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碱催化的 β-酮腈与偶氮二甲酸酯的化学选择性取代反应

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摘要 开发了 β-酮腈与偶氮二甲酸酯的碱催化 C—N 偶联反应. 在 Et_3N 催化下, 高选择性地得到了一系列二取代的 C—N 偶联产物, 收率从良好到优秀. 在 K_2CO_3 催化下进行的单取代 C—N 键形成反应也得到了新型烯醇基目标产物. 该方法简单温和, 化学选择性高, 底物相容性好, 可容忍多种官能团, 并实现了克级规模的合成. 该反应是一个亲核取代过程, 没有自由基的参与.

关键词 碱催化; β-酮腈; 选择性取代; 偶氮二甲酸酯

Base-Catalyzed Chemoselective Substitution of β-Ketonitrile with Azodicarboxylates

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Abstract Base-catalyzed nucleophilic substitution reactions of β-ketonitrile with azodicarboxylates have been developed. A series of disubstituted C—N coupling products were obtained in good to excellent yields under Et_3N catalysis. Monosubstitution C—N bond formation reaction catalyzed by K_2CO_3 also gave novel enol-based target products. This method is simple and mild, with good chemoselectivity, excellent substrate compatibility and tolerance for various functional groups, and achieves gram-scale synthesis. The reaction is a nucleophilic substitution process without the involvement of free radicals.

Keywords base-catalysis; β-ketonitrile; selective substitution; azodicarboxylate

1 Introduction

Since the development of the trinitrotoluene reaction,[1] various azodicarboxylate reagents have been synthesized and used for coupling reactions with different substrates,[2-5] such as dimethyl azodicarboxylate (DMAD), diethyl azodicarboxylate (DEAD), diisopropyl azodicarboxylate (DIAD), dibenzyl azodicarboxylate (DBAD), di-*tert*-butyl azodicarboxylate (DTBAD) and bisbenzylbis(trichloroethyl) azodicarboxylate (BTCEAD).[6] Due to their electrophilic nature, azodicarboxylic acid esters are used as prodienes in cyclisation reactions[7] and click chemistry.[8-9] The use of azodicarboxylates in carbonylation reactions is now well documented,[6,10-11] and their use as substrates for C—N bond formation has also been realized.[12-14] In addition, the use of azodicarboxylates in many oxidative C—H activation reactions does not require the involvement of a metal catalyst, providing a more environmentally friendly and sustainable approach to the construction of complex molecules.[15-16] In 2013, Zhou *et al*.[17] reported an efficient method for the preparation of stable enols via the reaction of various β-carbonyl esters (or β-carbonyl ketones) with azodicarboxylates. The authors found that the β-group of the carbonyl group in the substrate is important for the formation of enols, as these groups can either balance electrons via p-π conjugation, or form intramolecular hydrogen bonds with hydroxyl groups (Scheme 1, a). On this basis, we considered whether similar results could be obtained for the reaction of β-ketonitrile with azodicarboxylic acid esters. Interestingly, we found that the reaction of β-ketonitrile with dialkyl azodicarboxylate in the presence of a base similarly produced the desired stable enol. And further studies have shown that single- or dual-nucleophilic substitution products can be selectively generated under the catalysis of different types of base (Scheme 1, b).

2 Results and discussion

Firstly, 3-oxo-3-phenylpropanenitrile (**1a**) and diethyl

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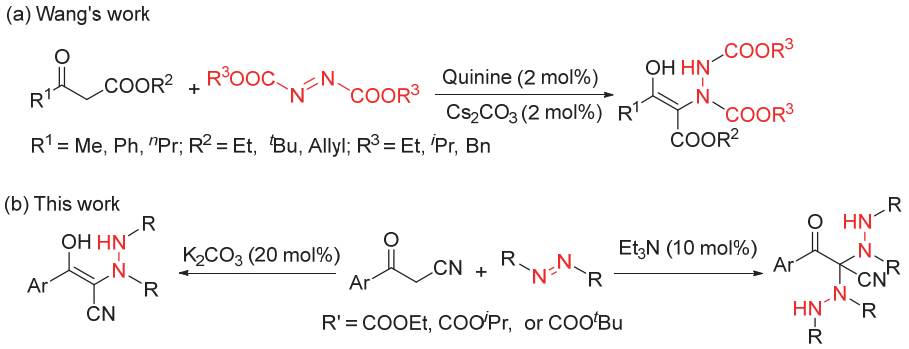
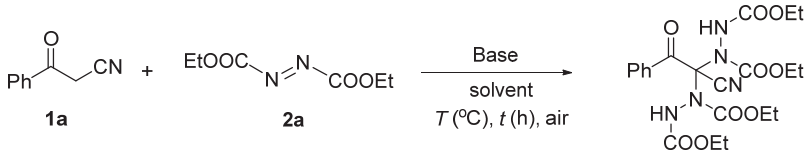
(*E*)-diazene-1,2-dicarboxylate (**2a**) were chosen as model substrates to assess the feasibility of the reaction (Table 1). The experimental results showed that the reaction of **1a** with **2a** in the ratio of 1∶2 in dichloromethane (DCM) solution for 12 h at 35 ℃ afforded the tetraethyl-1,1'-(1-cyano-2-oxo-2-phenylethane-1,1-diyl)bis(hydrazine-1,2-dicarboxylate) product **3a** in a yield of 75% (Entry 1). The structure of the product **3a** was confirmed by single crystal diffraction (CCDC: 2358107, Figure 1). When the ratio was adjusted to 1∶2.5, the yield increased slightly (Entry 2). In addition, we found that *n*-hexane, EtOH and dimethylsulfoxide (DMSO) were well compatible with the reaction system (Entries 3～5), whereas the other solvents behaved averagely and toluene even inhibited the reaction (Entries 6～10). Increasing the reaction time or temperature was not favourable (Entries 11 and 12). The addition of quinine (2 mol%) and Cs_2CO_3 (2 mol%) as catalysts to the reaction system gave only 58% yield (Entry 13). When Cs_2CO_3 (2 mol%) was added alone, the yield was 67% (Entry 14). However, when the organic base Et_3N (20 mol%) was used as catalyst, the yield of product **3a** was increased to 85% (Entry 15). Further studies showed that similar yields were obtained with 10 mol% Et_3N (Entries 16 and 17). Therefore, the optimal reaction conditions for dual-nucleophilic substitution were set to a **1a**/**2a** ratio of 1∶2.5, 10 mol% Et_3N as catalyst and dichloromethane (DCM) as solvent at 35 ℃ for 12 h.



Scheme 1 Reactions of azodicarboxylic acid ester

Table 1 Optimization of the reaction conditions[a]



Entry	*n*(**1a**)∶*n*(**2a**)	Base (dosage/mol%)	Solvent	*T*/℃	*t*/h	Yield[b]/%
1	1∶2	—	DCM	35	12	75
2[c]	1∶2.5	—	DCM	35	12	78
3	1∶2.5	—	*n*-Hexane	35	12	72
4	1∶2.5	—	EtOH	35	12	71
5	1∶2.5	—	DMSO	35	12	73
6	1∶2.5	—	1,4-Dioxane	35	12	48
7	1∶2.5	—	CH_3CN	35	12	28
8	1∶2.5	—	THF	35	12	57
9	1∶2.5	—	Toluene	35	12	NR
10	1∶2.5	—	H_2O	35	12	23
11	1∶2.5	—	DCM	35	16	57
12	1∶2.5	—	DCM	60	12	33
13	1∶2.5	Quinine (2)＋Cs_2CO_3 (2)	DCM	35	12	58
14	1∶2.5	Cs_2CO_3 (2)	DCM	35	12	67
15	1∶2.5	Et_3N (20)	DCM	35	12	85
16	1∶2.5	Et_3N (2)	DCM	35	12	78
17	**1∶2.5**	**Et_3N (10)**	DCM	**35**	**12**	**84**

[a] Reaction conditions: **1a** (0.3 mmol), **2a** (0.6 or 0.75 mmol), solvent (1 mL), base, under air. [b] Isolated yield.

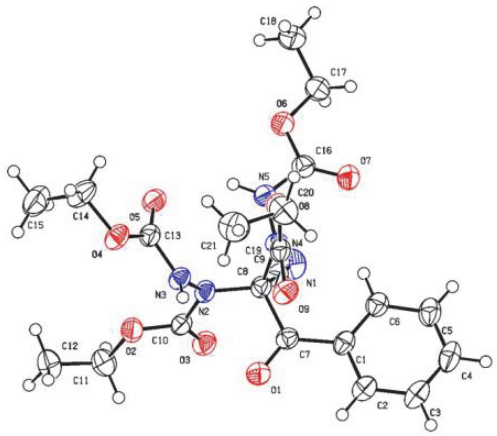
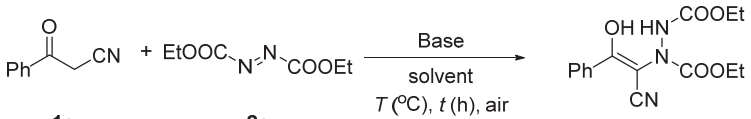


Figure 1 X-crystal structures of **3a**

The feasibility of single-nucleophilic substitution of 3-oxo-3-phenylpropionitrile (**1a**) with diethyl (*E*)-diazene-1,2-dicarboxylate (**2a**) was then investigated (Table 2). The experimental results showed that the reaction of **1a**/**2a** in a ratio of 1∶2.5 in CH_2Cl_2 solution at room temperature for 12 h in the presence of 20 mol% K_2CO_3 as catalyst afforded the diethyl (*Z*)-1-(1-cyano-2-hydroxy-2-phenylvinyl)hydrazine-1,2-dicarboxylate (**4a**) in 43% yield (Entry 1). When other inorganic bases such as KOH, Na_2CO_3 and NaOH were used, no increase in yield was observed (Entries 2～4). When the ratio of **1a**/**2a** was 1∶1, the reaction was difficult to proceed smoothly (Entry 5). However, by adjusting the **1a**/**2a** ratio to 1∶1.5, the reaction yield was rapidly increased to 72% (Entry 6). Reducing the amount of K_2CO_3 was detrimental to the reaction and was accompanied by the formation of the doubly substituted product **4a** (Entries 7 and 8). It is noteworthy that the substitution reaction was difficult to carry out when the ratio of **1a**/**2a** was 2∶1 (Entry 9), and the substitution of other solvents as reaction medium did not give satisfactory results (Entries 10～12). In addition, increasing the reaction temperature and prolonging the reaction time did not promote the yield of **4a** (Entries 13 and 14). Therefore, the optimal reaction conditions for single-nucleophilic substitution were set to a **1a**/**2a** ratio of 1∶1.5, a catalyst of 20 mol% K_2CO_3 and a solvent of CH_2Cl_2 at 35 ℃ for 12 h.

The range of substrates for the reaction of *β*-ketonitrile with azodicarboxylate disubstitution (Table 3) was investigated under optimal experimental conditions. It was shown that the reactions of various types of aryl-substituted *β*-ketonitrile with diethyl azodicarboxylate, containing either electron donating aryl group (*e.g.* Me, OMe and *n*-Pr) or electron withdrawing aryl group (*e.g.* F, Cl and Br), could proceed smoothly and the target products **3a**～**3l** were obtained in 61%～84% yields. In this process, the reactivity of the substrates containing electron-donating group substitutions was slightly higher than that with electron-absorbing group substitutions. In addition, when ethyl 3-oxo-3-phenylpropanoate and 2-nitro-1-phenylethan-1-one were used to react with diethyl azodicarboxylate, the corresponding bis-substituted products **3m** and **3n** were also obtained in 68% and 74% yields, respectively. When different aryl-substituted *β*-ketonitriles were used for the reaction with diisopropyl azodicarboxylate, the desired products **3o**～**3x** were successfully obtained in 59%～80% yields. Similarly, the reaction of aryl substituted *β*-ketonitrile with di-*tert*-butyl azodicarboxylate afforded **3y**～**3ad** in good to excellent yields. In particular, 3-(naphthalen-2-yl)-3-oxopropionitrile

Table 2 Optimization of the reaction conditions[a]

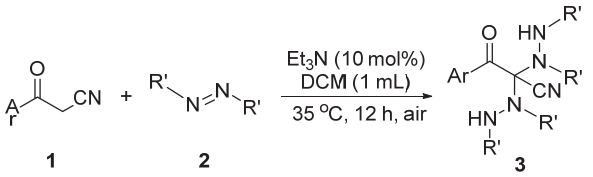


1a **2a** **4a**

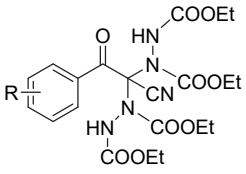
Entry	**1a**∶**2a**	Base (dosage/mol%)	Solvent	*T*/℃	*t*/h	Yield[b]/%
1	1∶2.5	K_2CO_3 (20)	DCM	35	12	43
2[c]	1∶2.5	KOH (20)	DCM	35	12	20
3	1∶2.5	Na_2CO_3 (20)	DCM	35	12	30
4	1∶2.5	NaOH (20)	DCM	35	12	35
5	1∶1	K_2CO_3 (20)	DCM	35	12	NR
6	1∶1.5	K_2CO_3 (20)	DCM	35	12	72
7	1∶1.5	K_2CO_3 (2)	DCM	35	12	0 (64)[c]
8	1∶1.5	K_2CO_3 (10)	DCM	35	12	46 (31)[c]
9[d]	2∶1	K_2CO_3 (20)	DCM	35	12	NR
10	1∶1.5	K_2CO_3 (20)	DMSO	35	12	68
11	1∶1.5	K_2CO_3 (20)	THF	35	12	61
12	1∶1.5	K_2CO_3 (20)	Toluene	35	12	NR
13	1∶1.5	K_2CO_3 (20)	DCM	60	12	59
14	1∶1.5	K_2CO_3 (20)	DCM	35	16	66

[a] Reaction conditions: **1a** (0.3 mmol), **2a** (0.75, 0.45 mmol or 0.3 mol), solvent (1 mL), catalyst, 12 h, 35 ℃, under air. [b] Isolated yield. [c] Yield of **3a**. [d] **1a** (0.6 mmol), **2a** (0.3 mmol).

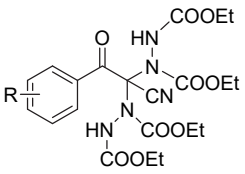
Table 3 Et_3N-catalysed reaction of *β*-ketonitrile with azodicarboxylates[a]



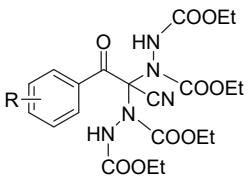
1 2 3



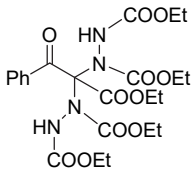
3a, R = 4-H, 84%
3b, R = 4-F, 67%
3c, R = 4-Cl, 72%
3d, R = 4-Br, 74%
3e, R = 4-Me, 68%
3f, R = 4-OMe, 67%
3g, R = 4-Pr, 80%



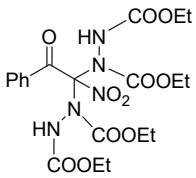
3h, R = 3-Me, 61%
3i, R = 3-Cl, 77%
3j, R = 3-Br, 56%



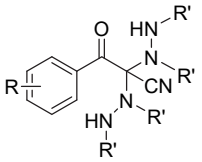
3k, R = 2-Me, 76%
3l, R = 2-OMe, 81%



3m, 68%

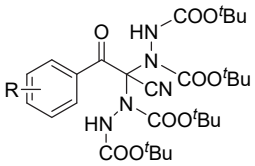


3n, 74%

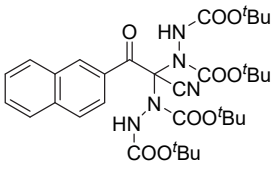


3o, R = 4-H, 78%
3p, R = 4-F, 72%
3q, R = 4-Cl, 75%
3r, R = 4-Br, 80%
3s, R = 4-Me, 74%

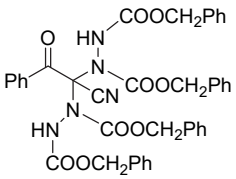
3t, R = 4-Pr, 67%
3u, R = 4-OMe, 70%
3v, R = 3-Br, 68%
3w, R = 3-Me, 59%
3x, R = 2-Me, 66%



3y, R = 4-H, 83%
3z, R = 4-Me, 90%
3aa, R = 4-Cl, 80%
3ab, R = 4-Br, 82%
3ac, R = 4-OMe, 88%
3ad, R = 4-F, 78%



3ae, 86%



3af, 81%

[a] Reaction conditions: **1a** (0.3 mmol), **2a** (0.75 mmol), DCM (1 mL), Et_3N (10 mol%) under air, 35 ℃, 12 h. [b] Isolated yield.

showed good performance when reacted with di-*tert*-butyl azodicarboxylate to afford **3ae** in 86% yield. In addition, dibenzyl azodicarboxylate and **1a** also reacted well to give the substituted enolisation product **3af** in 81% yield.

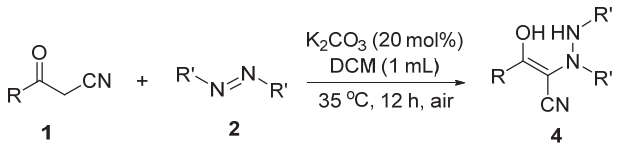
The scope of the monosubstitution reaction of *β*-ketonitrile with azodicarboxylate was then set out to investigate (Table 4). The reaction of *β*-ketonitrile with diethyl azodicarboxylate using different aryl-substituted *β*-ketonitriles containing electron-donating aryl groups (Me, OMe, *n*-Pr) and electron-withdrawing aryl groups (fluorine, chlorine and bromine) proceeded smoothly under alkaline conditions in K_2CO_3 to give the desired products **4a**～**4k** in 60%～77% yields. 3-Oxo-3-(4-pyridyl)propionitrile, 3-(naphthalen-2-yl)-3-oxopropanenitrile and 3-oxo-3-(thiophen-3-yl)propanenitrile were used in this reaction and the target products **4l**～**4n** were obtained in good yields. In addition, the benzoylacetone substrate was also suitable for this reaction and the mono-substituted product **4o** was obtained in 40% yield. When different aryl-substituted *β*-ketonitriles were used in the reaction with diisopropyl azodicarboxylate, the target products **4p**～**4y** were obtained in 42%～77% yields. Subsequently, aryl-substituted *β*-ketonitriles were used in the reaction with di-*tert*-butyl azodicarboxylate, both giving the target products **4z**～**4ab** in satisfactory yields.

To confirm the applicability of this reaction, 3 mmol of *β*-ketonitrile and 7.5 mmol of diethyl azodicarboxylate were added to 15 mL of DCM, and 1.352 g of **3a** was successfully obtained in 91% yield using 10 mol% Et_3N as catalyst (Scheme 2, a). Under similar conditions, the reaction of 4.8 mmol of *β*-ketonitrile with 7.2 mmol of diethyl azodicarboxylate also gave 1.046 g of the target product **4a** in 68% yield by using 20 mol% K_2CO_3 as catalyst (Scheme 2, b). To further demonstrate the utility of this reaction product, the product **4a** can be further reacted in trifluoroacetic acid at 0 ℃ by the action of phenyliodine(III) diacetate (PIDA) to give the product **4ac** in 93% yield (Scheme 2, c).

A series of controlled experiments were carried out to investigate the underlying reaction mechanism. First, the double substitution reaction in the presence of Et_3N was subjected to radical trapping experiments by the addition of 2,6-di-*tert*-butyl-4-methylphenol (BHT) and 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO). The results showed that the product **3a** could still be obtained with 77% and 81% yields, respectively (Scheme 3, a). Similarly, by adding BHT and TEMPO to the monosubstitution reaction in the presence of K_2CO_3, the target product **4a** was obtained in 43% and 65% yields, respectively (Scheme 3, b). The above experimental results indicate that this C—N bond formation reaction excludes the involvement of free radicals.

On the basis of controlled experiments, a possible reaction mechanism is proposed (Scheme 4). In the absence of a base (Route 1), an equilibrium exists between the *β*-ketonitrile and the enol intercalation isomers, whereby the enol

Table 4 K_2CO_3-catalysed reaction of β-ketonitrile with azodicarboxylates



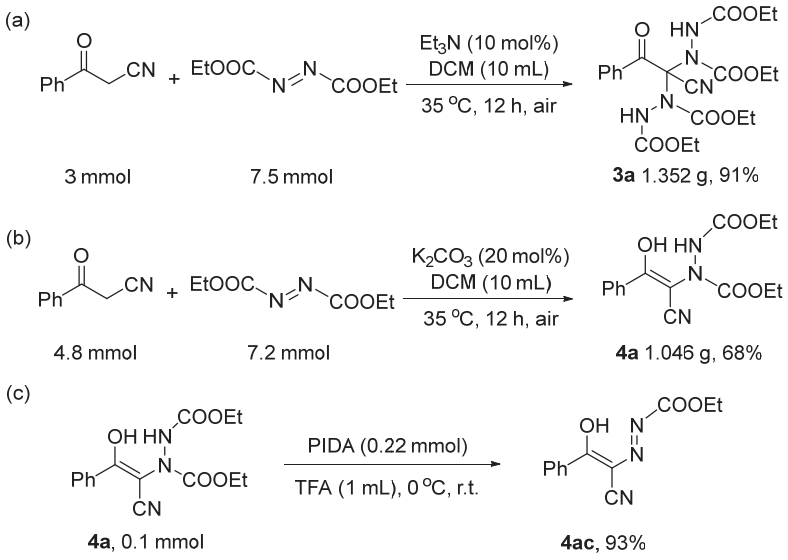
1 2 4

4a, R = 4-H, 72%
4b, R = 4-Me, 58% (77%)[c]
4c, R = 4-MeO, 73%
4d, R = 4-Br, 76%
4e, R = 4-F, 49% (70%)[c]
4f, R = 4-Pr, 36% (64%)[c]
4g, R = 4-Cl, 77%
4h, R = 3-Cl, 38% (69%)[c]
4i, R = 3-F, 32% (63%)[c]
4j, R = 3-Me, 56%
4k, R = 2-Me, 33% (60%)[c]

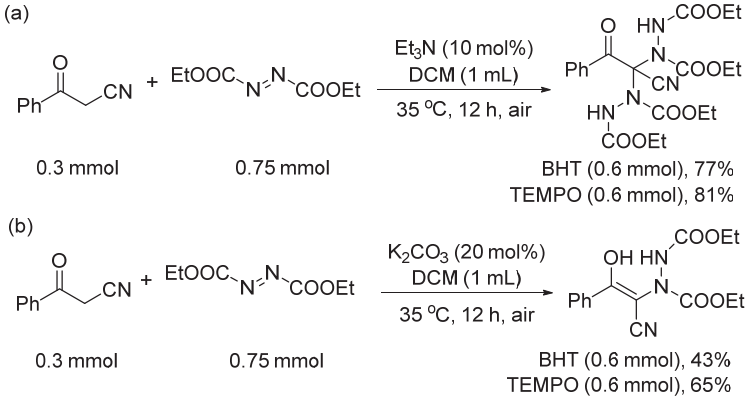
4l, 64%
4m, 42%
4n, 51%
4o, 40 %
4p, R = 4-H, 77%
4q, R = 4-F, 57%
4r, R = 4-Br, 55%
4s, R = 4-Cl, 52%
4t, R = 4-OMe, 59%
4u, R = 3-Cl, 51%
4v, R = 3-Me, 42%

4w, 52%
4x, 63%
4y, 67%
4z, R = 4-Br, 66%
4aa, R = 4-OMe, 47% (68%)[c]
4ab, 55%

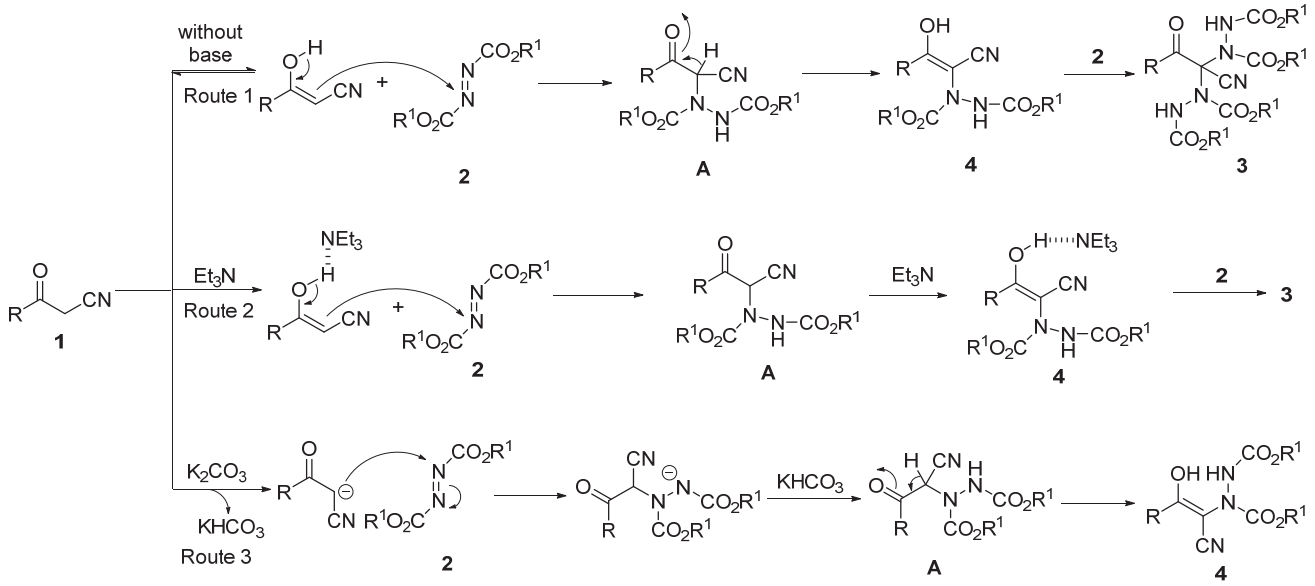
[a] Reaction conditions: **1a** (0.3 mmol), **2a** (0.45 mmol), DCM (1 mL), K_2CO_3 (20 mol%), under air. [b] Isolated yield. [c] 24 h.



Scheme 2 Gram-scale synthesis and derivatization



Scheme 3 Control experiments



Scheme 4 Possible reaction mechanisms

isomer undergoes a Michael addition with the azodicarboxylate **2** to form intermediate **A**. Intermediate **A** is further converted to the structurally stable enol structure product **4** due to intramolecular hydrogen bonding. Subsequently, the Michael addition of product **4** with **2** took place again to produce the target product **3**. In the presence of Et_3N (Route 2), due to the intermolecular hydrogen bonding, the *β*-ketonitrile is more readily present in the form of the enol isomer, and thus more favourable to the subsequent Michael addition, which lead to the final bisubstituted product **3**. In the presence of K_2CO_3 (Route 3), the *β*-ketonitrile loses its hydrogen to form the corresponding anionic intermediate, which subsequently reacts with the azodicarboxylate to form the addition product. Further hydrogen is obtained from $KHCO_3$ to yield the intermediate **A**. Finally, **A** undergoes hydrogen migration to give the product **4**.

3 Conclusions

In summary, the base-catalysed selective nucleophilic substitution reactions of *β*-ketonitrile with azodicarboxylates were successfully developed. On the one hand, a wide range of disubstituted products were synthesised in good to excellent yields under the catalysis of Et_3N. On the other hand, single-nucleophilic substitution reactions catalyzed by K_2CO_3 also yielded significant amounts of enol-based target products. This method has several advantages, including simplicity of operation, mild reaction conditions, excellent chemoselectivity, broad substrate compatibility and remarkable functional group tolerance. The practical significance of the reaction has been further validated by gram-scale reactions. Mechanistic studies suggest that the reaction involves a nucleophilic substitution process with non-radical participation.

4 Experimental section

4.1 General methods

Unless otherwise noted, all reactions were performed in Schlenk tubes. Melting points were determined with a fusiometer and were not corrected. The materials obtained from commercial suppliers were used without further purification. For chromatography, Qingdao Ocean Chemical 200～300 mesh silica gel was employed. ^1H NMR, ^{13}C NMR and ^{19}F NMR spectra were recorded on a Bruker Avance III HD 400 MHz spectrometer in $CDCl_3$ or DMSO-d_6 solution with tetramethylsilane (TMS) as the internal standard. High-resolution mass spectrometry (HRMS) was performed on a Thermo Scientific LTQ or bitrap XL mass spectrometer, thermo fisher Q Exactive.

4.2 General procedure for the synthesis of 1

Malononitrile (0.8 mmol), arylboronic acid (0.4 mmol), palladium acetate (0.08 mmol), 2,2'-bipyridine (0.16 mmol), *p*-toluenesulphonic acid (1.6 mmol), toluene (5 mL) and water (1 mL) were added to a Schlenk tube (10 mL) equipped with a magnetic stirring bar. The reaction mixture was allowed to react at 80 ℃ for 24 h. The reaction mixture was allowed to cool to room temperature, washed with saturated $NaHCO_3$ and extracted with ethyl acetate (10 mL×3). The organic layer was dried over anhydrous Na_2SO_4, concentrated by rotary evaporator and separated by silica gel column chromatography [petroleum ether (PE)/EtOAc, V∶V=5∶1] to give pure *β*-ketonitrile **1**.[18]

4.3 General procedure for the synthesis of 3

β-Ketonitrile **1** (0.3 mmol), azodicarboxylate **2** (0.75 mmol) and Et_3N (10 mol%) in DCM (1 mL) were added to a Schlenk tube (10 mL) equipped with a magnetic stirring bar. The mixture was stirred in air and the reaction was carried out at 35 ℃ for 12 h. The solution was then evaporated

under reduced pressure and the residue was purified by silica gel column chromatography using PE/EtOAc (V∶V=5∶1) as eluent to give product **3**.

Tetraethyl 1,1'-(1-cyano-2-oxo-2-phenylethane-1,1-diyl)-bis(hydrazine-1,2-dicarboxylate) (**3a**): 139.6 mg, 85% yield, yellow solid. m.p. 132.4～133.7 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.60 (d, J=7.8 Hz, 2H), 7.72～7.42 (m, 3H), 4.28 (dq, J=21.3, 7.9, 7.3 Hz, 8H), 1.52～1.00 (m, 12H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 165.17, 155.37, 151.38, 133.10, 132.99, 128.85, 127.76, 64.18, 62.56, 62.47, 62.33, 62.28, 14.46, 14.30, 14.18; HRMS (ESI) calcd for $C_{21}H_{27}N_5O_9Na$ $[M+Na]^+$ 516.1706, found 516.1701.

Tetraethyl 1,1'-(1-cyano-2-(4-fluorophenyl)-2-oxoethane-1,1-diyl)bis(hydrazine-1,2-dicarboxylate) (**3b**): 114.3 mg, 67% yield, yellow solid. m.p. 137.4～139.5 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.65 (s, 2H), 7.19 (d, J=8.5 Hz, 2H), 4.27 (t, J=8.9 Hz, 8H), 1.48～1.09 (m, 12H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 167.91, 165.35, 132.92, 128.66, 116.42, 116.20, 111.82, 100.11, 64.67, 63.10, 14.51, 14.21; HRMS (APCI) calcd for $C_{21}H_{27}FN_5O_9$ $[M+H]^+$ 512.1793, found 512.1787.

Tetraethyl 1,1'-(2-(4-chlorophenyl)-1-cyano-2-oxoethane-1,1-diyl)bis(hydrazine-1,2-dicarboxylate) (**3c**): 126.7 mg, 72% yield, yellow solid. m.p. 128.5～130.4 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.55 (d, J=8.3 Hz, 2H), 7.50 (d, J=8.4 Hz, 2H), 7.23～6.51 (m, 2H), 4.36～4.03 (m, 8H), 1.46～0.94 (m, 12H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 179.47, 155.30, 141.25, 131.33, 129.37, 111.68, 65.57, 64.67, 63.09, 60.48, 21.13, 14.47, 14.17; HRMS (APCI) calcd for $C_{21}H_{27}ClN_5O_9$ $[M+H]^+$ 528.1497, found 528.1492.

Tetraethyl 1,1'-(2-(4-bromophenyl)-1-cyano-2-oxoethane-1,1-diyl)bis(hydrazine-1,2-dicarboxylate) (**3d**): 141.3 mg, 74% yield, yellow solid. m.p. 134.7～135.9 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.47 (d, J=8.3 Hz, 2H), 7.68 (d, J=8.3 Hz, 2H), 4.26 (s, 8H), 1.29 (s, 12H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 179.71, 155.28, 132.37, 131.35, 131.00, 130.19, 111.66, 65.57, 64.67, 63.09, 60.48, 14.47, 14.29, 14.18; HRMS (APCI) calcd for $C_{21}H_{27}BrN_5O_9$ $[M+H]^+$ 572.0992, found 572.0987.

Tetraethyl 1,1'-(1-cyano-2-oxo-2-(*p*-tolyl)ethane-1,1-diyl)bis(hydrazine-1,2-dicarboxylate) (**3e**): 115.0 mg, 68% yield, yellow solid. m.p. 145.8～147.1 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.48 (d, J=7.9 Hz, 2H), 7.33 (d, J=8.9 Hz, 2H), 4.36～4.15 (m, 8H), 2.41 (s, 3H), 1.42～1.17 (m, 12H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 155.29, 145.86, 142.79, 130.07, 129.74, 129.31, 128.66, 64.54, 64.25, 63.01, 62.66, 62.37, 21.99, 21.71, 14.52, 14.39, 14.25; HRMS (APCI) calcd for $C_{22}H_{30}N_5O_9$ $[M+H]^+$ 508.2044, found 508.2038.

Tetraethyl 1,1'-(1-cyano-2-(4-methoxyphenyl)-2-oxoethane-1,1-diyl)bis(hydrazine-1,2-dicarboxylate) (**3f**): 117.0 mg, 67% yield, yellow solid. m.p. 142.7～144.3 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.58 (d, J=8.5 Hz, 2H), 7.00 (d, J=8.6 Hz, 2H), 4.40～4.02 (m, 8H), 3.86 (s, 3H), 1.27 (d, J=7.3 Hz, 12H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 164.72, 132.48, 130.57, 125.07, 114.32, 112.17, 64.48, 63.06, 62.33, 55.68, 14.52, 14.21; HRMS (APCI) calcd for $C_{22}H_{30}N_5O_{10}$ $[M+H]^+$ 524.1993, found 524.1987.

Tetraethyl 1,1'-(1-cyano-2-oxo-2-(4-propylphenyl)ethane-1,1-diyl)bis(hydrazine-1,2-dicarboxylate) (**3g**): 142.8 mg, 80% yield, yellow solid. m.p. 121.6～122.4 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.50 (d, J=8.1 Hz, 2H), 7.33 (d, J=8.0 Hz, 2H), 4.28 (dd, J=14.8, 7.3 Hz, 12H), 1.66 (q, J=7.4 Hz, 3H), 1.30 (dt, J=18.1, 8.4 Hz, 12H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 180.17, 150.40, 130.06, 129.13, 129.04, 128.72, 127.76, 112.05, 64.52, 64.23, 63.01, 38.31, 38.03, 24.33, 24.00, 14.51, 14.37, 14.20, 13.93; HRMS (APCI) calcd for $C_{24}H_{34}N_5O_9$ $[M+H]^+$ 536.2357, found 536.2351.

Tetraethyl 1,1'-(1-cyano-2-oxo-2-(*m*-tolyl)ethane-1,1-diyl)bis(hydrazine-1,2-dicarboxylate) (**3h**): 103.2 mg, 61% yield, yellow solid. m.p. 135.5～136.7 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.41 (d, J=47.5 Hz, 1H), 7.44 (s, 2H), 7.35 (d, J=18.9 Hz, 1H), 4.43～4.10 (m, 8H), 2.43 (s, 3H), 1.48～1.12 (m, 12H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 155.52, 138.83, 135.59, 132.91, 130.40, 129.15, 128.92, 128.51, 125.87, 64.56, 63.00, 21.44, 14.51; HRMS (APCI) calcd for $C_{22}H_{30}N_5O_9$ $[M+H]^+$ 508.2044, found 508.2038.

Tetraethyl 1,1'-(2-(3-chlorophenyl)-1-cyano-2-oxoethane-1,1-diyl)bis(hydrazine-1,2-dicarboxylate) (**3i**): 135.5 mg, 77% yield, yellow solid. m.p. 128.4～130.4 ℃; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 7.94～7.79 (m, 2H), 7.67 (d, J=7.5 Hz, 1H), 7.52 (t, J=7.8 Hz, 1H), 4.18 (d, J=7.1 Hz, 8H), 1.22 (dt, J=27.6, 7.1 Hz, 12H); ^{13}C NMR (101 MHz, DMSO-d_6) δ: 164.55, 151.41, 135.27, 133.14, 132.28, 130.35, 128.04, 127.01, 61.18, 60.45, 14.19, 14.09; HRMS (ESI) calcd for $C_{21}H_{26}ClN_5O_9Na$ $[M+Na]^+$ 550.1317, found 550.1318.

Tetraethyl 1,1'-(2-(3-bromophenyl)-1-cyano-2-oxoethane-1,1-diyl)bis(hydrazine-1,2-dicarboxylate) (**3j**): 106.8 mg, 56% yield, yellow solid. m.p. 126.5～127.4 ℃; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 8.05 (s, 1H), 7.92～7.49 (m, 2H), 7.51～7.24 (m, 1H), 4.28～4.00 (m, 8H), 1.19 (dt, J=14.0, 7.2 Hz, 12H). ^{13}C NMR (101 MHz, DMSO-d_6) δ: 164.46, 151.42, 135.46, 135.18, 130.89, 130.60, 127.39, 121.56, 61.19, 60.47, 20.77, 14.54, 14.19; HRMS (ESI) calcd for $C_{21}H_{26}BrN_5O_9Na$ $[M+Na]^+$ 594.0812, found 594.0812.

Tetraethyl 1,1'-(1-cyano-2-oxo-2-(*o*-tolyl)ethane-1,1-diyl)bis(hydrazine-1,2-dicarboxylate) (**3k**): 128.6 mg, 76% yield, yellow solid. m.p. 117.8～119.5 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.36 (s, 1H), 7.30 (d, J=18.5 Hz, 1H), 7.17 (d, J=6.5 Hz, 2H), 4.30～4.07 (m, 8H), 2.35 (s, 3H), 1.36～1.11 (m, 12H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 155.33, 137.39, 137.39, 131.03, 130.90, 129.24, 125.89, 116.88, 93.60, 64.30, 62.68, 19.40, 14.53; HRMS (APCI) calcd for $C_{22}H_{30}N_5O_9$ $[M+H]^+$ 508.2044, found 508.2038.

Tetraethyl 1,1'-(1-cyano-2-(2-methoxyphenyl)-2-oxoethane-1,1-diyl)bis(hydrazine-1,2-dicarboxylate) (**3l**): 141.3 mg, 81% yield, yellow solid. m.p. 100.2～103.1 ℃; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 7.65 (d, J=8.1 Hz, 1H), 7.48 (d, J=7.3 Hz, 1H), 7.16 (dd, J=37.2, 8.7 Hz, 1H), 7.02 (s, 1H), 4.35～3.93 (m, 8H), 3.83 (s, 3H), 1.32～1.06 (m, 12H); ^{13}C NMR (101 MHz, DMSO-d_6) δ: 165.81,

156.53, 151.19, 132.57, 129.45, 124.02, 120.43, 112.53, 111.85, 65.29, 63.81, 62.09, 61.04, 55.90, 55.66, 39.94, 39.73, 39.52, 39.31, 39.10, 14.17; HRMS (ESI) calcd for $C_{22}H_{29}N_5O_{10}Na$ [M + Na]$^+$ 546.1812546.1816, found 546.1816.

Tetraethyl 1,1'-(1-ethoxy-1,3-dioxo-3-phenylpropane-2,2-diyl)bis(hydrazine-1,2-dicarboxylate) (**3m**): 122.5 mg, 68% yield, yellow solid. m.p. 103.3～104.6 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.03 (d, J=7.8 Hz, 2H), 7.63～7.39 (m, 5H), 4.48～3.77 (m, 10H), 1.26 (t, J=7.1 Hz, 15H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 191.08, 156.10, 155.18, 134.97, 134.19, 129.06, 128.81, 77.48, 77.16, 76.84, 63.81, 62.42, 62.03, 14.42, 14.08; HRMS (ESI) calcd for $C_{23}H_{32}N_4O_{11}Na$ [M+Na]$^+$ 563.1965, found 563.1986.

Tetraethyl 1,1'-(1-nitro-2-oxo-2-phenylethane-1,1-diyl)-bis(hydrazine-1,2-dicarboxylate) (**3n**): 126.7 mg, 74% yield, yellow solid. m.p. 152.7～154.3 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.02 (s, 1H), 7.67 (t, J=7.4 Hz, 2H), 7.52 (t, J=7.7 Hz, 2H), 4.49 (q, J=7.1 Hz, 8H), 1.47～1.28 (m, 12H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 160.40, 154.70, 135.25, 133.15, 129.40, 128.99, 65.57, 65.09, 62.60, 14.23, 14.11; HRMS (ESI) calcd for $C_20H_{27}N_5O_{11}Na$ [M+Na]$^+$ 536.1605, found 536.1613.

1,1'-(1-Cyano-2-oxo-2-phenylethane-1,1-diyl)bis(hydrazine-1,2-dicarboxylate) (**3o**): 142.9 mg, 78% yield, yellow solid. m.p. 119.2～201.3 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.67～8.38 (m, 2H), 7.56 (d, J=34.3 Hz, 3H), 4.89 (d, J=115.7 Hz, 4H), 1.51～0.81 (m, 24H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 180.71, 154.99, 134.44, 132.36, 129.84, 128.90, 128.64, 72.91, 70.58, 60.45, 22.03, 21.75, 21.64, 14.27; HRMS (ESI) calcd for $C_{25}H_{35}N_5O_9Na$ [M + Na]$^+$ 572.2332, found 572.2328.

Tetraisopropyl 1,1'-(1-cyano-2-(4-fluorophenyl)-2-oxo-ethane-1,1-diyl)bis(hydrazine-1,2-dicarboxylate) (**3p**): 136.2 mg, 72% yield, yellow solid. m.p. 130.3～131.7 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.72～8.43 (m, 2H), 7.20 (t, J=8.6 Hz, 2H), 4.89 (d, J=108.9 Hz, 4H), 1.51～0.84 (m, 24H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 167.81, 155.07, 132.81, 128.86, 116.34, 116.12, 73.06, 70.73, 27.02, 22.07, 21.79, 21.68; HRMS (ESI) calcd for $C_{25}H_{34}FN_5O_9Na$ [M+Na]$^+$ 590.2238, found 590.2231.

Tetraisopropyl 1,1'-(2-(4-chlorophenyl)-1-cyano-2-oxo-ethane-1,1-diyl)bis(hydrazine-1,2-dicarboxylate) (**3q**): 146.0 mg, 75% yield, yellow solid. m.p. 147.7～149.1 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.46 (dd, J=67.5, 8.4 Hz, 2H), 7.51 (d, J=8.5 Hz, 2H), 4.90 (d, J=112.7 Hz, 4H), 1.52～0.83 (m, 24H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 155.04, 141.04, 131.28, 130.83, 129.35, 73.11, 70.74, 27.02, 22.06, 21.93, 21.78, 21.67; HRMS (ESI) calcd for $C_{25}H_{34}ClN_5O_9Na$ [M+Na]$^+$ 606.1943, found 606.1938.

Tetraisopropyl 1,1'-(2-(4-bromophenyl)-1-cyano-2-oxo-ethane-1,1-diyl)bis(hydrazine-1,2-dicarboxylate) (**3r**): 167.6 mg, 80% yield, yellow solid. m.p. 102.6～104.5 ℃; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 7.80 (d, J=8.6 Hz, 2H), 7.69 (d, J=8.5 Hz, 2H), 5.07～4.81 (m, 4H), 1.31 – 1.16 (m, 24H); ^{13}C NMR (101 MHz, DMSO-d_6) δ: 165.13, 151.03, 132.48, 131.36, 130.38, 126.38, 74.02, 71.94, 68.85, 21.65; HRMS (ESI) calcd for $C_{25}H_{34}BrN_5O_9Na$ [M+Na]$^+$ 650.1438, found 650.1429.

Tetraisopropyl 1,1'-(1-cyano-2-oxo-2-(*p*-tolyl)ethane-1,1-diyl)bis(hydrazine-1,2-dicarboxylate) (**3s**): 139.0 mg, 74% yield, yellow solid. m.p. 104.6～106,7 ℃; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 8.51～8.07 (m, 2H), 7.38 (d, J=7.9 Hz, 2H), 4.82 (d, J=92.5 Hz, 4H), 2.46～2.31 (m, 3H), 1.43～0.97 (m, 24H); ^{13}C NMR (101 MHz, DMSO-d_6) δ: 129.34, 128.88, 128.38, 70.06, 68.63, 26.36, 21.84, 21.70, 21.60, 21.37, 21.25, 21.21; HRMS (ESI) calcd for $C_{26}H_{37}N_5O_9Na$ [M+Na]$^+$ 586.2489, found 586.2480.

Tetraisopropyl 1,1'-(1-cyano-2-oxo-2-(4-propylphenyl)-ethane-1,1-diyl)bis(hydrazine-1,2-dicarboxylate) (**3t**): 132.1 mg, 67% yield, yellow solid. m.p. 91.0～93.6 ℃; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 8.34 (d, J=64.1 Hz, 2H), 7.55～7.08 (m, 2H), 5.12～4.50 (m, 4H), 2.65 (d, J=8.7 Hz, 2H), 1.71～1.56 (m, 2H), 1.56～0.93 (m, 24H), 0.89 (d, J=5.6 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 180.38, 155.07, 150.09, 129.96, 129.04, 112.30, 72.77, 71.28, 70.49, 38.27, 23.97, 22.04, 21.75, 21.64, 13.91; HRMS (ESI) calcd for $C_{28}H_{41}N_5O_9Na$ [M+Na]$^+$ 614.2802, found 614.2811.

Tetraisopropyl 1,1'-(1-cyano-2-(4-methoxyphenyl)-2-oxoethane-1,1-diyl)bis(hydrazine-1,2-dicarboxylate) (**3u**): 135.2 mg, 70% yield, yellow solid. m.p. 107.5～108.8 ℃; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 8.69 (d, J=145.3 Hz, 2H), 7.10 (d, J=8.6 Hz, 2H), 5.03～4.59 (m, 4H), 3.89 (s, 3H), 1.22 (dd, J=29.0, 5.9 Hz, 25H); ^{13}C NMR (101 MHz, DMSO-d_6) δ: 156.17, 131.75, 130.49, 114.10, 113.60, 70.05, 67.83, 55.75, 55.48, 21.92, 21.70, 21.33; HRMS (ESI) calcd for $C_{26}H_{37}N_5O_{10}Na$ [M+Na]$^+$ 602.2438, found 602.2435.

Tetraisopropyl 1,1'-(2-(3-bromophenyl)-1-cyano-2-oxo-ethane-1,1-diyl)bis(hydrazine-1,2-dicarboxylate) (**3v**): 142.5 mg, 68% yield, yellow solid. m.p. 82.6～84.3 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.37 (dd, J=136.4, 8.8 Hz, 2H), 7.54 (d, J=11.4 Hz, 1H), 7.33 (s, 1H), 5.04 (d, J=6.1 Hz, 4H), 1.29 (d, J=19.3 Hz, 24H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 155.04, 141.04, 131.28, 130.82, 129.35, 129.10, 73.11, 70.74, 27.02, 22.06, 21.93, 21.78, 21.67; HRMS (ESI) calcd for $C_{25}H_{34}BrN_5O_9Na$ [M + Na]$^+$ 650.1438, found650.1433.

Tetraisopropyl 1,1'-(1-cyano-2-oxo-2-(*m*-tolyl)ethane-1,1-diyl)bis(hydrazine-1,2-dicarboxylate) (**3w**): 110.8 mg, 59% yield, yellow solid. m.p. 96.2～99.3 ℃; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 7.75～7.58 (m, 2H), 7.39 (dd, J=15.9, 7.4 Hz, 2H), 5.17～4.62 (m, 4H), 2.36 (s, 3H), 1.38～1.13 (m, 24H); ^{13}C NMR (101 MHz, DMSO-d_6) δ: 165.88, 151.12, 137.68, 133.25, 133.07, 128.76, 128.23, 125.44, 74.02, 71.94, 68.65, 21.67, 21.33, 20.80; HRMS (ESI) calcd for $C_{26}H_{37}N_5O_9Na$ [M+Na]$^+$ 586.2489, found 586.2476.

Tetraisopropyl 1,1'-(1-cyano-2-oxo-2-(*o*-tolyl)ethane-1,1-diyl)bis(hydrazine-1,2-dicarboxylate) (**3x**): 124.0 mg, 66% yield, yellow oily liquid. ^{1}H NMR (400 MHz, DMSO-d_6) δ: 7.69 (d, J=32.2 Hz, 1H), 7.53 (d, J=7.0 Hz, 2H), 7.50～7.32 (m, 1H), 5.25～4.86 (m, 4H), 2.68 (s, 3H), 1.53～1.19 (m, 24H); ^{13}C NMR (101 MHz, DMSO-d_6) δ:

168.78, 151.02, 135.57, 135.28, 130.39, 130.06, 127.29, 125.42, 124.18, 120.42, 74.03, 71.94, 69.97, 69.22, 68.69, 21.59, 19.23; HRMS (ESI) calcd for $C_{26}H_{37}N_5O_9Na$ [M+Na]$^+$ 586.2489, found 586.2499.

Tetra-*tert*-butyl 1,1'-(1-cyano-2-oxo-2-phenylethane-1,1-diyl)bis(hydrazine-1,2-dicarboxylate) (**3y**): 167.6 mg, 83% yield, yellow solid. m.p. 161.4～163.2 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.61 (dd, J=41.4, 7.7 Hz, 2H), 7.55 (d, J=11.9 Hz, 3H), 1.80～1.12 (m, 36H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 181.24, 155.81, 134.67, 134.05, 130.52, 129.77, 128.74, 128.49, 84.54, 81.44, 28.27, 28.22, 28.05, 27.92; HRMS (ESI) calcd for $C_{29}H_{43}N_5O_9Na$ [M + Na]$^+$ 628.2958, found 628.2963.

Tetra-*tert*-butyl 1,1'-(1-cyano-2-oxo-2-(*p*-tolyl)ethane-1,1-diyl)bis(hydrazine-1,2-dicarboxylate) (**3z**): 185.9 mg, 90% yield, yellow solid. m.p. 192.5～194.6 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.50 (d, J=38.9 Hz, 2H), 7.33 (d, J=9.1 Hz, 2H), 7.21 (d, J=8.4 Hz, 0H), 2.40 (s, 3H), 1.69～1.08 (m, 36H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 171.17, 154.60, 154.06, 145.80, 145.05, 130.63, 129.88, 129.51, 129.21, 86.41, 84.44, 83.05, 81.68, 60.43, 28.22, 27.94, 27.81, 27.44, 21.91, 14.27, 11.50; HRMS (ESI) calcd for $C_{30}H_{45}N_5O_9Na$ [M+Na]$^+$ 642.3115, found 642.3118.

Tetra-*tert*-butyl 1,1'-(2-(4-chlorophenyl)-1-cyano-2-oxoethane-1,1-diyl)bis(hydrazine-1,2-dicarboxylate) (**3aa**): 170.7 mg, 80% yield, yellow solid. m.p. 124.4～125.8 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.91～8.03 (m, 2H), 7.49 (d, J=8.4 Hz, 2H), 1.74～1.06 (m, 36H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 180.24, 154.24, 140.59, 131.96, 131.23, 129.15, 128.91, 84.79, 81.94, 28.26, 27.94; HRMS (ESI) calcd for $C_{29}H_{42}ClN_5O_9Na$ [M+Na]$^+$ 662.2569, found 662.2573.

Tetra-*tert*-butyl 1,1'-(2-(4-bromophenyl)-1-cyano-2-oxoethane-1,1-diyl)bis(hydrazine-1,2-dicarboxylate) (**3ab**): 187.1 mg, 82% yield, yellow solid. m.p. 123.7～124.9 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.45 (d, J=8.3 Hz, 2H), 7.66 (d, J=8.3 Hz, 2H), 1.50 (d, J=23.3 Hz, 36H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 180.28, 154.31, 132.39, 132.14, 131.93, 131.65, 131.26, 130.92, 129.50, 112.61, 86.86, 84.81, 82.79, 81.93, 60.45, 36.15, 29.14, 28.26, 27.94, 27.50, 22.71, 21.12, 19.53, 18.86, 14.29, 11.52; HRMS (ESI) calcd for $C_{29}H_{42}BrN_5O_9Na$ [M + Na]$^+$ 706.2064, found 706.2062.

Tetra-*tert*-butyl 1,1'-(1-cyano-2-(4-methoxyphenyl)-2-oxoethane-1,1-diyl)bis(hydrazine-1,2-dicarboxylate) (**3ac**): 186.5 mg, 88% yield, yellow solid. m.p. 186.3～187.6 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.57 (d, J=28.7 Hz, 2H), 6.94 (d, J=38.4 Hz, 2H), 3.84 (s, 3H), 1.71～1.18 (m, 36H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 171.17, 164.24, 133.04, 132.24, 114.19, 114.06, 113.76, 86.26, 84.31, 81.71, 60.43, 55.56, 28.22, 27.94, 21.09, 14.26; HRMS (ESI) calcd for $C_{30}H_{45}BrN_5O_{10}Na$ [M+Na]$^+$ 658.3064, found 658.3062.

Tetra-*tert*-butyl 1,1'-(1-cyano-2-(4-fluorophenyl)-2-oxoethane-1,1-diyl)bis(hydrazine-1,2-dicarboxylate) (**3ad**): 162.2 mg, 78% yield, yellow solid. m.p. 107.2～108.7 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.67 (d, J=43.1 Hz, 2H), 7.19 (d, J=10.0 Hz, 2H), 1.81～1.09 (m, 36H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 167.56, 165.02, 154.41, 154.16, 133.54, 132.71, 129.28, 128.84, 115.89, 84.70, 81.92, 60.46, 41.44, 36.16, 33.80, 29.14, 28.29, 27.95, 22.71, 19.52, 18.85, 14.40, 11.52; HRMS (ESI) calcd for $C_{29}H_{42}FN_5O_9Na$ [M+Na]$^+$ 646.2864, found 646.2868.

Tetra-*tert*-butyl 1,1'-(1-cyano-2-(naphthalen-2-yl)-2-oxoethane-1,1-diyl)bis(hydrazine-1,2-dicarboxylate) (**3ae**): 188.0 mg, 86% yield, yellow solid. m.p. 93.8～95.4 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.45 (d, J=8.3 Hz, 1H), 8.16 (d, J=19.8 Hz, 1H), 7.91 (d, J=34.6 Hz, 3H), 7.59 (d, J=8.1 Hz, 2H), 1.55 (d, J=36.6 Hz, 37H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 153.97, 136.10, 132.75, 132.59, 131.07, 130.67, 129.99, 129.60, 129.04, 128.43, 127.63, 126.95, 126.64, 124.79, 86.48, 81.88, 53.55, 28.28, 28.00; HRMS (APCI) calcd for $C_{33}H_{46}N_5O_9$ [M+H]$^+$ 656.3296, found 656.3290.

Tetrabenzyl 1,1'-(1-cyano-2-oxo-2-phenylethane-1,1-diyl)bis(hydrazine-1,2-dicarboxylate) (**3af**): 180.1 mg, 81% yield, yellow oily liquid. ^{1}H NMR (400 MHz, Chloroform-*d*) δ: 8.67～8.52 (m, 1H), 8.31～8.06 (m, 1H), 7.65～7.51 (m, 2H), 7.47～7.27 (m, 20H), 5.20 (d, J=19.9 Hz, 8H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 135.60, 134.73, 134.53, 130.01, 128.97, 128.67, 128.57, 128.52, 128.49, 128.21, 128.03, 127.05, 111.66, 77.48, 77.16, 76.84, 69.66, 69.08, 68.40, 67.95, 60.49; HRMS (APCI) calcd for $C_{41}H_{34}N_5O_9$ [M−H]$^+$ 740.2435, found 740.2362.

4.4 General procedure for the synthesis of 4

β-Ketonitrile **1** (0.3 mmol), azodicarboxylate **2** (0.45 mmol), K_2CO_3 (20 mol%) in DCM (1 mL) were added to a Schlenk tube (10 mL) equipped with a magnetic stirrer. The mixture was stirred in air and the reaction was carried out at 35 ℃ for 12 h. The solution was then evaporated under reduced pressure and the residue was purified by silica gel column chromatography using PE/EtOAc (V∶V=5∶1) as eluent to give product **4**.

Diethyl 1-(1-cyano-2-oxo-2-phenylethyl)hydrazine-1,2-dicarboxylate (**4a**): 69.0 mg, 72% yield, yellow oily liquid. ^{1}H NMR (400 MHz, DMSO-d_6) δ: 10.94 (s, 1H), 7.87 (d, J=7.9 Hz, 2H), 7.60 (t, J=7.4 Hz, 1H), 7.49 (t, J=7.7 Hz, 2H), 4.26～4.03 (m, 4H), 1.30～1.16 (m, 6H); ^{13}C NMR (101 MHz, DMSO-d_6) δ: 165.82, 151.62, 133.28, 132.54, 128.37, 128.29, 63.29, 61.05, 14.22; HRMS (APCI) calcd for $C_{15}H_{18}N_3O_5$ [M+H]$^+$ 320.1246, found 320.1241.

Diethyl 1-(1-cyano-2-oxo-2-(*p*-tolyl)ethyl)hydrazine-1,2-dicarboxylate (**4b**): 77.0 mg, 77% yield, yellow oily liquid. ^{1}H NMR (400 MHz, DMSO-d_6) δ: 10.85 (s, 1H), 7.79 (d, J=7.9 Hz, 2H), 7.29 (d, J=7.9 Hz, 2H), 4.17 (q, J=7.2 Hz, 4H), 2.36 (s, 3H), 1.30～1.10 (m, 6H); ^{13}C NMR (101 MHz, DMSO-d_6) δ: 165.52, 151.65, 142.83, 130.43, 128.91, 128.38, 63.28, 60.97, 60.85, 21.04, 14.23, 14.01; HRMS (APCI) calcd for $C_{16}H_{18}N_3O_5$ [M−H]$^+$ 332.1247, found 332.1252.

Diethyl 1-(1-cyano-2-(4-methoxyphenyl)-2-oxoethyl)-hydrazine-1,2-dicarboxylate (**4c**): 76.5 mg, 73% yield, yellow oily liquid. ^{1}H NMR (400 MHz, DMSO-d_6) δ: 10.77 (s, 1H), 7.88 (d, J=8.9 Hz, 2H), 7.01 (d, J=8.5 Hz, 2H),

4.17 (q, J=7.1 Hz, 4H), 3.83 (d, J=2.8 Hz, 3H), 1.33～1.09 (m, 6H); ^{13}C NMR (101 MHz, DMSO-d_6) δ: 164.87, 162.69, 151.70, 130.48, 125.27, 113.63, 60.91, 55.50, 39.94, 39.73, 39.52, 39.31, 39.10, 14.25; HRMS (APCI) calcd for $C_{16}H_{20}N_3O_6$ $[M+H]^+$ 350.1352, found 350.1347.

Diethyl 1-(2-(4-bromophenyl)-1-cyano-2-oxoethyl)hydrazine-1,2-dicarboxylate (**4d**): 90.8 mg, 76% yield, yellow oily liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.22 (s, 1H), 7.71 (d, J=8.3 Hz, 2H), 7.61 (d, J=8.3 Hz, 2H), 4.29 (d, J=7.1 Hz, 4H), 1.32 (d, J=6.9 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 164.41, 151.17, 132.24, 131.96, 129.40, 128.10, 62.72, 62.45, 14.36; HRMS (APCI) calcd for $C_{15}H_{15}BrN_3O_5$ $[M-H]^+$ 396.0195, found 396.0201.

Diethyl 1-(1-cyano-2-(4-fluorophenyl)-2-oxoethyl)-hydrazine-1,2-dicarboxylate (**4e**): 70.8 mg, 70% yield, yellow oily liquid. ^{1}H NMR (400 MHz, DMSO-d_6) δ: 10.97 (s, 1H), 7.95 (dd, J=8.7, 5.6 Hz, 2H), 7.32 (t, J=8.8 Hz, 2H), 4.17 (s, 4H), 1.26 (s, 6H); ^{13}C NMR (101 MHz, DMSO-d_6) δ: 164.70, 151.54, 131.26, 131.16, 129.76, 115.48, 115.26, 63.28, 61.08, 14.21; HRMS (APCI) calcd for $C_{15}H_{15}FN_3O_5$ $[M-H]^+$ 336.0996, found 336.1001.

Diethyl 1-(1-cyano-2-oxo-2-(4-propylphenyl)ethyl)hydrazine-1,2-dicarboxylate (**4f**): 69.4 mg, 64% yield, yellow oily liquid. ^{1}H NMR (400 MHz, DMSO-d_6) δ: 10.84 (s, 1H), 7.80 (d, J=7.9 Hz, 2H), 7.30 (d, J=7.9 Hz, 2H), 4.13 (d, J=28.0 Hz, 4H), 2.61 (s, 2H), 1.61 (s, 2H), 1.22 (d, J=27.4 Hz, 6H), 0.90 (d, J=7.3 Hz, 3H); ^{13}C NMR (101 MHz, DMSO-d_6) δ: 165.54, 151.63, 151.32, 147.30, 130.73, 128.38, 128.31, 60.96, 23.73, 14.22, 14.20, 13.59; HRMS (APCI) calcd for $C_{18}H_{22}N_3O_5$ $[M-H]^+$ 360.1560, found 360.1565.

Diethyl 1-(2-(4-chlorophenyl)-1-cyano-2-oxoethyl)hydrazine-1,2-dicarboxylate (**4g**): 81.7 mg, 77% yield, yellow oily liquid. ^{1}H NMR (400 MHz, DMSO-d_6) δ: 11.02 (s, 1H), 7.88 (d, J=8.4 Hz, 2H), 7.56 (d, J=8.4 Hz, 2H), 4.38～3.90 (m, 4H), 1.38～1.04 (m, 6H); ^{13}C NMR (101 MHz, DMSO-d_6) δ: 164.90, 151.50, 137.40, 132.06, 130.25, 128.45, 61.13, 60.84, 14.20; HRMS (APCI) calcd for $C_{15}H_{15}ClN_3O_5$ $[M-H]^+$ 352.0700, found 353.0703.

Diethyl 1-(2-(3-chlorophenyl)-1-cyano-2-oxoethyl)hydrazine-1,2-dicarboxylate (**4h**): 73.2 mg, 69% yield, yellow oily liquid. ^{1}H NMR (400 MHz, DMSO-d_6) δ: 11.06 (s, 1H), 7.92～7.79 (m, 2H), 7.67 (d, J=8.1 Hz, 1H), 7.52 (t, J=7.9 Hz, 1H), 4.18 (d, J=7.1 Hz, 4H), 1.26 (t, J=7.1 Hz, 6H); ^{13}C NMR (101 MHz, DMSO-d_6) δ: 164.54, 151.40, 135.27, 133.13, 132.27, 130.34, 128.04, 127.01, 61.17, 60.84, 14.19; HRMS (APCI) calcd for $C_{15}H_{15}ClN_3O_5$ $[M-H]^+$ 352.0700, found 352.0706.

Diethyl 1-(1-cyano-2-(3-fluorophenyl)-2-oxoethyl)hydrazine-1,2-dicarboxylate (**4i**): 63.8 mg, 63% yield, yellow oily liquid. ^{1}H NMR (400 MHz, DMSO-d_6) δ: 11.03 (s, 1H), 7.70 (dd, J=13.5, 8.8 Hz, 2H), 7.61～7.38 (m, 3H), 4.18 (d, J=7.1 Hz, 4H), 1.30～1.13 (m, 6H); ^{13}C NMR (101 MHz, DMSO-d_6) δ: 164.56, 164.53, 162.94, 160.51, 151.43, 130.60, 130.52, 124.50, 124.47, 119.54, 119.33, 115.20, 114.97, 63.28, 61.18, 60.85, 14.19, 14.01; HRMS (APCI) calcd for $C_{15}H_{15}FN_3O_5$ $[M-H]^+$ 336.0996, found 336.1001.

Diethyl 1-(1-cyano-2-oxo-2-(*m*-tolyl)ethyl)hydrazine-1,2-dicarboxylate (**4j**): 56.0 mg, 56% yield, yellow oily liquid. ^{1}H NMR (400 MHz, DMSO-d_6) δ: 10.87 (s, 1H), 7.70 (s, 1H), 7.66 (d, J=7.6 Hz, 1H), 7.43～7.30 (m, 2H), 4.17 (d, J=7.1 Hz, 4H), 2.36 (s, 3H), 1.26 (s, 6H); ^{13}C NMR (101 MHz, DMSO-d_6) δ: 165.81, 151.57, 137.72, 133.21, 133.11, 128.77, 128.26, 125.44, 60.99, 60.84, 20.81, 14.22; HRMS (APCI) calcd for $C_{16}H_{18}N_3O_5$ $[M-H]^+$ 332.1247, found 332.1252.

Diethyl 1-(1-cyano-2-oxo-2-(*o*-tolyl)ethyl)hydrazine-1,2-dicarboxylate (**4k**): 60.0 mg, 60% yield, yellow oily liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.99 (s, 1H), 7.47 (d, J=7.5 Hz, 2H), 7.29 (d, J=7.0 Hz, 2H), 4.28 (s, 4H), 2.59 (s, 3H), 1.30 (d, J=4.9 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 142.37, 142.37, 133.85, 132.54, 131.62, 130.91, 126.49, 125.92, 112.23, 64.51, 63.00, 23.05, 14.53, 14.22; HRMS (APCI) calcd for $C_{16}H_{18}N_3O_5$ $[M-H]^+$ 332.1247, found 332.1252.

Diethyl 1-(1-cyano-2-oxo-2-(pyridin-4-yl)ethyl)hydrazine-1,2-dicarboxylate (**4l**): 61.5 mg, 64% yield, yellow oily liquid. ^{1}H NMR (400 MHz, DMSO-d_6) δ: 11.22 (s, 1H), 8.75 (d, J=13.3 Hz, 2H), 7.74 (d, J=6.1 Hz, 2H), 4.19 (d, J=7.1 Hz, 4H), 1.34～1.08 (m, 7H); ^{13}C NMR (101 MHz, DMSO-d_6) δ: 164.98, 151.33, 150.19, 149.99, 140.52, 121.77, 65.27, 61.36, 14.15; HRMS (APCI) calcd for $C_{14}H_{15}N_4O_5$ $[M-H]^+$ 319.1043, found 319.0148.

Diethyl 1-(1-cyano-2-(naphthalen-2-yl)-2-oxoethyl)hydrazine-1,2-dicarboxylate (**4m**): 46.5 mg, 42% yield, yellow oily liquid. ^{1}H NMR (400 MHz, DMSO-d_6) δ: 11.10 (s, 1H), 8.57 (s, 1H), 8.05 (d, J=7.8 Hz, 1H), 8.00 (t, J=6.7 Hz, 2H), 7.91 (d, J=8.5 Hz, 1H), 7.63 (dd, J=16.6, 7.4 Hz, 2H), 4.22 (s, 4H), 1.23 (d, J=38.5 Hz, 6H); ^{13}C NMR (101 MHz, DMSO-d_6) δ: 165.87, 151.63, 151.35, 134.69, 131.85, 130.47, 129.29, 129.20, 128.33, 128.01, 127.63, 126.92, 124.51, 61.07, 60.85, 14.24, 14.20; HRMS (APCI) calcd for $C_{19}H_{18}N_3O_5$ $[M-H]^+$ 368.1247, found 368.1243.

Diethyl 1-(1-cyano-2-oxo-2-(thiophen-3-yl)ethyl)hydrazine-1,2-dicarboxylate (**4n**): 49.8 mg, 51% yield, yellow oily liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.07 (s, 1H), 7.49 (d, J=5.1 Hz, 1H), 7.42～7.27 (m, 1H), 4.28 (s, 4H), 1.30 (d, J=26.3 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 159.92, 151.33, 136.18, 131.00, 127.14, 126.80, 62.60, 62.43, 14.54, 14.39; HRMS (APCI) calcd for $C_{13}H_{14}N_3O_5S$ $[M-H]^+$ 324.0654, found 324.06601.

Diethyl 1-(3-oxo-3-phenylpropanoyl)hydrazine-1,2-dicarboxylate (**4o**): 40.4 mg, 40% yield, yellow oily liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.01 (s, 1H), 7.82 (d, J=7.3 Hz, 2H), 7.59 (t, J=7.2 Hz, 1H), 7.49 (d, J=7.2 Hz, 2H), 4.26 (dd, J=43.8, 7.0 Hz, 4H), 1.59 (s, 2H), 1.37～1.24 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 185.63, 155.94, 134.28, 129.31, 128.89, 126.72, 63.77, 62.38, 22.84, 14.82, 14.45; HRMS (APCI) calcd for $C_{15}H_{17}N_2O_6$ $[M-H]^+$ 321.1087, found 321.1092.

Diisopropyl 1-(1-cyano-2-oxo-2-phenylethyl)hydrazine-1,2-dicarboxylate (**4p**): 70.9 mg, 68% yield, yellow oily liquid. ^{1}H NMR (400 MHz, DMSO-d_6) δ: 10.88 (s, 1H),

7.90～7.82 (m, 2H), 7.58 (d, J=7.5 Hz, 1H), 7.48 (t, J=7.6 Hz, 2H), 5.16～4.79 (m, 2H), 1.27 (d, J=6.3 Hz, 12H); ^{13}C NMR (101 MHz, DMSO-d_6) δ: 165.88, 151.16, 133.32, 132.48, 128.32, 128.28, 68.72, 21.66; HRMS (APCI) calcd for $C_{17}H_{20}N_3O_5$ [M－H]$^+$ 346.1403, found 346.1408.

Diisopropyl 1-(1-cyano-2-(4-fluorophenyl)-2-oxoethyl)-hydrazine-1,2-dicarboxylate (**4q**): 62.5 mg, 57% yield, yellow oily liquid. ^{1}H NMR (400 MHz, DMSO-d_6) δ: 10.91 (s, 1H), 7.95 (dd, J=8.7, 5.6 Hz, 2H), 7.31 (t, J=8.8 Hz, 2H), 4.93 (s, 2H), 1.27 (d, J=6.3 Hz, 8H); ^{13}C NMR (101 MHz, DMSO-d_6) δ: 165.82, 164.77, 163.33, 151.09, 131.25, 131.16, 129.84, 129.81, 115.43, 115.21, 68.77, 21.65; HRMS (APCI) calcd for $C_{17}H_{19}FN_3O_5$ [M－H]$^+$ 364.1309, found 364.1314.

Diisopropyl 1-(2-(4-bromophenyl)-1-cyano-2-oxoethyl)-hydrazine-1,2-dicarboxylate (**4r**): 70.3 mg, 55% yield, yellow oily liquid. ^{1}H NMR (400 MHz, DMSO-d_6) δ: 10.96 (s, 1H), 7.80 (d, J=8.4 Hz, 2H), 7.69 (d, J=8.4 Hz, 2H), 4.93 (s, 2H), 1.26 (d, J=6.2 Hz, 12H); ^{13}C NMR (101 MHz, DMSO-d_6) δ: 165.12, 151.02, 132.47, 131.35, 130.38, 126.38, 71.23, 68.84, 21.65; HRMS (APCI) calcd for $C_{17}H_{19}BrN_3O_5$ [M－H]$^+$ 424.0508, found 424.0514.

Diisopropyl 1-(2-(4-chlorophenyl)-1-cyano-2-oxoethyl)-hydrazine-1,2-dicarboxylate (**4s**): 59.6 mg, 52% yield, yellow oily liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.78 (d, J=6.1 Hz, 2H), 7.44 (d, J=6.0 Hz, 2H), 5.07 (s, 2H), 1.31 (d, J=6.3 Hz, 12H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 164.33, 150.58, 139.45, 131.60, 130.06, 129.26, 129.21, 70.71, 22.06, 21.91; HRMS (APCI) calcd for $C_{17}H_{19}ClN_3O_5$ [M－H]$^+$ 380.1073, found 380.1089.

Diisopropyl 1-(1-cyano-2-(4-methoxyphenyl)-2-oxoethyl)hydrazine-1,2-dicarboxylate (**4t**): 66.8 mg, 59% yield, yellow oily liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.57 (d, J=8.7 Hz, 1H), 8.22 (d, J=152.6 Hz, 1H), 7.01 (d, J=8.6 Hz, 2H), 5.04 (s, 2H), 3.87 (s, 3H), 1.26 (d, J=6.2 Hz, 12H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 164.59, 133.06, 132.41, 125.31, 114.29, 114.29, 113.96, 72.75, 70.56, 70.18, 68.58, 55.67, 22.16, 22.08; HRMS (APCI) calcd for $C_{18}H_{22}N_3O_6$ [M－H]$^+$ 376.1509, found 376.1514.

Diisopropyl 1-(2-(3-chlorophenyl)-1-cyano-2-oxoethyl)-hydrazine-1,2-dicarboxylate (**4u**): 58.4 mg, 51% yield, yellow oily liquid. ^{1}H NMR (400 MHz, DMSO-d_6) δ: 10.99 (s, 1H), 7.91 (s, 1H), 7.81 (d, J=7.9 Hz, 1H), 7.66 (d, J=8.0 Hz, 1H), 7.51 (t, J=7.9 Hz, 1H), 4.93 (s, 2H), 1.27 (d, J=6.3 Hz, 12H); ^{13}C NMR (101 MHz, DMSO-d_6) δ: 164.59, 150.94, 135.31, 133.11, 132.21, 130.29, 128.04, 127.00, 68.88, 21.63; HRMS (APCI) calcd for $C_{17}H_{19}ClN_3O_5$ [M－H]$^+$ 380.1073, found 380.1089.

Diisopropyl 1-(1-cyano-2-oxo-2-(m-tolyl)ethyl)hydrazine-1,2-dicarboxylate (**4v**): 45.5 mg, 42% yield, yellow oily liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.63～7.57 (m, 1H), 7.36 (d, J=7.4 Hz, 3H), 5.09 (s, 2H), 2.41 (s, 3H), 1.32 (d, J=6.2 Hz, 12H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 165.15, 150.54, 138.99, 133.81, 133.27, 128.83, 128.35, 124.63, 70.45, 21.96, 21.47; HRMS (APCI) calcd for $C_{18}H_{22}N_3O_6$ [M－H]$^+$ 360.1560, found 360.1564.

Diisopropyl 1-(1-cyano-2-oxo-2-(thiophen-3-yl)ethyl)-hydrazine-1,2-dicarboxylate (**4w**): 55.1 mg, 52% yield, yellow oily liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 9.19 (s, 1H), 7.90 (s, 1H), 7.34 (s, 1H), 5.04 (s, 2H), 1.45～1.03 (m, 12H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 174.87, 155.08, 136.08, 128.10, 126.26, 112.26, 72.93, 70.85, 22.05, 21.93, 21.77, 21.66; HRMS (APCI) calcd for $C_{15}H_{18}N_3O_5S$ [M－H]$^+$ 352.0967, found 352.0973.

Diisopropyl 1-(1-cyano-2-(naphthalen-2-yl)-2-oxoethyl)-hydrazine-1,2-dicarboxylate (**4x**): 75.1 mg, 63% yield, yellow oily liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.34 (s, 1H), 8.24 (s, 1H), 8.02～7.85 (m, 3H), 7.70 – 7.40 (m, 2H), 5.25～4.99 (m, 2H), 1.36 (s, 12H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 165.14, 150.65, 135.45, 132.52, 130.45, 129.30, 128.98, 128.67, 128.61, 127.96, 127.25, 123.75, 70.55, 21.98; HRMS (APCI) calcd for $C_{21}H_{22}N_3O_5$ [M－H]$^+$ 396.1560, found 369.1565.

Diisopropyl 1-(1-cyano-2-oxo-2-(pyridin-4-yl)ethyl)hydrazine-1,2-dicarboxylate (**4y**): 70.0 mg, 67% yield, yellow oily liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.91～7.74 (m, 1H), 7.56 (d, J=7.3 Hz, 1H), 7.47 (d, J=7.6 Hz, 2H), 6.56 (s, 1H), 4.18 (d, J=7.1 Hz, 2H), 1.29 (d, J=29.8 Hz, 12H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 165.06, 151.30, 133.16, 133.05, 128.94, 127.76, 62.56, 62.36, 14.37; HRMS (APCI) calcd for $C_{16}H_{19}N_4O_5$ [M－H]$^+$ 347.1356, found 347.1361.

Di-*tert*-butyl 1-(2-(4-bromophenyl)-1-cyano-2-oxoethyl)-hydrazine-1,2-dicarboxylate (**4z**): 90.0 mg, (66% yield, yellow oily liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.70 (d, J=7.4 Hz, 2H), 7.61 (d, J=8.7 Hz, 2H), 1.58～1.00 (m, 18H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 164.45, 150.53, 132.22, 132.07, 129.36, 128.03, 70.73, 21.93; HRMS (APCI) calcd for $C_{19}H_{23}BrN_3O_5$ [M－H]$^+$ 452.0821, found 452.0827.

Di-*tert*-butyl 1-(1-cyano-2-(4-methoxyphenyl)-2-oxoethyl)hydrazine-1,2-dicarboxylate (**4aa**): 82.7 mg, 68% yield, yellow oily liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.79 (d, J=8.4 Hz, 2H), 6.92 (d, J=8.4 Hz, 2H), 3.84 (s, 3H), 1.52 (s, 18H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 164.68, 163.32, 149.97, 129.80, 125.63, 114.07, 82.65, 55.61, 28.16; HRMS (APCI) calcd for $C_{20}H_{26}N_3O_6$ [M－H]$^+$ 404.1822, found 404.1828.

Di-*tert*-butyl 1-(1-cyano-2-oxo-2-(thiophen-3-yl)ethyl)-hydrazine-1,2-dicarboxylate (**4ab**): 63.0 mg, 55% yield, yellow oily liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.02 (s, 1H), 7.88 (s, 1H), 7.46 (d, J=5.0 Hz, 1H), 7.37 (d, J=2.6 Hz, 1H), 1.53 (s, 18H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 160.24, 149.77, 136.50, 130.66, 127.06, 126.72, 82.99, 28.19; HRMS (APCI) calcd for $C_{17}H_{22}N_3O_5S$ [M－H]$^+$ 380.1280, found 380.1286.

4.5 Gram-synthesis of **3a**

β-Ketonitrile (3 mmol), azodicarboxylic acid diethylester (7.5 mmol), Et_3N (10 mol%) and DCM (10 mL) were added to a sealed tube (100 mL) with a magnetic stirring bar. The mixture was stirred in air and the reaction was carried out at 35 ℃ for 12 h. The solution was then evaporated under reduced pressure and the residue was purified by silica gel column chromatography using PE/EtOAc (V∶V=5∶1) as

eluent to give product **3a** (1.352 g, 91%).

4.6 Gram-synthesis of **4a**

β-Ketonitrile (4.8 mmol), azodicarboxylic acid diethylester (7.2 mmol), K_2CO_3 (20 mol%) and DCM (10 mL) were added to a sealed tube (100 mL) with a magnetic stirring bar. The mixture was stirred in air and the reaction was carried out at 35 ℃ for 12 h. The solution was then evaporated under reduced pressure and the residue was purified by silica gel column chromatography using PE/EtOAc (*V*∶*V*=5∶1) as eluent to give product **4a** (1.046 g, 68%).

4.7 Synthesis of **4ac**

4a (0.1 mmol), PIDA (0.22 mmol) and trifluoroacetic acid (TFA) (1 mL) were added to a 10 mL reaction tube and the solution was stirred for 10 min at 0 ℃. Subsequently, the mixture was brought to room temperature and stirring was continued for 2 h. The solution was then evaporated under reduced pressure and the mixture was purified by column chromatography on silica gel using PE/EA (*V*∶*V*=3∶1) as the eluent to give product **4ac** in 93% yield. Ethyl (*E*)-2-((*Z*)-1-cyano-2-hydroxy-2-phenylvinyl)diazene-1-carboxylate (**4ac**): 22.8 mg, 93% yield, White solid, ^{1}H NMR (600 MHz, Chloroform-*d*) *δ*: 8.17 (s, 1H), 7.92～7.74 (m, 2H), 7.65～7.36 (m, 3H), 4.30 (q, *J*=7.1 Hz, 2H), 1.34 (t, *J*=7.1 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) *δ*: 165.00, 151.20, 133.18, 133.08, 128.98, 127.73, 77.37, 77.16, 76.95, 62.56, 14.39; HRMS (APCI) calcd for $C_{12}H_{10}N_3O_3$ $[M-H]^+$ 244.0800, found 244.0728.

Supporting Information NMR spectra of the products **3** and **4**. The Supporting Information is available free of charge via the Internet at http://sioc-journal.cn.

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