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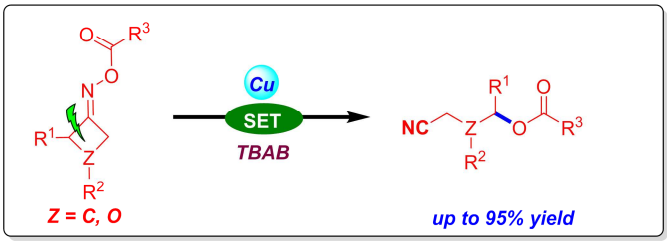

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ABSTRACT

Copper-catalyzed fragementation-rearrangement sequence of cycloketoxime esters is reported. This strategy provides direct access to diverse ring-opening acyloxylation nitriles avoiding the use of toxic cyanic reagents with good atom economy and well functional group tolerance. Experimental exploration showed that tetrabutylammonium bromide (TBAB) played an irreplaceable role in this transformation. Based on the primary mechanistic experiments, a plausible mechanism was also proposed.

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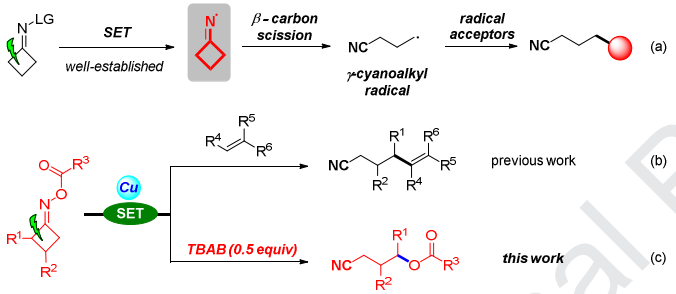
Intruction

Varieties of strained rings are highly valuable synthon for building interesting chemical skeletons *via* C−C bond cleavage.[1] Cyclobutanones are important building blocks and synthetic intermediates for the construction of functional molecules and natural products.[2] Meanwhile, cyclobutanones and derivatives could also be employed as flexible motifs to design new reactions through selective C-C bond cleavage. Transition-metal-catalyzed C-C bonds cleavage has already been an well-established strategy for the synthesis of complex products. Among these, rhodium,[3] palladium,[4] nickel[5] are efficient candidates to activate the inert C-C bonds directly *via* the formation of C-M (metals) bonds. In addition, with the rapid development of radical chemistry, the single-electron-transfer (SET) strategy can also be widely applied to achieve the cleavage of C-C bonds through the *β*-scission of strained ring radical intermediate. The iminyl radicals[6, 7] induced by suitable transition-metals, photoredox catalysts and other initiators are versatile reactive intermediates for multifarious transformations including C-C bond cleavage. In general, some cyclic iminyl radical intermediates underwent *β*-scission providing *γ*-cyanoalkyl radical, which was rapidly trapped by a wide range of radical acceptors leading to potentially functional compounds (Scheme 1a).



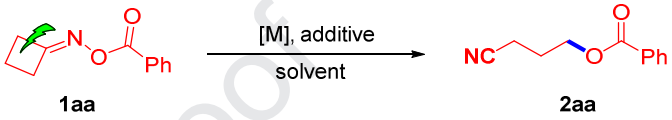
Scheme 1. Radical-mediated C-C bond cleavage of cyclobutanone oximes.

In 1991, Zard first employed cyclobutanone sulfenlimines or carboxymethyl oximes as the substrates realizing C-C bond cleavage *via* the formation of iminyl radicals under classic radical reaction conditions.[8] In 2005 Uemura and his co-workers reported an iridium-catalyzed ring cleavage reaction of cyclobutanone *O*-benzoyloximes proceeded *via* an iminyl radical to afford the saturated nitriles.[9] Until 2017, some organic chemistry researchers devoted themselves to the study of cycloketoximes again which are employed as effective distal-cyanoalkyl radical precursors, to realize varieties of interesting transformations. Meanwhile, we developed a copper-catalyzed intermolecular Heck-like coupling of cyclobutanone oximes and alkenes involving SET pathway (Scheme 1b).[10] Subsequently, Selander,[11] Zhou,[12] Guo,[13] Leonori,[14] Xiao,[15] Waser[16] and other groups[17] demonstrated a series of approaches giving the distal-cyanoalkyl radicals from the cyclobutane oximes and strainless cycloketoximes. In most of these transformations, benzoyl anion unit of substrates became part of waste stream during the process. Very recently, Liu[18] and we[19] discovered that *ortho*-aryl substituted cycloketoximes could be transformed to the rearrangement product cyano-containing benzoates *via* copper catalyst and photoredox catalyst respectively. However, achieving fragmentation-rearrangement of *ortho*-alkyl substituted or non-substituted cycloketoximes is under developed. As a sequence, with our ongoing interest in the research of radical-induced of C-C bond cleavage, [20] we herein successfully developed the first copper-catalyzed *ortho*-alkyl substituted or non-substituted cycloketoximes to afford cyano-containing benzoates *via* a fragmentation-rearrangement sequence, wherein TBAB played an irreplaceable role in this transformation (Scheme 1c).

1. Results and discussion

Cyclobutanone *O*-benzoyl oxime (**1aa**) was chosen as the standard substrate for an initial investigation. Only trace amount of desired product **2aa** was detected in GC-MS, when **1aa** was treated under the optimized conditions of our previous work (Table 1, entry 1). To our surprise, the yield of **2aa** increased up to 53% with the addition of TBAB (Table 1, entry 2). A brief evaluation of catalysts showed that $Cu(OTf)_2$ was superior to other catalysts (Table 1, entries 3-7). Notably, TBAB was critical in the reaction system. When the additive was replaced with other additives, only trace amount of product **3aa** was observed (Table 1, entries 8-9). Solvent screening indicated that 1,4-dioxane was the best solvent (Table 1, entries 10-12). What's more, Increasing the amount of TBAB from 20 mol% to 50 mol% gave the desired

Table 1. Reaction Development[a]



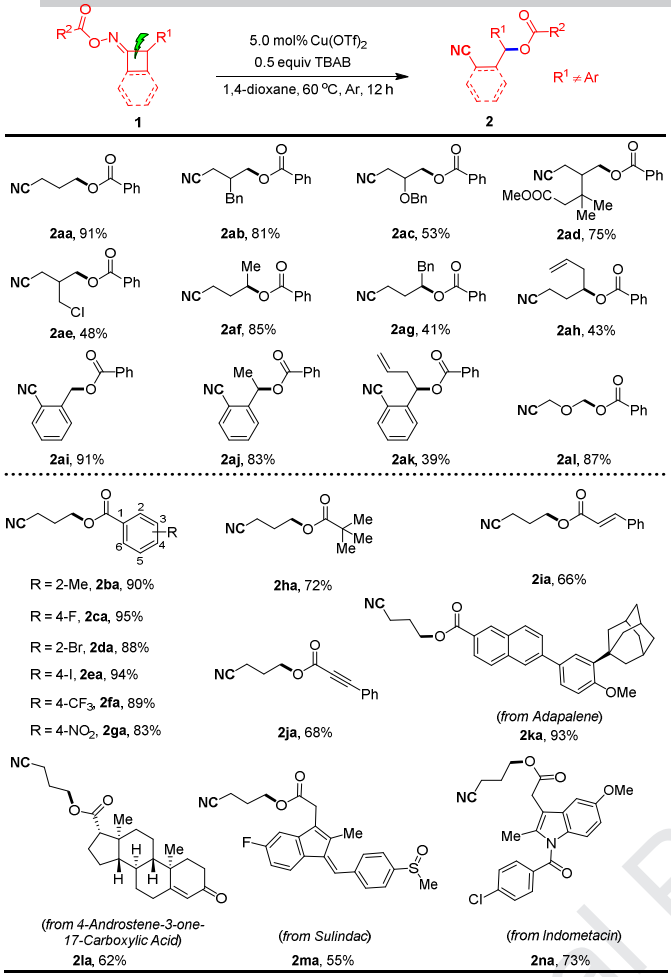
Entry	[M] (X mol%)	Additive (X mol%)	Solvent	Temperature (°C)	Yield[b] (%)
1	$Cu(OTf)_2$ (10)		1,4-dioxane	100	trace
2	$Cu(OTf)_2$ (10)	TBAB (20)	1,4-dioxane	100	53
3	$Ni(OTf)_2$ (10)	TBAB (20)	1,4-dioxane	100	12
4	$Fe(OTf)_2$ (10)	TBAB (20)	1,4-dioxane	100	18
5	$Cu(OAc)_2$ (10)	TBAB (20)	1,4-dioxane	100	47
6	$Cu(acac)_2$ (10)	TBAB (20)	1,4-dioxane	100	45
7	CuTc (10)	TBAB (20)	1,4-dioxane	100	40
8	$Cu(OTf)_2$ (10)	TBAI (20)	1,4-dioxane	100	trace
9	$Cu(OTf)_2$ (10)	LiBr (20)	1,4-dioxane	100	trace
10	$Cu(OTf)_2$ (10)	TBAB (20)	THF	100	48
11	$Cu(OTf)_2$ (10)	TBAB (20)	Toluene	100	38
12	$Cu(OTf)_2$ (10)	TBAB (20)	CH_3CN	100	19
13	$Cu(OTf)_2$ (10)	TBAB (50)	1,4-dioxane	100	93
14	$Cu(OTf)_2$ (5)	TBAB (50)	1,4-dioxane	100	93
15	$Cu(OTf)_2$ (5)	TBAB (50)	1,4-dioxane	60	95 (91)[c]

[a]Reaction conditions: **1aa** (0.20 mmol), 5 mol% of $Cu(OTf)_2$, 50 mol% of TBAB in 1,4-dioxane (1.0 mL), 60 °C, 12 h, under Ar.

[b]Determined by GC analysis.

[c]Isolated yield.

Table 2. Substrate Scope[a]



[a]Reaction conditions: **1** (0.20 mmol), 5 mol% of Cu (OTf)$_2$, 50 mol% of TBAB in 1,4-dioxane (1.0 mL), 60 °C, 12 h, under Ar.

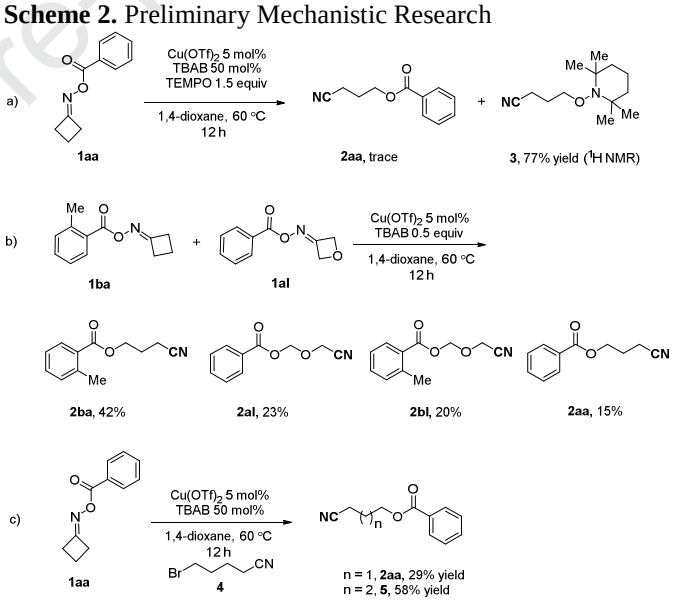
[b]Isolated yield.

product in good yield (Table 1, entry 13). Reducing the number of equivalent of Cu(OTf)$_2$ by half to 5 mol% made no difference to the yield of **3aa** (Table 1, entry 14). Reducing the reaction temperature to 60 °C further improved the yield of desired product to 95%, and 91% yield of **3aa** was isolated (Table 1, entry 15).

With the optimized reaction conditions in hand (5 mol% of Cu(OTf)$_2$, 50 mol% of TBAB, in 1,4-dioxane, 60 °C), we then focused our attention on evaluating the scope and generality of the reaction. As summarized in Table 2, the mild reaction conditions were compatible with diverse functional groups. A wide range of cyclobutanone oximes containing Bn, OBn, alkyl ester and chloromethyl groups on the *β*-position could react smoothly, resulted the corresponding products in 48% to 81% yields (Table 2, **2ab**-**2ae**). Variations of substituted groups on the *α*-position of cyclobuanone oximes were further tested, and *α*-methyl substituted cyclobutanone oximes showed effective performance affording 4-cyanobutan-2-yl benzoate (Table 2, **2af**) in 85% yield. However, the conversion rate of *α*-benzyl and allyl substituted cyclobuanone oximes is also very high but only about 40% yield of products (Table 2, **2ag**-**2ah**) were isolated due to the formation of the corresponding alkene products, which were detected in GC-MS. In addition, bicyclo[4.2.0]octa-1,3,5-trien-7-one *O*-benzoyl oxime and its derivatives are good candidates for the fragmentation-rearrangement reaction to genenrate the ester nitriles in 39% to 91% yields (Table 2, **2ai**-**2ak**). Similarity to **2ag** and **2ah**, the by-product formation of 2-(buta-1,3-dien-1-yl) benzonitrile also resulted in 39% yield of the desired product **2ak**. Moreover, oxetan-3-one oxime was also a suitable substrate in this transformation to generate (cyanomethoxy) methyl benzoate (**2al**) in 87% yield.

We further tested the protecting groups of the cyclobutanone oximes. According to the experimental results, diverse protecting groups were well tolerated and the corresponding ester nitriles were obtained in 55% to 95% yields. This reaction was successfully amenable to a wide range of substituted benzoyl oximes, good to excellent yields were achieved with substrates bearing functional groups such as methyl (**2ba**), fluoro (**2ca**), bromo (**2da**), iodo (**2ea**), trifluromethyl (**2fa**) and nitro (**2ga**) groups. Furthermore, the pivaloyl protected cyclobutanone oxime (**2ha**) was a suitable substrate for this conversion, and the rearrangement product **2ha** was obtained in 72% yield. Meanwhile, the alkenyl and alkynyl groups were also well compatible under the reaction conditions providing products **2ia** and **2ja** in medium yields, which allow for the further transformation. It is worthy noting that some complex substrates easily prepared from cyclobutanone and natural products could also be served as good candidates for the synthesis of functional ester nitriles. These functional frameworks could be transformed into the corresponding ester nitriles in one step, demonstrating the potential of this approach for rapid and direct modification of functional compounds (Table 2, **2ka**-**2na**).

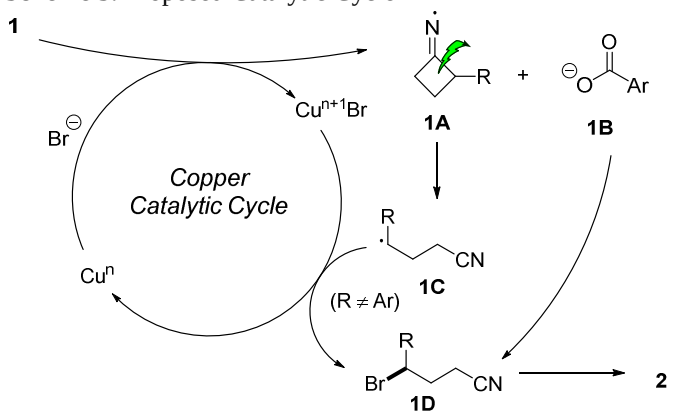
Scheme 2. Preliminary Mechanistic Research



In order to explore the mechanism of this transformation, we conducted the reaction with the addition of TEMPO to the standard reaction conditions. After 12 h we observed the alkyl-TEMPO **3** as a main product with a trace amount of ester product **2aa** by ^{1}H NMR and GC-MS analysis, which indicated that the γ-cyanoalkyl radical is involved in the transformation (Scheme 2a). Furthermore, we employed the mixture of **1ba** and **1al** under the standard conditions. We detected four products in different yields including the crossover products **2bl** and **2aa**, which indicated that the copper-catalyzed fragmentation-rearrangement sequence underwent an intermolecular pathway instead of an intramolecular pathway (Scheme 2b). During the copper-catalyzed process, we postulated that the alkyl fragment would undergo bromination *via* SET to generate a brominated intermediate in the presence of TBAB.[21] When we added an analogue 5-bromopentanenitrile (**3**) to the reaction system, the mixed products **2aa** and **5** were observed (Scheme 2c).

Based on the above-mentioned experimental results and earlier literature reports, we formulated a plausible mechanism as

Scheme 3. Proposed Catalytic Cycle



depicted in Scheme 3. In the first step, nitrogen-centered radical **1A** and anion **1B** were generated from cyclobutanone oximes **1** *via* a SET reduction process releasing a Cu^{n+1} species. Then, *β*-scission of strained ring radical intermediate **1A** led to the distal-cyanoalkyl radicals **1C**. Subsequently, **1C** reacted with $Cu^{n+1}Br$ species furnishing alkyl bromide **1D**. And Cu^{n+1} was reduced to Cu^n to furnish the copper catalytic cycle. Finally, a nucleophilic attack happened between **1B** and **1D** giving the desired rearrangement product **2**.

In summary, we have developed an efficient copper-catalyzed redox-neutral iminyl radical-mediated C-C bond cleavage approach for the synthesis of diverse ring-opening acyloxylation nitriles with high functional group tolerance. The reaction is superior in only requirement of copper catalyst without the addition of oxidant, base, ligand or toxic cyanide reagents. Moreover, the addition of TBAB is crucial for the success of this transformation. TBAB could react with distal-cyanoalkyl radical resulting in electrophilic mediate *via* SET reduction process in the presence of copper salts. Further studies are directed at explaining some details of the mechanism.

Experimental section

All new compounds were fully characterized. NMR-spectra were recorded on Bruker ARX-400 MHz or a ARX-500 Associated. Mass spectra were conducted at Micromass Q-Tof instrument (ESI) and Agilent Technologies 5973N (EI). All reactions were carried out in flame-dried reaction vessels with Teflon screw caps under argon. $Cu(OTf)_2$ was purchased from TCI, TBAB was purchased from Acros. All of the cyclobutanone *O*-acyl oximes **1** were synthesized from the corresponding cyclobutanones and carboxylic acids according to the literature.[10] All of the NMR spectra of the known compounds were in full accordance with the data in the literature. Unless otherwise noted, materials obtained from commercial suppliers were used without further purification.

Characterization of New Starting Materials. ***3-(Chloromethyl)cyclobutan-1-one O-benzoyl oxime (1ae).*** A white soild. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.03 (d, *J* = 7.2 Hz, 2H), 7.58 (t, *J* = 7.4 Hz, 1H), 7.45 (t, *J* = 7.8 Hz, 2H), 3.84 – 3.51 (m, 2H), 3.40 – 3.22 (m, 2H), 3.00 – 2.93 (m, 2H), 2.90 – 2.84 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.9, 163.8, 133.3, 129.6, 128.7, 128.5, 47.7, 35.7, 35.6, 30.0; ATR-FTIR (cm^{-1}): 1738, 1600, 1462, 1249, 1059, 708; HRMS m/z (ESI) calcd for $C_{12}H_{12}ClNNaO_2$ $(M + Na)^+$ 260.0449, found 260.0450.

Cyclobutanone O-(2-methylbenzoyl) oxime (1ba). A white soild. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, *J* = 7.9 Hz, 1H), 7.43 – 7.39 (m, 1H), 7.26 – 7.22 (m, 2H), 3.15 – 3.06 (m, 4H), 2.60 (s, 3H), 2.14 – 2.06 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.0, 165.3, 139.9, 132.1, 131.6, 130.3, 128.7, 125.7, 32.1, 31.8, 21.6, 14.2; ATR-FTIR (cm^{-1}):1739, 1553, 1460, 1242, 1066, 732; HRMS m/z (ESI) calcd for $C_{12}H_{13}NNaO_3$ $(M + Na)^+$ 226.0838, found 226.0839.

Cyclobutanone O-(4-fluorobenzoyl) oxime (1ca). A white soild: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 – 8.01 (m, 2H), 7.18 – 7.05 (m, 2H), 3.13 (t, *J* = 8.1 Hz, 4H), 2.18 – 2.06 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.4, 165.83 (d, *J* = 254.5 Hz), 163.1, 132.1 (d, *J* = 9.3 Hz), 125.2, 115.7 (d, *J* = 22.0 Hz), 31.83, 31.79, 14.2; ^{19}F NMR (376 MHz, $CDCl_3$) δ -104.9; ATR-FTIR (cm^{-1}):1742, 1600, 1508, 1269, 1243, 1064, 741; HRMS m/z (ESI) calcd for $C_{11}H_{10}FNNaO_2$ $(M + Na)^+$ 230.0588, found 230.0588.

Cyclobutanone O-(2-bromobenzoyl) oxime (1da) . A white soild. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (dd, *J* = 7.5, 2.0 Hz, 1H), 7.66 – 7.64 (m, 1H), 7.39 – 7.31 (m, 2H), 3.15 – 3.07 (m, 4H), 2.13 – 2.04 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.0, 164.2, 134.1, 132.6, 131.7, 131.3, 127.2, 121.2, 32.4, 31.7, 14.1; ATR-FTIR (cm^{-1}):1740, 1601, 1545, 1462, 1265, 1066, 754; HRMS m/z (ESI) calcd for $C_{11}H_{10}BrNNaO_2$ $(M + Na)^+$ 289.9787, found 289.9790.

Cyclobutanone O-(4-iodobenzoyl) oxime (1ea). A white soild. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 – 7.80 (m, 2H), 7.74 – 7.72 (m, 2H), 3.13 (td, *J* = 8.0, 1.2 Hz, 4H), 2.16 – 2.07 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.6, 163.6, 137.8, 130.9, 128.5, 101.0, 31.8, 31.8, 14.2; ATR-FTIR (cm^{-1}): 1748, 1582, 1393, 1271, 1067, 1003, 741; HRMS m/z (ESI) calcd for $C_{11}H_{10}INNaO_2$ $(M + Na)^+$ 337.9648, found 337.9649.

Cyclobutanone O-(4-(trifluoromethyl)benzoyl) oxime (1fa). A white soild. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 (d, *J* = 8.1 Hz, 2H), 7.72 (d, *J* = 8.2 Hz, 2H), 3.15 (t, *J* = 8.1 Hz, 4H), 2.17 – 2.09 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.0, 162.8, 134.7 (q, *J* = 32.7 Hz), 131.4 (d, *J* = 187.8 Hz), 130.0, 125.5 (q, *J* = 3.7 Hz), 123.5 (d, *J* = 272.7 Hz), 31.9, 31.8, 14.2; ^{19}F NMR (376 MHz, $CDCl_3$) δ -63.2; ATR-FTIR (cm^{-1}): 1743, 1564, 1549, 1262, 1160, 1022, 742; HRMS m/z (ESI) calcd for $C_{12}H_{13}FNNaO_2$ $(M + Na)^+$ 280.0556, found 280.0559.

Cyclobutanone O-cinnamoyl oxime (1ia). A white soild. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, *J* = 16.0 Hz, 1H), 7.52 – 7.49 (m, 2H), 7.36 – 7.32 (m, 3H), 6.45 (d, *J* = 16.0 Hz, 1H), 3.05 (t, *J* = 8.1 Hz, 4H), 2.08 – 2.00 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.6, 164.6, 145.8, 134.0, 130.4, 128.7, 128.0, 115.4, 31.7, 31.6, 14.1; ATR-FTIR (cm^{-1}):1734, 1578, 1550, 1496, 1329, 1202, 1124, 742; HRMS m/z (ESI) calcd for $C_{13}H_{13}NNaO_2$ $(M + Na)^+$ 238.0838, found 238.0840.

Cyclobutanone O-(3-phenylpropioloyl) oxime (1ja). A white soild. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 – 7.57 (m, 2H), 7.46 – 7.43 (m, 1H), 7.36 (t, *J* = 7.5 Hz, 2H), 3.11 – 3.04 (m, 4H), 2.11 – 2.03 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.5, 152.2, 132.9, 130.8, 128.5, 119.3, 88.8, 78.8, 32.0, 31.6, 14.1; ATR-FTIR (cm^{-1}):2222, 1692, 1480, 1371, 1276, 1174, 758; HRMS m/z (ESI) calcd for $C_{13}H_{12}NO_2$ $(M + H)^+$ 214.0863, found 214.0863.

Cyclobutanone O-(3-phenylpropioloyl) oxime (1ka). A white soild. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.62 (s, 1H), 8.09 – 7.97 (m, 3H), 7.92 (d, *J* = 8.7 Hz, 1H), 7.81 (dd, *J* = 8.5, 1.7 Hz, 1H), 7.61 (d, *J* = 2.3 Hz, 1H), 7.54 (dd, *J* = 8.4, 2.3 Hz, 1H), 6.99 (d, *J* = 8.5 Hz, 1H), 3.90 (s, 3H), 3.24 – 3.15 (m, 7H), 2.23 – 2.08 (m, 11H), 1.80 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.2, 164.3, 158.9, 141.5, 139.0, 136.0, 132.4, 131.1, 131.0, 129.7, 128.3, 126.5, 125.9, 125.7, 125.6, 125.3, 124.7, 112.0, 55.1, 40.5, 37.2,

37.1, 31.9, 29.1, 14.3; ATR-FTIR (cm $^{-1}$):1740, 1600, 1545, 1462, 1266, 1025, 755; HRMS m/z (ESI) calcd for $C_{32}H_{33}NNaO_3$ $(M + Na)^+$ 502.2353, found 502.2351.

(8S,9S,10R,13S,14S,17S)-17-(((Cyclobutylideneamino)oxy)carbonyl)-10,13-dimethyl-1,2,6,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-3H-cyclopenta[a]phenanthren-3-one (1la). A white soild. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.72 (s, 1H), 3.06 – 2.96 (m, 4H), 2.42 – 2.16 (m, 6H), 2.09 – 1.98 (m, 4H), 1.87 – 1.82 (m, 2H), 1.75 – 1.64 (m, 3H), 1.60 – 1.51 (m, 1H), 1.47 – 1.25 (m, 3H), 1.17 (s, 3H), 1.13 – 0.92 (m, 3H), 0.76 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.5, 171.0, 168.2, 123.9, 55.3, 53.8, 53.6, 43.9, 38.5, 37.9, 35.6, 33.9, 32.7, 32.0, 31.8, 31.7, 24.4, 23.5, 20.9, 17.3, 14.1, 13.4; ATR-FTIR (cm $^{-1}$):1756, 1678, 1565, 1361, 1270, 1003, 741; HRMS m/z (ESI) calcd for $C_{24}H_{33}NNaO_3$ (M + Na)+ 406.2353, found 406.2356.

Cyclobutanone O-(2-(5-fluoro-2-methyl-1-(4-(methylsulfinyl)benzylidene)-1H-inden-3-yl)acetyl) oxime (1ma). A white soild. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 – 7.54 (m, 4H), 7.13 (d, *J* = 6.2 Hz, 2H), 6.89 (d, *J* = 8.8 Hz, 1H), 6.54 (t, *J* = 8.7 Hz, 1H), 3.62 (s, 2H), 3.00 (t, *J* = 7.9 Hz, 2H), 2.89 (t, *J* = 7.9 Hz, 2H), 2.79 (s, 3H), 2.20 (s, 3H), 2.05 – 1.92 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.1, 167.2, 163.2 (d, *J* = 246.5 Hz), 146.5, 146.4, 145.4, 141.4, 139.5, 131.1 (d, *J* = 2.4 Hz), 130.1, 129.4 (d, *J* = 2.8 Hz), 128.3 (d, *J* = 1.5 Hz), 123.7, 123.5 (d, *J* = 9.0 Hz), 110.7 (d, *J* = 22.6 Hz), 106.1 (d, *J* = 24.0 Hz), 43.8, 31.5, 30.5, 14.0, 10.5; ^{19}F NMR (376 MHz, $CDCl_3$) δ -113.1; ATR-FTIR (cm $^{-1}$):1756, 1689, 1602, 1467, 1265, 1088, 1013, 740; HRMS m/z (ESI) calcd for $C_{24}H_{22}FNNaO_3S$ $(M + Na)^+$ 446.1197, found 446.1196.

2-(1-(4-Chlorobenzoyl)-5-methoxy-2-methyl-1H-indol-3-yl)-1-((cyclobutylideneamino)oxy)ethan-1-one (1na) . A white soild. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 – 7.63 (m, 2H), 7.47 – 7.44 (m, 2H), 6.98 (d, *J* = 2.5 Hz, 1H), 6.86 (d, *J* = 9.0 Hz, 1H), 6.65 (dd, *J* = 9.0, 2.5 Hz, 1H), 3.82 (s, 3H), 3.73 (s, 2H), 3.03 – 2.98 (m, 2H), 2.93 – 2.88 (m, 2H), 2.38 (s, 3H), 2.05 – 1.97 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.9, 168.2, 167.9, 155.9, 139.2, 135.9, 133.7, 131.1, 130.7, 130.4, 129.0, 114.8, 111.9, 111.6, 101.3, 55.6, 31.8, 31.5, 29.2, 14.1, 13.3; ATR-FTIR (cm $^{-1}$):1758, 1681, 1592, 1478, 1357, 1322, 1089, 1014, 754; HRMS m/z (ESI) calcd for $C_{23}H_{21}ClN_2NaO_4$ $(M + Na)^+$ 447.1082, found 447.1079.

General Procedures of Copper-Catalyzed Fragmentation-Rearrangement Sequence of Cycloketoxime Esters.

Flame-dried 25 mL Schlenk tube filled with argon, cyclobutanone oxime **1aa** (37.8 mg, 0.2 mmol), $Cu(OTf)_2$ (3.6 mg, 5 mol%), TBAB (32.2 mg, 0.5 equiv), absolute dry 1,4-dioxane (1.0 mL) were added under Ar. The formed mixture was stirred at 60 ºC under Ar for 12 h as monitored by TLC. The solution was then cooled to room temperature, and the solvent was removed under vaccum directly. The crude product was purified by flash column chromatography on silica gel (PE : EA = 20:1) to afford 34.5 mg (91%) of **2aa** as a colorless oil.

3-Cyanopropyl benzoate (2aa). A colorless oil (34.5 mg, 91%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 – 7.95 (m, 2H), 7.66 – 7.52 (m, 1H), 7.52 – 7.33 (m, 2H), 4.44 (t, *J* = 6.0 Hz, 2H), 2.54 (t, *J* = 7.2 Hz, 2H), 2.29 – 2.01 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.2, 133.2, 129.6, 129.6, 128.4, 118.8, 62.7, 25.0, 14.4; ATR-FTIR (cm $^{-1}$): 2245, 1719, 1452, 1385, 1267, 1115, 1071, 741; HRMS m/z (ESI) calcd for $C_{11}H_{11}NNaO_2$ $(M + Na)^+$ 212.0682, found 212.0677.

2-Benzyl-3-cyanopropyl benzoate (2ab). A colorless oil (45.2 mg, 81%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23 – 7.91 (m, 2H), 7.66 – 7.50 (m, 1H), 7.50 – 7.42 (m, 2H), 7.36 – 7.32 (m, 2H), 7.30 – 7.18 (m, 3H), 4.45 (dd, *J* = 11.4, 4.4 Hz, 1H), 4.27 (dd, *J* = 11.4, 6.8 Hz, 1H), 3.00 – 2.77 (m, 2H), 2.57 – 2.39 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.1, 137.4, 133.3, 129.6, 129.5, 129.0, 128.8, 128.5, 126.9, 117.8, 65.6, 37.1, 36.6, 19.2; ATR-FTIR (cm $^{-1}$): 2247, 1720, 1605, 1455, 1380, 1067, 765; HRMS m/z (ESI) calcd for $C_{18}H_{17}NNaO_2$ $(M + Na)^+$ 302.1151, found 302.1154.

2-(Benzyloxy)-3-cyanopropyl benzoate (2ac). A colorless oil (31.1 mg, 53%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 – 8.03 (m, 2H), 7.62 – 7.58 (m, 1H), 7.50 – 7.44 (m, 2H), 7.40 – 7.29 (m, 5H), 4.77 – 4.70 (m, 2H), 4.47 (dd, *J* = 5.0, 1.4 Hz, 2H), 4.09 – 4.03 (m, 1H), 2.72 (dd, *J* = 5.9, 2.1 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.0, 136.8, 133.4, 129.7, 129.3, 128.6, 128.5, 128.2, 127.9, 116.9, 72.4, 72.1, 64.3, 21.2; ATR-FTIR (cm $^{-1}$): 2245, 1721, 1601, 1584, 1452, 1384, 1177, 804; HRMS m/z (ESI) calcd for $C_{18}H_{17}NNaO_3$ $(M + Na)^+$ 318.1101, found 318.1098.

2-(Cyanomethyl)-5-methoxy-3,3-dimethyl-5-oxopentyl benzoate (2ad). A colorless oil (45.2 mg, 75%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 – 8.04 (m, 2H), 7.58 (t, *J* = 7.4 Hz, 1H), 7.45 (t, *J* = 7.6 Hz, 2H), 4.64 (dd, *J* = 11.7, 4.0 Hz, 1H), 4.37 (dd, *J* = 11.7, 7.4 Hz, 1H), 3.67 (s, 3H), 2.68 (dd, *J* = 17.1, 4.8 Hz, 1H), 2.57 (dd, *J* = 17.1, 7.4 Hz, 1H), 2.43 – 2.40 (m, 3H), 1.15 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.5, 166.3, 133.3, 130.1, 129.6, 128.5, 119.0, 63.9, 51.6, 44.5, 42.1, 35.3, 25.4, 25.3, 16.1; ATR-FTIR (cm $^{-1}$): 2245, 1723, 1602, 1452, 1272, 1071, 713; HRMS m/z (ESI) calcd for $C_{17}H_{21}NNaO_4$ $(M + Na)^+$ 326.1363, found 326.1368.

3-Chloro-2-(cyanomethyl)propyl benzoate (2ae). A colorless oil (22.9 mg, 48%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 – 7.92 (m, 2H), 7.60 (tt, *J* = 7.0, 1.3 Hz, 1H), 7.55 – 7.41 (m, 2H), 4.49 – 4.41 (m, 2H), 3.89 – 3.67 (m, 2H), 2.71 – 2.70 (m, 2H), 2.69 – 2.63 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.0, 133.5, 129.7, 129.2, 128.6, 117.0, 63.7, 43.7, 37.6, 17.7; ATR-FTIR (cm $^{-1}$): 2246, 1722, 1602, 1565, 1456, 1380, 1070, 757; HRMS m/z (ESI) calcd for $C_{12}H_{13}ClNO_2$ $(M + H)^+$ 238.0629, found 238.0635.

4-Cyanobutan-2-yl benzoate (2af). A colorless oil (34.3 mg, 85%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 – 8.03 (m, 2H), 7.60 – 7.56 (m, 1H), 7.47 – 7.44 (m, 2H), 5.26 – 5.22 (m, 1H), 2.48 (td, *J* = 7.3, 1.5 Hz, 2H), 2.09 – 2.05 (m, 2H), 1.41 (d, *J* = 6.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.9, 133.2, 130.0, 129.6, 128.4, 119.1, 69.7, 31.8, 19.8, 13.7; ATR-FTIR (cm $^{-1}$): 2247, 1723, 1600, 1545, 1462, 1381, 1069, 714; HRMS m/z (ESI) calcd for $C_{12}H_{13}NNaO_2$ $(M + Na)^+$ 226.0838, found 226.0834.

4-Cyano-1-phenylbutan-2-yl benzoate (2ag) . A colorless oil (23.2 mg, 41%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 – 8.02 (m, 2H), 7.61 – 7.57 (m, 1H), 7.48 – 7.44 (m, 2H), 7.32 – 7.23 (m, 5H), 5.40 – 5.34 (m, 1H), 3.14 (dd, *J* = 13.7, 5.8 Hz, 1H), 2.94 (dd, *J* = 13.8, 7.1 Hz, 1H), 2.47 – 2.40 (m, 2H), 2.11 – 1.98 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.0, 136.2, 133.3, 129.7, 129.5, 128.7, 128.5, 127.0, 119.1, 73.7, 40.3, 29.3, 13.8; ATR-FTIR (cm $^{-1}$): 2246, 1721, 1605, 1465, 1381, 1070, 763; HRMS m/z (ESI) calcd for $C_{18}H_{17}NNaO_2$ $(M + Na)^+$302.1151, found 302.1149.

1-Cyanohex-5-en-3-yl benzoate (2ah) . A colorless oil (19.8 mg, 43%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (dd, *J* = 8.2, 1.1 Hz, 2H), 7.58 (t, *J* = 7.4 Hz, 1H), 7.46 (t, *J* = 7.7 Hz, 2H), 5.85 – 5.75 (m, 1H), 5.26 – 5.20 (m, 1H), 5.19 – 5.12 (m, 2H), 2.56 – 2.43 (m, 4H), 2.13 – 2.03 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$)

δ 166.0, 133.3, 132.3, 129.7, 129.6, 128.5, 119.1, 119.0, 72.1, 38.3, 29.5, 13.7; ATR-FTIR (cm $^{-1}$): 2247, 1722, 1657, 1600, 1266, 1071, 738; HRMS m/z (ESI) calcd for $C_{14}H_{15}NNaO_2$ (M + Na)$^+$ 252.0995, found 252.0998.

2-Cyanobenzyl benzoate (2ai). A colorless oil (43.0 mg, 91%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 – 8.09 (m, 2H), 7.72 (d, *J* = 7.6 Hz, 1H), 7.62 (dd, *J* = 4.9, 1.0 Hz, 2H), 7.60 – 7.56 (m, 1H), 7.48 – 7.44 (m, 3H), 5.55 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.0, 139.4, 133.3, 133.1, 133.0, 129.8, 129.4, 128.8, 128.5, 117.0, 112.2, 64.1; ATR-FTIR (cm $^{-1}$): 2247, 2225, 1723, 1607, 1545, 1266, 1067, 749; HRMS m/z (ESI) calcd for $C_{15}H_{12}NNaO_2$ (M + Na)$^+$ 238.0863, found 238.0857.

1-(2-Cyanophenyl)ethyl benzoate (2aj). A colorless oil (41.4 mg, 83%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 – 8.11 (m, 2H), 7.68 (d, *J* = 7.6 Hz, 1H), 7.60 – 7.56 (m, 3H), 7.48 – 7.45 (m, 2H), 7.42 – 7.37 (m, 1H), 6.34 (q, *J* = 6.7 Hz, 1H), 1.76 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.4, 145.6, 133.3, 133.2, 133.1, 129.8, 129.7, 128.4, 128.2, 126.4, 117.2, 110.3, 71.1, 21.9; ATR-FTIR (cm $^{-1}$): 2246, 2225, 1722, 1603, 1465, 1264, 1071, 750; HRMS m/z (ESI) calcd for $C_{16}H_{13}NNaO_2$ (M + Na)$^+$ 274.0838, found 274.0840.

1-(2-Cyanophenyl)but-3-en-1-yl benzoate (2ak) . A colorless oil (21.4 mg, 39%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 – 8.11 (m, 2H), 7.69 – 7.67 (m, 1H), 7.61 – 7.53 (m, 3H), 7.48 – 7.45 (m, 2H), 7.41 – 7.37 (m, 1H), 6.26 (dd, *J* = 7.6, 5.9 Hz, 1H), 5.87 – 5.76 (m, 1H), 5.17 – 5.10 (m, 2H), 2.93 – 2.76 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.4, 143.9, 133.30, 133.32, 132.9, 132.1, 129.8, 129.7, 128.5, 128.3, 127.1, 119.2, 117.3, 110.8, 74.0, 40.2; ATR-FTIR (cm $^{-1}$): 2246, 2225, 1722, 1658, 1601, 1263, 1070, 711; HRMS m/z (ESI) calcd for $C_{18}H_{15}NNaO_2$ (M + Na)$^+$ 300.0995, found 300.0999.

(Cyanomethoxy)methyl benzoate (2al). A colorless oil (33.3 mg, 87%). ^{1}H NMR (400 MHz, $CDCl_3$) δ δ 8.09 (dd, *J* = 8.3, 1.3 Hz, 2H), 7.61 (tt, *J* = 7.0, 1.3 Hz, 1H), 7.52 – 7.38 (m, 2H), 5.61 (s, 2H), 4.48 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.6, 133.8, 129.9, 128.8, 128.6, 115.3, 88.1, 54.7; ATR-FTIR (cm $^{-1}$): 2247, 1722, 1631, 1451, 1316, 1095, 710; HRMS m/z (ESI) calcd for $C_{10}H_9NNaO_3$ (M + Na)$^+$ 214.0475, found 214.0471.

3-Cyanopropyl 2-methylbenzoate (2ba). A colorless oil (36.7 mg, 90%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 – 7.90 (m, 1H), 7.42 (td, *J* = 7.6, 1.4 Hz, 1H), 7.27 – 7.24 (m, 2H), 4.41 (t, *J* = 6.0 Hz, 2H), 2.60 (s, 3H), 2.54 (t, *J* = 7.2 Hz, 2H), 2.17 – 2.11 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.0, 140.4, 132.3, 131.8, 130.5, 128.9, 125.7, 118.8, 62.3, 24.9, 21.8, 14.4; ATR-FTIR (cm $^{-1}$): 2247, 1723, 1600, 1452, 1386, 1266, 1091, 732; HRMS m/z (ESI) calcd for $C_{12}H_{13}NNaO_2$ (M + Na)$^+$ 226.0838, found 226.0837.

3-Cyanopropyl 4-fluorobenzoate (2ca). A colorless oil (39.5 mg, 95 %). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 – 8.01 (m, 2H), 7.15 – 7.08 (m, 2H), 4.42 (t, *J* = 6.0 Hz, 2H), 2.53 (t, *J* = 7.1 Hz, 2H), 2.17 – 2.11 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.7 (d, *J* = 240.8 Hz), 167.2, 165.0 (d, *J* = 70.9 Hz), 132.3 (d, *J* = 9.4 Hz), 118.9, 115.7 (d, *J* = 22.0 Hz), 63.0, 25.0, 14.5; ^{19}F NMR (376 MHz, $CDCl_3$) δ -105.0; ATR-FTIR (cm $^{-1}$): 2246, 1721, 1603, 1548, 1262, 1154, 1091, 766; HRMS m/z (ESI) calcd for $C_{11}H_{10}FNNaO_2$ (M + Na)$^+$ 230.0588, found 230.0585.

3-Cyanopropyl 2-bromobenzoate (2da). A colorless oil (47.4 mg, 88 %). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 – 7.72 (m, 1H), 7.70 – 7.58 (m, 1H), 7.42 – 7.29 (m, 2H), 4.50 – 4.30 (m, 2H), 2.56 (t, *J* = 7.2 Hz, 2H), 2.27 – 2.04 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.8, 134.3, 132.8, 131.6, 131.3, 127.2, 121.4, 118.8, 63.2, 24.7, 14.4; ATR-FTIR (cm $^{-1}$): 2246, 1716, 1600, 1545, 1261, 1085, 811; HRMS m/z (ESI) calcd for $C_{11}H_{10}BrNNaO_2$ (M + Na)$^+$ 289.9787, found 289.9783.

3-Cyanopropyl 4-iodobenzoatee (2ea) . A colorless oil (63.0 mg, 94%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (d, *J* = 8.4 Hz, 2H), 7.73 (d, *J* = 8.5 Hz, 2H), 4.42 (t, *J* = 6.0 Hz, 2H), 2.53 (t, *J* = 7.1 Hz, 2H), 2.17 – 2.10 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.7, 137.8, 131.0, 129.0, 118.8, 101.1, 63.0, 24.8, 14.4; ATR-FTIR (cm $^{-1}$): 2246, 1715, 1585, 1468, 1263, 1103, 805; HRMS m/z (ESI) calcd for $C_{11}H_{10}INNaO_2$ (M + Na)$^+$ 337.9648, found 337.9643.

3-Cyanopropyl 4-(trifluoromethyl)benzoate (2fa) . A colorless oil (45.9 mg, 89%). ^{1}H NMR (400 MHz, CDCl3) δ 8.15 (d, *J* = 8.1 Hz, 2H), 7.71 (d, *J* = 8.2 Hz, 2H), 4.47 (t, *J* = 6.0 Hz, 2H), 2.55 (t, *J* = 7.1 Hz, 2H), 2.20 – 2.13 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.1, 134.6 (q, *J* = 32.7 Hz), 132.8, 130.0, 125.5 (q, *J* = 3.5 Hz), 123.5 (q, *J* = 272.8 Hz), 118.8, 63.3, 24.8, 14.4; ^{19}F NMR (376 MHz, $CDCl_3$) δ -63.2; ATR-FTIR (cm $^{-1}$): 2245, 1723, 1586, 1513, 1412, 1326, 1266, 1066, 775; HRMS m/z (ESI) calcd for $C_{12}H_{10}F_3NNaO_2$ (M + Na)$^+$ 280.0556, found 280.0552.

3-Cyanopropyl 4-nitrobenzoate (2ga) . A colorless oil (38.7 mg, 83%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.30 – 8.28 (m, 2H), 8.24 – 8.21 (m, 2H), 4.51 (t, *J* = 6.0 Hz, 2H), 2.57 (t, *J* = 7.0 Hz, 2H), 2.22 – 2.15 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.4, 150.6, 134.9, 130.8, 123.6, 118.7, 63.8, 24.8, 14.5; ATR-FTIR (cm $^{-1}$): 2245, 1724, 1607, 1527, 1349, 1264, 1103, 805; HRMS m/z (ESI) calcd for $C_{11}H_{10}N_2NaO_4$ (M + Na)$^+$ 257.0533, found 257.0532.

3-Cyanopropyl pivalate (2ha). A colorless oil (24.5 mg, 72%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.18 – 4.15 (m, 2H), 2.44 (t, *J* = 7.2 Hz, 2H), 2.01 – 1.98 (m, 2H), 1.20 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.0, 118.6, 62.4, 38.6, 26.9, 24.6, 14.0; ATR-FTIR (cm $^{-1}$): 2246, 1728, 1631, 1565, 1511, 1263, 1096, 850; HRMS m/z (ESI) calcd for $C_9H_{15}NNaO_2$ (M + Na)$^+$ 192.0995, found 192.0999.

3-Cyanopropyl cinnamate (2ia). A colorless oil (28.3 mg, 66%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, *J* = 16.0 Hz, 1H), 7.57 – 7.49 (m, 2H), 7.48 – 7.33 (m, 3H), 6.44 (d, *J* = 16.0 Hz, 1H), 4.32 (t, *J* = 6.0 Hz, 2H), 2.51 (t, *J* = 7.2 Hz, 2H), 2.16 – 2.01 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.6, 145.5, 134.1, 130.5, 128.9, 128.1, 118.9, 117.2, 62.2, 24.9, 14.3; ATR-FTIR (cm $^{-1}$): 2246, 1727, 1545, 1469, 1264, 1090, 843; HRMS m/z (ESI) calcd for $C_{13}H_{13}NNaO_2$ (M + Na)$^+$ 238.0838, found 238.0841.

3-Cyanopropyl 3-phenylpropiolate (2ja) . A colorless oil (29.1 mg, 68%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 – 7.55 (m, 2H), 7.51 – 7.44 (m, 1H), 7.40 – 7.36 (m, 2H), 4.34 (t, *J* = 6.0 Hz, 2H), 2.53 (t, *J* = 7.2 Hz, 2H), 2.18 – 2.03 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.6, 133.0, 130.9, 128.6, 119.2, 118.6, 87.2, 80.0, 63.4, 24.7, 14.2; ATR-FTIR (cm $^{-1}$): 2247, 1709, 1641, 1490, 1263, 1097, 1021, 863; HRMS m/z (ESI) calcd for $C_{13}H_{11}NNaO_2$ (M + Na)$^+$ 236.0682, found 236.0678.

3-Cyanopropyl 6-(3-((3r,5r,7r)-adamantan-1-yl)-4-methoxyphenyl)-2-naphthoate (2ka) . A white solid (89.4 mg, 93%). ^{1}H NMR (400 MHz, DMSO) δ 8.68 (s, 1H), 8.20 (s, 1H), 8.13 (d, *J* = 8.6 Hz, 1H), 8.09 – 7.99 (m, 2H), 7.88 (d, *J* = 9.8 Hz, 1H), 7.66 – 7.53 (m, 2H), 7.07 (d, *J* = 8.6 Hz, 1H), 4.39 (t, *J* = 6.0 Hz, 2H), 3.83 (s, 3H), 2.75 (t, *J* = 7.0 Hz, 2H), 2.16 – 1.95 (m, 11H), 1.72 (s, 6H); ^{13}C NMR (100 MHz, DMSO) δ 165.8, 158.6, 140.5, 138.0, 135.7, 131.4, 130.9, 130.5, 129.9, 128.5, 126.4, 126.1, 125.8, 125.2, 125.1, 124.1, 120.4, 112.7, 63.4, 55.3, 40.1, 36.6, 36.6, 28.4, 24.4, 13.7; ATR-FTIR (cm $^{-1}$): 2247, 1720,

1643, 1545, 1498, 1264, 1076, 788; HRMS m/z (ESI) calcd for $C_{32}H_{33}NNaO_3$ $(M + Na)^+$ 502.2353, found 502.2350.

3-Cyanopropyl (8S,9S,10R,13S,14S,17S)-10,13-dimethyl-3-oxo-2,3,6,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1H-cyclopenta[a]phenanthrene-17-carboxylatee (2la). A colorless oil (47.8 mg, 62%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.71 (s, 1H), 4.25 – 4.08 (m, 2H), 2.45 (t, J = 7.2 Hz, 2H), 2.42 – 2.23 (m, 5H), 2.17 – 2.07 (m, 1H), 2.04 – 1.94 (m, 4H), 1.87 – 1.78 (m, 2H), 1.76 – 1.68 (m, 2H), 1.63 – 1.49 (m, 2H), 1.45 – 1.24 (m, 3H), 1.17 (s,3H), 1.13 – 0.91 (m, 3H), 0.70 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.5, 173.5, 171.0, 123.8, 118.7, 61.8, 55.2, 55.0, 53.6, 43.9, 38.5, 38.1, 35.6, 33.9, 32.7, 31.8, 24.8, 24.3, 23.5, 20.8, 17.3, 14.4, 13.5; ATR-FTIR (cm $^{-1}$): 2246, 1730, 1673, 1615, 1451, 1229, 1163, 1051, 739; HRMS m/z (ESI) calcd for $C_{24}H_{33}NNaO_3$ $(M + Na)^+$ 406.2353, found 406.2349.

3-Cyanopropyl (E)-2-(5-fluoro-2-methyl-1-(4-(methylsulfinyl)benzylidene)-1H-inden-3-yl)acetate (2ma) **.** A yelow oil (47.6 mg, 55%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 – 7.56 (m,4H), 7.18 – 7.12 (m, 2H), 6.87 (dd, *J* = 8.8, 2.4 Hz, 1H), 6.57 (td, *J* = 8.9, 2.4 Hz, 1H), 4.23 (t, *J* = 6.0 Hz, 2H), 3.59 (s ,2H), 2.81 (s, 3H), 2.37 (t, *J* = 7.1 Hz, 2H), 2.21 (s, 3H), 2.02 – 1.96 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.9, 163.3 (d, *J* = 246.8 Hz), 146.5 (d, *J* = 8.8 Hz), 145.5, 141.5, 139.5, 138.3, 131.4, 130.2, 129.4, 128.5, 123.8, 118.7, 110.9 (d, *J* = 22.7 Hz), 105.9 (d, *J* = 23.9 Hz), 62.8, 43.9, 31.6, 24.7, 14.1, 10.6; ^{19}F NMR (376 MHz, $CDCl_3$) δ -112.8; ATR-FTIR (cm $^{-1}$): 2247, 1728, 1601, 1565, 1462, 1263, 1090, 805; HRMS m/z (ESI) calcd for $C_{24}H_{22}FNNaO_3S$ $(M + Na)^+$ 446.1197, found 446.1201..

3-Cyanopropyl 2-(1-(4-chlorobenzoyl)-5-methoxy-2-methyl-1H-indol-3-yl)acetate (2na). A yelow oil (62.1 mg, 73%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (d, *J* = 8.5 Hz, 2H), 7.47 (d, *J* = 8.5 Hz, 2H), 6.95 (d, *J* = 2.5 Hz, 1H), 6.86 (d, *J* = 9.0 Hz, 1H), 6.67 (dd, *J* = 9.0, 2.5 Hz, 1H), 4.22 (t, *J* = 6.0 Hz, 2H), 3.83 (s, 3H), 3.69 (s, 2H), 2.38 (s, 3H), 2.35 (t, *J* = 7.1 Hz, 2H), 2.01 – 1.94 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.5, 168.2, 156.0, 139.2, 136.0, 133.7, 131.1, 130.7, 130.4, 129.1, 118.7, 114.9, 112.1, 111.5, 101.2, 62.6, 55.7, 30.1, 24.7, 14.1, 13.3; ATR-FTIR (cm $^{-1}$): 2246, 1737, 1681, 1552, 1478, 1385, 1321, 1089, 1035, 804, 754; HRMS m/z (ESI) calcd for $C_{23}H_{21}ClN_2NaO_4$ $(M + Na)^+$ 447.1082, found 447.1087.

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1. The first copper-catalyzed ortho-alkyl substituted or non-substituted cycloketoximes is achieved to afford cyano-containing benzoates via a fragmentation-rearrangement sequence.
2. The reaction is superior in only requirement of copper catalyst without extra addition of oxidant, base, ligand or toxic cyanide reagents.

Declaration of interests

☒ The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

☐The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: