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Note

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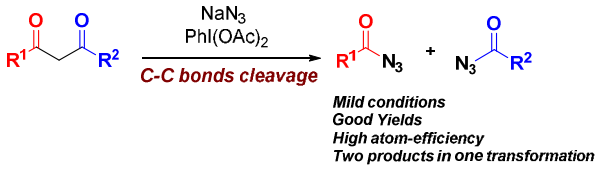
Synthesis of Acyl Azides from 1,3-Diketones via Oxidative Cleavage of Two C−C Bonds

Tian-Yang Yu[†,§], Zhao-Jing Zheng[‡,§], Tong-Tong Dang[†], Fang-Xia Zhang[†] and Hao Wei[*,†]

† Key Laboratory of Synthetic and Natural Functional Molecular Chemistry of the Ministry of Education, College of Chemistry & Materials Science, Northwest University, Xi'an 710127, P. R. China

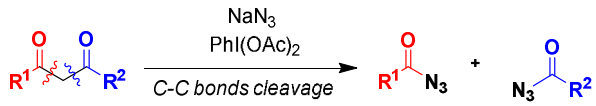
‡ State Key Laboratory of Applied Organic Chemistry College of Chemistry and Chemical Engineering Lanzhou University, Lanzhou 730000, P. R. China



ABSTRACT: A metal-free $PhI(OAc)_2$-mediated method for the synthesis of acyl azides through oxidative cleavage of 1,3-diketones is described. This method is shown to have a broad substrate scope, providing a useful tool for multiproduct synthesis in single procedure. A possible reaction pathway is proposed based on mechanistic studies

C−C bonds are one of the most fundamental chemical bonds in organic compounds. As compared to C−C bond-forming reactions, reactions for formation of C−X bonds through the selective cleavage of C−C bonds remain a major challenge.[1,2] The cleavage of unstrained C−C bonds with subsequent functionalization would not only provide unusual retrosynthetic disconnections, but also improve industrial processes. Traditionally, harsh conditions with high-costing transition-metal catalysts and stoichiometric oxidants are required to cleave C−C bonds. Thus, the development of green approaches toward unstrained C−C bond cleavage is highly desirable. 1,3-Dicarbonyl moieties are found in various natural products, drugs, and biologically active compounds. Despite the thermodynamic stability of C−C bonds, the oxidative cleavage of 1,3-diketones has evolved into a powerful tool for synthesis of carboxylic acids.[3] Also, several elegant examples of the construction of new C−C,[4] C−O,[5] C−N[6] or other bonds[7] have been reported through fragmentation of 1,3-dicarbonyl compounds. On the other hand, acyl azides are valuable intermediates in synthesis and building

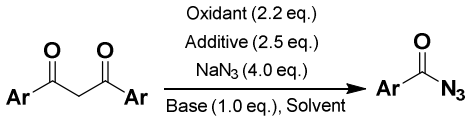
blocks in organic chemistry.[8] Classical procedures for synthesis of acyl azides are based on combining activated acid derivatives (acyl chlorides, anhydrides and N-acyl benzotriazoles) with metal azides.[9] To our knowledge, no examples of acyl azide preparation through the direct oxidative cleavage of 1,3-diketones under metal-free conditions have been reported previously. Herein, we disclose the development of a method for the oxidative cleavage of 1,3-diketone compounds, which provides facile access to a series of functionalized acyl azides (Scheme 1).



Scheme 1. Synthesis of two azides.

Initially, we investigated the reaction of compound (**1a**) in the presence of (diacetoxyiodo)benzene, NaBr, K_2CO_3, and NaN_3 in different solvents. Among these solvents, acetone gave the most promising results, but the yields were not high (Table 1, entries 1–3). It was found that aqueous solutions of acetone were required to obtain higher product yields, probably due to the low solubility of sodium azide in organic solvents (Table 1, entries 4 and 5). This result encouraged us to further optimize with the volume of water used. To our delight, acyl azide **2a** was obtained in 60% yield in acetone/H_2O (5:1, *v/v*) (Table 1, entry 5). Other hypervalent iodine(III) reagents, such as [bis(trifluoroacetoxy)iodo]benzene and iodobenzene dichloride, were also examined, but were found to be less efficient than $PhI(OAc)_2$ (Table 1, entries 5–7). Next, NaI, NH_4Br and CuBr were tested as additives, with the results showing that NaBr was the best option (Table 1, entries 5, 8−10). Finally, a screening of different bases showed that NaOAc was slightly superior to K_2CO_3 (Table 1, entries 5, 11–13).

Table 1. Optimization of $PhI(OAc)_2$-mediated cleavage of 1,3-diketones[a]



1a Ar = 4-$MeOC_6H_4$ **2a**

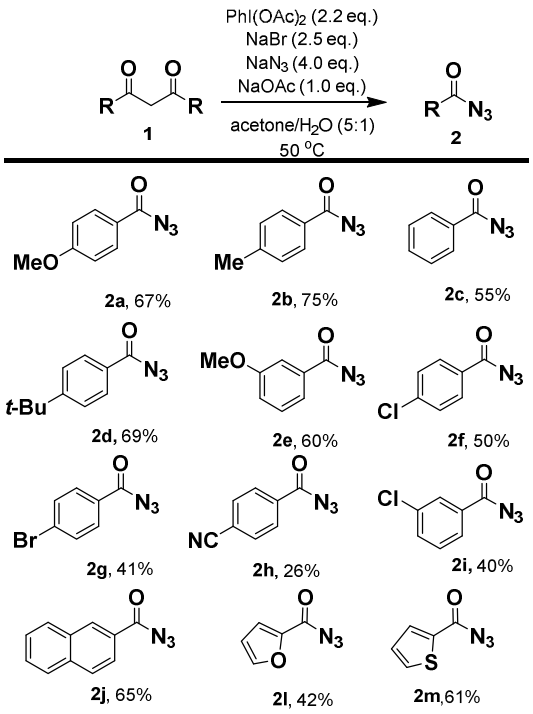
Entry	Oxidant	addtive	base	Yield[b] (%)

1[c]	$PhI(OAc)_2$	NaBr	K_2CO_3	23
2[d]	$PhI(OAc)_2$	NaBr	K_2CO_3	21
3[e]	$PhI(OAc)_2$	NaBr	K_2CO_3	trace
4[f]	$PhI(OAc)_2$	NaBr	K_2CO_3	44
5[g]	$PhI(OAc)_2$	NaBr	K_2CO_3	60
6[g]	$PhI(OCOCF_3)_2$	NaBr	K_2CO_3	trace
7[g]	$PhICl_2$	NaBr	K_2CO_3	43
8[g]	$PhI(OAc)_2$	NaI	K_2CO_3	46
9[g]	$PhI(OAc)_2$	NH_4Br	K_2CO_3	45
10[g]	$PhI(OAc)_2$	CuBr	K_2CO_3	trace
11[g]	$PhI(OAc)_2$	NaBr	Na_2CO_3	62
12[g]	$PhI(OAc)_2$	NaBr	NaOAc	67
13[g]	$PhI(OAc)_2$	NaBr	---	58

[a]Reaction conditions: **1a** (0.2 mmol), oxidant (0.44 mmol), additive (0.5 mmol), base (0.2 mmol) and NaN_3 (0.8 mmol) in the indicated solvent (1.0 mL) at 50 °C for 4 h. [b]Yields were determined by ^1H NMR with 1,1,2,2-tetrachloroethane as an internal standard. [c]In acetone. [d]In CH_3CN. [e]In DCE. [f]In the solvent of acetone and H_2O (10:1, V/V). [g]In the solventof acetone and H_2O (5:1, V/V).

Next, the generality of the method was then investigated using a variety of symmetrical 1,3- diketones (Scheme 2). In general, the reaction was effective for a broad range of 1,3- diketones, affording acyl azide products in moderate to good yields. This reaction exhibited excellent compatibility with a variety ofsubstituents, including aryl halides (**2f**, **2g**, and **2i**), ethers (**2a** and **2e**), heteroaromatics (**2l** and **2m**), nitrile (**2h**), and 2-naphthoyl (**2j**).

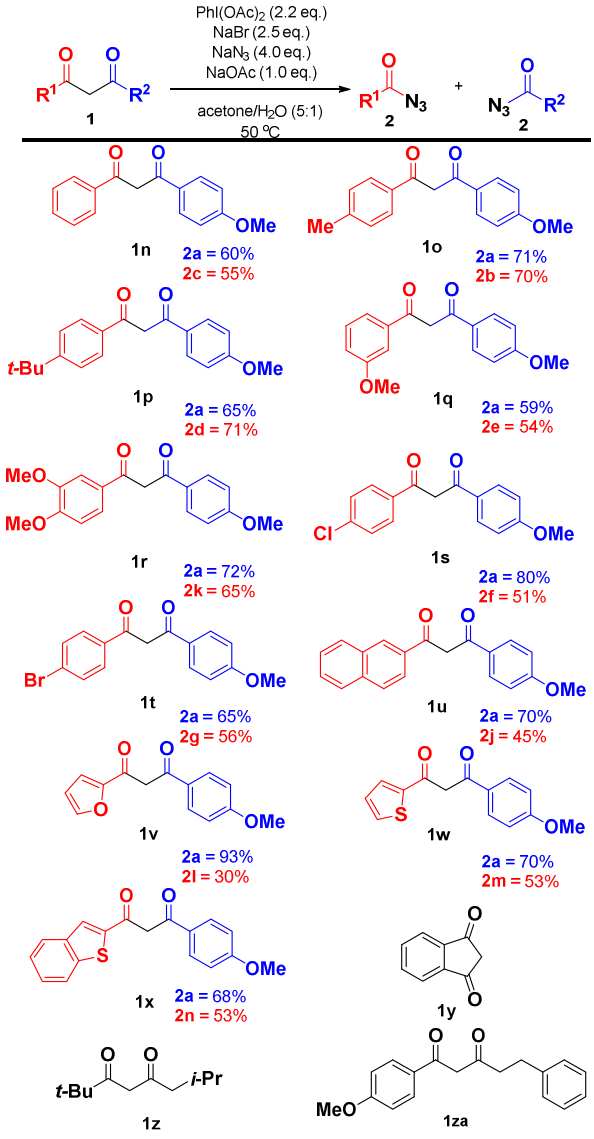
Scheme 2. Substrate scope of symmetric 1,3-diketone[a]



[a] Reaction conditions: **1** (0.2 mmol), $PhI(OAc)_2$ (0.44 mmol), NaBr (0.5 mmol), NaOAc (0.2 mmol) and NaN_3 (0.8 mmol) in acetone/H_2O (5/1, V/V) (1.0 mL) at 50 °C for 4 h, yields were determined by ^1H NMR with 1,1,2,2-tetrachloroethane as an internal standard.

To further explore the generality of this azidation method, we applied this fragmentation reaction to various unsymmetrical 1,3-diketones. As shown in Scheme 3, all reactions proceeded smoothly, furnishing two different azides in one pot with moderate to good yields. Importantly, these two acyl azides could be separated by column chromatography. Unfortunately, indanedione **1y** and aliphatic 1, 3-diketones (**1z** and **1za**) did not react smoothly under the optimized reaction conditions.

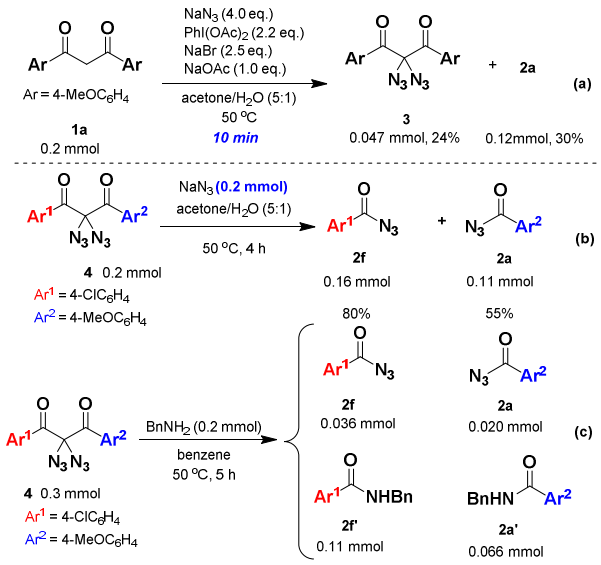
Scheme 3. Substrate scope of unsymmetrical 1,3-diketones[a]



[a]Reaction conditions: diketone (0.2 mmol), $PhI(OAc)_2$ (0.44 mmol), NaBr (0.5 mmol), NaOAc (0.2 mmol) and NaN_3 (0.8 mmol) in acetone/H_2O (5/1, V/V) (1.0 mL) at 50 °C for 4 h, yields were determined by ^1H NMR with 1,1,2,2-tetrachloroethane as an internal standard.

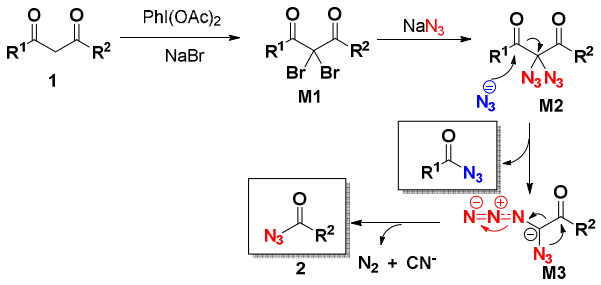
A series of control experiments were performed to investigate the reaction pathway. The reaction of **1a** was initially conducted under the optimal conditions, but with a shorter reaction time, which resulted in diazido intermediate **3** and desired product **2a** being obtained in 24% and 30% yields, respectively (Scheme 4a). Furthermore, treating diazides **4** with NaN_3 led to smooth fragmentation of the dicarbonyl core, without the need for additional reagents. These results indicated that the reaction proceeded via an

intermediate diazido 1,3-diketone. Moreover, we noticed that NaN_3 (0.2 mmol) generated acyl azide (0.28 mmol), which indicated that a part of azido of products originated from the diazido 1,3-diketone intermediate itself. Other nucleophiles were tested to demonstrate the transformation of the diazido intermediate. As shown in Scheme 4c, the reaction of diazides **4** (0.3 mmol) with benzylamine (0.2 mmol) afforded amide **2f'** (0.11 mmol) and **2a'**(0.066mmol), in addition to acyl azides **2f** (0.036 mmol) and **2a** (0.020 mmol).



Scheme 4. Control experiments

Based on control experiments and related reports,[10,11] a possible reaction pathway is outlined in Scheme 5. The reaction begins with the oxidative dibromination of diketone **1**, which produces dibrominated diketone **M1**. Next, intermediate **M2** is formed *via* nucleophilic substitution of **M1** with NaN_3. Nucleophilic attack on the carbonyl group then leads to C−C bond cleavage of **M2** and formation of the acyl azide and **M3**. Finally, **M3** undergoes a rearrangement to produce another acyl azide molecule with the release of N_2 and a cyanide ion.



Scheme 5. Possible reaction pathway

In summary, a novel, atom-economical strategy for generating acyl azides from the cleavage of two C−C bonds in 1,3-diketones has been developed. The use of environmentally friendly hypervalent iodine(III) reagent ($PhI(OAc)_2$) under aerobic conditions makes this protocol green and highly practical. Furthermore, this chemistry provides an approach to a new methodologically diverse synthetic strategy for obtaining two differently substituted acyl azides in one pot from unsymmetrical 1,3-diketones. Several experiments were performed to investigate the possible pathway. This simple and practical method complements classical acyl azide preparation methods and provides new ideas for the design of novel 1,3-diketone transformations.

Experimental Section

General Information: Commercial reagents and solvents were purchased from TCI, Strem Chemicals and Alfa Aesar. Deuterated solvents were purchased from Cambridge Isotope Laboratories, Inc. and were stored over 4Å molecular sieves prior to use. Flash column chromatography was carried out using silica gel (200–300 mesh) at increased pressure. NMR spectra were recorded on WNMR-I spectrometer and JEOL JNM-ECZ600R/S3 spectrometer. The spectra were recorded in $CDCl_3$ or other solvents at room temperature. ^{1}H and ^{13}C chemical shifts are reported in ppm relative to either the residual solvent peak (^{13}C) or TMS (^{1}H) as an internal standard. MS were performed on Bruker Daltonics MicroTof-Q II mass spectrometer and SHIMADZU GCMS-QP2010. IR spectra were recorded using Bruker Tensor27 FT-IR instrument and are reported in wavenumbers (cm^{-1}).

Caution! Acyl azide and cyanide may cause potentially damage and should be

carefully handled. The maximum reaction scale was limited to 0.2 mmol. Protective gear was needed with larger scales. The temperature of water bath of rotary evaporator was 35 °C.

General procedure for the synthesis of acyl azides: A mixture of ketone **1**[12] (0.2 mmol), $PhI(OAc)_2$ (0.44 mmol), NaBr (0.5 mmol), NaN_3 (0.8 mmol) and NaOAc (0.2 mmol) in 1 mL solvent (acetone : water = 5:1) was stirred at 50 ^oC. After 4 hours, the mixture was cooled to room temperature and diluted with Et_2O, washed with water and brine. Then the solution was dried with sodium sulfate anhydrous, concentrated using rotary evaporator. The residue was purified by column chromatography to provide the acyl azide **2**.

4-methoxybenzoyl azide (2a).[13a] White solid (67% yield, 47.4 mg); ^1H NMR (400 MHz, $CDCl_3$): δ 7.98 (d, *J* = 9.2 Hz, 2H), 6.92 (d, *J* = 8.8 Hz, 2H), 3.87 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.6, 164.6, 131.7, 123.2, 113.9, 55.5; FT-IR (KBr): 2137, 1680, 1598, 1318, 985 cm^{-1}; MS (EI) m/z: 177.0 (31) $[M]^+$, 149 (63) $[M-N_2]^+$.

4-methylbenzoyl azide (2b).[13a] Colorless oil (75% yield, 48.2 mg); ^1H NMR (400 MHz, $CDCl_3$): δ 7.91 (d, *J* = 8.4 Hz, 2H), 7.24 (d, *J* = 8.0 Hz, 2H), 2,41 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.3, 145.4, 129.5, 129.3, 128.0, 21.7; FT-IR (KBr): 2136, 1691, 1255, 1023, 735 cm^{-1}; MS (EI) m/z: 161.0 (17)$[M]^+$, 133.0 (28)$[M-N_2]^+$.

Benzoyl azide (2c).[13a] Colorless oil (55% yield, 32.3 mg); ^1H NMR (400 MHz, $CDCl_3$): δ 8.03 (d, *J* = 7.2 Hz, 2H), 7.62 (t, *J* = 7.2 Hz, 1H), 7.46 (t, *J* = 7.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.5, 134.5, 130.7, 129.4, 128.6; FT-IR (KBr): 2139, 1691, 1242, 1191, 993, 700 cm^{-1}; MS (EI) m/z : 147.1 (31) $[M]^+$, 123.1 (72) $[M-N_2]^+$.

4-(tert-butyl)benzoyl azide (2d).[13a] White solid (69% yield, 56.1 mg); ^1H NMR (600 MHz, $CDCl_3$): δ 7.95 (d, *J* = 8.4 Hz, 2H), 7.46 (d, *J* = 9.0 Hz, 2H), 1.33 (s, 9H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 172.2, 158.2, 129.3, 127.9, 125.6, 35.2, 31.0; FT-IR (KBr): 2967, 2132, 1693, 1258, 689 cm^{-1}; MS (EI) m/z: 203.0 (26) $[M]^+$, 161.1 (100) $[M-N_3]^+$.

3-methoxybenzoyl azide (2e).[13a] Colorless oil (60% yield, 42.2 mg). ^1H NMR (600 MHz, $CDCl_3$): δ 7.63 − 7.61 (m, 1H), 7.54 − 7.53 (m, 1H), 7.35 (t, *J* = 8.4 Hz, 1H), 7.17−7.15 (m, 1H), 3.85 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 172.3, 159.7, 131.9, 129.6, 121.9, 121.0, 113.5, 55.4; FT-IR (KBr): 2141, 1696, 1599, 1271, 1047, 678 cm^{-1};

MS (EI) m/z: 177.0 (31) $[M]^+$, 149.1 (63) $[M\text{-}N_2]^+$.

4-chlorobenzoyl azide (2f).[13a] White solid (50% yield, 36.1 mg). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.96 (d, *J* = 8.4 Hz, 2H), 7.43 (d, *J* = 8.4 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 171.5, 140.9, 132.3, 130.8, 129.0; FT-IR (KBr): 2136, 1682, 1253, 995, 744 cm^{-1}; MS (EI) m/z: 181.0 (3) $[M]^+$, 153.0 (14) $[M\text{-}N_2]^+$, 139.0 (100) $[M\text{-}N_3]^+$.

4-bromobenzoyl azide (2g).[13a] White solid (41% yield, 36.8 mg). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.88 (d, *J* = 8.4 Hz, 2H), 7.60 (d, *J* = 9.0 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 171.7, 132.0, 130.8, 129.7, 129.5; FT-IR (KBr): 2134, 1680, 1534, 1250, 991, 740 cm^{-1}; MS (EI) m/z: 224.9 (14) $[M]^+$, 196.9 (30) $[M\text{-}N_2]^+$, 182.9 (100) $[M\text{-}N_3]^+$.

4-cyanobenzoyl azide (2h).[13a] White solid (26% yield, 28.0 mg). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.13 (d, *J* = 8.4 Hz, 2H), 7.76 (d, *J* = 9.0 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 171.7, 134.1, 132.4, 129.8, 117.6, 117.5; FT-IR (KBr): 2230, 2139, 1698, 1245, 1024, 678 cm^{-1}; MS (EI) m/z: 172.0 (4) $[M]^+$, 144.0 (54) $[M\text{-}N_2]^+$, 130.0 (100) $[M\text{-}N_3]^+$.

3-chlorobenzoyl azide (2i). Colorless oil (40% yield, 28.9 mg). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.00 (t, *J* = 1.8 Hz, 1H), 7.91 (dt, *J* = 1.8 Hz, 7.8 Hz, 1H), 7.59 − 7.57 (m, 1H), 7.40 (t, *J* = 7.8 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 171.3, 134.9, 134.2, 132.2, 129.9, 129.4, 127.5; FT-IR (KBr): 2140, 1696, 1237, 1002, 728 cm^{-1}; MS (EI) m/z: 181.0(16) $[M]^+$, 139.0(100) $[M\text{-}N_3]^+$.

2-naphthoyl azide (2j).[13b] White solid (65% yield, 51.1 mg). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.57 (s, 1H), 8.01 (dd, *J* = 1.8 Hz, 8.4 Hz, 1H), 7.93 (d, *J* = 8.4 Hz, 1H), 7.87 − 7.85 (m, 2H), 7.62 − 7.59 (m, 1H), 7.55 − 7.53 (m, 1H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 172.5, 136.1, 132.3, 131.4, 129.6, 128.9, 128.5, 127.8, 127.8, 126.9, 124.5; FT-IR (KBr): 2139, 1685, 1200, 996, 722 cm^{-1}; MS (EI) m/z: 197.0 (10) $[M]^+$; 169.0 (100) $[M\text{-}N_2]^+$.

3,4-dimethoxybenzoyl azide (2k).[13c] White solid (65% yield, 26.8 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.67 (d, *J* = 8.4 Hz, 1H), 7.51 (s, 1H), 6.88 (d, *J* = 8.8 Hz, 1H), 3.95 (s, 3H), 3.93 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.6, 154.2, 148.8, 123.9, 123.2, 111.3, 110.2, 56.0, 55.9; FT-IR (KBr): 2137, 1675, 1267, 1020, 644 cm^{-1}; MS (EI) m/z: 207.0 (8) $[M]^+$; 179.0 (54) $[M\text{-}N_2]^+$.

Furan-2-carbonyl azide (2l).[13d] White solid (42% yield, 22.8 mg). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.66 (dd, *J* = 1.2 Hz, 1.5Hz, 1H), 7.28 − 7.21 (m, 1H), 6.56 − 6.55 (m, 1H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 162.5, 148.1, 145.5, 120.0, 112.5; FT-IR (KBr): 2142, 1686, 1290, 1030, 789 cm^{-1}; MS (EI) m/z: 137(18) $[M]^+$, 109 (59) $[M\text{-}N_2]^+$.

Thiophene-2-carbonyl azide (2m).[13a] White solid (61% yield, 37.1 mg). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.84 (dd, *J* = 3.6 Hz, 1.2 Hz, 1H), 7.66 (dd, *J* = 5.4 Hz, 1.2 Hz, 1H), 7.14 (dd, *J* = 4.8 Hz, 3.6 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 166.6, 134.8, 134.7, 134.4, 128.4; FT-IR (KBr): 2156, 1685, 1519, 1255, 739 cm^{-1}; MS (EI) m/z: 153.0 (24) $[M]^+$, 125.1 (34) $[M\text{-}N_2]^+$, 111.0 (100) $[M\text{-}N_3]^+$.

Benzothiophene-2-carbonyl azide (2n).[13e] White solid (53% yield, 21.6 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.10 (s, 1H), 7.88 (t, *J* = 8.8 Hz, 2H), 7.51 − 7.41 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.6, 143.0, 138.7, 134.7, 131.7, 127.8, 126.0, 125.2, 122.9; FT-IR (KBr): 2158, 1668, 1514, 1243, 758 cm^{-1}; MS (EI) m/z: 203(100) $[M]^+$.

Mechanism study: A mixture of ketone (0.2 mmol), $PhI(OAc)_2$ (0.44 mmol), NaBr (0.5 mmol), NaN_3 (0.8 mmol) and NaOAc (0.2 mmol) in 1 mL solvent (acetone : water = 5:1) was stirred at 50 ^{o}C for 10 min. The mixture was cooled to room temperature and diluted with Et_2O. The solution was washed with water and brine. Then the solution was dried with sodium sulfate anhydrous, concentrated using rotary evaporator. The residue was purified by column chromatography to provide the acyl azide **2a** (21.2 mg) and compound **3** (17.3 mg).

A mixture of **4** (0.2 mmol) and NaN_3 (0.2 mmol) in 1 mL solvent (acetone: water = 5:1) was stirred at 50 ^{o}C for 4 h. The mixture was cooled and purified by column chromatography on silica gel to provide the acyl azide **2a** (0.11 mmol) and acyl azide **2f** (0.16 mmol), yields were determined by ^{1}H NMR with 1,1,2,2-tetrachloroethane as an internal standard.

A mixture of **4** (0.3 mmol) and benzylamine (0.2 mmol) in 2 mL benzene was stirred at 50 ^{o}C for 5 h. The mixture was cooled and purified by column chromatography on silica gel to provide the acyl azide **2a** (0.020 mmol), **2f** (0.036 mmol) and amide **2f'** (0.11 mmol), **2a'** (0.066 mmol), yields were determined by ^{1}H NMR with 1,1,2,2-tetrachloroethane as an internal standard.

2,2-diazido-1,3-bis(4-methoxyphenyl)propane-1,3-dione (3). White solid (24% yield, 17.3 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.00 (d, J = 8.8 Hz, 4H), 6.84 (d, J = 9.2 Hz, 4H), 3.82 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 187.0, 164.5, 133.0, 125.1, 114.0, 88.5, 55.5; HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{17}H_{14}N_6NaO_4$ 389.0969; Found 389.0963.

2,2-diazido-1-(4-chlorophenyl)-3-(4-methoxyphenyl)propane-1,3-dione (4). White solid (30% yield, 22.1 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.99 − 7.93 (m, 4H), 7.35 (d, J = 8.4 Hz, 2H), 6.85 (d, J = 8.8 Hz, 2H), 3.83 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 187.9, 186.7, 164.7, 141.2, 133.0, 131.7, 130.6, 129.1, 124.9, 114.1, 88.1, 55.5; FT-IR (KBr): 2113, 1679, 1594, 1272, 889 cm^{-1}; MS (EI) m/z: 314 (0.36) $[M-N_2-N_2]^+$, 316 (0.12); HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{16}H_{11}ClN_6NaO_3$ 393.0473 Found 393.0478.

N-benzyl-4-methoxybenzamide (2a').[13f] White solid (55% yield, 15.1 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.76 (d, J = 8.8 Hz, 2H), 7.34−7.26 (m, 5H), 6.90 (d, J = 8.4 Hz, 2H), 6.51 (s, 1H), 4.61 (d, J = 5.6 Hz, 2H), 3.83 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.8, 162.1, 138.4, 128.7, 128.7, 127.8, 127.5, 126.6, 113.7, 55.4, 44.0.

N-benzyl-4-chlorobenzamide (2f').[13f] White solid (33% yield, 26.8 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.72 (d, J = 8.8 Hz, 2H), 7.38 (d, J = 8.4 Hz, 2H), 7.35−7.30 (m, 5H), 6.53 (s, 1H), 4.61 (d, J = 5.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.3, 137.9, 137.8, 132.7, 128.8, 128.4, 127.9, 127.7, 44.2.

The one-pot transformation of compound 2i: A mixture of ketone (0.2 mmol), $PhI(OAc)_2$ (0.44 mmol), NaBr (0.5 mmol), NaN_3 (0.8 mmol) and NaOAc (0.2 mmol) in 1 mL solvent (acetone : water = 5:1) was stirred at 50 ^{o}C for 4 h. After the reaction was complete, the mixture was cooled to room temperature and diluted with Et_2O. The solution was washed with H_2O and NaCl (sat.). Then the solution was dried with Na_2SO_4, concentrated using rotary evaporator. The residue was transferred to a schlenk tube and the tube was evacuated and backfilled with N_2 three times before the addition of toluene (1.0 mL). The mixture was heated at 100 ^{o}C for 1 hour. Then, (4-methoxyphenyl)methanamine (0.4 mmol) was added and the mixture was stirred at room temperature overnight. The mixture was concentrated under reduced pressure and

purified by column chromatography to provide the 1-(3-chlorophenyl)-3-(4-methoxybenzyl)urea.

1-(3-chlorophenyl)-3-(4-methoxybenzyl)urea. White solid (13.5 mg, 23%). ^{1}H NMR (400 MHz, *d6*-DMSO): δ 8.78 (s, 1H), 7.73 (s, 1H), 7.30-7.22 (m, 4H), 6.99-6.93 (m, 3H), 6.67 (t, J = 5.6 Hz, 1H), 4.27 (d, J = 6.0 Hz, 2H), 3.78 (s, 3H); ^{13}C NMR (100 MHz, *d6*-DMSO): δ 158.2, 154.9, 142.1, 133.1, 132.0, 130.2, 128.5, 120.7, 117.0, 116.0, 113.7, 55.1, 42.2. HRMS (ESI-TOF) m/z: [M + Na]+ Calcd for $C_{15}H_{15}ClN_2NaO_2$ 313.0714; Found 313.0708.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website.

Detection of cyanide, ^{1}H and ^{13}C NMR spectra (PDF)

AUTHOR INFORMATION

Corresponding Author

*Email: haow@nwu.edu.cn.

Author Contributions

[§]These authors contributed equally to this work.

Notes

The authors declare no competing financial interest.

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