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Note

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C-N Bond Activation of *N,N'*-Dialkylacylhydrazines Mediated by β-Fragmentation of Nitrogen-centered Radical

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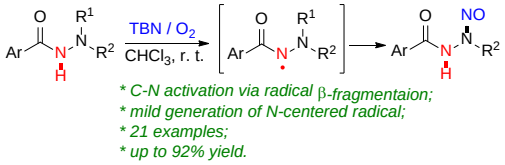


Abstract: In the presence of *tert*-butylnitrite and dioxygen, the C-N bond activation of N,N'-dialkylacylhydrazines was realized, providing a series of N-nitrosoacylhydrazines in high yields. Different from transition-metal and other radical catalysis, this reaction is mediated by a nitrogen-centered radical of the corresponding N,N'-dialkylacylhydrazine and further β-fragmentation, which was supported by the mechanistic study.

As one of the basic chemical bonds, C-N bond is ubiquitous in organic compounds, biomolecules, drugs and natural products. These nitrogen-containing molecules not only exhibit various biologically reactivity, but also are a kind of synthetically important intermediates, participating in construction of diverse functionalized skeletons. Therefore, C-N bond formation attracted chemists' persistent research interests. [1] On the contrary, due to the inert nature of C-N bond, efficient

transformations involving C-N bond cleavage are still limited, [2, 3, 4] and in the tide of research on inert chemical bond activation, [5, 6, 7] C-N bond activation occupies a unique place, worth deeply studies. Since Trost's poineering work of allylic amines activation in 1980, transition-metal enabled C-N bond activation has become increasingly mature, in which a carbon-metal-nitrogen species is generated by oxidative addition of transition-metal to C-N bond, followed by further functionalization (Figure 1, eq 1). [3] Based on this process, both C- and N- functionalization could be smoothly realized under controlled reaction conditions.

With the development of sp^3 C-H bond activation, oxidation of the C-H bond adjacent to nitrogen provided a different approach to cleave the C-N bond, in which an iminium intermediate might be created by C-H bond oxidation. [4] After further hydrolysis, an amine and aldehyde are released, participating followed transformations (Figure 1, eq 2). For example, in 2011, under aerobic conditions, Huang and co-workers reported a $CuBr_2$ catalyzed amination of benzoxazoles using tertiary amines as nitrogen source. [4a] Recently, this group developed a novel multicomponent reactions through C-N bond cleavage of cyclic tertiary amines, realizing the difunctionalization of saturated C-N bond. [4f] Using tertiary anilines as the substrates, Lei and co-workers efficiently constructed indolin-2-one skeleton by palladium/copper-catalyzed oxidative tandem alkenylation/dealkylative carbonylation of tertiary anilines. [4b] In 2017, Jiao's group described a Rh-catalyzed C–H cyclization of tertiary anilines with alkynes and CO, synthesizing a series of biologically significant quinolin-2(1H)-ones and related N-heterocycles via C–N bond cleavage. [4e]

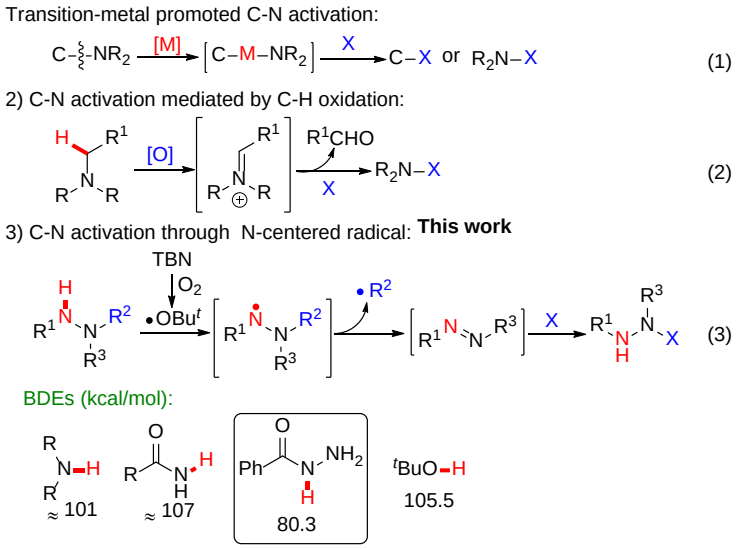


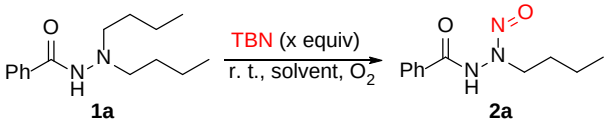
Figure 1. C-N bond activation through different strategies.

Although various elegant methods have been established to enable C-N bond cleavage, we still wonder whether C-N bond activation could be achieved by new reaction process. As part of our ongoing research program, we are interested in free radical intermediate mediated organic transformations. [8] It is well-known that β-fragmentation is one of elemental radical reactions, [9] and heteroatom centered radicals can readily undergo β-fragmentation to give an alkyl radical as well as an unsaturated product, such as Kolbe, [10] Hunsdiecker, [11] Barton reaction [12] and so on. For β-fragmentation, the driving force is the formation of stable unsaturated product, and the formation of a more stable alkyl radical (carbon-centered radical) than the heteroatom centered radical. Therefore, we questioned whether β-fragmentation could act as a handle to promote the activation of inert C-N bond. However, due to their highly active nature, generation of N-centered radicals is not facile. Besides homolysis of N-heteroatom bond, oxidation of N-H bond is an efficient way to generate N-centered radicals. Generally, the high bond dissociation energy (BDE) of N-H bond (> 100 kacl/mol, see Figure 1) [13] results in the difficulty to directly create N-centered radicals from amines or amides, therefore, strong oxidants are generally needed. [14] After broadly survey of amines' BDEs, we found

that the N-H bond of acylhydrazines is relatively weak, and the corresponding BDE is about 80 kcal/mol. So we hypothesized that if we can select an appropriate initiator to create the N-centered radical of acylhydrazines, this radical might undergo β-fragmentation to cleave the saturated C-N bond, realizing C-N bond activation of alkylacylhydrazines (Figure 1, eq 3). From the view of enthalpy change, this process will generate a relatively stable acylazo intermediate, providing sufficient reaction driving force.

Alkyl nitrites were an important kind of metal-free reagents, and have various advantages such as commercial availability, inexpensiveness, good solubility in organic solvents, easy handing, and so on. Due to their vertisale reactivities, alkyl nitrites can participate in a variety of organic transformations, including nitrosation, oximation, nitration, diazotization and so on. [15, 16] Recently, we reported a series of TBN (*tert*-butylnitrite) initiated activation of C-H, C-N and C-C bonds, [4g-i, 7h] and in these reactions, the tBuO radicals were released from TBN, which abstracted the hydrogen adjacent to nitrogen, affording an α-amino radical. After further oxidation and hydrolysis of the generated iminium intermediate, the C-N bond was cleaved smoothly. Since the BDE of O-H bond is obviously higher than that of N-H bond in acylhydrazines, we believe that TBN could also be employed to create the N-centered radical of acylhydrazines, initiating further β-fragmentation to realize the C-N bond cleavage. If this idea is feasible, we will provide a new way to promote C-N bond activation, enriching the direct transformations of C-N bond containing molecules.

Table 1. Optimization of reaction conditions [a]



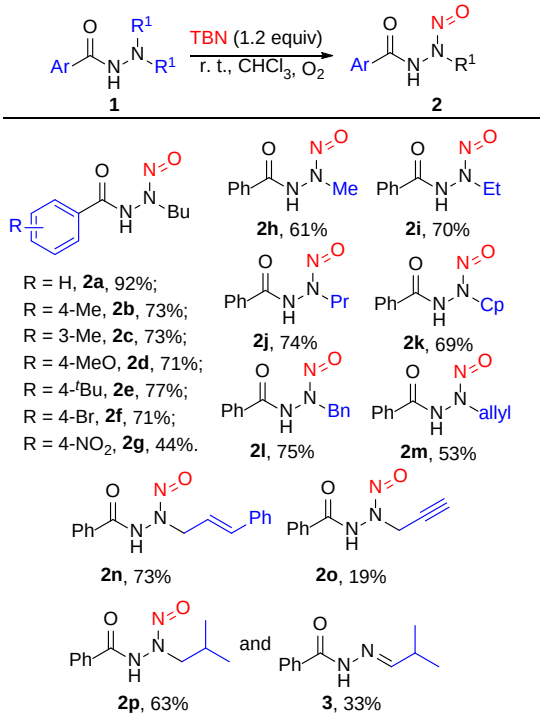
1a **2a**

Entry	TBN (x equiv.)	Solvent	Time (h)	Yield (%) [b]
1	1.0	MeCN	1	65
2	1.2	MeCN	0.8	74

3	1.2	DCM	1.5	67
4	1.2	DCE	1.1	63
5	**1.2**	**$CHCl_3$**	**4.5**	**92**
6	1.2	1,4-dioxane	7	85
7	1.2	THF	2.5	80
8	1.2	n-hexane	24	84

[a] Unless otherwise specified, the reaction was carried out with **1a** (0.1 mmol) and in the presence of TBN (x equiv.), and anhydrous solvent (1.0 mL). [b] Isolated yield.

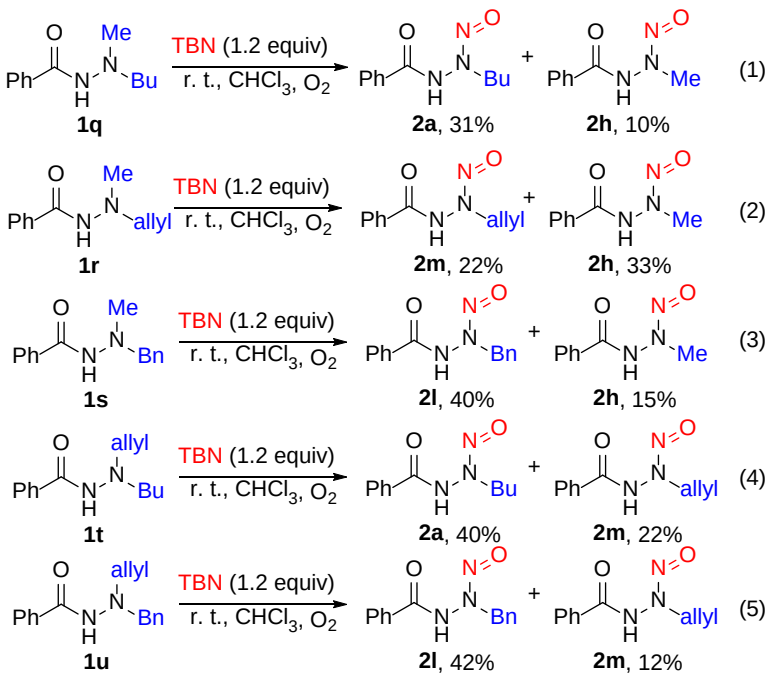
With this idea in mind, N,N'-dialkylacylhydrazine **1a** was chosen as the model substrate to test the possibility of TBN initiated C-N bond activation (Table 1). In the presence of one equivalent of TBN under dioxygen atmosphere, the C-N bond was cleaved smoothly, giving the N-nitrosoacylhydrazine **2a** in 65% yield (entry 1). Increasing the amount of TBN to 1.2 equivalent, the yield of the desired product was raised to 74% (entry 2). Then a brief solvent screen was performed (entries 2-8), and $CHCl_3$ gave the best result, affording the expected product in 92% yield (entry 5).



Scheme 1. Reaction scope of C-N bond cleavage of N,N'-dialkylacylhydrazines.

With the best reaction conditions established, the reaction scope was then investigated, and the results were shown in Scheme 1. First, the effect of substituents on the phenyl ring was evaluated. The results show that electron-donating groups, such as methyl, methoxyl and *tert*-butyl groups, did not affect the reaction efficiency, providing the desired C-N bond cleaved products **2a-2e** in 77-92% yields. Weak electron-withdrawing group, Br, did not exert negative effect on the reaction, and the corresponding *N*-nitrosoacylhydrazine **2f** was isolated in 71% yield. However, the substrate with strong electron-withdrawing nitro group exhibited lower reactivity, giving the expected product **2g** in 44% yield. It is probably due to that the nitro group dramatically decrease the electron density on the nitrogen, destabilizing the nitrogen-centered radical intermediate. Then the various alkyl groups on nitrogen were tested. Generally, the substrates with linear alkyl groups were fully tolerated in this reaction, and comparable yields of the desired products **2h-2j** were obtained. Even bulky cyclopentyl group gave the N-NO derivative **2k** in 69% yield. This result is different with our previous research of TBN initiated C-H activation, in which the C-H bond cleavage was dramatically affected by steric effect, and the C-H bond adjacent to bulky groups could not be activated. [4g] Therefore, this reaction might proceed via different reaction pathway, and the C-H bond cleavage might not be the initial step. Dibenzylacylhydrazine is also compatible substrate, affording the expected product **2l** in 75% yield. It is well-known that in the presence of dioxygen, TBN can liberate NO_2 radical, which can add to C-C unsaturated bonds, realizing difunctionalization of alkenes and alkynes. [16] Consequently, *N*-allyl and -propargyl substituted substrates **1m** and **1o** was subjected to the standard reaction conditions. As expected, the reaction efficiency was decreased, and the desired N-NO products **2m** and **2o** were isolated in lower yields

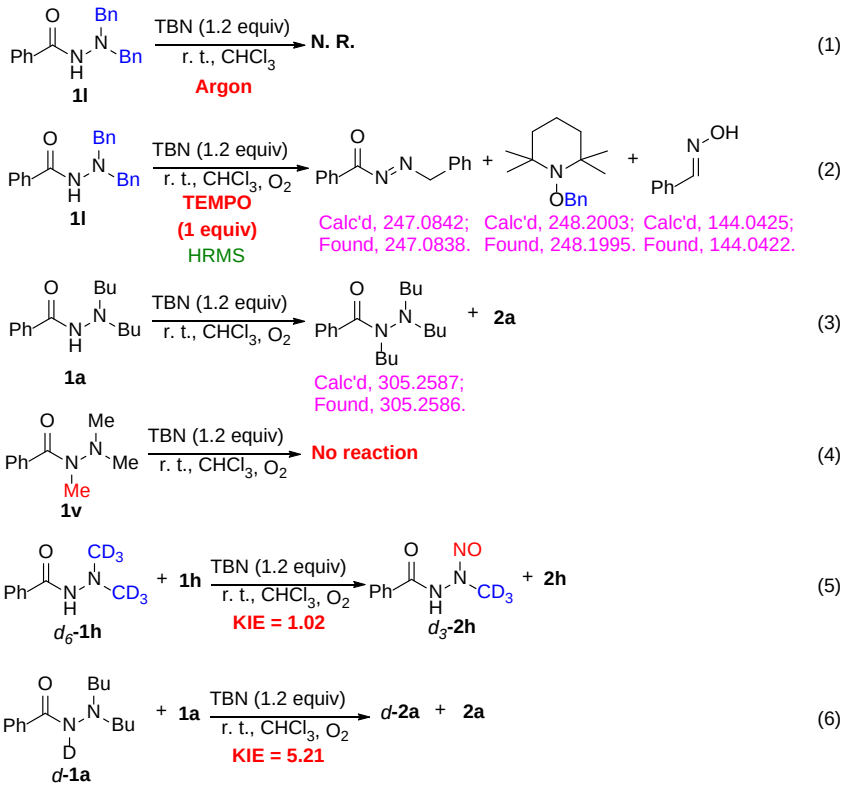
as well as other unidentified products. This result suggested that electron-rich C-C unsaturated could not be well tolerated in TBN initiated reaction. Differently, the reaction of N,N'-dicinnamylacylhydrazine **1n** occurred smoothly, providing the desired product **2n** in 73%. Although the exact reason remains unknown, we believed that the relatively higher steric hindrance of the cinnamyl group might impede the attack of NO_2 radical to C-C double bond. For isobutyl substituted acylhydrazine, besides the normal C-N cleaved product **2p**, an imine side-product **3** was also isolated in 33% yield, which was generated from isomerization of the acylazo intermediate **B** (see Scheme 4).



Scheme 2. Evaluation of the selectivity of C-N bond cleavage.

With the success of TBN initiated C-N bond cleavage, unsymmetrical acylhydrazines were synthesized to investigate the selectivity (Scheme 2). When N-methyl-N'-butylacylhydrazine **1q** was subjected to the standard reaction condition, a mixture of **2a** and **2h** were obtained, in which the cleavage of N-Me bond was favored (eq 1). The existence of allyl group reversed the reaction

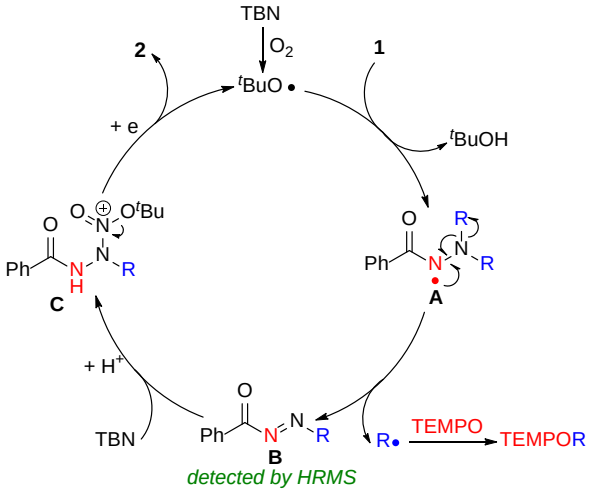
selectivity, and the deallylated N-NO acylhydrazines **2h** and **2a**, respectively, were isolated in slightly higher yields (eqs 2 and 4). The selectivity of N-Me and N-Bn was then evaluated, and the result showed that N-Me cleavage is preferred (eq 3). For the pair of N-allyl and N-Bn, the N-allyl bond was still cleaved preferentially (eq 5). From the results of selectivity evaluation we can see that the selectivity follows the following sequence: allyl > Me > Bu ~ Bn. This sequence is obviously different from the stability of the corresponding alkyl radicals, and the reasons might be attributed to synergistic influence of radical stability and entropy effect. For allyl group, both radical intermediate stability and entropy effect are beneficial to this reaction, resulting in its highest reactivity. However, the dichotomy of entropy effect and stability for methyl, butyl and benzyl groups lead to their relatively lower reactivity, compared with allyl group.



Scheme 3. Control experiments.

To reveal the mechanistic details, a series of control experiments were performed (Scheme 3). First, the reaction of **1l** was conducted under argon atmosphere, however, no reaction occurred, and the

starting material was fully recovered (eq 1). This result suggested that dioxygen is crucial to promote homolysis of TBN, releasing the tBuO radical to initiate this C-N bond cleavage. Then, the model reaction was performed in the presence of one equivalent of TEMPO (eq 2). By HRMS analysis of the reaction mixture, a series of intermediates were smoothly detected. The existence of acylazo intermediate suggested that the C-N bond cleavage might be mediated by a β-fragmentation of N-centered radical of acylhydrazine. Furthermore, a TEMPO captured benzyl radical as well as an oxime of benzaldehyde, which was generated through trapping of benzyl radical by NO and the followed isomerization, were also be detected. These results all supported that the C-N bond might be cleaved via β-fragmentation of N-centered radical of acylhydrazine. Then the HRMS detection of the model reaction of **1a** was conducted, and fortunately, a radical cross-coupling product was detected smoothly (eq 3), which supported the existence of intermediate **A** and R radicals (see Scheme 4). To further confirm this different reaction pathway of C-N bond activation, the reaction of substrate **1v**, in which the N-H bond was replaced by N-Me bond to block the generation of the N-centered radical, was investigated under the standard reaction conditions (eq 4). As expected, no reaction occurred, and only the starting material was recovered. Then, a KIE value 1.02 was obtained by an intermolecular competition between d_6-**1h** and **1h** (eq 5). This KIE value implied that the C-H bond cleavage is not the rate-determining step, and different from other radical C-N bond activation, this reaction is not mediated by C-H bond oxidation and the following hydrolysis of the generated iminium intermediate. On the contrary, when the reaction of mixture of *d*-**1a** and **1a** was performed under the standard conditions (eq 6), a KIE value 5.21 was obtained, implying that the cleavage of the N-H bond is the rate-determining step and the C-N bond might be cleaved through β-fragmentation of the N-centered radical intermediate.



Scheme 4. Proposed mechanism.

Based on the control experiments and the references precedent, [16] a plausible mechanism was proposed (Scheme 4). First, in the presence of dioxygen, tBuO radical is liberated, which abstracts a hydrogen from the relatively weak N-H bond of acylhydrazine, giving a nitrogen-centered radical **A**. Then, β-fragmentation of the acylhydrazine radical occurred, releasing an acylazo intermediate **B** as well as the carbon-centered radical intermediate, which can be captured by TEMPO and NO radical (see Scheme 3). Consequently, a Michael type addition between the acylazo intermediate and TBN provides intermediate **C**. After further single electron transfer, [18] the N-nitroso acylhydrazine products are afforded, and the tBuO radical is regenerated to participate next catalytic cycle.

In summary, using TBN/O_2 as the metal-free catalyst system, we accomplished an efficient C-N bond activation of derivatives of acylhydrazines, providing a series of N-nitrosoacylhydrazines in high yields. The mechanistic study revealed that different from other transition-metal catalysis and radical C-H bond activation enabled C-N bond cleavage, this reaction is initiated by nitrogen centered radical intermediate and further β-fragmentation. Therefore, this reaction provided a new

method to accomplish C-N bond activation and the corresponding C- or N-functionalization of nitrogen-containing compounds. Further applications and mechanistic study are still underway in our laboratory.

Experimental Section

General

All solvents are anhydrous. TBN were purchased from commercial source and used without further purification. Flash chromatography was carried out with silica gel (200-300 mesh). Analytical TLC was performed with silica gel GF254 plates, and the products were visualized by UV detection. ^{1}H NMR and ^{13}C NMR (400 MHz, 600MHz and 100 MHz, 150MHz respectively) spectra were recorded in $CDCl_3$. Chemical shifts (δ) are reported in ppm using TMS as internal standard and spin-spin coupling constants (J) are given in Hz. The high resolution mass spectra (HRMS) were measured on an electrospray ionization (ESI) apparatus using time of flight (TOF) mass spectrometry.

Substrate Preparation

Compounds **1a-u** were prepared according to the literatures, [17] and the compounds spectra data are in agreement with the reports.

General Experimental Procedure

A solution of **1a** (1 mmol, 248mg) in $CHCl_3$ (5 mL) was mixed fully, then TBN (1.2 mmol, 124mg) was added dropwise under dioxygen atmosphere. The reaction solution was stirred under room temperature. After completion monitored by TLC (by UV visualization), the solvent was removed under reduced pressure. The products were separated by silica gel column chromatography eluted

with petroleum ether/acetone (v/v 5:1) to afford the products.

TEMPO Trapping Experiment

A solution of **1a** (1 mmol, 248mg) in $CHCl_3$ (5 mL) was mixed fully, then TBN (1.2 mmol, 124mg) was added dropwise under dioxygen atmosphere. The reaction solution was stirred under room temperature for 20 minutes, followed by the addition of one equivalent of TEMPO (1 mmol, 156mg). Then the HRMS detection of the reaction mixture was performed immediately to detect the reaction intermediate.

***N'*-Benzoyl-*N*-butylnitrous hydrazide (2a)**

Compound **2a** was isolated in 92% yield (203 mg, yellow oil); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.22 (brs, *NH*, 1H), 7.80 (d, *J* = 8.0 Hz, 2H), 7.54 (t, *J* = 7.4 Hz, 1H), 7.41 (t, *J* = 7.5 Hz, 2H), 4.48 (t, *J* = 7.1 Hz, 2H), 1.89 – 1.69 (m, 2H), 1.45 – 1.29 (m, 2H), 0.94 (t, *J* = 7.4 Hz, 3H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 165.5, 133.0, 130.8, 128.8, 127.7, 54.0, 29.4, 19.6, 13.5; HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{11}H_{15}N_3O_2Na$, 244.1057; found, 244.1058.

***N*-Butyl-*N'*-(4-methylbenzoyl)nitrous hydrazide (2b)**

Compound **2b** was isolated in 73% yield (172 mg, yellow oil); ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.33 (brs, *NH*, 1H), 7.71 (d, *J* = 7.6 Hz, 2H), 7.20 (d, *J* = 7.9 Hz, 2H), 4.45 (t, *J* = 7.1 Hz, 2H), 2.38 (s, 3H), 1.78 (p, *J* = 7.2 Hz, 2H), 1.44 – 1.30 (m, 2H), 0.94 (t, *J* = 7.4 Hz, 3H); ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 165.6, 143.7, 129.4, 128.0, 127.8, 54.1, 29.4, 21.6, 19.6, 13.5; HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{12}H_{17}N_3O_2Na$, 258.1213; found, 258.1217.

***N*-Butyl-*N'*-(3-methylbenzoyl)nitrous hydrazide (2c)**

Compound **2c** was isolated in 73% yield (172 mg, yellow oil); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.30 (brs, *NH*, 1H), 7.65 – 7.55 (m, 2H), 7.37 – 7.22 (m, 2H), 4.46 (t, *J* = 7.1 Hz, 2H), 2.34 (s, 3H), 1.86 – 1.66 (m, 2H), 1.44 – 1.32 (m, 2H), 0.93 (t, *J* = 7.4 Hz, 3H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 165.7, 138.7, 133.7, 130.8, 128.6, 128.3, 124.7, 54.0, 29.4, 21.2, 19.6, 13.5; HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{12}H_{17}N_3O_2Na$, 258.1213; found, 258.1215.

***N*-Butyl-*N'*-(4-methoxybenzoyl)nitrous hydrazide (2d)**

Compound **2d** was isolated in 71% yield (178 mg, yellow oil); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.27 (brs, *NH*, 1H), 7.76 (d, *J* = 8.9 Hz, 2H), 6.85 (d, *J* = 8.9 Hz, 2H), 4.43 (t, *J* = 7.1 Hz, 2H), 3.80 (s, 3H), 1.90 – 1.62 (m, 2H), 1.52 – 1.19 (m, 2H), 0.91 (t, *J* = 7.4 Hz, 3H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 165.1, 163.3, 129.8, 122.9, 114.0, 55.5, 54.1, 29.4, 19.6, 13.5; HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{12}H_{17}N_3O_3Na$, 274.1162; found, 274.1157.

***N*-Butyl-*N'*-(4-(tert-butyl)benzoyl)nitrous hydrazide (2e)**

Compound **2e** was isolated in 77% yield (213 mg, yellow oil); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.43 (brs, *NH*, 1H), 7.76 (d, *J* = 8.6 Hz, 2H), 7.40 (d, *J* = 8.6 Hz, 2H), 4.44 (t, *J* = 7.1 Hz, 2H), 1.82 – 1.71 (m, 2H), 1.42 – 1.32 (m, 2H), 1.29 (s, 9H), 0.91 (t, *J* = 7.4 Hz, 3H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 165.4,

156.6, 127.8, 127.7, 125.7, 54.1, 35.1, 31.0, 29.4, 19.6, 13.5; HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{15}H_{23}N_3O_2Na$, 300.1683; found, 300.1692.

***N′*-(4-Bromobenzoyl)-*N*-butylnitrous hydrazide (2f)**

Compound **2f** was isolated in 71% yield (212 mg, yellow oil); ^1H NMR (400 MHz, $CDCl_3$) δ 9.28 (brs, *NH*, 1H), 7.66 (d, *J* = 8.6 Hz, 2H), 7.54 (d, *J* = 8.5 Hz, 2H), 4.46 (t, *J* = 7.1 Hz, 2H), 1.88 – 1.68 (m, 2H), 1.46 – 1.29 (m, 2H), 0.93 (t, *J* = 7.4 Hz, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 164.6, 132.1, 129.6, 129.3, 129.2, 128.0, 54.1, 29.4, 19.6, 13.5; HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{11}H_{14}BrN_3O_2Na$, 322.0162; found, 322.0163.

***N*-Butyl-*N′*-(4-nitrobenzoyl)nitrous hydrazide (2g)**

Compound **2g** was isolated in 44% yield (117 mg, yellow oil); ^1H NMR (400 MHz, d_6-DMSO) δ 11.33 (brs, 1H), 8.36 (d, *J* = 8.6 Hz, 2H), 8.08 (d, *J* = 8.3 Hz, 2H), 4.34 (t, *J* = 6.4 Hz, 2H), 1.77 – 1.65 (m, 2H), 1.42 – 1.30 (m, 2H), 0.91 (t, *J* = 7.2 Hz, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, d_6-DMSO) δ 163.2, 150.2, 137.1, 129.8, 124.3, 53.6, 29.4, 19.5, 13.9; HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{11}H_{14}N_4O_4Na$, 289.0907; found, 289.0911.

***N′*-Benzoyl-*N*-methylnitrous hydrazide (2h)**

Compound **2h** was isolated in 61% yield (109 mg, white solid: 115 °C-118 °C;) ^1H NMR (400 MHz, $CDCl_3$) δ 9.27 (brs, *NH*, 1H), 7.82 (d, *J* = 7.6 Hz, 2H), 7.59 (t, *J* = 7.4 Hz, 1H), 7.47 (t, *J* = 7.2 Hz, 2H), 4.16 (s, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 165.4, 133.2, 130.8, 128.9, 127.7, 41.2; HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_8H_9N_3O_2Na$, 202.0587; found, 202.0593.

***N′*-Benzoyl-*N*-ethylnitrous hydrazide (2i)**

Compound **2i** was isolated in 70% yield (135 mg, yellow oil); ^1H NMR (400 MHz, $CDCl_3$) δ 9.40 (s, 1H), 7.77 (d, J = 7.5 Hz, 2H), 7.49 (t, J = 7.1 Hz, 1H), 7.35 (t, J = 7.4 Hz, 2H), 4.47 – 4.34 (m, 2H), 1.42 – 1.29 (m, 3H).$^{13}C\{^1H\}$ NMR (101 MHz, CDCl3) δ 165.8, 133.0, 132.9, 130.7, 128.7, 127.8, 127.7, 49.5, 13.0. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_9H_{11}N_3O_2Na$, 216.0744; found, 216.0742.

***N′*-Benzoyl-*N*-propylnitrous hydrazide (2j)**

Compound **2j** was isolated in 74% yield (153 mg, yellow oil); ^1H NMR (400 MHz, $CDCl_3$) δ 9.28 (brs, *NH*, 1H), 7.83 – 7.75 (m, 2H), 7.55 – 7.49 (m, 1H), 7.43 – 7.35 (m, 2H), 4.42 (t, *J* = 7.1 Hz, 2H), 1.90 – 1.71 (m, 2H), 0.95 (t, *J* = 7.4 Hz, 3H); $^{13}C\{^1H\}$ NMR (101MHz, $CDCl_3$) δ 165.6, 133.0, 130.8, 128.8, 127.7, 56.0, 20.8, 11.0; HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{10}H_{13}N_3O_2Na$, 230.0900; found, 230.0894.

***N′*-Benzoyl-*N*-cyclopentylnitrous hydrazide (2k)**

Compound **2k** was isolated in 69% yield (161 mg, yellow solid:108 °C-111 °C); ^1H NMR (400 MHz, $CDCl_3$) δ 8.90 (brs, *NH*, 1H), 7.80 (d, *J* = 7.2 Hz, 2H), 7.51 (t, *J* = 7.4 Hz, 1H), 7.38 (t, *J* = 7.8 Hz, 2H), 5.19 – 5.05 (m, 1H), 2.14 – 1.96 (m, 4H), 1.85 – 1.54 (m, 4H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 166.2, 132.9, 130.9, 128.7, 127.8, 66.5, 30.3, 23.8; HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{12}H_{15}N_3O_2Na$, 256.1057; found, 256.1054.

***N′*-Benzoyl-*N*-benzylnitrous hydrazide (2l)**

Compound **2l** was isolated in 75% yield (191 mg, white solid:113 °C-116 °C); ^1H NMR (400 MHz, $CDCl_3$) δ 9.05 (brs, *NH*, 1H), 7.65 (d, *J* = 7.7 Hz, 2H), 7.50 (t, *J* = 7.4 Hz, 1H), 7.39 – 7.32 (m, 2H), 7.31 (s, 5H), 5.59 (s, 2H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 165.4, 133.5, 133.0, 130.7, 129.1, 128.9, 128.8, 128.2, 127.7, 57.6; HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{14}H_{13}N_3O_2Na$, 278.0900; found, 278.0909.

***N*-Allyl-*N′*-benzoylnitrous hydrazide (2m)**

Compound **2m** was isolated in 53% yield (109 mg, yellow oil); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.21 (brs, *NH*, 1H), 7.76 (d, *J* = 7.7 Hz, 2H), 7.52 (t, *J* = 7.4 Hz, 1H), 7.39 (t, *J* = 7.8 Hz, 2H), 5.99 – 5.84 (m, 1H), 5.40 – 5.25 (m, 2H), 5.02 (d, *J* = 6.5 Hz, 2H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 165.5, 133.0, 130.7, 130.3, 128.8, 127.7, 121.1, 56.7; HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{10}H_{11}N_3O_2Na$, 228.0744; found, 228.0748.

***N'*-Benzoyl-*N*-cinnamylnitrous hydrazide (2n)**

Compound **2n** was isolated in 73% yield (205 mg, yellow oil); ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.04 (brs, *NH*, 1H), 7.79 (d, *J* = 7.9 Hz, 2H), 7.54 (t, *J* = 7.1 Hz, 1H), 7.41 (t, *J* = 7.6 Hz, 2H), 7.36 (d, *J* = 7.7 Hz, 2H), 7.30 (t, *J* = 7.4 Hz, 2H), 7.26 (d, *J* = 6.8 Hz, 1H), 6.70 (d, *J* = 15.8 Hz, 1H), 6.34 – 6.25 (m, 1H), 5.26 (d, *J* = 6.9 Hz, 2H); ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 165.4, 136.3, 135.8, 133.1, 130.9, 128.9, 128.7, 128.4, 127.7, 126.7, 121.1, 56.3; HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{16}H_{15}N_3O_2Na$, 304.1057; found, 304.1057.

***N'*-Benzoyl-*N*-(prop-2-yn-1-yl)nitrous hydrazide (2o)**

Compound **2o** was isolated in 19% yield (39 mg, yellow solid: 97 °C-100 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.65 (brs, *NH*, 1H), 7.84 (d, *J* = 6.4 Hz, 2H), 7.59 (d, *J* = 6.9 Hz, 1H), 7.49 (d, *J* = 6.2 Hz, 2H), 5.35 (s, 2H), 2.43 (s, 1H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 165.3, 133.2, 130.6, 128.9, 127.7, 75.6, 74.8, 43.7; HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{10}H_9N_3O_2Na$, 226.0587; found, 226.0590.

***N'*-Benzoyl-*N*-isobutylnitrous hydrazide (2p)**

Compound **2p** was isolated in 63% yield (139 mg, yellow solid: 111 °C-116 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.43 (brs, *NH*, 1H), 7.83 – 7.75 (m, 2H), 7.51 (t, *J* = 7.5 Hz, 1H), 7.38 (t, *J* = 7.8 Hz, 2H), 4.26 (d, *J* = 7.2 Hz, 2H), 2.14 (m, 1H), 0.95 (d, *J* = 6.7 Hz, 6H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 165.6, 133.0, 130.8, 128.8, 127.8, 61.4, 26.8, 19.8; HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{11}H_{15}N_3O_2Na$, 244.1057; found, 244.1063.

(E)-*N'*-(2-Methylpropylidene)benzohydrazide (3)

Compound **3** was isolated in 33% yield (63 mg, yellow oil); ^{1}HNMR (400 MHz, $CDCl_3$) δ 10.48 (brs, *NH*, 1H), 7.80 (d, *J* = 7.5 Hz, 2H), 7.59 (d, *J* = 5.9 Hz, 1H), 7.40 (t, *J* = 7.3 Hz, 1H), 7.29 (t, *J* = 7.4 Hz, 2H), 2.60 – 2.45 (m, 1H), 1.01 (d, J = 6.8 Hz, 6H); ^{13}C{^{1}H} NMR (101 MHz,$CDCl_3$) δ 164.6, 158.0, 133.2, 131.6, 128.4, 127.5, 31.6, 19.8. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{11}H_{14}N_2ONa$, 213.0998; found, 213.1004.

Supporting Information. Mechanistic study and Copies of all ^{1}H NMR and ^{13}C NMR spectra of all compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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[18] Although we did not exactly know the electron donor, there are several possibilities. First, another molecule of substrate **1** might be oxidized by intermediate **C**, generating intermediate **A** after the release of a proton. Second, in the case of the model reaction of **1l**, benzoic acid and benzaldehyde were also be detected by GC-MS and HRMS. This result suggested that the generated Bn radical was oxidized and might act as the electron donor.