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ARTICLE

$AlCl_3$ Catalyzed Coupling of N-benzylic Sulfonamides with 2-Substituted Cyanoacetates through Carbon-Nitrogen Bond Cleavage

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A new cross-coupling reaction of *N*-benzylic sulfonamides with 2-substituted cyanoacetates for the synthesis of 2-substituted benzylbenzene was reported. In the presence of the $AlCl_3$, a broad range of *N*-benzylic sulfonamides reacted smoothly with 2-substituted cyanoacetates to afford structurally diverse benzylbenzenes in moderate to excellent yields. The conversion could be enlarged to gram-scale efficiently. The practicability of this approach was further manifested in the synthesis of a related bioactive agent with high anti-inflammatory activity.

Introduction

The functionalized nitrile derivatives represent an important class of precursors to amines, carboxylic acids, ketones and even heterocycles.[1] Compounds containing nitrile group, which are frequently employed as building blocks in drug discovery programs, play significant roles in biological activities.[2] Due to its adequate possibility of derivatization, nitriles often appear as key intermediates in total synthesis.[3] Till now, over 50 nitriles-containing agents have been reported in the previous work.[4] For example, Zeneca,[5] Arensin,[6] Milrinone,[7] are widely prescribed for the treatment of the prostate cancer, human aromatase inhibitors, and myocardial infarction, respectively. Cilomilast, a well-studied nitriles-containing anti-inflammatory agent, has been widely prescribed for the treatment of the inflammatory component of diseases (Figure 1).[8]

The cleavage of carbon-nitrogen bond or carbon-oxygen bond under acidic conditions was broadly applied to the formation of carbon-carbon bond in organic synthesis.[9] Owning to the leaving ability of amino groups,[10] sulfonyl-activated primary benzylic amines (*N*-benzylic sulfonamides) can generate benzylic cation with primary sulfonamides as byproducts.[11] For example, the [3+2] cyclization of sulfonyl-activated benzylic amines with disubstituted alkynes to generate indene derivatives was developed by Tian and his co-workers in the presence of a Fe catalyst (Scheme 1, a).[9] Meanwhile, they

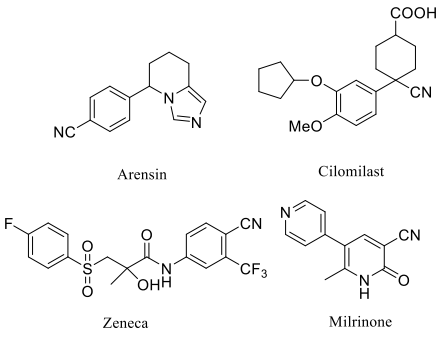

Figure 1 Selected examples of pharmaceutical agent containing nitriles

accomplished a catalyst-free alkylation of sulfonic acids with sulfonamides (Scheme 1, b).[12] In 2016, our group developed transition metal-free direct arylation of 2-substituted cyanoacetates with diaryliodonium salts (Scheme 1, c).[4b] We reasoned that 2-substituted cyanoacetates could also react with sulfonamides to afford structurally diverse nitrile containing benzylbenzene. Herein, we reported Lewis-acid catalyzed 2-subsituted cyanoacetates coupling of sulfonamides *via* sp^3 carbon-nitrogen bond cleavage. And its application to the simple synthesis of substituted 2-cyanopropanoic amide, which are useful for the treatment of inflammatory component of diseases.[2a]

Results and discussion

Our initial investigation began by employing the ethyl 2-cyanopropanoate **1a** (0.25 mmol) with *N*-benzhydryl-4-methybenznesulfonamide **2a** (0.3 mmol) as the model substrates to optimize the reaction condition. To our delight, the expected product **3a** was isolated with 52% yield in presence of $AlCl_3$ (10 mol %) in the 1,2-dichloroethane (1,2-DCE) at 80 °C for 12 h (Table

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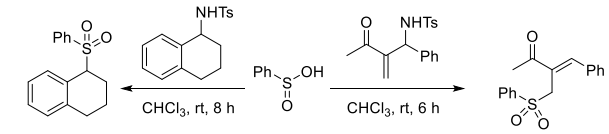
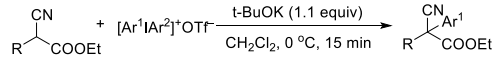
a.Reaction of indene complexes derived from N-benzylic sulfonamides with alkynes.

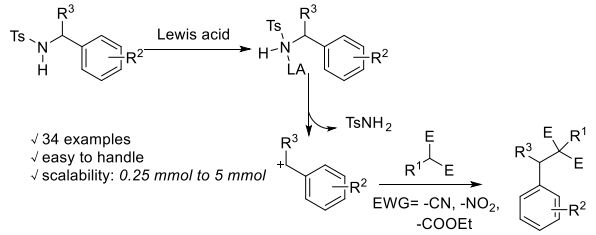
b.Reaction of alkylation of sulfinic acids with sulfonamides.



c.Our previous work: Arylation of 2-substituted cyanoacetates with diaryliodonium salts



d. This work.

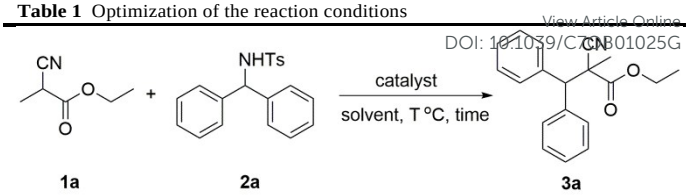


Scheme 1 Summary of previous studies toward sulfonamides and our previous work

1, entry 1). Rare earth perfluorooctanoates [$Sc(OPF)_3$] and pentafluorobenzoates [$La(Pfb)_3$] that developed by our group were also applied to catalyze the reaction. After a comprehensive screening, we found that $AlCl_3$ was superior to other rare-earth metal catalysis, such as $Yb(OTf)_3$, $Sc(OTf)_3$, $La(Pfb)_3$ and $Sc(OPF)_3$ (Table 1, entries 2-5). It was found that a range of different Lewis acids such as $BF_3{\cdot}OEt_2$, $FeCl_3$ and $TsOH{\cdot}H_2O$ also worked in this reaction system, and gave product **3a** in 35-49% yield (Table 1, entries 6-8). Then the amount of $AlCl_3$ was screened. The yield was increased to 68% by increasing the catalyst loading to 100 mol % (Table 1, entries 9 and 10). When screening solvents, we cannot gain the desired products in CH_3CN and 1,4 –dioxane (Table 1, entries 11 and 12). Meanwhile, efforts to enhance yield by replacing $CHCl_3$ with other solvents such as DMSO, EtOH, H_2O and DCM (Table 1, entries 13-16) proved that the yield gradually decreased, while $CHCl_3$ had positive effect on the reaction affording the product in 90% yield (Table 1, entry 17). Subsequently, the investigation on the effect of temperature showed that this transformation was most efficiently when conducted at 80 °C (Table 1, entries 17-19). Shortening the reaction time led to the decrease of the yield (Table 1, entries 20-21). A slightly decrease in the yield was observed when the reaction was conducted under argon (Table 1, entry 22). So the optimal conditions were determined to be **1a** (0.25 mmol) and *N*-benzhydryl-4-methybenznesulfonamide **2a** (0.30 mmol) in the presence of $AlCl_3$ (100 mol %) in $CHCl_3$ (1 mL) at 80 °C for 12 h.

With the optimal reaction conditions in hand, the scope of this transformation was then explored by employing a variety of 2-substituted cyanoacetates **1** to react with **2** (Table 2).

Table 1 Optimization of the reaction conditions



1a **2a** **3a**

Entry[a]	Catalyst (mol %)	Solvent	T (°C)	time (h)	Yield (%)[b]
1	$AlCl_3$ (10)	1,2-DCE	80	12	52
2	$Yb(OTf)_3$ (10)	1,2-DCE	80	12	21
3	$Sc(OTf)_3$ (10)	1,2-DCE	80	12	37
4	$Sc(OPF)_3$ (10)	1,2-DCE	80	12	31
5	$La(Pfb)_3$ (10)	1,2-DCE	80	12	26
6	$BF_3{\cdot}OEt_2$ (10)	1,2-DCE	80	12	40
7	$FeCl_3$ (10)	1,2-DCE	80	12	49
8	$TsOH{\cdot}H_2O$ (10)	1,2-DCE	80	12	35
9[c]	$AlCl_3$ (20\50\70)	1,2-DCE	80	12	53\58\62
10	$AlCl_3$ (100\130)	1,2-DCE	80	12	68\65
11	$AlCl_3$ (100)	CH_3CN	80	12	trace
12	$AlCl_3$ (100)	1,4-dioxane	80	12	trace
13	$AlCl_3$ (100)	DMSO	80	12	64
14	$AlCl_3$ (100)	DCM	80	12	65
15	$AlCl_3$ (100)	EtOH	80	12	0
16	$AlCl_3$ (100)	H_2O	80	12	0
17	$AlCl_3$ (100)	$CHCl_3$	80	12	90
18	$AlCl_3$ (100)	$CHCl_3$	60	12	81
19	$AlCl_3$ (100)	$CHCl_3$	100	12	88
20	$AlCl_3$ (100)	$CHCl_3$	80	4	82
21	$AlCl_3$ (100)	$CHCl_3$	80	8	87
22[d]	$AlCl_3$ (100)	$CHCl_3$	80	12	88

[a] Reaction conditions: **1a** (0.25 mmol), **2a** (0.3 mmol), Lewis acid (x mol %), and solvent (1 mL), at 80 °C. [b] Isolated yield. [c] x mol % of $AlCl_3$. [d] Under argon.

Substrates **1** containing alkyl group were efficiently coupled with *N*-benzhydryl-4-methybenznesulfonamide **2a**, furnishing the corresponding products **3b**-**3g** in moderate yields of 57-86%. Among them, when R^1 is fluoroalkyl or allyl, **3f** and **3e** can be furnished in 60% and 57% yield, respectively. Moreover, substrates with benzyl and aromatic rings underwent coupling reaction to give the corresponding products in generally good yields of 70-84% (**3j**-**3p**). Moreover, H-substituted cyanoacetate **1q** was suitable substrate for this protocol and generated anticipated product in 70% yield (**3q**). Cyclic alkyl substituded cyanoacetates **1h** and **1i** could not afford the desired product (**3h** and **3i**).

Next, the reactions of variously substituted *N*-benzylic sulfonamides with **1a** were examined and the results were listed in Table 2. For substrates bearing either electron-rich (Me) or electron-deficient (F, Cl, Br) substituents on the benzene rings of symmetrical *N*-benzylic sulfonamides, the coupling reactions performed well and gave desired products with the yields ranging from 84% to 93% (**3r**, **3s**, **3t**).

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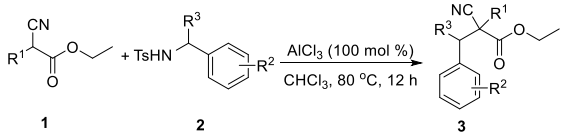
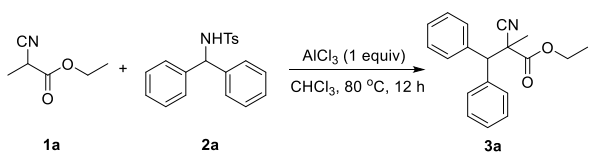
Table 2 Coupling reactions of 2-substituted cyanoacetates **1** with **2**



1 2 3

Entry[a]	R^1	R^2	R^3	3	Yield (%)[b]
1	$CH_2CH_2CH_2CH_3$	H	C_6H_5	**3b**	86
2	$CH_2CH_2CH_2Cl$	H	C_6H_5	**3c**	72
3	$CH(CH_3)_2$	H	C_6H_5	**3d**	80
4	$CH_2CH=CH_2$	H	C_6H_5	**3e**	57
5	$CH_2CH_2(CF_2)_2CF_3$	H	C_6H_5	**3f**	60
6	CH_2CH_3	H	C_6H_5	**3g**	62
7	cyclohexyl	H	C_6H_5	**3h**	0
8	cyclopentane	H	C_6H_5	**3i**	0
9	$C_6H_5CH_2$	H	C_6H_5	**3j**	70
10	4-$BrC_6H_4CH_2$	H	C_6H_5	**3k**	84
11	4-$FC_6H_4CH_2$	H	C_6H_5	**3l**	81
12	4-$MeC_6H_4CH_2$	H	C_6H_5	**3m**	79
13	4-BrC_6H_4	H	C_6H_5	**3n**	72
14	4-MeC_6H_4	H	C_6H_5	**3o**	77
15	C_6H_5	H	C_6H_5	**3p**	75
16	H	H	C_6H_5	**3q**	70
17	CH_3	4-F	4-FC_6H_4	**3r**	93
18	CH_3	4-Br	4-BrC_6H_4	**3s**	85
19	CH_3	4-Me	4-MeC_6H_4	**3t**	84
20	CH_3	4-Me	naphthyl	**3u**	72
21	CH_3	4-Me	C_6H_5	**3v**	85
22	CH_3	4-F	C_6H_5	**3w**	87
23	CH_3	4-Br	C_6H_5	**3x**	78
24	CH_3	4-Cl	C_6H_5	**3y**	79
25	CH_3	H	naphthyl	**3z**	46
26	CH_3	H	2,4,6-$triMeC_6H_2$	**3aa**	40
27	CH_3	H	thienyl	**3ab**	trace
28	CH_3	4-Br	CH_3	**3ac**	trace

[a]Reaction conditions: **1a** (0.25 mmol), **2** (0.3 mmol), $AlCl_3$ (100 mol %) and $CHCl_3$ (1 mL) at 80 °C for indicated time. [b]Isolated yields.



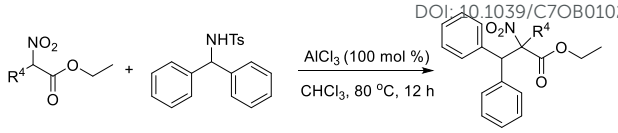
1a 2a 3a

1a=635.70 mg, 5 mmol, **2a**=2.02 g, 6 mmol
3a= 1.17 g, 81% yield

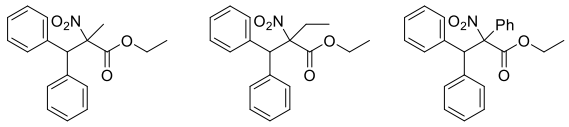
Scheme 2 Synthesis of **3a** on gram-scale

Meanwhile, reactions of unsymmetrical *N*-benzylic sulfonamides also proceeded smoothly, leading to the efficient generation of the corresponding products in 40-87% yields (**3u**, **3v**, **3w**, **3x**, **3y**, **3z**, **3aa**). However, heteroaryl-substituted and alkyl-substituted sulfonamides were not effective under the reaction conditions (**3ab**, **3ac**).

Table 3 Coupling reactions of nitro esters with **2a**



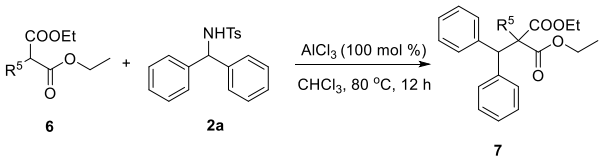
4 2a 5



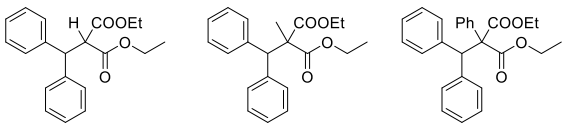
5a, 56% **5b**, 48% **5c**, 53%

[a]Reaction conditions: **4** (0.25 mmol), **2a** (0.3 mmol), $AlCl_3$ (100 mol %), and $CHCl_3$ (1 mL), at 80 °C. [b]Isolated yield.

Table 4 Coupling reactions of diethyl malonates with **2a**



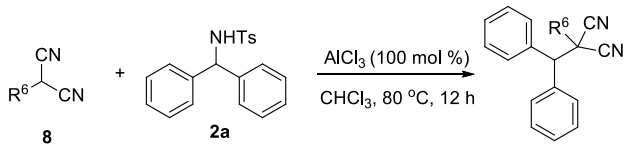
6 2a 7



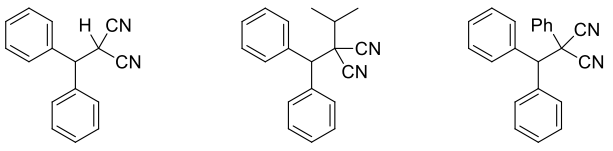
7a, 60% **7b**, trace **7c**, 25%

[a]Reaction conditions: **6** (0.25 mmol), **2a** (0.3 mmol), $AlCl_3$ (100 mol %), and $CHCl_3$ (1 mL), at 80 °C. [b]Isolated yield.

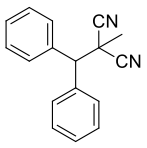
Table 5 Coupling reactions of malononitriles with **2a**



8 2a 9

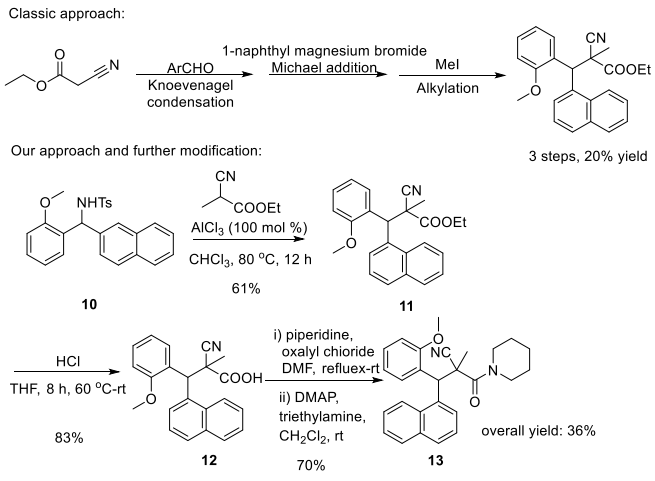


9a, 83% **9b**, 52% **9c**, 71%



9d, 94%

[a]Reaction conditions: **8** (0.25 mmol), **2a** (0.3 mmol), $AlCl_3$ (100 mol %), and $CHCl_3$ (1 mL), at 80 °C. [b]Isolated yield.



Scheme 3 Application to the improved synthesis of anti-inflammatory agent **13**

To test whether the reaction was amenable to scale-up, we attempted the reaction using 5 mmol of 2-cyanopropanoate (**1a**) and 6 mmol of *N*-benzhydryl-4-methybenznesulfonamide (**2a**) (Scheme 2). Gratifyingly, the coupling reaction gave the corresponding product in 81% yield.

Subsequently, 2-nitroesters **4** were reacted with **2a** under standard conditions to test the efficiency of this methodology (Table 3).[13] Both alkyl and aryl substituted nitroester derivatives can proceed smoothly affording the corresponding products in 48%-56% yields (**5a**, **5b**, **5c**). Meanwhile, the malononitriles and diethyl malonates were also tested under the standard conditions. The reactions of H and aryl substituted diethyl malonate were also found to be compatible with the reaction and led to the expected products in 60% and 25% yields (**7a**, **7c**) (Table 4). Unfortunately, the methyl-substituted diethyl malonate could not progress well under the optimal conditions (Table 4, **7b**). Malononitriles bearing alkyl and aryl substituents were well implemented to form the desired products (**9a**, **9b**, **9c, 9d**) in 52%-94% yield (Table 5).

Further, to demonstrate the utility of this mothod for the synthesis of medicinally relavant molecules, we targeted a common intermediate route to the agent **13** with high anti-inflammatory activity (Scheme 3). The reported routes to compound **11** involved a three-step sequence from benzaldehyde derivatives.[2a] The highest yielding route reported occurs in only 20% yield over three steps. By employing the mothod reported here with N-benzylic sulfonamides derivative **10**, the target molecular **11** was formed in 61% yield. This short synthesis was further highlighted by its modification to the final compound **13** in 36% overall yield.

Conclusions

In conclusion, we have demonstrated an efficient coupling reaction of *N*-benzylic sulfonamides with 2-substituted cyanoacetates in the present of $AlCl_3$. The newly developed protocol features good functional group tolerance, mild reaction conditions. More importantly, the synthetic utility has been demonstrated by an improved route to the intermediate by an anti-inflammatory agent. Considering the valuable nitrile containing structure, further extension of this process for the synthesis of structurally diverse nitrile containing compounds is in progress.

Experimental section

General Information

^{1}H NMR , ^{13}C NMR and ^{19}F NMR spectra were recorded at 400 MHz , 100 MHz and 376 MHz respectively using tetramethylsilane as an internal reference. Chemical shifts (δ) and coupling constants (J) were expressed in parts per million and hertz, respectively. High-resolution mass spectrometry (HRMS) was performed on an ESI-TOF spectrometer. Chemicals were commercially available and used without purification. Chromatography: Column chromatography was performed with silica gel (200-300 mesh ASTM). Sulfonamides compound substrates were prepared according to the literature procedure.[14] Substituted cyanoacetates,[15] 2-nitroesters,[16] diethyl malonate[17] and malononitrile[18] were synthesized according to the reported procedure, respectively.

Typical procedure for N-benzylic sulfonamides with 2-substituted cyanoacetates

2-subsituted cyanoacetates (0.25 mmol, 1 equiv), N-benzylic sulfonamides (0.3 mmol, 1.2 equiv), $AlCl_3$ (100 mol %), dry $CHCl_3$ (1 mL) and a stir bar were added to a sealed tube. After being stirred at 80 °C for indicated time, the mixture was evaporated under vacuum. The corresponding product was isolated by silica gel column chromatography with a dichloromethane/petroleum ether mixture as eluent.

Ethyl 2-cyano-2-methyl-3,3-diphenylpropanoate (3a)

Yellow oil, 90% yield. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.58–7.52 (m, 2H), 7.51–7.46 (m, 2H), 7.41–7.26 (m, 6H), 4.51 (s, 1H), 4.03 (q, J = 7.1 Hz, 2H), 1.55 (s, 3H), 0.93 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 168.5, 139.5, 138.0, 129.5, 128.5, 128.4, 128.0, 127.7, 127.4, 119.8, 62.4, 55.8, 48.3, 23.8, 13.4. HRMS (ESI-TOF) m/z: [M + Na]$^+$ Calcd for $C_{19}H_{19}NO_2Na$ 316.1313; Found 316.1310.

Ethyl 2-benzhydryl-2-cyanohexanoate (3b)

Colorless oil, 86% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58–7.58 (m, 4H), 7.38–7.26 (m, 5H), 7.25–7.21 (m, 1H), 4.34 (s, 1H), 4.06 (q, J = 7.1 Hz, 2H), 1.98–1.90 (m, 1H), 1.77–1.67 (m, 1H), 1.30–1.16 (m, 4H), 1.02 (t, J = 7.1 Hz, 3H), 0.85 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.8, 139.3, 138.2, 129.6, 128.8, 128.6, 128.5, 127.8, 127.5, 119.3, 62.7, 57.7, 54.6, 37.6, 27.5, 22.4, 13.8, 13.7. HRMS (ESI-TOF) m/z: [M + Na]$^+$ Calcd for $C_{22}H_{25}NO_2Na$ 358.1783; Found 358.1782.

Ethyl 2-benzhydryl-4-chloro-2-cyanobutanoate (3c)

Yellow oil, 72% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59–7.49 (m, 4H), 7.39–7.26 (m, 5H), 7.26–7.20 (m, 1H), 4.36 (s, 1H), 4.07 (q, J = 7.1 Hz, 2H), 3.51 (m, 1H), 3.42 (m, 1H), 2.22–2.13 (m, 1H), 2.11–2.01 (m, 1H), 1.84 (q, J = 3.3 Hz, 1H), 1.77–1.63 (m, 1H), 1.02 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.3, 139.0, 137.8, 129.5, 128.9, 128.7, 128.5, 128.0, 127.7, 118.9, 63.0, 57.7, 54.2, 43.7, 35.1, 28.5, 13.7. HRMS (ESI-TOF) m/z: [M + Na]$^+$ Calcd for $C_{21}H_{22}ClNO_2Na$ 378.1237; Found 378.1241.

Ethyl 2-benzhydryl-2-cyano-3-methylbutanoate (3d)

Colorless oil, 80% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67–7.58 (m, 2H), 7.54–7.49 (m, 2H), 7.38–7.26 (m, 5H), 7.25–7.16 (m, 1H), 4.62 (s, 1H), 4.12–4.02 (m, 2H), 2.29–2.21 (m, 1H), 1.13–1.03 (m, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.1, 139.6, 138.5, 129.3, 129.0, 128.8, 128.6, 127.6, 127.4, 119.9, 62.8, 58.6, 54.1, 34.5, 19.5, 17.2, 13.9. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{21}H_{23}NO_2Na$ 344.1626; Found 344.1624.

Ethyl 2-benzhydryl-2-cyanopent-4-enoate (3e)

Colorless oil, 57% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58–7.51 (m, 4H), 7.39–7.27 (m, 5H), 7.25–7.20 (m, 1H), 5.84–5.69 (m, 1H), 5.20–5.13 (m, 2H), 4.39 (s, 1H), 4.05 (q, *J* = 7.1 Hz, 2H), 2.70–2.62 (m, 1H), 2.51–2.44 (m, 1H), 1.03 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.1, 139.1, 137.9, 130.5, 129.6, 128.9, 128.7, 128.5, 128.0, 127.6, 120.9, 118.8, 62.7, 57.2, 54.5, 42.1, 13.8. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{21}H_{21}NO_2Na$ 342.1470; Found 342.1469.

Ethyl 2-benzhydryl-2-cyano-5,5,6,6,7,7,8,8,8-nonafluorooctanoate (3f)

White solid, 60% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59–7.50 (m, 4H), 7.40–7.35 (m, 2H), 7.34–7.29 (m, 3H), 7.27–7.23 (m, 1H), 4.37 (s, 1H), 4.08 (q, *J* = 7.2 Hz, 2H), 2.44–2.23 (m, 2H), 2.12–1.94 (m, 2H), 1.01 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.8, 138.6, 137.3, 129.3, 129.1, 128.8, 128.5, 128.3, 127.9, 118.1, 63.3, 57.7, 53.7, 28.5, 27.2, 13.3; ^{19}F NMR (376 MHz, $CDCl_3$) δ -75.14–-84.48 (m, 3F), -114.53 (t, *J* = 13.6 Hz, 2F), -124.27 (d, *J* = 10.2 Hz, 2F), -126.07–-126.15 (m, 2F). HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{24}H_{20}F_9NO_2Na$ 548.1248; Found 548.1243.

Ethyl 2-benzhydryl-2-cyanobutanoate (3g)

Colorless oil, 62% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57–7.50 (m, 4H), 7.36–7.27 (m, 5H), 7.25–7.20 (m, 1H), 4.35 (s, 1H), 4.07 (q, *J* = 7.1 Hz, 2H), 2.04–1.95 (m, 1H), 1.84–1.74 (m, 1H), 1.03 (q, *J* = 7.3 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.7, 139.4, 138.2, 129.6, 128.8, 128.6, 128.5, 127.8, 127.5, 119.1, 62.7, 57.6, 55.5, 31.5, 13.8, 9.7. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{20}H_{21}NO_2Na$ 330.1470; Found 330.1453.

Ethyl 2-benzyl-2-cyano-3,3-diphenylpropanoate (3j)

Colorless oil, 70% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69–7.61 (m, 2H), 7.59–7.51 (m, 2H), 7.44–7.37 (m, 2H), 7.36–7.25 (m, 5H), 7.25–7.18 (m, 4H), 4.56 (s, 1H), 3.97–3.72 (m, 2H), 3.21 (d, *J* = 13.3 Hz, 1H), 2.97 (d, *J* = 13.3 Hz, 1H), 0.82 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.0, 139.1, 138.0, 134.0, 130.0, 129.7, 129.0, 128.7, 128.6, 128.5, 128.0, 127.8, 127.6, 118.8, 62.6, 57.9, 56.4, 43.7, 13.5. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{25}H_{23}NO_2Na$ 392.1626; Found 392.1625.

Ethyl 2-(4-bromobenzyl)-2-cyano-3,3-diphenylpropanoate (3k)

Yellow oil, 84% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67–7.62 (m, 2H), 7.57–7.52 (m, 2H), 7.43–7.37 (m, 4H), 7.35–7.27 (m, 3H), 7.25–7.20 (m, 1H), 7.10–7.05 (m, 2H), 4.52 (s, 1H), 4.01–3.78 (m, 2H), 3.18 (d, *J* = 13.4 Hz, 1H), 2.91 (d, *J* = 13.4 Hz, 1H), 0.84 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.9, 138.8, 137.8, 133.1, 131.7, 131.6, 129.7, 129.0, 128.7, 128.6, 128.2, 127.7, 122.1, 118.6, 62.8, 58.0, 56.2, 42.9, 13.5. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{25}H_{22}BrNO_2Na$ 470.0732; Found 470.0722.

Ethyl 2-cyano-2-(4-fluorobenzyl)-3,3-diphenylpropanoate (3l)

White solid, 81% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65–7.63 (m, 2H), 7.58–7.55 (m, 2H), 7.43–7.40 (m, 2H), 7.36–7.27 (m, 3H), 7.25–7.14 (m, 3H), 6.99–6.91 (m, 2H), 4.53 (s, 1H), 3.96–3.78 (m, 2H), 3.20 (d, *J* = 13.5 Hz, 1H), 2.94 (d, *J* = 13.6 Hz, 1H), 0.84 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.0, 163.7, 161.3, 138.9, 137.9, 131.7, 131.6, 129.7, 129.0, 128.7, 128.6, 128.1, 127.7, 118.8, 115.5, 115.3, 62.7, 57.9, 56.4, 42.8, 13.5, ^{19}F NMR (376 MHz, $CDCl_3$) δ -114.47. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{25}H_{22}FNO_2Na$ 410.1532; Found 410.1529.

Ethyl 2-cyano-2-(4-methylbenzyl)-3,3-diphenylpropanoate (3m)

Yellow solid, 79% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69–7.62 (m, 2H), 7.58–7.52 (m, 2H), 7.41-7.35 (m, 2H), 7.33–7.26 (m, 3H), 7.24–7.18 (m, 1H), 7.10–7.03 (m, 4H), 4.54 (s, 1H), 4.02–3.70 (m, 2H), 3.19 (d, *J* = 13.4 Hz, 1H), 2.93 (d, *J* = 13.4 Hz, 1H), 2.29 (s, 3H), 0.83 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.1, 139.2, 138.1, 137.5, 130.9, 129.8, 129.7, 129.2, 129.0, 128.7, 128.6, 128.0, 127.6, 118.9, 62.6, 57.9, 56.5, 43.3, 21.2, 13.5. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{26}H_{25}NO_2Na$ 406.1783; Found 406.1790.

Ethyl 2-(4-bromophenyl)-2-cyano-3,3-diphenylpropanoate (3n)

White oil, 72% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60–7.53 (m, 2H), 7.50–7.39 (m, 4H), 7.38–7.26 (m, 3H), 7.15–7.05 (m, 5H), 5.03 (s, 1H), 4.25–3.97 (m, 2H), 1.10 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.8, 139.2, 137.4, 132.7, 132.0, 129.6, 128.8, 128.7, 128.3, 127.7, 127.4, 123.3, 117.9, 63.6, 59.0, 58.0, 53.5, 29.7, 13.7. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{24}H_{20}BrNO_2Na$ 456.0575; Found 456.0574.

Ethyl 2-cyano-3,3-diphenyl-2-(p-tolyl)propanoate (3o)

Yellow solid, 77% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62–7.54 (m, 2H), 7.50–7.43 (m, 2H), 7.36–7.30 (m, 2H), 7.25–7.23 (m, 1H), 7.14–7.04 (m, 7H), 5.08 (s, 1H), 4.20–3.99 (m, 2H), 2.29 (s, 3H), 1.08 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.3, 139.8, 138.8, 137.9, 130.5, 129.7, 129.5, 128.9, 128.6, 128.1, 127.5, 127.1, 127.0, 118.4, 68.0, 63.3, 59.1, 57.8, 25.6, 21.0, 13.7. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{25}H_{23}NO_2Na$ 392.1626; Found 392.1613.

Ethyl 2-cyano-2,3,3-triphenylpropanoate (3p)

White solid, 75% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55–7.47 (m, 4H), 7.32–7.24 (m, 2H), 7.23–7.16 (m, 4H), 7.04–6.93 (m, 5H), 5.01 (s, 1H), 4.22–3.88 (m, 2H), 1.02 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.1, 139.7, 137.7, 133.5, 129.8, 129.7, 128.9, 128.8, 128.6, 128.4, 128.1, 127.5, 127.2, 127.1, 126.5, 118.3, 63.4, 59.4, 58.1, 13.7. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{24}H_{21}NO_2Na$ 378.1470; Found 378.1463.

Ethyl 2-cyano-3,3-diphenylpropanoate (3q)

Colorless oil, 70% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38–7.28 (m, 8H), 7.27–7.21 (m, 2H), 4.73 (d, *J* = 8.5 Hz, 1H), 4.23 (d, *J* = 8.7 Hz, 1H), 4.13–4.03 (m, 2H), 1.07 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.1, 139.4, 138.8, 128.9, 128.8, 128.3, 127.9, 127.8, 127.7, 115.9, 62.9, 51.1, 43.6, 13.8. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{18}H_{17}NNaO_2$ 302.1157; Found 302.1153.

Ethyl 2-cyano-3,3-bis(4-fluorophenyl)-2-methylpropanoate (3r)

Colorless oil, 93% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52–7.44 (m, 4H), 7.10–6.96 (m, 4H), 4.35 (s, 1H), 4.11 (q, *J* = 7.1 Hz, 2H), 1.59 (s, 3H), 1.08 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.1, 135.0, 134.9, 133.5, 133.4, 131.2, 131.1, 129.9, 119.5, 115.9, 115.8, 115.7, 115.6, 63.1, 55.8, 48.8, 24.4, 13.7, ^{19}F NMR (376 MHz, $CDCl_3$) δ -114.28, -114.70. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{19}H_{17}F_2NO_2Na$ 352.1125; Found 352.1121.

Ethyl 3,3-bis(4-bromophenyl)-2-cyano-2-methylpropanoate (3s)

Colorless oil, 85% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ7.52–7.42 (m, 4H), 7.39–7.30 (m, 4H), 4.30 (s, 1H), 4.12 (q, *J* = 7.2 Hz, 2H), 1.59 (s, 3H), 1.11 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.9, 137.8, 136.4, 132.1, 131.9, 131.8, 131.1, 130.1, 129.5, 128.9, 122.4, 121.9, 119.3, 63.2, 56.0, 48.3, 24.4, 13.8. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{19}H_{17}Br_2NO_2Na$ 471.9524; Found 471.9521.

Ethyl 2-cyano-2-methyl-3,3-di-p-tolylpropanoate (3t)

White solid, 84% yield. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.42–7.36 (m, 2H), 7.35–7.30 (m, 2H), 7.16 –7.11 (m, 4H), 4.40 (s, 1H), 4.03 (q, *J* = 7.1 Hz, 2H), 2.26 (d, *J* = 9.0 Hz, 6H), 1.53 (s, 3H), 0.97 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 168.6, 136.9, 136.7, 136.5, 135.2, 129.4, 129.0, 127.8, 119.9, 62.4, 55.1, 54.8, 48.4, 23.9, 20.5, 20.4, 13.4. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{21}H_{23}NO_2Na$ 344.1626; Found 344.1628.

Ethyl 2-cyano-2-methyl-3-(naphthalen-2-yl)-3-(p-tolyl)propanoate (3u)

Colorless oil, 72% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07–7.93 (m, 1H), 7.88–7.71 (m, 3H), 7.70–7.36 (m, 4H), 7.33–7.30 (m, 1H), 7.26–7.15 (m, 1H), 7.13–7.00 (m, 1H), 4.50 (d, *J* = 2.7 Hz, 1H), 4.19–4.00 (m, 2H), 2.31 (d, *J* = 12.1 Hz, 3H), 1.65 (d, *J* = 7.0 Hz, 3H), 1.02 (dt, *J* = 45.1, 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.5, 139.2, 138.5, 138.3, 137.8, 137.1, 135.6, 130.6, 129.4, 128.6, 127.1, 125.3, 120.0, 119.9, 62.9, 57.3, 48.6, 24.7, 21.5, 13.7. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{24}H_{23}NNaO_2$ 380.1626; Found 380.1620.

Ethyl 2-cyano-2-methyl-3-phenyl-3-(p-tolyl)propanoate (3v)

Colorless oil, 85% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56–7.47 (m, 2H), 7.44–7.36 (m, 2H), 7.35–7.25 (m, 2H), 7.24–7.17 (m, 1H), 7.12 (dd, *J* = 21.0, 7.9 Hz, 2H), 4.31 (d, *J* = 5.3 Hz, 1H), 4.14–4.02 (m, 2H), 2.30 (d, *J* = 12.3 Hz, 3H), 1.60 (d, *J* = 3.9 Hz, 3H), 1.13–0.97 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.4, 129.5, 129.4, 129.3, 128.7, 128.6, 128.3, 128.2, 127.8, 127.5, 119.9, 62.8, 57.0, 48.8, 29.7, 24.5, 21.0, 13.7. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{20}H_{21}NO_2Na$ 330.1470; Found 330.1471.

Ethyl 2-cyano-3-(4-fluorophenyl)-2-methyl-3-phenylpropanoate (3w)

Colorless oil, 87% yield. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.63–7.50 (m, 3H), 7.49–7.46 (m, 1H), 7.42–7.26 (m, 3H), 7.25–7.17(m, 2H), 4.56 (d, *J* = 12.0 Hz, 1H), 4.08–3.98 (m, 2H), 1.55 (d, *J* = 3.3 Hz, 3H), 0.95 (dt, *J* = 14.2, 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.2, 131.3, 130.1, 129.4, 128.9, 128.7, 128.2, 128.0, 127.7, 115.8, 115.6, 115.4, 63.0, 56.6, 48.8, 29.7, 24.4, 13.8; ^{19}F NMR (376 MHz, $CDCl_3$) δ -113.99. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{19}H_{18}FNO_2Na$ 334.1219; Found 334.1215.

Ethyl 3-(4-bromophenyl)-2-cyano-2-methyl-3-phenylpropanoate (3x)

Colorless oil, 78% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51–7.44 (m, 3H), 7.43–7.34 (m, 4H), 7.34–7.26 (m, 2H), 4.32 (d, *J* = 11.6 Hz, 1H), 4.10 (dq, *J* = 14.3, 7.1 Hz, 2H), 1.60 (s, 3H), 1.08 (dt, *J* = 26.8, 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.2, 138.4, 131.9, 131.2, 130.1, 129.5, 128.9, 128.8, 128.3, 128.1, 127.8, 121.7, 119.6, 63.1, 56.7, 48.5, 24.4, 13.8. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{19}H_{18}BrNO_2Na$ 394.0419; Found 394.0414.

Ethyl 3-(4-chlorophenyl)-2-cyano-2-methyl-3-phenylpropanoate (3y)

Yellow oil, 79% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53–7.43 (m, 4H), 7.38–7.23 (m, 5H), 4.34 (d, *J* = 1.8 Hz, 1H), 4.10 (dq, *J* = 14.1, 7.1 Hz, 2H), 1.60 (d, *J* = 2.4 Hz, 3H), 1.07 (dt, *J* = 24.9, 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.1, 130.9, 129.78, 129.5, 129.0, 128.9, 128.8, 128.3, 128.1, 127.8, 119.6, 63.1, 56.7, 48.6, 24.4, 13.8. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{19}H_{18}ClNO_2Na$ 350.0924; Found 350.0927.

Ethyl 2-cyano-2-methyl-3-(naphthalen-2-yl)-3-phenylpropanoate (3z)

Colorless oil, 46% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11–7.95 (m, 1H), 7.87–7.73 (m, 3H), 7.69–7.45 (m, 5H), 7.44–7.26 (m, 3H), 4.54 (d, *J* = 1.5 Hz, 1H), 4.18–4.01 (m, 2H), 1.66 (d, *J* = 4.7 Hz, 3H), 1.03 (dt, *J* = 36.6, 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.4, 129.8, 128.8, 128.7, 128.5, 128.1, 128.0, 127.9, 127.6, 127.1, 126.9, 126.6, 126.4, 126.3, 119.9, 119.8, 63.0, 57.5, 48.7, 24.7, 13.7. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{23}H_{21}NO_2Na$ 366.1470; Found 366.1469.

Ethyl 2-cyano-3-mesityl-2-methyl-3-phenylpropanoate (3aa)

Colorless oil, 40% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24–7.16 (m, 3H), 7.15–7.09 (t, *J* = 7.0 Hz, 3H), 6.86 (d, *J* = 2.0 Hz, 1H), 5.40 (s, 1H), 4.40–4.20 (m, 2H), 2.42 (s, 3H), 2.21 (s, 3H), 1.96 (s, 3H), 1.42 (s, 3H), 1.29 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.1, 140.0, 138.9, 137.2, 132.3, 131.9, 129.3, 128.5, 126.8, 126.3, 120.9, 63.5, 48.7, 46.4, 24.7, 22.5, 22.4, 20.8, 14.0. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for$C_{22}H_{25}NNaO_2$ 358.1783; Found 358.1780.

Ethyl 2-methyl-2-nitro-3,3-diphenylpropanoate (5a)

Colorless oil, 56% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37–7.33 (m, 4H), 7.32–7.26 (m, 4H), 7.25–7.18 (m, 2H), 5.37 (s, 1H), 4.12–4.01 (m, 2H), 1.98 (s, 3H), 1.05 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.4, 138.2, 138.1, 129.9, 129.7, 128.5, 128.4, 127.5, 96.7, 63.0, 56.1, 20.9, 15.7, 13.9, 13.5. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{18}H_{19}NO_4Na$ 336.1212; Found 336.1219.

Ethyl 2-benzhydryl-2-nitrobutanoate (5b)

Yellow oil, 48% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77–7.70 (m, 1H), 7.44–7.35 (m, 3H), 7.30–7.21 (m, 4H), 7.18–7.13 (m, 2H), 5.04 (s, 1H), 4.22 (q, *J* = 7.1 Hz, 2H), 4.11–3.95 (m, 2H), 1.25 (d, *J* = 7.2 Hz, 3H), 0.76 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.4, 138.3, 138.1, 129.9, 129.7, 128.5, 128.4, 127.5, 96.7, 63.0, 56.1, 20.9, 13.5. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{19}H_{21}NNaO_4$ 350.1368; Found 350.1363.

Ethyl 2-nitro-2,3,3-triphenylpropanoate (5c)

Colorless oil, 53% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96–7.90 (m, 2H), 7.77–7.68 (m, 2H), 7.55–7.44 (m, 4H), 7.42–7.38 (m, 2H), 7.34–7.28 (m, 4H), 7.22–7.18 (m, 1H), 5.23 (d, *J* = 24.0 Hz, 1H), 4.37 (q, *J* = 7.2 Hz, 2H), 1.34 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 186.5, 163.9, 137.6, 134.9, 132.5, 132.4,

130.1, 130.0, 128.9, 128.8, 128.5, 128.3, 128.1, 128.0, 62.4, 59.2, 14.1, 14.0. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{23}H_{21}NO_4Na$ 398.1368; Found 398.1359.

Diethyl 2-benzhydrylmalonate (7a)

Colorless oil, 60% yield. ^1H NMR (400 MHz, $CDCl_3$) δ 7.25–7.20 (m, 4H), 7.19–7.14 (m, 4H), 7.12–7.04 (m, 2H), 4.67 (d, *J* = 12.2 Hz, 1H), 4.25 (d, *J* = 12.2 Hz, 1H), 3.96–3.85 (m, 4H), 0.93 (t, *J* = 7.1 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.7, 141.4, 128.6, 127.8, 126.9, 126.6, 61.5, 57.5, 51.2, 13.8. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{20}H_{22}NaO_4$ 349.1416; Found 349.1411.

Diethyl 2-benzhydryl-2-phenylmalonate (7c)

Colorless oil, 25% yield. 1H NMR (400 MHz, $CDCl_3$) δ 7.34–7.27 (m, 1H), 7.24–7.19 (m, 2H), 7.19–7.13 (m, *3*H), 7.12–7.06 (m, 4H), 7.04–6.99 (m, 5H), 4.51 (d, *J* = 9.0 Hz, 1H), 4.16–4.03 (m, 4H), 1.15 (t, *J* = 7.2 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.3, 168.2, 143.9, 143.7, 130.8, 129.7, 129.5, 129.3, 129.3, 128.6, 128.4, 126.4, 61.8, 58.0, 57.6, 56.6, 14.1. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{26}H_{26}NaO_4$ 425.1729; Found 425.1725.

2-benzhydrylmalononitrile (9a)

Colorless oil, 83% yield. ^1H NMR (400 MHz, $CDCl_3$) δ 7.34–7.27 (m, 5H), 7.25-7.16 (m, 5H), 4.53 (d, *J* = 8.1 Hz, 1H), 4.32 (d, *J* = 8.1 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.1, 129.3, 128.7, 127.9, 112.0, 51.6, 29.0. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{16}H_{12}N_2Na$ 255.0898; Found 255.0890.

2-benzhydryl-2-isopropylmalononitrile (9b)

White oil, 52% yield. ^1H NMR (400 MHz, $CDCl_3$) δ 7.53–7.45 (m, 4H), 7.33–7.18 (m, 6H), 4.28 (s, 1H), 2.18–2.10 (m, 1H), 1.17 (d, *J* = 6.7 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.7, 129.1, 129.0, 128.5, 114.9, 54.5, 49.4, 33.9, 18.4. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{19}H_{18}N_2Na$ 297.1368; Found 297.1375.

2-benzhydryl-2-phenylmalononitrile (9c)

White oil, 71% yield. ^1H NMR (400 MHz, $CDCl_3$) δ 7.31–7.26 (m, 10H), 7.20–7.17 (m, 5H), 4.44 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.3, 130.8, 128.8, 128.1, 128.0, 127.7, 127.4, 125.8, 113.9, 61.3, 46.3. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{22}H_{16}N_2Na$ 331.1211; Found 331.1202.

2-benzhydryl-2-methylmalononitrile (9d)

Colorless oil, 94% yield. ^1H NMR (400 MHz, $CDCl_3$) δ 7.58–7.49 (m, 4H), 7.44–7.31 (m, 6H), 4.23 (d, *J* = 2.7 Hz, 1H), 1.81 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.8, 129.12, 128.8, 128.6, 116.1, 58.4, 36.4, 25.5. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{17}H_{14}N_2Na$ 269.1055; Found 269.1062.

N-((2-methoxyphenyl)(naphthalen-1-yl)methyl)-4-methylbenzenesulfonamide (10)

White solid, 80% yield. ^1H NMR (400 MHz, $CDCl_3$) δ 7.79–7.72 (m, 1H), 7.69–7.65 (m, 2H), 7.58–7.51 (m, 3H), 7.45–7.39 (m, 2H), 7.35–7.31 (m, 1H), 7.21–7.14 (m, 1H), 7.05–6.99 (m, 3H), 6.82–6.77 (m, 1H), 6.70–6.66 (m, 1H), 5.82 (d, *J* = 9.1 Hz, 1H), 3.57 (s, 3H), 2.29 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.4, 142.9, 138.0, 137.5, 133.1, 132.5, 129.7, 129.1, 128.1, 127.9, 127.6, 127.5, 127.0, 126.0, 125.9, 125.4, 125.3, 120.7, 111.1, 59.0, 55.3, 21.4. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{25}H_{23}NNaO_3S$ 440.1296; Found 440.1295.

Ethyl 2-cyano-3-(2-methoxyphenyl)-2-methyl-3-(naphthalen-1-yl)propanoate (11)

Yellow solid, 61% yield. ^1H NMR (400 MHz, $CDCl_3$) δ 8.20 (d, *J* = 7.3 Hz, 1H), 8.06–7.96 (m, 1H), 7.79–7.71 (m, 2H), 7.52–7.37 (m, 4H), 7.23–7.16 (m, 1H), 6.97–6.92 (m, 1H), 6.87–6.79 (m, 1H), 5.94 (s, 1H), 4.03 (s, 3H), 4.01–3.90 (m, 2H), 1.73 (s, 3H), 0.88 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.5, 156.7, 136.8, 134.0, 131.8, 131.0, 130.0, 128.9, 128.0, 126.4, 126.0, 125.6, 125.0, 123.7, 123.4, 121.1, 120.3, 110.4, 62.6, 55.6, 49.5, 42.6, 24.6, 13.6. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{24}H_{23}NNaO_3$ 396.1576; Found 396.1578.

2-cyano-3-(2-methoxyphenyl)-2-methyl-3-(naphthalen-1-yl)propanoic acid (12)

White solid, 83% yield. ^1H NMR (400 MHz, DMSO-d_6) δ 8.13 (d, *J* = 7.2 Hz, 1H), 7.93–7.83 (m, 3H), 7.60 (t, *J* = 7.8 Hz, 1H), 7.49–7.43 (m, 2H), 7.25–7.21 (m, 1H), 7.18–7.10 (m, 2H), 6.81 (td, *J* = 7.5, 1.2 Hz, 1H), 5.80 (s, 1H), 4.05 (s, 3H), 1.64 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 170.6, 156.6, 136.9, 131.0, 130.0, 129.0, 128.8, 127.7, 126.6, 125.9, 125.0, 122.9, 122.8, 120.6, 120.4, 111.2, 56.0, 48.9, 42.0, 24.2. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{22}H_{19}NNaO_3$ 368.1263; Found 368.1263.

3-(2-methoxyphenyl)-2-methyl-3-(naphthalen-1-yl)-2-(piperidine-1-carbonyl)propanenitrile (13)

White solid, 70% yield. ^1H NMR (400 MHz, $CDCl_3$) δ 8.11 (d, *J* = 7.2 Hz, 1H), 7.97–7.87 (m, 1H), 7.71–7.62 (m, 2H), 7.44–7.27 (m, 4H), 7.15–7.07 (m, 1H), 6.85 (dd, *J* = 8.3, 1.1 Hz, 1H), 6.79–6.70 (m, 1H), 5.85 (s, 1H), 3.99–3,89 (m, 4H), 3.84–3.72 (m, 1H), 3.03 (t, *J* = 6.0 Hz, 2H), 1.66 (s, 3H), 1.40–0.99 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.5, 156.7, 136.8, 134.0, 131.7, 130.9, 129.1, 128.8, 128.1, 126.5, 125.8, 125.7, 125.1, 123.7, 123.3, 121.1, 120.2, 110.4, 65.7, 55.7, 49.8, 44.1, 42.5, 28.5, 25.6, 24.7. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{27}H_{28}N_2NaO_2$ 435.2048; Found 435.2050.

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