Nucleophilic heterocyclic carbene as a novel catalyst for cyclopropanation of cyano acrylates†

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Nucleophilic heterocyclic carbenes (NHCs) have been used for the first time as catalysts in the cyclopropanation of ethyl cyanocinnamates with phenacyl bromide by Michael-initiated ring-closure (MIRC).

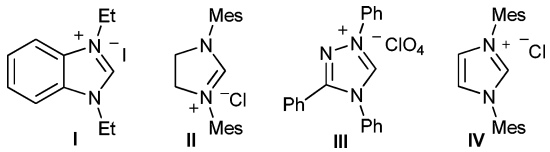
Introduction

Cyclopropane is an important structural motif present in a number of natural and unnatural molecules endowed with interesting biological properties.[1] Cyclopropane carboxylic acid derivatives occur naturally as insecticidal pyrethrins[2] or as the immediate biosynthetic precursor of the plant hormone ethylene.[3] The activation of α,β-unsaturated aldehydes and ketones toward conjugate addition by sulfur ylides[4] or secondary amines,[5] followed by an intramolecular ring closure reaction (Michael-initiated ring-closure, MIRC) is one of the most successful strategies for the synthesis of cyclopropanes.[6] The most popular MIRC synthesis of substituted cyclopropanes involves addition of α-halogenated nucleophiles to activated olefins. In 1922, Kohler reported the synthesis of 1-cyano cyclopropane carboxylates in moderate to good yields from cyanocinnamates following a MIRC involving benzylcinnamate and α,α-dibromo acetophenone.[7] Decades later, in 2007, arsenic ylide mediated cyclopropanation of cyanocinnamates was patented for the synthesis of similar cyclopropane carboxylates.[8] In the context of the general interest in using NHCs as reagents[9] and catalysts,[10–12] it was surmised that NHCs may serve as organocatalysts in the cyclopropanation of cyanocinnamates with phenacyl bromide in an MIRC reaction. The results of our work validating the assumption are presented in this paper.

Results and discussion

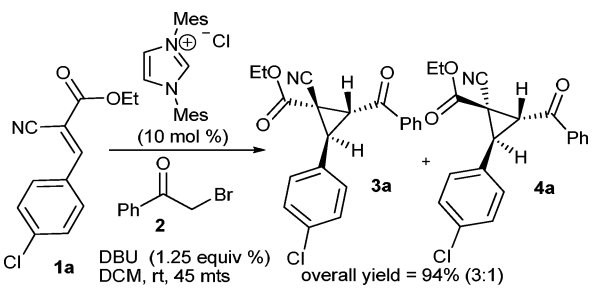
In a pilot experiment, the reaction of ethyl 2-cyano-3-(4-chlorophenyl)propenoate **1a** with phenacyl bromide **2** in the presence of dimesitylimidazocarbene afforded ethyl 2-benzoyl-3-(4-chlorophenyl)-1-cyanocyclopropanecarboxylate **3a** in 45% yield. Further studies for optimizing the reaction conditions were carried out using available carbene precursors and suitable amine bases (Table 1). Since 1-cyanocyclopropane carboxylates are more susceptible to ring opening reactions in the presence of a nucleophilic carbene,[13] the yield of the reaction was very poor under most of the reaction conditions. Thus dimesitylimidazocarbene, which is less nucleophilic compared to other nucleophilic heterocyclic carbene was found to be better yielding catalyst. The cyclopropane carboxylate **3a** was formed in excellent yield when the cyanocinnamate **1a** was treated with phenacyl bromide in the presence of 10 mol% dimesitylimidazolium chloride and 1.2 equivalent of DBU (0.75 mmol) in dichloromethane for 45 min (Scheme 1). It is noteworthy that under the optimized reaction conditions diastereomers **3** & **4** are selectively formed in an overall 94% yield.

Table 1 Catalyst screening



Entry	Catalyst	Reaction conditions	Yield (%)
1	**I** (20 mol%)	DBU (1.2 eq), DCM, rt, 2 h	27
2	**II** (10 mol%)	DIPEA (1.2 eq), DCM, rt, 2h	5
3	**III** (10 mol%)	DIPEA (1.2 eq), DCM, rt, 2 h	9
4	**III** (10 mol%)	DBU (20 mol%), DCM, rt, 2 h	9
5	**IV** (10 mol%)	DBU (20 mol%), DCM, rt, 2 h	33
6	None	DBU (1.2 equiv), DCM, rt, 4 h	22
7	**IV** (10 mol%)	DBU (50 mol%), DCM, rt, 2 h	45
8	**IV** (10 mol%)	DBU (1.2 eq), DCM, rt, 4 h	83
[a]9	**IV** (10 mol%)	DBU (1.2 eq), DCM, rt, 0.75 h	94

[a] (1*S*/*R*,2*S*,3*R*) isomers were formed as major components.



Scheme 1

In the ^{1}H NMR spectrum, the major isomer **3a** showed peaks at δ 3.57 (d, J = 8.5 Hz) and 3.71 (d, J = 8.5 Hz) due to cyclopropane ring protons, the minor isomer **4a** showed peaks

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at δ 3.92 (d, J = 8 Hz) and 4.27 (d, J = 8 Hz). In order to differentiate the *cis* isomer from the *trans* isomer, we isolated the *cis* isomer from a reaction of cyano cinnamate **1a** with phenacyl bromide in the presence of DBU and found that the cyclopropane ring protons resonate at δ 3.75 (d, J = 10.5 Hz) and 4.38 (d, J = 10.5 Hz). The separation of the two diastereomers **3a** (major) and **4a** (minor) by the usual column chromatographic techniques was difficult and so the ratio of two isomers **3a** & **4a** was calculated from the ^{1}H NMR spectrum as 3 : 1. Further investigations on this reaction using substituted cyanocinnamates **1** proved that the reaction is substantially general to afford 1-cyanocyclopropane carboxylates **3** and **4** in high yields (Table 2).

The minor isomer **4g** of ethyl 2-benzoyl-3-(3-nitrophenyl)-1-cyanocyclopropanecarboxylate was separated from the reaction mixture by repeated column chromatography and was characterized on the basis of single crystal X-ray analysis (Fig. 1).[14]

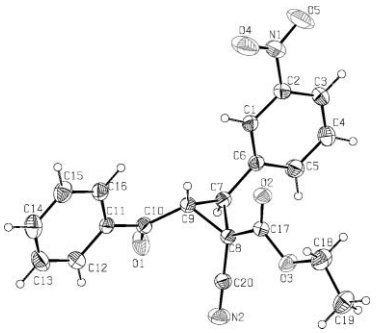
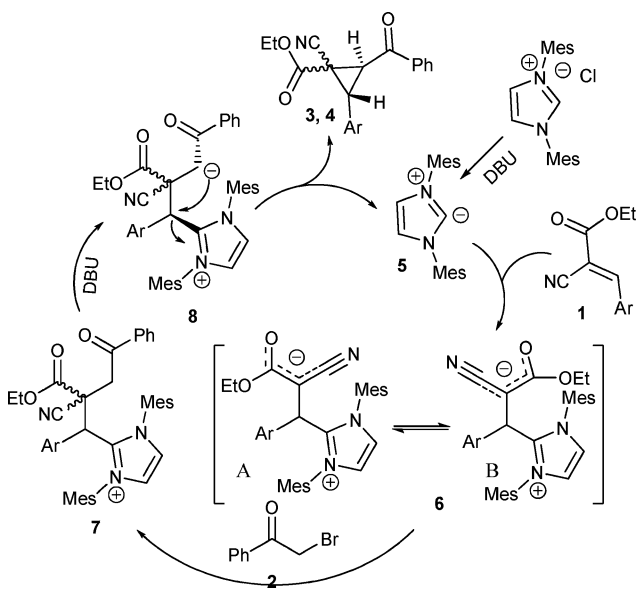


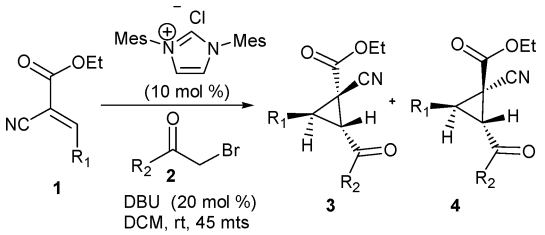
Fig. 1 ORTEP diagram of ethyl 2-benzoyl-1-cyano-3-(3-nitrophenyl)-cyclopropane carboxylate **4g**.

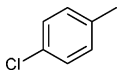
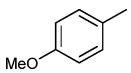
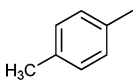
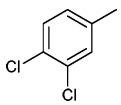
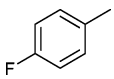
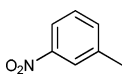
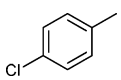
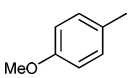
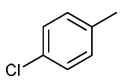
A mechanistic postulate for the reaction is outlined as follows: the dimesitylimidazocarbene **5** underwent Michael addition[15] with cyanocinnamate **1** generating a reactive intermediate **6**, which underwent alkylation with phenacyl bromide **2**, followed by intramolecular cyclization in the presence of DBU to afford cyclopropane carboxylates **3** (Scheme 2). The equilibration



Scheme 2

Table 2 Synthesis of ethyl 3-aryl-2-benzoyl-1-cyanocyclopropane-carboxylates



Entry	Products	R_1	R_2	Yield[a,b](% (**3** : **4**))
1	**3a**, **4a**			94 (3 : 1)
2	**3b**, **4b**			72 (3 : 1)
3	**3c**, **4c**			92 (4 : 1)
4	**3d**, **4d**			62 (1.25 : 1)
5	**3e**, **4e**			93 (4 : 1)
6	**3f**, **4f**			89 (3 : 1)
7	**3g**, **4g**			76 (1.7 : 1)
8	**3h**, **4h**			94 (9 : 1)
9	**3i**, **4i**			83 (2.6 : 1)
10	**3j**, **4j**			63 (2 : 1)
11	**3k**, **4k**			68 (4.12 : 1)

[a] Overall Yield. [b] Other isomers were formed in <5% yield.

between the initially formed enolates **6** A and **6** B determined the stereochemistry of the diastereomers **3** and **4**.

Conclusion

We have developed a convenient method for the synthesis of 2-benzoyl-1-cyanocyclopropane carboxylates from cyanocinnamates; this constitutes the first example for the use of NHCs as catalysts in cyclopropanation by MIRC.

Experimental

General

All reactions were carried out in oven-dried glassware. Progress of reactions was monitored by Thin Layer Chromatography while purification was effected by column chromatography on silica gel (100–200 mesh) using hexane–ethyl acetate (9 : 1) as the eluent. Melting points were recorded on a Buchi melting point apparatus and are uncorrected. NMR spectra were recorded at 500 MHz (for ^{1}H) and 125 MHz (for ^{13}C) respectively on Brucker Avance DPX-500 MHz. Chemical shifts are reported in δ (ppm) relative to TMS (^{1}H) and $CDCl_3$ (^{13}C) as internal standards. Mass spectra were recorded using JEOL JMS 600H high resolution mass spectrometer.

General procedure for the synthesis of ethyl 2-benzoyl-1-cyanocyclopropanecarboxylates

DBU (57 mg, 0.75 mmol) was added to a suspension of 1,3-dimesitylimidazolium chloride (17 mg, 10 mol%), cyanocinnamate **1** (0.5 mmol) and phenacyl bromide **2** (150 mg, 0.75 mmol) in 3 ml dry dichloromethane under argon atmosphere. This solution was stirred for 45 min at room temperature (30 °C). The reaction mixture was then passed through a short pad of Celite®, the solvent was removed by distillation and residue was subjected to column chromatography on a silica gel (100–200 mesh) using hexane–ethyl acetate (9 : 1) as the eluent to afford 2-benzoyl-1-cyanocyclopropanecarboxylates **3**.

Ethyl 2-benzoyl-3-(4-chlorophenyl)-1-cyanocyclopropanecarboxylate (3a : 4a = 3 : 1). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 1.03–1.09 (m, 3.9 H, **3** & **4**), 3.57 (d, J = 8.5 Hz, 1H, **3**), 3.71 (d, J = 8.5 Hz, 1H, **3**), 3.92 (d, J = 8 Hz, 0.3 H, **4**), 4.02–4.06 (m, 2.6 H, **3** & **4**), 4.27 (d, J = 8 Hz, 0.3 H, **4**), 7.24 (d, J = 8 Hz, 0.6 H, **4**), 7.30–7.32 (m, 2.6 H, **3** & **4**), 7.39 (d, J = 8 Hz, 2H, **3**), 7.51 (t, J = 8 Hz, 2H, **3**), 7.55 (t, J = 8 Hz, 0.3H, **4**), 7.63 (t, J = 8 Hz, 1H, **3**), 7.67 (t, J = 8 Hz, 0.3H, **4**), 8.00 (d, J = 8 Hz, 2H, **3**), 8.10 (d, J = 8 Hz, 0.6H, **4**) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 13.65 (**3**), 13.93 (**4**), 29.53 (**3**), 29.54 (**4**), 34.37 (**4**), 35.59 (**3**), 38.74 (**4**), 39.76 (**3**), 63.49 (**4**), 63.60 (**3**), 114.79 (**4**), 115.20 (**3**), 128.45 (**3**), 128.73 (**4**), 129.11 (**4**), 129.25 (**4**), 129.41 (**3**), 129.70 (**3**), 130.45 (**3**), 130.49 (**4**), 134.41 (**3**), 134.67 (**4**), 135.36 (**3**), 135.95 (**4**), 162.69 (**4**), 163.60 (**3**), 189.34 (**3**), 190.75 (**4**); IR (KBr) ν_{max} = 22340, 1741, 1679, 1268 cm^{-1}; LRMS (FAB$^+$) m/z = 354.38; HRMS (EI) for $C_{20}H_{16}ClNO_3$: Calcd.: 353.0819, found :353.0811.

Ethyl 2-benzoyl-1-cyano-3-(4-methoxyphenyl)cyclopropanecarboxylate (3b : 4b = 3 : 1). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 1.136–1.14 (m, 4 H, **3** & **4**), 3.61 (d, J = 8 Hz, 1H, **3**), 3.79 (d, J = 8 Hz, 1H, **3**), 3.83 (s, 3H, **3**), 3.87 (s, 1H, **4**), 3.92 (d, J = 8 Hz, 0.33 H, **4**), 4.11–4.14 (m, 2.66 H, **3** & **4**), 4.27 (d, J = 8 Hz, 0.33 H, **4**), 6.84 (d, J = 8 Hz, 0.66 H, **4**), 6.93 (d, J = 8 Hz, 2H, **3**), 7.22 (d, J = 8 Hz, 0.66H, **4**), 7.30 (d, J = 8 Hz, 2H, **3**), 7.53 (d, J = 8 Hz, 2H, **3**), 7.56 (t, J = 8 Hz, 0.66H, **4**), 7.62 (t, J = 8 Hz, 1H, **3**), 7.64 (t, J = 8 Hz, 0.33H, **4**), 8.02 (d, J = 8 Hz, 2H, **3**), 8.11 (d, J = 8 Hz, 0.66H, **4**) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 13.96 (**3**), 14.24 (**4**), 29.52 (**4**), 34.34 (**4**), 36.21(**3**), 39.28 (**4**), 39.96 (**3**), 55.21 (**3**), 62.31 (**4**), 63.16 (**3**), 113.93 (**4**), 114.43 (**3**), 114.74 (**4**), 115.37 (**4**), 122.54 (**4**), 123.67 (**3**), 128.44 (**3**), 128.70 (**4**), 128.99 (**3**), 129.1 (**3**), 130.19 (**4**), 133.61 (**4**), 134.11 (**3**), 134.24 (**4**), 135.57 (**3**), 154.23 (**4**), 160.01 (**3**), 163.83, 189.44 (**3**), 191.12 (**4**); IR (KBr) ν_{max} = 2236, 1739, 1684, 1268 cm^{-1}; LRMS (FAB$^+$) m/z = 350.38 HRMS (EI) for $C_{21}H_{19}NO_4$: Calcd.: 349.1314, found :349.1306.

Ethyl 2-benzoyl-1-cyano-3-(4-methylphenyl)cyclopropanecarboxylate (3c : 4c = 4 : 1). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 1.12–1.15 (m, 3.73 H, **3** & **4**), 2.34 (s, 0.72 H, **4**), 2.38 (s, 3H, **3**), 3.63 (d, J = 8 Hz, 1H, **3**), 3.79 (d, J = 8 Hz, 1H, **3**), 3.94 (d, J = 8 Hz, 0.24 H, **4**), 4.09–4.17 (m, 2.48 H, A & **4**), 4.27 (d, J = 8 Hz, 0.24 H, **4**), 7.12 (d, J = 8 Hz, 0.48 H, **4**), 7.18 (d, J = 8 Hz, 0.48 H, **4**), 7.22 (d, J = 8 Hz, 2 H, **3**), 7.26 (d, J = 8 Hz, 2H, **3**), 7.51 (t, J = 8 Hz, 2H, **3**), 7.55 (t, J = 8 Hz, 0.48H, **4**), 7.62 (t, J = 8 Hz, 1H, **3**), 7.67 (t, J = 8 Hz, 0.24H, **4**), 8.01 (d, J = 8 Hz, 2H, **3**), 8.12 (d, J = 8 Hz, 0.48H, **4**) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 13.82 (**3**), 13.94 (**4**), 21.25 (**3**), 22.71 (**4**), 29.71 (**3**), 31.94 (**4**), 34.26 (**4**), 36.35 (**3**), 39.45 (**4**), 39.80 (**3**), 63.19 (**3** & **4**), 115.22 (**4**), 115.30 (**3**), 128.11 (**3**), 128.45 (**4**), 128.72 (**4**), 128.79 (**3**), 128.89 (**4**), 129 (**3**), 129.24 (**4**), 129.70 (**3**), 134.12 (**4**), 134.24 (**3**), 135.58 (**3**), 138.39 (**4**), 138.70 (**3**), 163.81 (**3**), 161.90 (**4**), 189.45 (**3**), 191.10 (**4**); LRMS (FAB$^+$) m/z = 334.45; IR (KBr) ν_{max} = 2244, 1749, 1673, 1267 cm^{-1}; HRMS (EI) for $C_{21}H_{19}NO_3$: Calcd.: 333.1365, found: 334.1427 (M$^+$ + 1).

Ethyl 2-benzoyl-1-cyano-3-(3,4-dichlorophenyl)cyclopropanecarboxylate (3d : 4d = 1.25 : 1). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 1.16–1.21 (m, 5.16 H, **3** & **4**), 3.36 (d, J = 8 Hz, 1H, **3**), 3.79 (d, J = 8 Hz, 1 H, **3**), 3.94 (d, J = 8 Hz, 0.72 H, **4**), 4.05–4.18 (m, 3.44 H, **3** & **4**), 4.26 (d, J = 8 Hz, 0.72 H, **4**), 7.01 (dd, J_1 = 8 Hz, J_2 = 2 Hz, 1.44 H, **4**), 7.18 (dd, J_1 = 8 Hz, J_2 = 2 Hz, 2 H, **3**), 7.23–7.25 (m, 1.72 H, **3** & **4**), 7.28 (s, 1H, **3**), 7.29 (s, 0.72 H, **4**), 7.53 (t, J = 8 Hz, 2H, **3**), 7.60 (t, J = 8 Hz, 1.44H, **4**), 7.65 (t, J = 8 Hz, 1H, **3**), 7.69 (t, J = 8 Hz, 0.72H, **4**), 8.01 (d, J = 8 Hz, 2H, **3**), 8.11 (d, J = 8 Hz, 1.44H, **4**) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 12.62 (**3**), 12.92 (**4**), 28.35 (**3**), 28.60 (**4**), 33.72 (**3**), 36.77 (**4**), 38.54 (**4**), 39.45 (**3**), 62.06 (**3**), 62.43 (**4**), 112.33 (**3**), 113.68 (**4**), 126.25 (**3**), 127.37 (**3**), 127.39 (**3**), 127.65 (**4**), 127.78 (**3**), 128.02 (**4**), 128.39 (**3**), 129.53 (**3**), 129.67 (**4**), 129.90 (**3**), 130.08 (**4**), 130.28 (**3**), 131.13 (**4**), 131.24 (**3**), 131.82 (**4**), 132.19 (**3**), 132.27 (**4**), 132.31 (**4**), 133.18 (**3**), 133.31 (**4**), 133.46 (**4**), 158.75 (**4**), 162.09 (**3**), 187.59 (**3**), 191.94 (**4**); FAB$^+$ m/z = 388.70; IR (KBr) ν_{max} = 2200, 1739, 1679, 1268 cm^{-1}; HRMS (EI) for $C_{20}H_{15}Cl_2NO_3$: Calcd.: 387.0429, found: 388.0411 (M$^+$ + 1).

Ethyl 2-benzoyl-1-cyano-3-phenylcyclopropanecarboxylate (3e : 4e = 4 : 1). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 1.07–1.11 (m, 3.76 H, **3** & **4**), 3.70 (d, J = 8.5 Hz, 1H, **3**), 3.81 (d, J = 8.5 Hz, 1H, **3**), 3.95 (d, J = 8 Hz, 0.25 H, **4**), 4.04–4.14 (m, 2.57 H, **3** & **4**), 4.32 (d, J = 8 Hz, 0.25 H, **4**), 7.29–7.32 (m, 1.25 H, **3** & **4**), 7.36–7.41 (m, 4.97 H, **3** & **4**), 7.48 (t, J = 8 Hz, 2 H, **3**), 7.53 (t, J = 8 Hz, 0.5H, **4**), 7.60 (t, J = 8 Hz, 1H, **3**), 7.65 (t, J = 8 Hz, 0.25H, **4**), 8.00 (d, J = 8 Hz, 2H, **3**), 8.10 (d, J = 8 Hz, 0.5H, **4**) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 13.80 (**3**), 13.87 (**4**), 26.93 (**4**), 29.53 (**3**), 34.19 (**4**), 36.42 (**3**), 39.50 (**4**), 39.72 (**3**), 63.26 (**3** & **4**), 115.21 (**4**), 115.25 (**3**), 128.30 (**3**), 128.47 (**4**), 128.56 (**4**), 128.62 (**3**), 128.72 (**4**), 128.87 (**3**), 128.99 (**4**), 129.03 (**3**), 130.67 (**4**), 131.91 (**3**), 134.20 (**3**), 134.34 (**4**), 135.54 (**3**), 136.20 (**4**), 162.52 (**4**), 163.78 (**3**), 189.51 (**3**), 190.75 (**4**) ppm; IR (KBr) ν_{max} = 2239, 1739, 1677, 1268 cm^{-1}; LRMS (FAB$^+$) m/z = 320.79; HRMS (EI) for $C_{20}H_{17}NO_3$: Calcd.: 319.1208, found: 319.1215.

Ethyl 2-benzoyl-1-cyano-3-(4-fluorophenyl)cyclopropanecarboxylate (3f : 4f = 3 : 1). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 1.09–1.13 (m, 3.95 H, **3** & **4**), 3.65 (d, J = 8 Hz, 1H, **3**), 3.80 (d, J = 8 Hz, 1H, **3**), 3.86 (d, J = 8 Hz, 0.33 H, **4**), 4.09–4.13 (m, 2.66 H, **3** & **4**), 4.28 (d, J = 8 Hz, 0.33 H, **4**), 6.95 (t, J = 16 Hz, 0.66 H, **4**), 7.04 (t, J = 16 Hz, 2 H, **3**), 7.22 (dd, J_1 = 31 Hz, J_2 = 5 Hz, 0.66 H, **4**), 7.29 (dd, J_1 = 31 Hz, J_2 = 5 Hz, 2 H, **3**), 7.47 (t, J = 8 Hz, 2 H, **3**), 7.49 (t, J = 8 Hz, 0.66H, **4**), 7.56 (t, J = 8 Hz, 1H, **3**), 7.60 (t, J = 8 Hz, 0.33H, **4**), 7.94 (d, J = 8 Hz, 2H, **3**), 8.03 (d, J = 8 Hz, 0.66 H, **4**) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 13.78 (**3**), 13.94 (**4**), 29.45 (**3**), 29.82 (**4**), 34.36 (**4**), 35.53 (**3**), 38.63 (**4**), 39.88 (**3**), 63.30 (**4**), 63.39 (**3**), 114.57 (**4**), 115.10 (**3**), 115.54 (**4**), 115.72 (**4**), 116.01 (**3**), 116.18 (**3**), 126.61 (**4**), 127.77 (**4**), 128.43 (**3**), 128.71 (**4**), 129.04(**3**), 130.07 (**4**), 130.13(**3**), 130.86 (**4**), 134.23 (**3**), 134.37 (**4**), 135.45(**3**), 136.03 (**4**), 161.93 (**4**), 163.71(**3**), 189.13 (**3**), 190.47 (**4**) ppm; LRMS (FAB$^+$) m/z = 338.48; IR (KBr) ν_{max} = 2248, 1739, 1686, 1268, 1208 cm^{-1}; HRMS (EI) for $C_{20}H_{16}FNO_3$: Calcd.: 337.114, found: 338.1190 (M$^+$ + 1).

Ethyl 2-benzoyl-1-cyano-3-(3-nitrophenyl)cyclopropanecarboxylate (3g : 4g = 1.7 : 1). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 1.11 (t, J = 7 Hz, 3H, **3**), 1.18 (t, J = 7 Hz, 1.77 H, **4**), 3.85 (d, J = 8.5 Hz, 1H, **3**), 3.93 (d, J = 8.5 Hz, 1H, **3**), 4.07 (d, J = 8 Hz, 0.59 H, **4**), 4.11–4.15 (m, 3.18 H, **3** & **4**), 4.37 (d, J = 8 Hz, 0.59 H, **4**), 7.40 (t, J = 8 Hz, 1 H, **3**), 7.43 (t, J = 8 Hz, 0.59H, **4**), 7.52–7.76 (m, 3.18 H, **3** & **4**), 7.65 (d, J = 8 Hz, 2H, **3**), 7.68 (d, J = 8 Hz, 0.59 H, **4**), 7.70 (d, J = 8 Hz, 1H, **3**), 7.76 (d, J = 8 Hz, 1.18 H, **4**), 8.03 (dd, J_1 = 8 Hz, J_2 = 1.5 Hz, 2H, **3**), 8.12 (dd, J_1 = 8 Hz, J_2 = 1.5 Hz, 1.18H, **4**), 8.18 (s, 1H, **3**), 8.24 (s, 0.59 H, **4**) ppm; ^{1}H NMR (500 MHz, $CDCl_3$, isomer **4**) δ = 1.18 (t, J = 7 Hz, 1.77 H), 4.07 (d, J = 8 Hz, 1H), 4.15 (q, J = 7 Hz, 2H, **4**), 4.37 (d, J = 8 Hz, 1H, **4**), 7.54–7.60 (m, 3H), 7.70 (t, J = 8 Hz, 2H), 8.12 (dd, J_1 = 8 Hz, J_2 = 1.5 Hz, 2H), 8.13–8.21 (m, J = 8 Hz, 2H) ppm;^{13}C NMR (125 MHz, $CDCl_3$, isomer **4**) δ = 13.95, 29.63, 34.51, 37.98, 63.82, 114.06, 123.63, 124.05, 128.81, 129.17, 129.62, 133.23, 134.65, 135.27, 135.75, 148.24, 162.59, 189.88 ppm; IR (KBr) ν_{max} = 2250, 1732, 1680, 1533, 1361, 1268 cm^{-1}; LRMS (FAB$^+$) m/z = 365.66; HRMS (EI) for $C_{20}H_{16}N_2O_5$: Calcd.: 364.1059, found: 364.1052.

Ethyl 2-benzoyl-1-cyano-3-(1-naphthyl)cyclopropanecarboxylate (3h : 4h = 9 : 1). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 1.19 (m, 3.33 H, **3** & **4**), 3.89 (d, J = 8.5 Hz, 1H, **3**), 4.11–4.15 (m, 2.22 H, **3** & **4**), 4.18 (d, J = 8.5 Hz, 1H, **3**), 4.39 (d, J = 8 Hz, 0.11 H, **4**), 4.52 (d, J = 8 Hz, 0.11 H, **4**), 7.36–7.45 (m, 0.77 H, **4**), 7.51–7.56 (m, 7H, **3**), 7.81–7.90 (m, 0.33H, **4**), 7.93–7.94 (m, 3H, **3**), 8.12 (d, J = 8 Hz, 2H, **3**), 8.22 (d, J = 8 Hz, 0.22 H, **4**) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 13.80 (**3**), 13.87 (**4**), 29.55 (**3**), 29.86 (**4**), 34.19 (**4**), 36.42 (**3**), 39.48 (**4**), 39.69 (**3**), 63.23 (**3** & **4**), 114.93 (**4**), 115.25 (**3**), 128.34 (**3**), 128.48 (**4**), 128.55 (**3**), 128.61 (**4**), 128.72 (**3**), 128.84 (**4**), 128.97 (**3**), 129.03 (**4**), 129.07 (**3**), 130.94 (**4**), 131.96 (**3**), 134.19 (**3**), 134.34 (**4**), 135.55 (**3**), 136.13 (**4**), 162.71 (**4**), 163.80 (**3**) ppm; IR (KBr) ν_{max} = 2250, 1740, 1675, 1268 cm^{-1}; LRMS (FAB$^+$) m/z = 370.34.

Ethyl 2-benzoyl-1-cyano-3-(2-thienyl)cyclopropanecarboxylate (3i : 4i = 2.6 : 1). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 1.12–1.18 (m, 4.2 H, **3** & **4**), 3.64 (d, J = 8.5 Hz, 1H, **3**), 3.23 (d, J = 8.5 Hz, 1H, **3**), 4.00 (d, J = 8.5 Hz, 0.4 H, **4**), 4.10–4.16 (m, 2.8 H, **3** & **4**), 4.29 (d, J = 8.5 Hz, 0.4 H, **4**), 6.95 (d, J = 8 Hz, 0.4 H, **4**), 7.01 (d, J = 8 Hz, 0.4 H, **4**), 7.05 (d, J = 8 Hz, 1 H, **3**), 7.13 (d, J = 8 Hz, 1 H, **4**), 7.26 (t, J = 8 Hz, 0.4 H, **4**), 7.33 (t, J = 8 Hz, 1 H, **3**), 7.50–7.56 (m, 3 H, **3**), 7.61–7.67 (m, 1.2 H, **4**), 8.00 (d, J = 8 Hz, 2H, **3**), 8.10 (d, J = 8 Hz, 0.22 H, **4**) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 13.80 (**3**), 14.24 (**4**), 30.57 (**4**), 30.31 (**3**), 31.74 (**3**), 34.20 (**4**), 35.76 (**4**), 41.50 (**3**), 63.36 (**4**), 63.50 (**3**), 114.32 (**4**), 115.01 (**3**), 126.43 (**3**), 126.49 (**4**), 126.98 (**3**), 127.19 (**4**), 128.48 (**4**), 128.58 (**3**), 128.75 (**4**), 128.84 (**3**), 133.18 (**4**), 134.91 (**3**), 135.03 (**3**), 135.34 (**4**), 135.91 (**3**), 136.08 (**4**), 136.99 (**3**), 146.5 (**4**), 162.53 (**4**), 163.35 (**3**), 188.70 (**3**), 190.12 (**4**) ppm; IR (KBr) ν_{max} = 2250, 1739, 1680, 1267 cm^{-1}; LRMS (FAB$^+$) m/z = 326.50; HRMS (EI) for $C_{18}H_{15}NO_3S$: Calcd.: 325.0773, found: 326.0770 (M$^+$ + 1).

Ethyl 2-(4-chlorophenyl)-1-cyano-3-(4-methoxybenzoyl)cyclopropanecarboxylate (3j : 4j = 2 : 1). ^{1}H NMR (300 MHz, $CDCl_3$) δ = 1.18–1.24 (m, 4.5H, **3** & **4**), 3.68 (d, J = 8.5 Hz, 1H, **3**), 3.84 (d, J = 8.5 Hz, 1H, **3**), 3.95 (s, 1.5H, **4**), 3.97 (s, 3H, **3**), 4.11–4.21 (m, 3.5 H, **3** & **4**), 4.28 (d, J = 8 Hz, 0.5 H, **4**), 6.87 (d, J = 8 Hz, 0.5H, **3**), 7.01–7.40 (m, 7 H, **3** & **4**), 7.47 (d, J = 8 Hz, 1H, **3**), 7.56 (d, J = 8 Hz, 0.5H, **4**), 8.03 (d, J = 8 Hz, 2H, **3**), 8.15 (d, J = 8 Hz, 0.9H, **4**); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 13.95 (**3**), 14.16 (**4**), 29.52 (**3**), 29.71 (**4**), 34.16 (**4**), 35.41 (**3**), 38.49 (**4**), 39.79 (**3**), 55.52 (**4**), 55.47 (**3**), 63.27 (**4**), 63.39 (**3**), 114.05 (**4**), 114.24 (**3**), 114.69 (**4**), 115.16 (**3**), 128.50 (**4**), 128.74 (**4**), 129.01 (**4**), 129.05 (**3**), 129.20 (**3**), 129.65 (**3**), 130.43 (**3**), 130.65 (**3**), 130.81 (**3**), 131.96 (**4**), 133.87 (**4**), 134.88 (**3**), 162.77 (**4**), 163.49 (**3**), 164.26 (**3**), 164.60 (**4**), 187.34 (**3**), 188.55 (**4**); IR (KBr) ν_{max} = 2224, 1741, 1669, 1262 cm^{-1}; LRMS (FAB$^+$) m/z = 383.82.

Ethyl 2-(4-chlorobenzoyl)-3-(4-chlorophenyl)-1-cyanocyclopropanecarboxylate (3k : 4k = 4.12 : 1). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 1.17–1.20 (m, 3.69H, **3** & **4**), 3.58 (d, J = 8.5 Hz, 1H, **3**), 3.80 (d, J = 8.5 Hz, 1H, **3**), 3.95 (d, J = 8 Hz, 0.27 H, **4**), 4.14–4.19 (m, 2.54 H, **3** & **4**), 4.23 (d, J = 8 Hz, 0.27 H, **4**), 7.27 (d, J = 8 Hz, 0.5H, **3**), 7.32–7.34 (m, 2.48, **3** & **4**), 7.43 (d, J = 8 Hz, 2 H, **3**), 7.53 (d, J = 8 Hz, 2H, **3**), 7.56 (d, J = 8 Hz, 0.5H, **4**), 7.97 (d, J = 8 Hz, 2H, **3**), 8.06 (d, J = 8 Hz, 0.9H, **4**) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 13.83 (**3**), 13.95 (**4**), 29.43 (**3**), 29.86 (**4**), 34.18 (**4**), 35.60 (**3**), 38.60 (**4**), 39.51 (**3**), 63.50 (**4**), 63.39 (**3** & **4**), 114.37 (**4**), 114.83 (**3**), 128.52 (**4**), 128.83 (**4**), 129.14 (**4**), 129.29 (**3**), 129.45 (**3**), 129.59 (**3**), 129.74 (**3**), 130.06 (**3**), 130.21 (**4**), 130.35 (**4**), 133.75 (**3**), 134.25 (**4**), 134.83 (**4**), 135.12 (**3**), 140.99 (**3**), 141.19 (**4**), 162.49 (**4**), 163.40 (**3**), 187.95 (**3**), 189.33 (**4**) IR (KBr) ν_{max} = 2226, 1745, 1671, 1264 cm^{-1}; LRMS (FAB$^+$) m/z = 387.04.

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