.7, 138.7, 138.1, 137.4, 126.5, 124.8, 29.5, 21.1, 19.6. HRMS-ESI (m/z) [$\text{M} + \text{Na}$] $^+$ calculated for $\text{C}_{12}\text{H}_{11}\text{NNaO}_3$, 240.0631, found 240.0633.

2-(Acetoxyimino)-6-methoxy-2,3-dihydro-1H-inden-1-one (1c). **1c** was prepared from the corresponding 1-indanone (5.0 mmol) as white solid (481.2 mg, 41%). ($R_f = 0.2$, petroleum ether/ethyl acetate = 8/2). ^1H NMR (600 MHz, CDCl_3) δ 7.41 (d, $J = 8.4$ Hz, 1H), 7.32 (s, 1H), 7.28 (dd, $J = 8.4, 2.5$ Hz, 1H), 3.88 (s, 2H), 3.85 (s, 3H),

2.34 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3) δ 188.0, 168.8, 160.1, 159.9, 139.2, 138.6, 127.6, 126.4, 106.1, 55.8, 29.1, 19.7. HRMS-ESI (m/z) [$\text{M} + \text{Na}$] $^+$ calculated for $\text{C}_{12}\text{H}_{11}\text{NNaO}_4$, 256.0580, found 256.0583.

2-(Acetoxyimino)-5,6-dimethoxy-2,3-dihydro-1H-inden-1-one (1d). **1d** was prepared from the corresponding 1-indanone (5.0 mmol) as white solid (771.0 mg, 59%). ($R_f = 0.2$, petroleum ether/ethyl acetate = 8/2). ^1H NMR (600 MHz, CDCl_3) δ 7.28 (s, 1H), 6.89 (s, 1H), 4.00 (s, 3H), 3.91 (s, 3H), 3.83 (s, 2H), 2.34 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3) δ 186.2, 169.2, 159.8, 157.3, 150.2, 142.2, 131.0, 107.4, 105.3, 56.6, 56.3, 29.4, 19.7. HRMS-ESI (m/z) [$\text{M} + \text{Na}$] $^+$ calculated for $\text{C}_{13}\text{H}_{13}\text{NNaO}_5$, 286.0686, found 286.0695.

2-(Acetoxyimino)-5-chloro-2,3-dihydro-1H-inden-1-one (1e). **1e** was prepared from the corresponding 1-indanone (5.0 mmol) as white solid (446.9 mg, 38%). ($R_f = 0.2$, petroleum ether/ethyl acetate = 8/2). ^1H NMR (600 MHz, CDCl_3) δ 7.83 (d, $J = 8.2$ Hz, 1H), 7.52 (s, 1H), 7.45 (d, $J = 7.6$ Hz, 1H), 3.94 (s, 2H), 2.34 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3) δ 186.6, 168.6, 158.6, 147.6, 143.4, 135.8, 129.5, 127.1, 126.2, 29.6, 19.6. HRMS-ESI (m/z) [$\text{M} + \text{Na}$] $^+$ calculated for $\text{C}_{11}\text{H}_8\text{ClNNaO}_3$, 260.0085, found 260.0088.

2-(Acetoxyimino)-6-bromo-2,3-dihydro-1H-inden-1-one (1f). **1f** was prepared from the corresponding 1-indanone (5.0 mmol) as white solid (751.2 mg, 53%). ($R_f = 0.2$, petroleum ether/ethyl acetate = 8/2). ^1H NMR (600 MHz, CDCl_3) δ 8.05 (d, $J = 1.8$ Hz, 1H), 7.81 (dd, $J = 8.1, 1.9$ Hz, 1H), 7.43 (d, $J = 8.2$ Hz, 1H), 3.91 (s, 2H), 2.36 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3) δ 186.7, 168.7, 158.6, 144.7, 139.6, 138.9, 128.4, 128.0, 123.0, 29.5, 19.7. HRMS-ESI (m/z) [$\text{M} + \text{Na}$] $^+$ calculated for $\text{C}_{11}\text{H}_8\text{BrNNaO}_3$, 303.9579, found 303.9584.

2-(Acetoxyimino)-5-bromo-2,3-dihydro-1H-inden-1-one (1g). **1g** was prepared from the corresponding 1-indanone (5.0 mmol) as white solid (789.6 mg, 56%). ($R_f = 0.2$, petroleum ether/ethyl acetate = 8/2). ^1H NMR (600 MHz, CDCl_3) δ 7.76 (d, $J = 8.2$ Hz, 1H), 7.71 (s, 1H), 7.62 (d, $J = 8.1$ Hz, 1H), 3.95 (s, 2H), 2.35 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3) δ 186.8, 168.6, 158.5, 147.6, 136.2, 132.4, 132.3, 130.1, 126.2, 29.5, 19.7. HRMS-ESI (m/z) [$\text{M} + \text{Na}$] $^+$ calculated for $\text{C}_{11}\text{H}_8\text{BrNNaO}_3$, 303.9579, found 303.9584.

2-(Acetoxyimino)-4-bromo-2,3-dihydro-1H-inden-1-one (1h). **1h** was prepared from the corresponding 1-indanone (5.0 mmol) as white solid (477.9 mg, 34%). ($R_f = 0.2$, petroleum ether/ethyl acetate = 8/2). ^1H NMR (600 MHz, CDCl_3) δ 7.85 (d, $J = 7.9$ Hz, 1H), 7.83 (d, $J = 7.6$ Hz, 1H), 7.38 (t, $J = 7.7$ Hz, 1H), 3.86 (s, 2H), 2.35 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3) δ 187.4, 168.4, 158.3, 146.5, 139.4, 139.1, 130.3, 123.7, 122.1, 31.1, 19.6. HRMS-ESI (m/z) [$\text{M} + \text{Na}$] $^+$ calculated for $\text{C}_{11}\text{H}_8\text{BrNNaO}_3$, 303.9579, found 303.9585.

2-(Acetoxyimino)-4-(trifluoromethyl)-2,3-dihydro-1H-inden-1-one (1i). **1i** was prepared from the corresponding 1-indanone (5.0 mmol) as white solid (650 mg, 48%). ($R_f = 0.2$, petroleum ether/ethyl acetate = 8/2). ^1H NMR (600 MHz, CDCl_3) δ 8.09 (d, $J = 7.7$ Hz, 1H), 7.97 (d, $J = 7.7$ Hz, 1H), 7.64 (t, $J = 7.7$ Hz, 1H), 4.12 (s, 2H), 2.36 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3) δ 186.7, 168.3, 157.6, 143.5, 138.5, 133.2 (q, $J = 4.5$ Hz), 129.1, 128.7 (q, $J = 32.8$ Hz), 128.3, 123.4 (q, $J = 273.4$ Hz), 29.9 (q, $J = 1.4$ Hz), 19.6. HRMS-ESI (m/z) [$\text{M} + \text{Na}$] $^+$ calculated for $\text{C}_{12}\text{H}_8\text{F}_3\text{NNaO}_3$, 294.0348, found 294.0347.

2-(Acetoxyimino)-1-oxo-2,3-dihydro-1H-indene-4-carbonitrile (1j). **1j** was prepared from the corresponding 1-indanone (5.0 mmol) as white solid (193.0 mg, 17%). ($R_f = 0.2$, petroleum ether/ethyl acetate = 8/2). ^1H NMR (600 MHz, CDCl_3) δ 8.14 (d, $J = 7.7$ Hz, 1H), 8.01 (d, $J = 7.6$ Hz, 1H), 7.66 (t, $J = 7.7$ Hz, 1H), 4.15 (s, 2H), 2.37 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3) δ 186.1, 167.8, 157.1, 149.2, 139.3, 138.2, 129.5, 129.1, 115.4, 111.9, 29.5, 19.5. HRMS-ESI (m/z) [$\text{M} + \text{Na}$] $^+$ calculated for $\text{C}_{12}\text{H}_8\text{N}_2\text{NaO}_3$, 251.0427, found 251.0425.

2-(Acetoxyimino)-5-(((3R,5S,8R,9S,10S,13R,14S,17R)-10,13-dimethyl-17-((R)-6-methylheptan-2-yl)hexadecahydro-1H-cyclopenta[a]phenanthren-3-yl)oxy)-2,3-dihydro-1H-inden-1-one (1k). **1k** was prepared from the corresponding 1-indanone (5.0 mmol) as white solid (1234.0 mg, 42%). ($R_f = 0.2$, petroleum ether/ethyl acetate = 8/2). ^1H NMR (600 MHz, CDCl_3) δ 7.78 (d, $J = 8.6$ Hz,

1H), 6.91 (d, $J = 8.7$ Hz, 1H), 6.87 (s, 1H), 4.67 (s, 1H), 3.84 (s, 2H), 2.30 (s, 3H), 1.94 (d, $J = 12.6$ Hz, 1H), 1.87 (d, $J = 14.4$ Hz, 1H), 1.82–1.68 (m, 2H), 1.66–1.42 (m, 8H), 1.37–1.26 (m, 5H), 1.25–1.14 (m, 4H), 1.13–1.03 (m, 5H), 1.01–0.91 (m, 3H), 0.87 (d, $J = 6.5$ Hz, 3H), 0.83 (dd, $J = 6.6, 2.7$ Hz, 6H), 0.81 (s, 3H), 0.74 (td, $J = 12.3, 3.8$ Hz, 1H), 0.62 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3) δ 185.7, 169.0, 165.5, 160.0, 149.4, 130.5, 127.1, 117.4, 111.5, 73.4, 56.5, 56.3, 54.1, 42.6, 40.0, 39.6, 39.5, 36.2, 35.8, 35.8, 35.5, 32.6, 32.5, 31.9, 29.9, 28.4, 28.2, 28.0, 25.7, 24.2, 23.7, 22.8, 22.6, 20.8, 19.7, 18.7, 12.1, 11.4. HRMS-ESI (m/z) [$\text{M} + \text{Na}$] $^+$ calculated for $\text{C}_{38}\text{H}_{55}\text{NNaO}_4$ 612.4023, found 612.4027.

2-(Acetoxymino)-3,3-dimethyl-2,3-dihydro-1H-inden-1-one (1l).

1l was prepared from the corresponding 1-indanone (5.0 mmol) as white solid (924.1 mg, 80%). ($R_f = 0.2$, petroleum ether/ethyl acetate = 8/2). ^1H NMR (600 MHz, CDCl_3) δ 7.87 (d, $J = 7.7$ Hz, 1H), 7.74 (t, $J = 7.6$ Hz, 1H), 7.52 (d, $J = 7.8$ Hz, 1H), 7.47 (t, $J = 7.5$ Hz, 1H), 2.37 (s, 3H), 1.68 (s, 6H); $^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3) δ 187.8, 168.5, 164.4, 158.3, 137.2, 134.9, 128.6, 124.5, 123.6, 43.2, 25.6, 19.6. HRMS-ESI (m/z) [$\text{M} + \text{Na}$] $^+$ calculated for $\text{C}_{13}\text{H}_{13}\text{NNaO}_3$ 254.0787, found 254.0792.

Procedure A. Diethylamine (0.2 mmol, 2.0 equiv) was added to a solution of oxime ester **1a** (0.1 mmol, 1.0 equiv) in alcohol **2** (1.0 mL, 0.1 M) at room temperature. After 24 h, TLC indicated complete conversion of the starting material and the solvent was removed with a rotary evaporator. The pure product was obtained by flash chromatography on silica gel using petroleum ether and ethyl acetate as the eluent.

Procedure B. Diethylamine (0.4 mmol, 4.0 equiv) was added to a solution of oxime ester **1a** (0.1 mmol, 1.0 equiv) in alcohol **2** (0.1 mL) and CH_3CN (0.9 mL) at room temperature. After 24 h, TLC indicated complete conversion of the starting material and the solvent was removed with a rotary evaporator. The pure product was obtained by flash chromatography on silica gel using petroleum ether and ethyl acetate as the eluent.

Procedure C. Diethylamine (0.4 mmol, 4.0 equiv) was added to a solution of oxime ester **1a** (0.1 mmol, 1.0 equiv) and alcohol **2** (10.0 equiv) in DCM (1.0 mL) at room temperature. After 24 h, TLC indicated complete conversion of the starting material and the solvent was removed with a rotary evaporator. The pure product was obtained by flash chromatography on silica gel using petroleum ether and ethyl acetate as the eluent.

Procedure D. Diethylamine (0.2 mmol, 2.0 equiv) was added to a solution of oxime ester **1** (0.1 mmol, 1.0 equiv) in ethanol (1.0 mL, 0.1 M) at room temperature. After 24 h, TLC indicated complete conversion of the starting material and the solvent was removed with a rotary evaporator. The pure product was obtained by flash chromatography on silica gel using petroleum ether and ethyl acetate as the eluent.

Ethyl 2-(cyanomethyl)benzoate (3aa). Following General Procedure A: Colorless oil, 17.0 mg, 90% yield. ($R_f = 0.20$, petroleum ether/ethyl acetate = 20/1). ^1H NMR (600 MHz, CDCl_3) δ 8.08 (d, $J = 7.7$ Hz, 1H), 7.58–7.55 (m, 2H), 7.45–7.41 (m, 1H), 4.39 (q, $J = 7.1$ Hz, 2H), 4.22 (s, 2H), 1.41 (t, $J = 7.1$ Hz, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3) δ 166.3, 133.0, 131.9, 131.5, 130.2, 128.7, 128.3, 118.0, 61.4, 23.2, 14.2. Spectroscopic data matches that reported in the literature.⁴

Methyl 2-(cyanomethyl)benzoate (3ab). Following General Procedure A: White solid, 14.0 mg, 80% yield. ($R_f = 0.20$, petroleum ether/ethyl acetate = 20/1). ^1H NMR (600 MHz, CDCl_3) δ 8.07 (d, $J = 7.7$ Hz, 1H), 7.58–7.57 (m, 2H), 7.46–7.39 (m, 1H), 4.22 (s, 2H), 3.93 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3) δ 166.8, 133.2, 132.1, 131.6, 130.2, 128.4, 128.3, 117.9, 52.3, 23.2. Spectroscopic data matches that reported in the literature.¹³

Propyl 2-(cyanomethyl)benzoate (3ac). Following General Procedure A: Colorless oil, 19.8 mg, 98% yield. ($R_f = 0.20$, petroleum ether/ethyl acetate = 20/1). ^1H NMR (600 MHz, CDCl_3) δ 8.08 (d, $J = 7.7$ Hz, 1H), 7.58–7.56 (m, 2H), 7.45–7.40 (m, 1H), 4.29 (t, $J = 6.7$ Hz, 2H), 4.22 (s, 2H), 1.84–1.75 (m, 2H), 1.04 (t, $J = 7.4$ Hz, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3) δ 166.4, 133.0, 132.0, 131.5,

130.2, 128.7, 128.3, 118.0, 67.0, 23.2, 22.0, 10.6. HRMS-ESI (m/z) [$\text{M} + \text{Na}$] $^+$ calculated for $\text{C}_{12}\text{H}_{13}\text{NNaO}_2$ 226.0838, found 226.0839.

Butyl 2-(cyanomethyl)benzoate (3ad). Following General Procedure A: Colorless oil, 20.0 mg, 92% yield. ($R_f = 0.20$, petroleum ether/ethyl acetate = 20/1). ^1H NMR (600 MHz, CDCl_3) δ 8.07 (d, $J = 7.6$ Hz, 1H), 7.58–7.54 (m, 2H), 7.44–7.41 (m, 1H), 4.33 (t, $J = 6.7$ Hz, 2H), 4.22 (s, 2H), 1.81–1.70 (m, 2H), 1.53–1.41 (m, 2H), 0.98 (t, $J = 7.4$ Hz, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3) δ 166.4, 133.0, 132.0, 131.5, 130.6, 128.7, 128.3, 118.0, 65.3, 30.7, 23.2, 19.3, 13.7. HRMS-ESI (m/z) [$\text{M} + \text{Na}$] $^+$ calculated for $\text{C}_{13}\text{H}_{15}\text{NNaO}_2$ 240.0995, found 240.0997.

Isopropyl 2-(cyanomethyl)benzoate (3ae). Following General Procedure A: Colorless oil, 15.0 mg, 74% yield. ($R_f = 0.20$, petroleum ether/ethyl acetate = 20/1). ^1H NMR (600 MHz, CDCl_3) δ 8.05 (d, $J = 7.8$ Hz, 1H), 7.57–7.54 (m, 2H), 7.42 (m, 1H), 5.26 (m, 1H), 4.21 (s, 2H), 1.39 (d, $J = 6.3$ Hz, 6H); $^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3) δ 165.9, 132.9, 131.8, 131.5, 130.1, 129.2, 128.3, 118.0, 69.1, 23.2, 21.9. HRMS-ESI (m/z) [$\text{M} + \text{Na}$] $^+$ calculated for $\text{C}_{12}\text{H}_{13}\text{NNaO}_2$ 226.0838, found 226.0840.

Cyclopentyl 2-(cyanomethyl)benzoate (3af). Following General Procedure A: Colorless oil, 16.0 mg, 70% yield. ($R_f = 0.20$, petroleum ether/ethyl acetate = 20/1). ^1H NMR (600 MHz, CDCl_3) δ 8.02 (d, $J = 7.8$ Hz, 1H), 7.57–7.53 (m, 2H), 7.44–7.40 (m, 1H), 5.46–5.32 (m, 1H), 4.21 (s, 2H), 2.01–1.92 (m, 2H), 1.89–1.77 (m, 4H), 1.70–1.64 (m, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3) δ 166.2, 132.9, 131.8, 131.5, 130.1, 129.1, 128.3, 118.0, 78.4, 32.8, 23.8, 23.2. HRMS-ESI (m/z) [$\text{M} + \text{Na}$] $^+$ calculated for $\text{C}_{14}\text{H}_{15}\text{NNaO}_2$ 252.0995, found 252.0998.

Cyclohexyl 2-(cyanomethyl)benzoate (3ag). Following General Procedure A: Colorless oil, 21.9 mg, 90% yield. ($R_f = 0.20$, petroleum ether/ethyl acetate = 20/1). ^1H NMR (600 MHz, CDCl_3) δ 8.07 (d, $J = 7.7$ Hz, 1H), 7.57–7.54 (m, 2H), 7.42 (m, 1H), 5.09–4.95 (m, 1H), 4.21 (s, 2H), 2.01–1.92 (m, 2H), 1.81–1.77 (m, 2H), 1.65–1.52 (m, 3H), 1.50–1.40 (m, 2H), 1.39–1.30 (m, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3) δ 165.8, 132.9, 131.8, 131.5, 130.1, 129.2, 128.3, 118.0, 73.9, 31.2, 25.4, 23.8, 23.2. HRMS-ESI (m/z) [$\text{M} + \text{Na}$] $^+$ calculated for $\text{C}_{15}\text{H}_{17}\text{NNaO}_2$ 266.1152, found 266.1166.

4-Methylcyclohexyl 2-(cyanomethyl)benzoate (3ah). Following General Procedure A: The diastereomeric ratio was 6:1 (Isomer **3ah'**: Isomer **3ah''**) as determined by ^1H NMR analysis. Orange oil, 14.3 mg, 56% yield. ($R_f = 0.2$, petroleum ether/ethyl acetate = 20/1). Isomer **3ah'**: ^1H NMR (600 MHz, CDCl_3) δ 8.05 (d, $J = 7.8$ Hz, 1H), 7.57–7.54 (m, 2H), 7.43–7.39 (m, 1H), 4.93–1.89 (m, 1H), 4.20 (s, 2H), 2.15–2.06 (m, 2H), 1.85–1.75 (m, 2H), 1.56–1.47 (m, 2H), 1.46–1.41 (m, 1H), 1.14–1.07 (m, 2H), 0.93 (d, $J = 6.5$ Hz, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3) δ 165.9, 132.9, 131.8, 131.5, 130.1, 129.2, 128.3, 118.0, 74.8, 33.0, 31.7, 29.8, 23.3, 21.8.

Isomer **3ah''**: ^1H NMR (600 MHz, CDCl_3) δ 8.08 (d, $J = 7.7$ Hz, 1H), 7.58–7.57 (m, 2H), 7.47–7.44 (m, 1H), 5.29–5.21 (m, 1H), 4.25 (s, 2H), 2.03–1.94 (m, 2H), 1.68–1.65 (m, 2H), 1.61–1.59 (m, 2H), 1.37–1.35 (m, 1H), 1.27 (m, 2H), 0.96 (d, $J = 6.5$ Hz, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3) δ 165.7, 132.9, 132.0, 131.5, 130.1, 129.3, 128.3, 118.0, 71.2, 31.7, 31.4, 29.6, 23.2, 22.1. HRMS-ESI (m/z) [$\text{M} + \text{Na}$] $^+$ calculated for $\text{C}_{16}\text{H}_{19}\text{NNaO}_2$ 280.1308, found 280.1307.

4-Ethylcyclohexyl 2-(cyanomethyl)benzoate (3ai). Following General Procedure A: The diastereomeric ratio was 7:1 (Isomer **3ai'**: Isomer **3ai''**) as determined by ^1H NMR analysis. Colorless oil, 19.0 mg, 70% yield. ($R_f = 0.2$, petroleum ether/ethyl acetate = 20/1). Isomer **3ai'**: ^1H NMR (600 MHz, CDCl_3) δ 8.05 (d, $J = 7.7$ Hz, 1H), 7.55–7.54 (m, 2H), 7.44–7.40 (m, 1H), 4.95–4.89 (m, 1H), 4.20 (s, 2H), 2.18–2.08 (m, 2H), 1.91–1.83 (m, 2H), 1.54–1.45 (m, 2H), 1.29–1.22 (m, 2H), 1.21–1.15 (m, 1H), 1.11–1.02 (m, 2H), 0.90 (t, $J = 7.4$ Hz, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3) δ 165.9, 132.9, 131.8, 131.5, 130.1, 129.2, 128.3, 118.0, 75.1, 38.4, 31.7, 30.6, 29.2, 23.3, 11.7.

Isomer **3ai''**: ^1H NMR (600 MHz, CDCl_3) δ 8.08 (d, $J = 7.5$ Hz, 1H), 7.57–7.56 (m, 2H), 7.46–7.42 (m, 1H), 5.26–5.25 (m, 1H), 4.24 (s, 2H), 2.03–1.96 (m, 2H), 1.70–1.60 (m, 4H), 1.34–1.31 (m, 2H), 1.30–1.28 (m, 2H), 1.23–1.20 (m, 1H), 0.90 (t, $J = 7.4$ Hz,

3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3) δ 165.7, 132.9, 132.0, 131.5, 130.1, 129.3, 128.3, 118.0, 71.6, 38.1, 31.7, 29.7, 27.4, 23.2, 11.5. HRMS-ESI (m/z) [$\text{M} + \text{Na}$] $^+$ calculated for $\text{C}_{17}\text{H}_{21}\text{NNaO}_2$ 294.1465, found 294.1461.

2-Hydroxyethyl 2-(cyanomethyl)benzoate (3aj). Following General Procedure A: Colorless oil, 20.3 mg, 98% yield. ($R_f = 0.15$, petroleum ether/ethyl acetate = 8/2). ^1H NMR (600 MHz, CDCl_3) δ 8.10 (d, $J = 7.8$ Hz, 1H), 7.57 (t, $J = 7.5$ Hz, 1H), 7.53 (d, $J = 7.7$ Hz, 1H), 7.43 (t, $J = 7.6$ Hz, 1H), 4.54–4.41 (m, 2H), 4.18 (s, 2H), 4.01–3.93 (m, 2H), 2.08 (s, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3) δ 166.6, 133.3, 131.9, 131.7, 130.4, 128.5, 128.4, 118.2, 67.0, 61.0, 23.4. HRMS-ESI (m/z) [$\text{M} + \text{Na}$] $^+$ calculated for $\text{C}_{11}\text{H}_{11}\text{NNaO}_3$ 228.0631, found 228.0630.

4-Hydroxybutyl 2-(cyanomethyl)benzoate (3ak). Following General Procedure A: Colorless oil, 23.1 mg, 99% yield. ($R_f = 0.15$, petroleum ether/ethyl acetate = 8/2). ^1H NMR (600 MHz, CDCl_3) δ 8.06 (d, $J = 7.5$ Hz, 1H), 7.65–7.52 (m, 2H), 7.46–7.36 (m, 1H), 4.37 (t, $J = 6.6$ Hz, 2H), 4.20 (s, 2H), 3.71 (t, $J = 6.4$ Hz, 2H), 1.91–1.85 (m, 2H), 1.85 (s, 1H), 1.76–1.69 (m, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3) δ 166.4, 133.1, 132.0, 131.5, 130.3, 128.6, 128.4, 118.0, 65.3, 62.3, 29.2, 25.2, 23.2. HRMS-ESI (m/z) [$\text{M} + \text{H}$] $^+$ calculated for $\text{C}_{13}\text{H}_{16}\text{NO}_3$ 234.1125, found 234.1124.

2-Methoxyethyl 2-(cyanomethyl)benzoate (3al). Following General Procedure A: Colorless oil, 20.1 mg, 92% yield. ($R_f = 0.5$, petroleum ether/ethyl acetate = 8/2). ^1H NMR (600 MHz, CDCl_3) δ 8.10 (d, $J = 8.2$ Hz, 1H), 7.57 (m, 2H), 7.43 (m, 1H), 4.56–4.40 (m, 2H), 4.21 (s, 2H), 3.86–3.59 (m, 2H), 3.42 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3) δ 166.3, 133.2, 132.0, 131.8, 130.2, 128.4, 128.4, 118.0, 70.3, 64.3, 59.0, 23.2. HRMS-ESI (m/z) [$\text{M} + \text{H}$] $^+$ calculated for $\text{C}_{12}\text{H}_{14}\text{NO}_3$ 220.0968, found 220.0975.

2-Ethoxyethyl 2-(cyanomethyl)benzoate (3am). Following General Procedure A: Colorless oil, 22.6 mg, 97% yield. ($R_f = 0.7$, petroleum ether/ethyl acetate = 8/2). ^1H NMR (600 MHz, CDCl_3) δ 8.09 (d, $J = 7.9$ Hz, 1H), 7.60–7.51 (m, 2H), 7.48–7.38 (m, 1H), 4.52–4.41 (m, 2H), 4.21 (s, 2H), 3.83–3.73 (m, 2H), 3.58 (q, $J = 7.0$ Hz, 2H), 1.23 (t, $J = 7.0$ Hz, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3) δ 166.3, 133.2, 132.0, 131.8, 130.2, 128.6, 128.3, 118.0, 68.2, 66.7, 64.5, 23.2, 15.2. HRMS-ESI (m/z) [$\text{M} + \text{H}$] $^+$ calculated for $\text{C}_{13}\text{H}_{16}\text{NO}_3$ 234.1125, found 234.1129.

But-3-en-1-yl 2-(cyanomethyl)benzoate (3an). Following General Procedure B: Colorless oil, 13.6 mg, 63% yield. ($R_f = 0.20$, petroleum ether/ethyl acetate = 20/1). ^1H NMR (600 MHz, CDCl_3) δ 8.06 (d, $J = 7.7$ Hz, 1H), 7.59–7.56 (m, 2H), 7.45–7.41 (m, 1H), 5.87 (ddt, $J = 17.0, 10.3, 6.7$ Hz, 1H), 5.19 (dd, $J = 17.1, 1.6$ Hz, 1H), 5.13 (dd, $J = 10.3, 1.5$ Hz, 1H), 4.39 (t, $J = 6.6$ Hz, 2H), 4.21 (s, 2H), 2.59–2.48 (m, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3) δ 166.3, 134.0, 133.1, 132.0, 131.6, 130.2, 128.6, 128.4, 117.9, 117.6, 64.4, 33.1, 23.3. HRMS-ESI (m/z) [$\text{M} + \text{Na}$] $^+$ calculated for $\text{C}_{13}\text{H}_{13}\text{NNaO}_2$ 238.0839, found 238.0843.

But-3-yn-1-yl 2-(cyanomethyl)benzoate (3ao). Following General Procedure B: White solid, 19.1 mg, 89% yield. ($R_f = 0.15$, petroleum ether/ethyl acetate = 20/1). ^1H NMR (600 MHz, CDCl_3) δ 8.11 (d, $J = 7.6$ Hz, 1H), 7.60–7.57 (m, 2H), 7.49–7.42 (m, 1H), 4.44 (t, $J = 6.6$ Hz, 2H), 4.23 (s, 2H), 2.69 (td, $J = 6.6, 2.7$ Hz, 2H), 2.05 (t, $J = 2.7$ Hz, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3) δ 166.0, 133.3, 132.1, 131.8, 130.2, 128.4, 128.2, 117.9, 80.0, 70.3, 63.0, 23.3, 19.1. HRMS-ESI (m/z) [$\text{M} + \text{Na}$] $^+$ calculated for $\text{C}_{13}\text{H}_{11}\text{NNaO}_2$ 236.0682, found 236.0687.

Benzyl 2-(cyanomethyl)benzoate (3ap). Following General Procedure B: Colorless oil, 20.1 mg, 80% yield. ($R_f = 0.15$, petroleum ether/ethyl acetate = 20/1). ^1H NMR (600 MHz, CDCl_3) δ 8.12 (d, $J = 7.6$ Hz, 1H), 7.58 (m, 2H), 7.48–7.34 (m, 6H), 5.37 (s, 2H), 4.23 (s, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3) δ 166.1, 135.5, 133.3, 132.2, 131.7, 130.2, 128.7, 128.5, 128.4, 128.4, 128.3, 117.9, 67.2, 23.2. HRMS-ESI (m/z) [$\text{M} + \text{Na}$] $^+$ calculated for $\text{C}_{16}\text{H}_{13}\text{NNaO}_2$ 274.0839, found 274.0841.

Furan-2-ylmethyl 2-(cyanomethyl)benzoate (3aq). Following General Procedure B: Colorless oil, 17.7 mg, 73% yield. ($R_f = 0.15$, petroleum ether/ethyl acetate = 20/1). ^1H NMR (600 MHz, CDCl_3) δ 8.08 (d, $J = 7.6$ Hz, 1H), 7.58–7.55 (m, 2H), 7.46 (d, $J = 1.4$ Hz,

1H), 7.43–7.38 (m, 1H), 6.50 (d, $J = 3.2$ Hz, 1H), 6.39 (dd, $J = 3.2, 1.9$ Hz, 1H), 5.31 (s, 2H), 4.22 (s, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3) δ 165.9, 149.1, 143.5, 133.3, 132.2, 131.8, 130.1, 128.4, 128.1, 117.9, 111.1, 110.7, 58.8, 23.2. HRMS-ESI (m/z) [$\text{M} + \text{Na}$] $^+$ calculated for $\text{C}_{14}\text{H}_{11}\text{NNaO}_3$ 264.0631, found 264.0639.

(Tetrahydrofuran-2-yl)methyl 2-(cyanomethyl)benzoate (3ar). Following General Procedure B: Colorless oil, 16.9 mg, 69% yield. ($R_f = 0.20$, petroleum ether/ethyl acetate = 20/1). ^1H NMR (600 MHz, CDCl_3) δ 8.10 (d, $J = 7.7$ Hz, 1H), 7.58–7.55 (m, 2H), 7.43–7.41 (m, 1H), 4.41–4.34 (m, 1H), 4.30–4.24 (m, 2H), 4.22 (s, 2H), 3.95–3.88 (m, 1H), 3.87–3.78 (m, 1H), 2.12–2.03 (m, 1H), 2.00–1.87 (m, 2H), 1.71–1.63 (m, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3) δ 166.3, 133.2, 132.1, 131.7, 130.1, 128.4, 128.4, 118.0, 76.4, 68.5, 67.3, 28.1, 25.7, 23.2. HRMS-ESI (m/z) [$\text{M} + \text{Na}$] $^+$ calculated for $\text{C}_{14}\text{H}_{15}\text{NNaO}_3$ 268.0944, found 268.0945.

Cinnamyl 2-(cyanomethyl)benzoate (3as). Following General Procedure B: Colorless oil, 18.1 mg, 65% yield. ($R_f = 0.2$, petroleum ether/ethyl acetate = 20/1). ^1H NMR (600 MHz, CDCl_3) δ 8.13 (d, $J = 7.9$ Hz, 1H), 7.59–7.57 (m, 2H), 7.47–7.40 (m, 3H), 7.34 (t, $J = 7.6$ Hz, 2H), 7.28 (t, $J = 7.3$ Hz, 1H), 6.76 (d, $J = 15.9$ Hz, 1H), 6.41 (dt, $J = 15.8, 6.5$ Hz, 1H), 4.99 (d, $J = 6.5$ Hz, 2H), 4.25 (s, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3) δ 166.1, 136.1, 135.0, 133.2, 132.2, 131.7, 130.2, 128.7, 128.4, 128.3, 126.7, 122.7, 117.9, 66.0, 23.3. HRMS-ESI (m/z) [$\text{M} + \text{Na}$] $^+$ calculated for $\text{C}_{18}\text{H}_{15}\text{NNaO}_2$ 300.0995, found 300.1004.

(1,3-Dihydroisobenzofuran-5-yl)methyl 2-(cyanomethyl)benzoate (3at). Following General Procedure C: Colorless oil, 25.6 mg, 87% yield. ($R_f = 0.15$, petroleum ether/ethyl acetate = 20/1). ^1H NMR (600 MHz, CDCl_3) δ 8.08 (d, $J = 7.7$ Hz, 1H), 7.58–7.55 (m, 2H), 7.46–7.36 (m, 1H), 6.93–6.91 (m, 2H), 6.81 (d, $J = 7.8$ Hz, 1H), 5.97 (s, 2H), 5.25 (s, 2H), 4.21 (s, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3) δ 166.1, 147.9, 147.9, 133.2, 132.2, 131.7, 130.2, 129.2, 128.4, 128.3, 122.5, 117.9, 109.2, 108.4, 101.3, 67.1, 23.2. HRMS-ESI (m/z) [$\text{M} + \text{Na}$] $^+$ calculated for $\text{C}_{17}\text{H}_{13}\text{NNaO}_4$ 318.0737, found 318.0738.

3,7-Dimethyloct-6-en-1-yl 2-(cyanomethyl)benzoate (3au). Following General Procedure A: Colorless oil, 23.5 mg, 78% yield. ($R_f = 0.3$, petroleum ether/ethyl acetate = 20/1). ^1H NMR (600 MHz, CDCl_3) δ 8.06 (d, $J = 7.7$ Hz, 1H), 7.60–7.54 (m, 2H), 7.46–7.37 (m, 1H), 5.11–5.08 (m, 1H), 4.42–4.28 (m, 2H), 4.23 (s, 2H), 2.07–1.95 (m, 2H), 1.85–1.81 (m, 1H), 1.67 (s, 3H), 1.63–1.60 (m, 1H), 1.60 (s, 3H), 1.58–1.52 (m, 1H), 1.44–1.36 (m, 1H), 1.27–1.21 (m, 1H), 0.97 (d, $J = 6.5$ Hz, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3) δ 166.4, 133.0, 132.0, 131.5, 130.1, 128.7, 128.3, 124.5, 118.0, 64.0, 37.0, 35.4, 29.6, 25.7, 25.4, 23.2, 19.5, 17.7. HRMS-ESI (m/z) [$\text{M} + \text{Na}$] $^+$ calculated for $\text{C}_{19}\text{H}_{25}\text{NNaO}_2$ 322.1777, found 322.1773.

3,7-Dimethyloctyl 2-(cyanomethyl)benzoate (3av). Following General Procedure B: Colorless oil, 12.6 mg, 42% yield. ($R_f = 0.20$, petroleum ether/ethyl acetate = 20/1). ^1H NMR (600 MHz, CDCl_3) δ 8.06 (d, $J = 7.6$ Hz, 1H), 7.58–7.55 (m, 2H), 7.43 (m, 1H), 4.41–4.28 (m, 2H), 4.23 (s, 2H), 1.87–1.75 (m, 1H), 1.54 (m, 2H), 1.38–1.24 (m, 4H), 1.21–1.10 (m, 3H), 0.96 (d, $J = 6.5$ Hz, 3H), 0.87 (d, $J = 6.6$ Hz, 6H); $^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3) δ 166.4, 133.0, 132.0, 131.5, 130.1, 128.7, 128.3, 118.0, 64.1, 39.2, 37.1, 35.5, 30.0, 28.0, 24.6, 23.2, 22.7, 22.6, 19.6. HRMS-ESI (m/z) [$\text{M} + \text{H}$] $^+$ calculated for $\text{C}_{19}\text{H}_{28}\text{NO}_2$ 302.2114, found 302.2115.

(E)-3,7-Dimethylocta-2,6-dien-1-yl 2-(cyanomethyl)benzoate (3aw). Following General Procedure B: Colorless oil, 17.8 mg, 60% yield. ($R_f = 0.3$, petroleum ether/ethyl acetate = 20/1). ^1H NMR (600 MHz, CDCl_3) δ 8.07 (d, $J = 7.5$ Hz, 1H), 7.61–7.52 (m, 2H), 7.46–7.34 (m, 1H), 5.47 (td, $J = 7.1, 1.2$ Hz, 1H), 5.09 (ddd, $J = 6.9, 4.0, 1.3$ Hz, 1H), 4.84 (d, $J = 7.1$ Hz, 2H), 4.23 (s, 2H), 2.15–2.11 (m, 2H), 2.10–2.06 (m, 2H), 1.77 (s, 3H), 1.67 (d, $J = 0.6$ Hz, 3H), 1.60 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3) δ 166.4, 143.1, 133.0, 131.9, 131.6, 130.1, 128.7, 128.3, 123.7, 118.0, 117.9, 62.2, 39.6, 26.3, 25.7, 23.2, 17.7, 16.6. HRMS-ESI (m/z) [$\text{M} + \text{Na}$] $^+$ calculated for $\text{C}_{19}\text{H}_{23}\text{NNaO}_2$ 320.1621, found 320.1620.

(Z)-3,7-Dimethylocta-2,6-dien-1-yl 2-(cyanomethyl)benzoate (3ax). Following General Procedure B: Colorless oil, 19.9 mg, 67%

yield. ($R_f = 0.3$, petroleum ether/ethyl acetate = 20/1). ^1H NMR (600 MHz, CDCl_3) δ 8.10–7.96 (m, 1H), 7.62–7.51 (m, 2H), 7.46–7.34 (m, 1H), 5.48 (t, $J = 7.2$ Hz, 1H), 5.19–5.01 (m, 1H), 4.81 (d, $J = 7.3$ Hz, 2H), 4.23 (s, 2H), 2.21–2.16 (m, 2H), 2.13–2.11 (m, 2H), 1.80 (s, 3H), 1.67 (s, 3H), 1.60 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3) δ 166.3, 143.3, 133.0, 132.3, 132.0, 131.6, 130.0, 128.7, 128.3, 123.5, 118.8, 118.0, 62.0, 32.2, 26.7, 25.7, 23.5, 23.2, 17.7. HRMS-ESI (m/z) [$\text{M} + \text{Na}$] $^+$ calculated for $\text{C}_{19}\text{H}_{23}\text{NNaO}_2$ 320.1617, found 320.1620.

(4-(Prop-1-en-2-yl)cyclohex-1-en-1-yl)methyl 2-(cyanomethyl)benzoate (3ay). Following General Procedure B: Colorless oil, 17.0 mg, 58% yield. ($R_f = 0.15$, petroleum ether/ethyl acetate = 20/1). ^1H NMR (600 MHz, CDCl_3) δ 8.09 (d, $J = 7.7$ Hz, 1H), 7.67–7.54 (m, 2H), 7.49–7.35 (m, 1H), 5.86 (s, 1H), 4.73 (dd, $J = 12.3$, 3.5 Hz, 4H), 4.24 (s, 2H), 2.24–2.14 (m, 4H), 2.06–1.94 (m, 1H), 1.92–1.84 (m, 1H), 1.75 (s, 3H), 1.58–1.49 (m, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3) δ 166.2, 149.5, 133.1, 132.3, 132.1, 131.5, 130.1, 128.6, 128.3, 126.5, 118.0, 108.9, 69.4, 40.8, 30.5, 27.3, 26.6, 23.2, 20.8. HRMS-ESI (m/z) [$\text{M} + \text{Na}$] $^+$ calculated for $\text{C}_{19}\text{H}_{21}\text{NNaO}_2$ 318.1464, found 318.1468.

((1*R*, 4*aR*, 4*bR*, 10*aR*)-7-Isopropyl-1,4*a*-dimethyl-1,2,3,4,4*a*,4*b*,5,6,10,10*a*-decahydrophenanthren-1-yl)methyl 2-(cyanomethyl)benzoate (3az). Following General Procedure C: Colorless oil, 11.7 mg, 26% yield. ($R_f = 0.3$, petroleum ether/ethyl acetate = 20/1). ^1H NMR (600 MHz, CDCl_3) δ 8.04 (d, $J = 7.6$ Hz, 1H), 7.64–7.56 (m, 1H), 7.49–7.39 (m, 1H), 5.78 (s, 1H), 5.40 (d, $J = 2.4$ Hz, 1H), 4.29–4.14 (m, 2H), 4.05 (d, $J = 10.9$ Hz, 1H), 3.95 (d, $J = 10.9$ Hz, 1H), 2.24–2.20 (m, 1H), 2.15–2.01 (m, 4H), 1.90 (d, $J = 12.8$ Hz, 2H), 1.85–1.78 (m, 1H), 1.70–1.62 (m, 1H), 1.58–1.53 (m, 2H), 1.49–1.46 (m, 1H), 1.28–1.21 (m, 2H), 1.11–1.07 (m, 1H), 1.05 (s, 3H), 1.01 (dd, $J = 6.8$, 5.0 Hz, 6H), 0.86 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3) δ 166.3, 145.4, 135.4, 133.1, 132.2, 131.3, 130.1, 128.6, 128.4, 122.4, 120.6, 117.9, 73.8, 50.8, 44.9, 38.8, 36.8, 36.6, 34.9, 34.8, 27.5, 24.1, 23.2, 22.7, 21.4, 20.8, 18.1, 17.9, 14.2. HRMS-ESI (m/z) [$\text{M} + \text{H}$] $^+$ calculated for $\text{C}_{29}\text{H}_{38}\text{NO}_2$ 432.2824, found 432.2882.

Ethyl 2-(cyanomethyl)-5-methylbenzoate (3ba). Following General Procedure D: Colorless oil, 14.8 mg, 73% yield. ($R_f = 0.2$, petroleum ether/ethyl acetate = 20/1). ^1H NMR (600 MHz, CDCl_3) δ 7.87 (m, 1H), 7.42 (d, $J = 7.8$ Hz, 1H), ^1H NMR (600 MHz, CDCl_3) δ 7.42 (d, $J = 7.8$ Hz, 1H), 7.35 (dd, $J = 7.8$, 1.2 Hz, 1H), 4.37 (q, $J = 7.1$ Hz, 2H), 4.15 (s, 2H), 2.39 (s, 3H), 1.41 (t, $J = 7.1$ Hz, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3) δ 166.5, 138.3, 133.6, 132.0, 130.1, 128.9, 128.5, 118.2, 61.3, 22.7, 20.9, 14.3. HRMS-ESI (m/z) [$\text{M} + \text{Na}$] $^+$ calculated for $\text{C}_{12}\text{H}_{13}\text{NNaO}_2$ 226.0838, found 226.0833.

Ethyl 2-(cyanomethyl)-5-methoxybenzoate (3ca). Following General Procedure D: White solid, 16.9 mg, 77% yield. ($R_f = 0.2$, petroleum ether/ethyl acetate = 8/2). ^1H NMR (600 MHz, CDCl_3) δ 7.58 (d, $J = 2.8$ Hz, 1H), 7.43 (d, $J = 8.5$ Hz, 1H), 7.07 (dd, $J = 8.5$, 2.8 Hz, 1H), 4.39 (q, $J = 7.1$ Hz, 2H), 4.11 (s, 2H), 3.85 (s, 3H), 1.41 (t, $J = 7.1$ Hz, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3) δ 166.1, 159.2, 131.4, 129.8, 123.7, 118.4, 118.3, 116.8, 61.5, 55.6, 22.5, 14.2. HRMS-ESI (m/z) [$\text{M} + \text{Na}$] $^+$ calculated for $\text{C}_{12}\text{H}_{13}\text{NNaO}_3$ 242.0787, found 242.0784.

Ethyl 2-(cyanomethyl)-4,5-dimethoxybenzoate (3da). Following General Procedure D: White solid, 15.7 mg, 63% yield. ($R_f = 0.2$, petroleum ether/ethyl acetate = 8/2). ^1H NMR (600 MHz, CDCl_3) δ 7.57 (s, 1H), 6.98 (s, 1H), 4.37 (d, $J = 7.1$ Hz, 2H), 4.19 (s, 2H), 3.96 (s, 3H), 3.92 (s, 3H), 1.40 (t, $J = 7.1$ Hz, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3) δ 166.0, 152.5, 148.2, 126.0, 120.6, 118.3, 113.9, 112.6, 61.2, 56.2, 56.2, 23.0, 14.3. HRMS-ESI (m/z) [$\text{M} + \text{H}$] $^+$ calculated for $\text{C}_{13}\text{H}_{16}\text{NO}_4$ 250.1074, found 250.1075.

Ethyl 4-chloro-2-(cyanomethyl)benzoate (3ea). Following General Procedure D: White solid, 21.4 mg, 89% yield. ($R_f = 0.2$, petroleum ether/ethyl acetate = 20/1). ^1H NMR (600 MHz, CDCl_3) δ 8.02 (d, $J = 8.4$ Hz, 1H), 7.57 (d, $J = 2.0$ Hz, 1H), 7.40 (dd, $J = 8.4$, 2.0 Hz, 1H), 4.38 (q, $J = 7.1$ Hz, 2H), 4.21 (s, 2H), 1.40 (t, $J = 7.1$ Hz, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3) δ 165.5, 139.4, 133.9,

132.9, 130.3, 128.6, 127.0, 117.3, 61.7, 23.0, 14.2. HRMS-ESI (m/z) [$\text{M} + \text{Na}$] $^+$ calculated for $\text{C}_{11}\text{H}_{10}\text{ClNNaO}_2$ 246.0292, found 246.0300.

Ethyl 5-bromo-2-(cyanomethyl)benzoate (3fa). Following General Procedure D: White solid, 24.1 mg, 90% yield. ($R_f = 0.2$, petroleum ether/ethyl acetate = 20/1). ^1H NMR (600 MHz, CDCl_3) δ 8.19 (d, $J = 2.2$ Hz, 1H), 7.68 (dd, $J = 8.3$, 2.2 Hz, 1H), 7.44 (d, $J = 8.3$ Hz, 1H), 4.39 (q, $J = 7.1$ Hz, 2H), 4.16 (s, 2H), 1.41 (t, $J = 7.1$ Hz, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3) δ 165.0, 135.9, 134.4, 131.7, 131.0, 130.3, 122.2, 117.4, 61.9, 22.8, 14.2. HRMS-ESI (m/z) [$\text{M} + \text{Na}$] $^+$ calculated for $\text{C}_{11}\text{H}_{10}\text{BrNNaO}_2$ 289.9787, found 289.9789.

Ethyl 4-bromo-2-(cyanomethyl)benzoate (3ga). Following General Procedure D: Yellow solid, 20.1 mg, 75% yield. ($R_f = 0.2$, petroleum ether/ethyl acetate = 20/1). ^1H NMR (600 MHz, CDCl_3) δ 7.93 (d, $J = 8.4$ Hz, 1H), 7.72 (d, $J = 1.8$ Hz, 1H), 7.56 (dd, $J = 8.4$, 1.8 Hz, 1H), 4.37 (q, $J = 7.1$ Hz, 2H), 4.19 (s, 2H), 1.40 (t, $J = 7.1$ Hz, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3) δ 165.6, 133.9, 133.2, 132.9, 131.6, 127.8, 127.5, 117.3, 61.7, 22.9, 14.2. HRMS-ESI (m/z) [$\text{M} + \text{Na}$] $^+$ calculated for $\text{C}_{11}\text{H}_{10}\text{BrNNaO}_2$ 289.9787, found 289.9775.

Ethyl 3-bromo-2-(cyanomethyl)benzoate (3ha). Following General Procedure D: White solid, 21.7 mg, 81% yield. ($R_f = 0.2$, petroleum ether/ethyl acetate = 20/1). ^1H NMR (600 MHz, CDCl_3) δ 7.98 (dd, $J = 7.8$, 1.2 Hz, 1H), 7.80 (dd, $J = 8.0$, 1.2 Hz, 1H), 7.30 (t, $J = 7.9$ Hz, 1H), 4.42 (q, $J = 7.1$ Hz, 2H), 4.36 (s, 2H), 1.42 (t, $J = 7.1$ Hz, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3) δ 165.8, 137.1, 132.1, 131.4, 130.6, 129.7, 126.9, 116.7, 62.1, 22.5, 14.2. HRMS-ESI (m/z) [$\text{M} + \text{Na}$] $^+$ calculated for $\text{C}_{11}\text{H}_{10}\text{BrNNaO}_2$ 289.9787, found 289.9781.

Ethyl 2-(cyanomethyl)-3-(trifluoromethyl)benzoate (3ia). Following General Procedure D: White solid, 23.4 mg, 91% yield. ($R_f = 0.2$, petroleum ether/ethyl acetate = 20/1). ^1H NMR (600 MHz, CDCl_3) δ 8.22 (d, $J = 7.3$ Hz, 1H), 7.89 (d, $J = 7.9$ Hz, 1H), 7.57 (t, $J = 7.9$ Hz, 1H), 4.45 (q, $J = 7.1$ Hz, 2H), 4.26 (s, 2H), 1.44 (t, $J = 7.2$ Hz, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3) δ 165.6, 134.9, 132.3, 130.7 (q, $J = 30.2$ Hz), 130.4, 130.1 (q, $J = 5.7$ Hz), 128.8, 123.6 (q, $J = 27.4$ Hz), 116.9, 62.3, 18.6 (q, $J = 2.6$ Hz), 14.1. HRMS-ESI (m/z) [$\text{M} + \text{Na}$] $^+$ calculated for $\text{C}_{12}\text{H}_{10}\text{F}_3\text{NNaO}_2$ 280.0556, found 280.0547.

Ethyl 3-cyano-2-(cyanomethyl)benzoate (3ja). Following General Procedure D: Colorless oil, 12.6 mg, 59% yield. ($R_f = 0.4$, petroleum ether/ethyl acetate = 8/2). ^1H NMR (600 MHz, CDCl_3) δ 8.30 (dd, $J = 8.0$, 1.4 Hz, 1H), 7.88 (dd, $J = 7.8$, 1.4 Hz, 1H), 7.59 (t, $J = 7.9$ Hz, 1H), 4.46 (q, $J = 7.1$ Hz, 2H), 4.39 (s, 2H), 1.44 (t, $J = 7.2$ Hz, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3) δ 164.8, 136.7, 135.7, 135.3, 131.2, 129.4, 116.2, 115.9, 115.5, 62.5, 21.2, 14.1. HRMS-ESI (m/z) [$\text{M} + \text{Na}$] $^+$ calculated for $\text{C}_{12}\text{H}_{10}\text{N}_2\text{NaO}_2$ 237.0634, found 237.0629.

Ethyl 2-(cyanomethyl)-4-(((3*R*,5*S*,8*R*,9*S*,10*S*,13*R*,14*S*,17*R*)-10,13-dimethyl-17-((*R*)-6-methylheptan-2-yl)hexadecahydro-ro-1*H*-cyclopenta[*a*]phenanthren-3-yl)oxy)benzoate (3ka). Following General Procedure D: White solid, 23.6 mg, 41% yield. ($R_f = 0.2$, petroleum ether/ethyl acetate = 20/1). ^1H NMR (600 MHz, CDCl_3) δ 8.05 (d, $J = 8.8$ Hz, 1H), 7.09 (d, $J = 2.2$ Hz, 1H), 6.88 (dd, $J = 8.8$, 2.2 Hz, 1H), 4.67 (s, 1H), 4.36 (q, $J = 7.1$ Hz, 2H), 4.24 (s, 2H), 1.99 (d, $J = 12.6$ Hz, 1H), 1.91 (d, $J = 14.4$ Hz, 1H), 1.87–1.80 (m, 1H), 1.77–1.49 (m, 11H), 1.41 (d, $J = 7.1$ Hz, 3H), 1.36 (m, 3H), 1.31–1.09 (m, 10H), 1.02 (dt, $J = 18.3$, 10.6 Hz, 4H), 0.92 (d, $J = 6.5$ Hz, 3H), 0.88 (dd, $J = 6.6$, 2.8 Hz, 6H), 0.85 (s, 3H), 0.68 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3) δ 166.1, 161.5, 134.4, 133.8, 119.9, 118.1, 117.6, 114.2, 72.7, 60.9, 56.5, 56.3, 54.1, 42.6, 40.0, 39.6, 39.5, 36.2, 35.84, 35.78, 35.5, 32.6, 32.5, 31.9, 28.4, 28.3, 28.0, 25.6, 24.2, 23.9, 23.5, 22.8, 22.6, 20.8, 18.7, 14.3, 12.1, 11.4. HRMS-ESI (m/z) [$\text{M} + \text{Na}$] $^+$ calculated for $\text{C}_{38}\text{H}_{57}\text{NNaO}_3$ 598.4231, found 598.4240.

Ethyl 2-(2-cyanopropan-2-yl)benzoate (3la). Following General Procedure D: Colorless oil, 18.4 mg, 85% yield. ($R_f = 0.2$, petroleum ether/ethyl acetate = 20/1). ^1H NMR (600 MHz, CDCl_3) δ 7.62 (d, $J = 7.6$ Hz, 1H), 7.47 (m, 2H), 7.40–7.31 (m, 1H), 4.43 (q, $J = 7.2$ Hz, 2H), 1.87 (s, 6H), 1.41 (t, $J = 7.2$ Hz, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3) δ 169.0, 139.4, 132.2, 131.3, 130.4, 127.8, 125.8, 124.3, 61.9, 36.6, 29.3, 14.1. HRMS-ESI (m/z) [$\text{M} + \text{Na}$] $^+$ calculated for $\text{C}_{13}\text{H}_{15}\text{NNaO}_2$ 240.0995, found 240.0994.

Ethyl 2-(3-cyanopropyl)benzoate (3ma). Following General Procedure D: Colorless oil, 13.4 mg, 62% yield. ($R_f = 0.2$, petroleum ether/ethyl acetate = 20/1). $^1\text{H NMR}$ (600 MHz, CDCl_3) δ 7.93 (d, $J = 7.7$ Hz, 1H), 7.45 (td, $J = 7.5, 1.0$ Hz, 1H), 7.30 (t, $J = 7.6$ Hz, 1H), 7.26 (d, $J = 7.6$ Hz, 1H), 4.36 (q, $J = 7.1$ Hz, 2H), 3.21–2.91 (m, 2H), 2.38 (t, $J = 7.2$ Hz, 2H), 2.01 (dd, $J = 15.0, 7.4$ Hz, 2H), 1.40 (t, $J = 7.1$ Hz, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3) δ 167.3, 141.9, 132.2, 131.2, 131.1, 129.7, 126.6, 119.7, 61.0, 33.4, 27.2, 16.9, 14.3. HRMS-ESI (m/z) $[\text{M} + \text{Na}]^+$ calculated for $\text{C}_{13}\text{H}_{15}\text{NNaO}_2$ 240.0995, found 240.0992.

Scale-Up Reaction. Diethylamine (8.0 mmol, 2.0 equiv) was added to a solution of oxime ester **1a** (4.0 mmol, 1.0 equiv) in ethanol (40 mL, 0.1 M) at room temperature. After 28 h, TLC indicated complete conversion of the starting material and the solvent was removed with a rotary evaporator. The pure product (**3aa** 0.67 g, 88%) was obtained by flash chromatography on silica gel using petroleum ether and ethyl acetate as the eluent.

Electrochemical Conditions. In an oven-dried undivided three-necked flask (25 mL) equipped with a stir bar, **1a** (0.3 mmol, 100 mg, 1.0 equiv), KI (50.0 mg, 1.0 equiv), ethanol (8.0 mL) were added. The flask was equipped with graphite electrodes (1.0 cm \times 1.0 cm \times 0.2 cm) as both the anode and cathode. The reaction mixture was stirred and electrolyzed at a constant current of 10 mA under room temperature for 8 h. TLC indicated complete conversion of the starting material and the solvent was removed with a rotary evaporator. The pure product (**3aa** 44.3 mg, 78%) was obtained by flash chromatography on silica gel using petroleum ether and ethyl acetate as the eluent.

In an oven-dried undivided three-necked flask (25 mL) equipped with a stir bar, **1a** (0.3 mmol, 100 mg, 1.0 equiv), KI (50.0 mg, 1.0 equiv), methanol (8.0 mL) were added. The flask was equipped with graphite electrodes (1.0 cm \times 1.0 cm \times 0.2 cm) as both the anode and cathode. The reaction mixture was stirred and electrolyzed at a constant current of 10 mA under room temperature for 8 h. TLC indicated complete conversion of the starting material and the solvent was removed with a rotary evaporator. The pure product (**3ab** 26.8 mg, 51%) was obtained by flash chromatography on silica gel using petroleum ether and ethyl acetate as the eluent.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at <https://pubs.acs.org/doi/10.1021/acs.joc.1c01131>.

^1H NMR and ^{13}C NMR spectra of all compounds (PDF)

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Notes

The authors declare no competing financial interest.

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