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In Situ-Generated Iodonium Ylides as Safe Carbene Precursors for the Chemoselective Intramolecular Buchner Reaction

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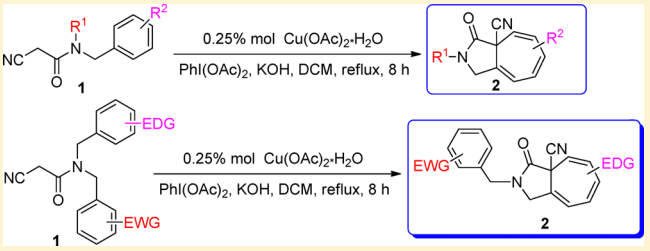
Supporting Information

ABSTRACT: A chemoselective intramolecular Buchner reaction employing iodonium ylides as safe carbene precursors has been developed. Iodonium ylides are generated in situ from *N*-benzyl-2-cyanoacetamides and $PhI(OAc)_2$ in the presence of base and undergo intramolecular Buchner reaction under catalysis from $Cu(OAc)_2{\cdot}H_2O$, affording fused cyclohepta-1,3,5-triene derivatives in up to 85% yield. The *N*,*N*-dibenzyl-2-cyanoacetamides with two different benzyl groups undergo intramolecular Buchner reaction on their electron-rich benzyl groups selectively. The reaction is not sensitive to air and moisture and uses a safe alternative version of the corresponding diazo starting materials. The overall transformation involving the carbene pathway has been verified.



INTRODUCTION

Since the first utilization of carbene for the cyclopropanation of ethyl diazoacetate by Eduard Buchner in 1903,[1] much progress has been achieved in carbene chemistry[2] and its application including carbene insertion into C−H or active heteroatom-H bonds,[3] cyclopropanation[3b,4] or cyclopropenation, and carbene polymerization.[5] Diazo compounds are the most traditional and effective carbene precursors. However, they suffer from major drawbacks such as explosiveness, carcinogenicity, and toxicity.[6] Thus, plenty of the carbene-related reactions are exclusively restricted to the research laboratory.

In the wake of great developments in hypervalent iodine chemistry, iodonium ylides have emerged as safe carbene precursors compared to diazo compounds.[7] Nevertheless, the application of iodonium ylides as carbene precursors is also limited because of their low solubility in most solvents, difficulty of purification, and instability.[8] Zhdankin and co-workers improved the solubility of aryliodonium ylides by introducing an alkoxy group in the ortho position of the phenyl group, extending the application of iodonium ylides.[7,9] However, the one-pot procedure, using iodonium-generated ylides in situ, is a more straightforward and effective process to overcome the shortcomings of iodonium ylides, because the procedure avoids isolation of the potentially unstable and low-solubility intermediates. The one-pot strategy has been applied in several synthetic transformations such as carbene C−H insertion[10] and cyclopropanation,[11] exhibiting a promising future.

The Buchner reaction is an efficient method to synthesize cyclohepta-1,3,5-triene derivatives,[12] which are the structure motifs of arcyriacyanin[13] and abeo-ergoline (Figure 1).[14] Very recently, we reported the $Cu(acac)_2$-catalyzed intramolecular Buchner reaction of *N*-benzyl-2-cyano-2-diazoacetamides.[15] By introducing a cyano group at the α-position of *N*-benzyl-2-diazoacetamides, specific chemoselectivity is realized for the intramolecular Buchner reaction, providing an economical and efficient approach to access 9-aza-1-cyanobicyclo[5.3.0]deca-2,4,6-trien-10-ones, 5,7-bicyclic compounds. Herein, we disclose the intramolecular Buchner reaction employing iodonium ylides as the corresponding safe alternative carbene precursors to *N*-benzyl-2-diazo-2-cyanoacetamides. Iodonium ylides are generated in situ from 2-cyanoacetamides and $PhI(OAc)_2$ in the presence of base and undergo chemoselective intramolecular Buchner reaction under catalysis from $Cu(OAc)_2{\cdot}H_2O$. The protocol avoids the purification of the carbene precursors, and the reactions proceed without inert gas protection, improving the practicality of the reaction. To the best of our knowledge, this is the first report of iodonium ylides being employed as carbene precursors for the Buchner reaction. The mechanistic studies suggest a carbene pathway in the overall transformation.

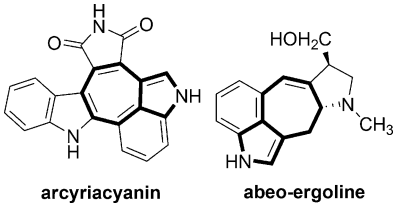


Figure 1. Pharmaceuticals containing 9-azabicyclo[5.3.0]decane structure motifs.

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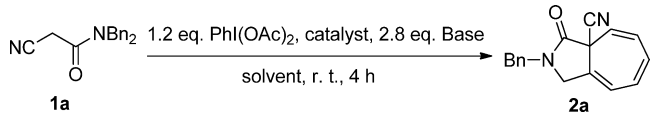
Table 1. Survey of Reaction Conditions



1a 2a

entry	catalyst (%)	solvent	base	yield[a] (%)
1	$Rh_2(OAc)_4$ (1)	DCM[b]	KOH	63
2	$Rh_2(OAc)_4$ (1)	DCM[b]	KOH	63[c]
3	$Rh_2(OAc)_4$ (1)	DCM	KOH	64
4	$Rh_2(OAc)_4$ (1)	THF	KOH	40
5	$Rh_2(OAc)_4$ (1)	CH_3CN	KOH	27
6	$Rh_2(OAc)_4$ (1)	DMF	KOH	0
7	$Rh_2(OAc)_4$ (1)	DCM	Cs_2CO_3	56
8	$Rh_2(OAc)_4$ (1)	DCM	TEA	20
9	$Rh_2(oct)_4$ (1)	DCM	KOH	55
10	$Cu(acac)_2$ (1)	DCM	KOH	48
11	Cu(OTf) (1)	DCM	KOH	51
12	Co(TMDPP) (1)	DCM	KOH	15
13	$Cu(OAc)_2·H_2O$ (1)	DCM	KOH	66
14	$CuCl_2·2H_2O$ (1)	DCM	KOH	63
15	CuCl (1)	DCM	KOH	64
16	$Cu(OAc)_2·H_2O$ (1)	DCM (0 °C)	KOH	32
17	$Cu(OAc)_2·H_2O$ (1)	DCM (reflux, 0.2 M[d])	KOH	72
18	$Cu(OAc)_2·H_2O$ (1)	$CHCl_3$ (reflux)	KOH	50
19	$Cu(OAc)_2·H_2O$ (1)	DCE (reflux)	KOH	67
20	$Cu(OAc)_2·H_2O$ (2)	DCM (reflux)	KOH	64
21	$Cu(OAc)_2·H_2O$ (0.25)	DCM (reflux)	KOH	75
22	$Cu(OAc)_2·H_2O$ (0.25)	DCM (reflux, 0.5 M[d])	KOH	75
23	$Cu(OAc)_2·H_2O$ (0.25)	DCM (reflux, 0.05 M[d])	KOH	78
24	$Cu(OAc)_2·H_2O$ (0.25)	DCM (reflux, 0.05 M,[d] 8 h)	KOH	87(84[e])
25	$Cu(OAc)_2·H_2O$ (0.25)	DCM (reflux, 0.05 M,[d] 8 h)	KOH	(72[e,f])
26	–	DCM (reflux, 0.05 M,[d] 8 h)	KOH	60

[a]Unless otherwise noted, the yield is determined by ^{1}H NMR with methyl maleate as an internal standard. All reactions were performed on 1 mmol scale and in open air. [b]DCM was dried over CaH_2. [c]The reaction was run under nitrogen atmosphere. [d]Concentration of cyanoacetamide **1a**. [e]Isolated yield after column chromatography on silica gel. [f]The reaction was conducted on 10 mmol scale.

RESULTS AND DISCUSSION

Optimization of Reaction Conditions. *N*,*N*-Dibenzyl-2-cyanoacetamide (**1a**) was selected as the model substrate for optimization of the reaction conditions (Table 1). In the presence of base, rhodium catalyst, and (diacetoxyiodo)-benzene, the desired product 5,7-bicyclic product 9-aza-9-benzyl-1-cyanobicyclo[5.3.0]deca-2,4,6-trien-10-one (**2a**) was successfully generated in 63% yield from **1a** (Table 1, entry 1). To be noted, the reaction yield in open atmosphere was comparable with that under nitrogen atmosphere (Table 1, entry 2). In addition, the reaction yield was the same whether the reaction was performed in freshly dried DCM (dichloromethane) or in commercially available DCM (Table 1, entry 3). The results indicated that the reaction is not affected by air or moisture.

The solvent effect for the reaction was investigated. Several common solvents including DCM, THF, CH_3CN, and DMF were scanned (Table 1, entries 1, 4–6). The results suggested that DCM is the best solvent for the reaction, while DMF was completely not applicable. Various bases were used, and KOH was found to be the most practical (Table 1, entries 1, 7, and 8). Subsequently, a variety of metal salts, including rhodium(II), cobalt(II), cupper(II), and cupper(I) salts, were used to attempt catalysis of the reaction (Table 1, entries 1, 9–15). The screening revealed that the best yield was obtained when $Cu(OAc)_2·H_2O$ was utilized. Further investigation of reaction temperature demonstrated that low temperature was unfavorable for the reaction (Table 1, entry 16). In contrast, when the reaction was conducted in refluxing solvent, the yield was improved to 72% (Table 1, entry 17). However, when the reaction was performed in higher boiling point solvents, the yield did not increase further (Table 1, entries 18 and 19). The effect of catalyst loading was surveyed (Table 1, entries 13, 20, and 21), and the results showed that a higher yield was achieved when a very small amount of catalyst (0.25%) was loaded (Table 1, entry 21). Studies on the concentration of the substrate proved that 0.05 M substrate led to better yield than other concentrations (Table 1, entries 17, 22, and 23). When reaction time was extended to 8 h, 87% yield was obtained (Table 1, entry 24). A 72% yield was obtained on a larger scale synthesis (Table 1, entry 25). The reaction also proceeded without any catalyst but with only 60% yield (Table 1, entry 26). Therefore, a set of reaction conditions was optimized.

Scope and Limitation of the Method. With the optimal reaction conditions in hand, we investigated the substrate scope and limitation of the intramolecular Buchner reaction with a range of *N*-benzyl-2-cyanoacetamides **1**, and the results are summarized in Table 2. The effect of the N-protecting group was surveyed. Substrates **1b–e** bearing *N*-benzyl and the other *N*-alkyl groups with benzylic, primary, and secondary C–H were converted into 5,7-bicyclic compounds **2b–e**, the intramolecular Buchner reaction products, in 40–84% yields

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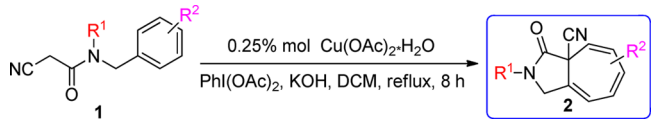
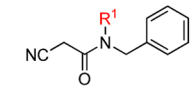
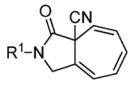
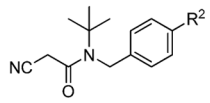
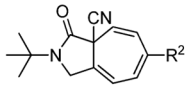
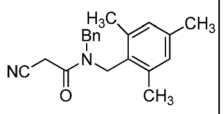
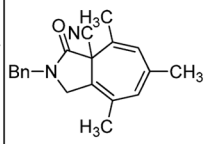
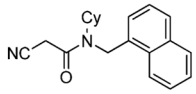
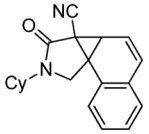
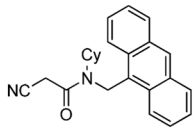
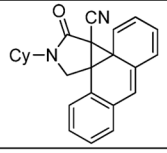
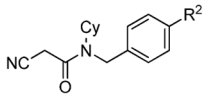
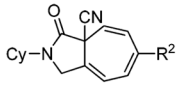
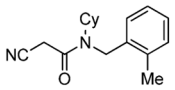
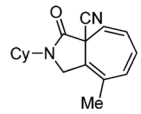
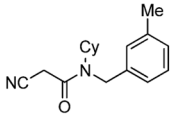
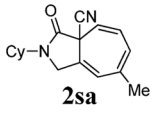
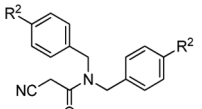
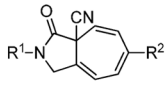
Table 2. Scope and Limitation of the Intramolecular Buchner Reaction



Entry	Substrate **1**	Product **2**	Yield[a] (%)
1		 **2a**, R^1 = Bn	84
2		**2b**, R^1 = Me	40
3		**2c**, R^1 = cHexyl (Cy)	60
4		**2d**, R^1 = 2,6-dichlorobenzyl	50
5		**2e**, R^1 = neopentyl	46
6		 **2f**, R^2 = H	0
7		**2g**, R^2 = Me	0
8		**2h**, R^2 = Br	0
9		 **2i**	50
10		 **2j**	75
11		 **2k**	85
12		 **2l**, R^2 = Br	34
13		**2m**, R^2 = CN	35
14		**2n**, R^2 = Me	52
15		**2o**, R^2 = ^{i}Pr	39
16		**2p**, R^2 = OMe	51
17		**2q**, R^2 = SMe	33
18		 **2r**	64
19		 **2sa** + **2sb**	60[b]
20		 **2t**, R^1 = 4-chlorobenzyl, R^2 = Cl	70
21		**2u**, R^1 = 4-methoxybenzyl, R^2 = OMe	82

[a]Isolated yield after column chromatography on silica gel. All reactions were performed on 1 mmol scale and in open air. [b]Two products, **2sa** and **2sb**, were obtained in a ratio of 1:1 after silical gel column chromatography.

(Table 2, entries 2–5). To our surprise, none of the substrates **1f–h** with the *N-tert*-butyl group gave the desired product (Table 2, entries 6–8). This phenomenon is not in accordance with that in our previous research, in which the corresponding diazo compounds were used as the carbene precursors and the *N-tert*-butyl-substituted substrates achieved higher yields.[15] Taking into account the present method with the key intermediate iodonium ylides, the phenyliodo group is very

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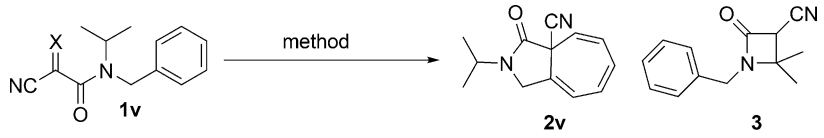
Scheme 1. Comparison between Two Types of the Buchner Reactions from *N*-Benzyl-2-cyano-*N*-isopropylacetamide (1v) and *N*-Benzyl-2-cyano-2-diazo-*N*-isopropylacetamide (4)



Method A: $Cu(OAc)_2{\cdot}H_2O$, $PhI(OAc)_2$, KOH, DCM, reflux, 8 h.
Method B: $Cu(acac)_2$, DCE, reflux, 0.5 h.

bulky; in addition, the steric hindrance of the *N*-*tert*-butyl group is very large, so the *N*-*tert*-butyl-substituted substrates **1f−h** cannot even generate the corresponding phenyliodonium ylides to produce intramolecular Buchner reaction products (Scheme 1). However, substrates **1a−e** with the other relatively less bulky N-protecting groups (Bn, Me, Cy, 2,6-dichlorobenzyl, neopentyl) are converted into the iodonium ylides and subsequently undergo the intramolecular Buchner reactions. Furthermore, substrate **1i** with the *N*-mesitylenemethyl group underwent the intramolecular Buchner reaction on the mesitylene ring, while substrate **1d** with both *N*-benzyl and *N*-2,6-dichlorobenzyl groups underwent the intramolecular Buchner reaction on the benzene ring rather than on the 2,6-dichlorobenzene ring, revealing that the electronic effect of the aromatic ring is much more important than the steric effect (Table 2, entries 4 and 9). However, the intramolecular Buchner reactions involving the polyaromatic ring substrates **1j** and **1k** only proceeded to the first stage for some reason, affording the corresponding cyclopropanation products in good yields (Table 2, entries 11 and 12). The electronic effect of the substituents at the para position of the benzyl group was studied (Table 2, entries 12−17). The *N*-benzyl substrates **1n−p** with electron-donating groups gave rise to the desired products **2n−p** in yields relatively higher than those (**1l** and **1m**) with electron-withdrawing groups. Therefore, the electronic effect shows certain influence in the Buchner reaction. For the ortho-substituted substrate **1r**, only one product **2r** was generated (Table 2, entry 18). However, the meta-substituted substrate **1s** produced two regioisomeric products **2sa** and **2sb** without regioselectivity (1:1) (Table 2, entry 19). The substrates **1t** and **1u** with two identical N-para-substituted benzyl groups were tested as well, affording the desired products **2t** and **2u** in satisfactory to good yields (Table 2, entries 20 and 21). When the substrate *N*-benzyl-2-cyano-*N*-isopropylacetamide (**1v**) was subjected to the reaction conditions, a mixture of two products, 5,7-bicyclic compound **2v** and *β*-lactam **3**, was obtained in a ratio of 47:53 in 66% yield (Scheme 1). However, unfortunately, they cannot be separated either upon recrystallization or on a chromatographic column due to their very close solubility and polarity. Their structures were identified on the basis of spectral analysis and by referring to similar compounds.[16] This is the first example that gave rise to byproduct *β*-lactam **3**. This prompted us to rerun the reactions, which produced products **2** in low yields, to check whether byproduct *β*-lactams were generated in those cases. Although all starting materials were consumed completely, even for all similar substrates with the secondary *N*-cyclohexyl group, no lactams (*β*-lactam and *γ*-lactam, C−H insertion products), carbene dimer, and polymers of carbene were observed besides the corresponding desired products **2** and some strong polar impurities on the basis of TLC and IR analyses of the reaction mixtures. The polar byproducts were difficult to completely isolate by column chromatography, even with MeOH as the eluent. Some of them were isolated, but their proton NMR spectra were very complicated, and thus these complexes were unable to be identified. Currently, it is still unclear why only substrate **1v** with the *N*-isopropyl group can yield the *β*-lactam byproduct.

The Buchner reaction generally includes two stages, cyclopropanation and ring-expansion. The mechanism for the cyclopropanation of the iodonium ylides is controversial. Moriaty proposed an ionic mechanism, and it is very rational for the cyclopropanation of the polar double bonds.[17] But Muller suggested a carbene mechanism for the cyclopropanation of alkenes and discovered some conclusive evidence.[8b] The first stage of the Buchner reaction is the cyclopropanation of the aromatic rings, and we are apt to assume the carbene mechanism for our reactions. In our previous investigation,[15] *N*-alkyl-*N*-arylmethyl-cyanodiazoacetamides underwent the first-stage cyclopropanation specifically under catalysis from $Cu(acac)_2$. The reaction occurred through the carbene mechanism. However, we did not test the corresponding diazo derivative of substrate **1v**. To verify the mechanism, the diazo derivative of **1v**, *N*-benzyl-2-cyano-2-diazo-*N*-isopropylacetamide (**4**), was prepared and subjected to the $Cu(acac)_2$-catalyzed reaction conditions for the intramolecular Buchner reaction. The products **2v** and **3** were obtained in very close (almost identical) yield and ratio as those in the reaction of **1v** (Scheme 1). This phenomenon reveals that these two reactions proceed with the same intermediates and mechanism. Because the metal catalysis of diazo compounds proceeds through the metallocarbene pathway, the $Cu(OAc)_2{\cdot}H_2O$-catalyzed decomposition of the ylides should also go through the metallocarbene pattern. In addition, the formation of the unusual C−H insertion product (*β*-lactam **3**) in the intramolecular Buchner reaction suggests the carbene mechanism as well, because these type of products are typical for carbenoid reactions.

The results indicate that both steric and electronic effects of the N-protecting groups control the intramolecular Buchner reaction. The steric effect controls the generation of the iodonium ylides. Too bulky N-substituents, such as *tert*-butyl, impede the formation of the key intermediate iodonium ylides. Less steric N-substituents are favorable for the ylide formation. The electronic effect impacts both yield and regioselectivity. Generally, the electron-rich substrates (**2n** and **2p**) give rise to yields higher than those of the electron-deficient ones (**2l** and **2m**). The intramolecular Buchner reactions generally take place on the electron-rich benzyl groups regioselectively if the substrates possess two different benzyl groups (Table 2, entries 4 and 9). The results suggest that the *π*−*π* stacking interaction

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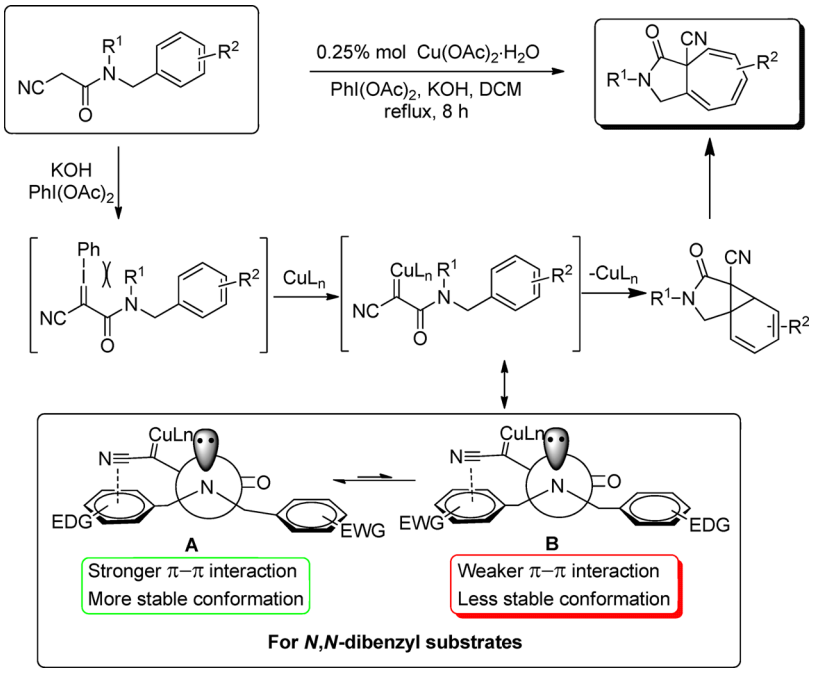
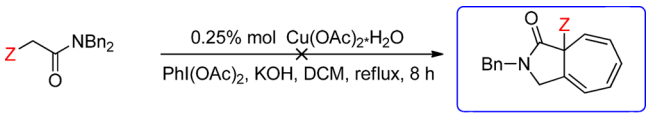
Scheme 2. Explanation of Chemo- and Regioselectivities



(actually a type of Lewis acid–base interaction) between the cyano and phenyl groups indeed plays an important role in stabilizing conformation **A** as proposed previously,[15,18] resulting in the formation of the Buchner products chemoselectively because the cyano group is an electron-deficient group and shows stronger interaction with the electron-rich phenyl groups. In the Newman projection of the intermediates, when R^1 are benzyls with electron-withdrawing groups and R^2 are electron-rich substituents, conformation **A** is more favorable than conformation **B** (Scheme 2). Conformation **A** is the reactive conformation that leads to the Buchner reaction chemoselectively.

Scheme 3. Attempts To Extend the Substrate Scope to *N,N*-Dibenzylacetamides with Other *α*-Electron-Withdrawing Substituents



Z = $PhSO_2$, **5**
Z = Ac, **6**

Finally, the *N,N*-dibenzylacetamides with other *α*-electron-withdrawing substituents ($PhSO_2$ and Ac) were used to attempt extension of the reaction substrate scope. Under the optimized reaction conditions, *N,N*-dibenzyl-2-phenylsulfonylacetamide (**5**) was completely inert and was recovered totally. 2-Acetyl-*N,N*-dibenzylacetamide (**6**) was completely consumed, but the reaction did not generate the corresponding desired product, leading only to formation of some unidentified complexes (Scheme 3).

CONCLUSION

We developed a $Cu(OAc)_2·H_2O$-catalyzed and chemoselective intramolecular Buchner reaction which employed iodonium ylides as carbene precursors. The iodonium ylides are generated in situ from *N*-benzyl-2-cyanoacetamides and $PhI(OAc)_2$ in the presence of KOH. For the *N,N*-dibenzyl-2-cyanoacetamides with two different benzyl groups, the intramolecular Buchner reaction occurs on the electron-rich benzyl groups selectively. The reactions are not sensitive to air and moisture, affording a variety of fused cyclohepta-1,3,5-triene derivatives. The reaction is proved to proceed through the carbene pathway and is a safe alternative version compared with the corresponding diazo starting materials.

EXPERIMENTAL SECTION

General Information. For the reactions conducted under anhydrous conditions, glassware was flame-dried or dried in an oven at 105 °C prior to use and the reactions were carried out under a nitrogen atmosphere.

1. Spectroscopy and Instruments. Melting points (mp) were determined on a melting point apparatus and are uncorrected. ^1H and ^{13}C NMR spectra were recorded on a 400 NMR spectrometer at 400 and 100 MHz, respectively, in $CDCl_3$ with TMS as the internal standard, and chemical shifts were reported in ppm. IR spectra were taken on an FT-IR spectrometer in dichloromethane (DCM). HRMS spectra were performed on an LC/MSD TOF mass spectrometer.

2. Solvents and Reagents. For the reactions conducted under anhydrous conditions, solvents were refluxed with drying reagents and freshly distilled prior to use. Dichloromethane (DCM) and acetonitrile were dried with calcium hydride. 1,2-Dichloroethane (DCE) and chloroform were dried with phosphorus pentoxide. Toluene and benzene were dried with sodium wire. Reagents used were obtained from commercial suppliers and used without purification except that triethylamine (TEA) was dried with calcium hydride and freshly distilled prior to use.

3. Column Chromatography. Column chromatography was carried out on silica gel (200–300 mesh) with petroleum ether (PE, 60–90 °C) and ethyl acetate (EA) as the eluent. All reactions were followed by thin-layer chromatography (TLC) where practical, using silica gel 60 F_{254} fluorescent-treated silica gel plates, which were visualized under UV light (250 nm).

General Procedure for the Preparation of 2-Cyanoacetamides Using DCC/DMAP as Condensation Reagents.[15,19] To a

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solution of secondary amine (10 mmol) and 2-cyanoacetic acid (936 mg, 11 mmol) in CH_2Cl_2 (10 mL) was added a solution of DCC (*N*,*N*′-dicyclohexylcarbodiimide, 2.27 g, 11 mmol) and DMAP [4-(*N*,*N*-dimethylamino)pyridine, 61 mg, 0.5 mmol] in CH_2Cl_2 (20 mL) at 0 °C. The resulting solution was stirred for 1 h. During this period, a white solid (1,3-dicyclohexylurea, DCU) was precipitated and subsequently filtered. After removal of the solvent under reduced pressure, the resulting crude product was recrystallized from EtOH to afford pure amide **1**.

*N,N-Dibenzyl-2-cyanoacetamide (**1a**).* 2.32 g, 88% yield. Colorless crystals, mp 117−119 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.41−7.30 (m, 6H), 7.26−7.23 (m, 2H), 7.14−7.12 (m, 2H), 4.65 (s, 2H), 4.44 (s, 2H), 3.52 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 162.5, 136.0, 134.8, 129.3, 128.8, 128.4, 128.2, 127.9, 126.1, 113.8, 50.6, 49.5, 25.3. IR (DCM) ν (cm^{-1}): 2254 (CN), 1654 (C═O).

*N-Benzyl-2-cyano-N-methylacetamide (**1b**).* 1.18 g, 63% yield. Colorless crystals, mp 45−47 °C. Exists as two different conformational isomers in solution. Major isomer (65%): ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.42−7.30 (m, 3H), 7.25 (d, *J* = 7.5 Hz, 2H), 4.60 (s, 2H), 3.55 (s, 2H), 2.96 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 161.8, 135.9, 128.8, 128.1, 126.1, 113.8, 51.5, 35.2, 25.2. Minor isomer (35%): ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.42−7.30 (m, 3H), 7.17 (d, *J* = 7.2 Hz, 2H), 4.53 (s, 2H), 3.51 (s, 2H), 3.03 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 162.1, 134.9, 129.3, 128.2, 127.8, 113.9, 53.9, 34.9, 24.9. IR (DCM) ν (cm^{-1}): 2260 (CN), 1653 (C═O).

*N-Benzyl-2-cyano-N-(2,6-dichlorobenzyl)acetamide (**1d**).* 2.89 g, 87% yield. Colorless crystals, mp 106−107 °C. Exists as two different conformational isomers in solution. Major isomer (66%): ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.36−7.27 (m, 3H), 7.23−7.18 (m, 2H), 7.15−7.08 (m, 3H), 5.12 (s, 2H), 4.37 (s, 2H), 3.45 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 162.5, 137.0, 135.5, 130.0, 129.2, 128.6, 128.0, 127.3, 125.5, 113.7, 49.9, 45.2, 25.3. Minor isomer (34%): ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.36−7.28 (m, 3H), 7.16−7.08 (m, 3H), 7.03−7.00 (m, 2H), 4.81 (s, 2H), 4.48 (s, 2H), 3.89 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 162.5, 136.5, 136.3, 131.0, 130.4, 128.8, 128.1, 127.1, 125.5, 113.7, 48.5, 48.0, 25.9. IR (DCM) ν (cm^{-1}): 2235 (CN), 1709 (C═O). HRMS (ESI) calcd for $C_{17}H_{15}Cl_2N_2O$ $[M + H]^+$ *m*/*z* 333.0556, found 333.0554.

*N-Benzyl-2-cyano-N-neopentylacetamide (**1e**).* 2.12 g, 87% yield. Colorless crystals, mp 48−51 °C. Exists as two different conformational isomers in solution. Major isomer (77%): ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.39 (t, *J* = 7.3 Hz, 2H), 7.34−7.32 (m, 1H), 7.11 (d, *J* = 7.3 Hz, 1H), 4.64 (s, 2H), 3.40 (s, 2H), 3.37 (s, 2H), 1.00 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 163.5, 135.8, 129.4, 128.0, 125.4, 114.1, 58.7, 53.8, 34.5, 28.3, 25.5. Minor isomer (23%): ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.34−7.28 (m, 3H), 7.20 (d, *J* = 7.0 Hz, 2H), 4.74 (s, 2H), 3.63 (s, 2H), 3.08 (s, 2H), 1.04 (s, 9H).^{13}C NMR (100 MHz, $CDCl_3$) δ: 163.2, 136.4, 128.7, 127.7, 127.6, 114.1, 58.3, 51.0, 34.2, 28.6, 25.8. IR (DCM) ν (cm^{-1}): 2259 (CN), 1666 (C═O). HRMS (ESI) calcd for $C_{15}H_{21}N_2O$ $[M + H]^+$ *m*/*z* 245.1648, found 245.1651.

*N-(tert-Butyl)-2-cyano-N-(4-methylbenzyl)acetamide (**1g**).* 1.76 g, 72% yield. Colorless crystals, mp 159−161 °C. Exists as two different conformational isomers in solution. Major isomer (74%): ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.20 (d, *J* = 8.0 Hz, 2H), 7.07 (d, *J* = 8.0 Hz, 2H), 4.53 (s, 2H), 3.43 (s, 2H), 2.35 (s, 3H), 1.46 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 162.9, 137.4, 134.2, 129.9, 125.1, 114.5, 59.2, 48.9, 28.4, 25.7, 20.9. Minor isomer (26%): ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.34 (d, *J* = 8.0 Hz, 2H), 7.11 (d, *J* = 8.0 Hz, 2H), 3.92 (s, 2H), 3.23 (s, 2H), 2.31 (s, 3H), 1.26 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 166.4, 138.8, 130.3, 129.3, 128.3, 116.4, 56.9, 45.3, 27.8, 26.6, 21.1. IR (DCM) ν (cm^{-1}): 2255 (CN), 1662 (C═O). HRMS (ESI) calcd for $C_{15}H_{21}N_2O$ $[M + H]^+$ *m*/*z* 245.1648, found 245.1644.

*N-(4-Bromobenzyl)-N-(tert-butyl)-2-cyanoacetamide (**1h**).* 2.46 g, 80% yield. Colorless crystals, mp 115−117 °C. Exists as two different conformational isomers in solution. Major isomer (94%): ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.53 (d, *J* = 8.3 Hz, 2H), 7.09 (d, *J* = 8.3 Hz, 2H), 4.52 (s, 2H), 3.42 (s, 2H), 1.46 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 162.8, 136.5, 132.4, 126.9, 121.6, 114.3, 59.3, 48.6, 28.4, 27.8. Minor isomer (6%): ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.23 (d, *J* = 7.4 Hz, 2H), 6.69 (d, *J* = 7.0 Hz, 2H), 3.89 (s, 2H), 3.24 (d, *J* = 12.7 Hz, 2H), 1.24 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 166.8, 140.5, 133.4, 132.5, 131.6, 106.5, 44.8, 39.9, 27.2, 25.7. IR (DCM) ν (cm^{-1}): 2258 (CN), 1660 (C═O). HRMS (ESI) calcd for $C_{14}H_{18}BrN_2O$ $[M + H]^+$ *m*/*z* 309.0597, found 309.0594.

*N-Benzyl-2-cyano-N-(2,4,6-trimethylbenzyl)acetamide (**1i**).* 2.17 g, 71% yield. Colorless crystals, mp 107−108 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.39−7.29 (m, 3H), 7.22 (s, 1H), 7.05 (d, *J* = 7.3 Hz, 1H), 6.83 (s, 2H), 4.84 (s, 2H), 4.22 (s, 2H), 3.46 (d, *J* = 3.3 Hz, 2H), 2.27 (s, 3H), 2.06 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 162.4, 138.3, 137.8, 135.6, 129.4, 129.4, 128.2, 128.0, 125.4, 113.9, 48.1, 43.1, 25.2, 20.9, 19.6. IR (DCM) ν (cm^{-1}): 2259 (CN), 1662 (C═O). HRMS (ESI) calcd for $C_{20}H_{23}N_2O$ $[M + H]^+$ *m*/*z* 307.1805, found 307.1807.

General Procedure for the Preparation of 2-Cyanoacetamides Using 2-Cyanoacetic Chloride as an Acylating Reagent.[15,20] To a stirred suspension of 2-cyanoacetic acid (1.10 g, 13.0 mmol) in CH_2Cl_2 (50 mL) was added oxalyl chloride (1.04 mL, 12.0 mmol) followed by seven drops of DMF at 0 °C. The reaction mixture was stirred at room temperature for 3 h. To the above clear pale yellow solution was added a solution of secondary amine (10.0 mmol) in dichloromethane (40 mL) followed by triethylamine (3.48 mL, 25.0 mmol) at 0 °C. The reaction mixture was stirred for 24 h and then washed with water (20 mL) and 1 mol/L HCl (20 mL). The organic layer was dried over MgSO4 and then evaporated. The resulting residue was purified by silica gel chromatography (petroleum ether/EtOAc, v/v 6:1−2:1) to give the amide **1**.

*N-Benzyl-2-cyano-N-cyclohexylacetamide (**1c**).* 1.23 g, 48% yield. Colorless crystals, mp 79−81 °C. Exists as two different conformational isomers in solution. Major isomer (61%): ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.40−7.19 (m, 5H), 4.49−4.46 (m, 3H), 3.32 (s, 2H), 1.83−1.63 (m, 4H), 1.51−1.24 (m, 4H), 1.11−1.04 (m, 1H), 0.90−0.87 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 162.5, 136.8, 129.1, 126.9, 125.5, 114.1, 55.1, 47.1, 31.8, 30.4, 25.7, 25.5, 25.2, 14.0. Minor isomer (39%): ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.40−7.19 (m, 5H), 4.58 (s, 2H), 3.64 (s, 2H), 3.52−3.47 (m, 1H), 1.83−1.63 (m, 4H), 1.51−1.24 (m, 4H), 1.11−1.04 (m, 1H), 0.90−0.87 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 161.8, 138.2, 128.4, 127.8, 126.9, 114.1, 59.1, 45.4, 31.5, 25.9, 25.5, 24.9, 22.6, 14.0. IR (DCM) ν (cm^{-1}): 2257 (CN), 1652 (C═O). HRMS (ESI) calcd for $C_{16}H_{21}N_2O$ $[M + H]^+$ *m*/*z* 257.1648, found 257.1652.

*N-Benzyl-N-tert-butyl-2-cyanoacetamide (**1f**).* 0.60 g, 26% yield. Colorless crystals, mp 97−99 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.40 (dd, *J* = 7.6, 7.6 Hz, 2H), 7.30 (t, *J* = 7.6 Hz, 1H), 7.19 (d, *J* = 7.6 Hz, 2H), 4.57 (s, 2H), 3.44 (s, 2H), 1.47 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 162.9, 137.4, 129.2, 127.7, 125.2, 114.5, 59.2, 49.1, 28.4, 27.8. IR (DCM) ν (cm^{-1}): 2256 (CN), 1650 (C═O). HRMS (ESI) calcd for $C_{14}H_{18}N_2NaO$ $[M + Na]^+$ *m*/*z* 253.1311, found 253.1315.

*2-Cyano-N-cyclohexyl-N-(naphthalen-1-ylmethyl)acetamide (**1j**).* 1.49 g, 49% yield. Colorless crystals, mp 121−124 °C. Exists as two different conformational isomers in solution. Major isomer (70%): ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.94−7.89 (m, 2H), 7.82 (d, *J* = 8.2 Hz, 1H), 7.62−7.54 (m, 2H), 7.49−7.44 (m, 2H), 7.31 (d, *J* = 7.0 Hz, 2H), 4.92 (s, 2H), 4.64−4.57 (m, 1H), 3.34 (s, 2H), 1.85 (d, *J* = 10.4 Hz, 1H), 1.75 (d, *J* = 10.0 Hz, 1H), 1.62 (d, *J* = 13.3 Hz, 1H), 1.45−1.28 (m, 4H), 1.05−0.94 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 162.9, 133.6, 133.6, 131.7, 129.1, 128.3, 126.7, 126.3, 125.3, 122.4, 121.6, 114.2, 55.1, 44.8, 30.2, 25.6, 25.5, 25.5. Minor isomer (30%): ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.95 (d, *J* = 9.3 Hz, 1H), 7.86 (d, *J* = 8.1 Hz, 1H), 7.73 (d, *J* = 8.3 Hz, 1H), 7.58−7.51 (m, 2H), 7.43−7.37 (m, 1H), 7.20 (d, *J* = 6.8 Hz, 1H), 5.04 (s, 2H), 3.72 (s, 2H), 3.67−3.61 (m, 1H), 1.85 (d, *J* = 10.4 Hz, 2H), 1.75 (d, *J* = 10.0 Hz, 2H), 1.62 (d, *J* = 13.3 Hz, 1H), 1.44−1.27 (m, 4H), 1.06−0.95 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 161.8, 133.6, 132.1, 129.8, 128.9, 127.4, 126.1, 125.6, 125.2, 123.0, 122.2, 114.2, 59.1, 43.2, 31.3, 25.5, 25.2, 24.8. IR (DCM) ν (cm^{-1}): 2259 (CN), 1659 (C═O). HRMS (ESI) calcd for $C_{20}H_{23}N_2O$ $[M + H]^+$ *m*/*z* 307.1805 found 307.1807.

*N-(Anthracen-9-ylmethyl)-2-cyano-N-cyclohexylacetamide (**1k**).* 1.75 g, 95% yield. Colorless crystals, mp 138−139 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.44 (s, 1H), 8.19 (d, *J* = 5.6 Hz, 2H), 8.01 (d, *J* = 8.3 Hz, 2H), 7.60−7.51 (m, 2H), 7.51−7.41 (m, 2H), 5.73 (s, 2H), 3.65 (s, 2H), 3.21−3.07 (m, 1H), 1.43 (d, *J* = 11.2 Hz, 2H), 1.34−1.26

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(m, 3H), 0.97−0.38 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 162.0, 131.2, 130.9, 129.4, 128.7, 128.6, 126.7, 125.1, 123.6, 114.3, 59.2, 40.0, 31.3, 26.6, 26.1, 24.8. IR (DCM) ν (cm^{-1}): 2258 (CN), 1645 (C═O). HRMS (ESI) calcd for $C_{24}H_{25}N_2O$ $[M + H]^+$ m/z 357.1961, found 357.1962.

*N-(4-Bromobenzyl)-2-cyano-N-cyclohexylacetamide (**1l**).* 1.67 g, 50% yield. Colorless crystals, mp 102−104 °C. Exists as two different conformational isomers in solution. Major isomer (55%): ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.41 (d, J = 8.3 Hz, 2H), 7.09 (d, J = 8.3 Hz, 2H), 4.51 (s, 2H), 3.64 (s, 2H), 3.52−3.45 (m, 1H), 1.85−1.61 (m, 5H), 1.49−1.24 (m, 4H), 1.11−0.99 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 162.0, 137.3, 131.5, 128.7, 120.8, 113.9, 59.1, 45.0, 31.9, 25.8, 25.7, 25.5. Minor isomer (45%): ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.51 (d, J = 8.2 Hz, 2H), 7.10 (d, J = 8.2 Hz, 2H), 4.46−4.42 (m, 3H), 3.32 (s, 2H), 1.85−1.63 (m, 5H), 1.49−1.24 (m, 4H), 1.11−0.98 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 162.5, 135.9, 132.3, 127.3, 121.7, 113.9, 55.2, 46.7, 30.4, 25.5, 25.2, 24.9. IR (DCM) ν (cm^{-1}): 2259 (CN), 1651 (C═O). HRMS (ESI) calcd for $C_{16}H_{20}BrN_2O$ $[M + H]^+$ m/z 335.0754, found 335.0755.

*2-Cyano-N-(4-cyanobenzyl)-N-cyclohexylacetamide (**1m**).* 1.55 g, 55% yield. Colorless crystals, mp 133−134 °C. Exists as two different conformational isomers in solution. Major isomer (73%): ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.59 (d, J = 8.0 Hz, 2H), 7.33 (d, J = 8.0 Hz, 2H), 4.60 (s, 2H), 3.67 (s, 2H), 3.52 (t, J = 11.1 Hz, 1H), 1.86−1.63 (m, 5H), 1.47−1.24 (m, 4H), 1.12−1.02 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 162.2, 143.7, 132.3, 127.5, 118.6, 113.8, 110.9, 59.0, 45.4, 31.8, 25.6, 25.5, 24.8. Minor isomer (27%): ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.59 (d, J = 8.0 Hz, 2H), 7.33 (d, J = 8.0 Hz, 2H), 4.60 (s, 2H), 3.67 (s, 2H), 3.52 (t, J = 11.1 Hz, 1H), 1.86−1.63 (m, 5H), 1.47−1.24 (m, 4H), 1.12−1.02 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 162.3, 142.4, 132.9, 126.4, 118.1, 113.8, 111.9, 55.3, 47.0, 33.9, 30.4, 25.8, 25.1. IR (DCM) ν (cm^{-1}): 2258 (CN), 2227 (CN), 1652 (C═O). HRMS (ESI) calcd for $C_{17}H_{20}N_3O$ $[M + H]^+$ m/z 282.1601, found 282.1612.

*2-Cyano-N-cyclohexyl-N-(4-methylbenzyl)acetamide (**1n**).* 1.13g, 47% yield. Colorless crystals, mp 99−100 °C. Exists as two different conformational isomers in solution. Major isomer (66%): ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.18 (d, J = 7.8 Hz, 2H), 7.07 (d, J = 7.8 Hz, 2H), 4.50−4.41 (m, 3H), 3.32 (s, 2H), 2.34 (s, 3H), 1.84−1.72 (m, 4H), 1.64 (d, J = 11.8 Hz, 1H), 1.50−1.26 (m, 4H), 1.08−1.01 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 162.5, 137.5, 133.7, 129.8, 125.4, 114.2, 55.0, 46.9, 30.3, 25.9, 25.7, 25.5, 20.9. Minor isomer (34%): ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.13−7.09 (m, 4H), 4.54 (s, 2H), 3.63 (s, 2H), 3.50−3.43 (m, 1H), 2.31 (s, 3H), 1.82−1.71 (m, 4H), 1.64 (d, J = 11.8 Hz, 1H), 1.50−1.25 (m, 4H), 1.10−1.00 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 161.8, 136.5, 135.2, 129.0, 126.9, 114.2, 59.0, 45.2, 31.9, 25.5, 25.2, 24.9, 20.9. IR (DCM) ν (cm^{-1}): 2258 (CN), 1651 (C═O). HRMS (ESI) calcd for $C_{17}H_{23}N_2O$ $[M + H]^+$ m/z 271.1805, found 271.1808.

*2-Cyano-N-cyclohexyl-N-(4-isopropylbenzyl)acetamide (**1o**).* 1.55 g, 59% yield. Colorless crystals, mp 111−112 °C. Exists as two different conformational isomers in solution. Major isomer (68%): ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.23 (d, J = 8.0 Hz, 2H), 7.10 (heptet, J = 8.0 Hz, 2H), 4.48−4.45 (m, 3H), 3.31 (s, 2H), 2.89 (d, J = 8.0 Hz, 1H), 1.84−1.74 (m, 4H), 1.64 (d, J = 11.1 Hz, 1H), 1.53−1.29 (m, 4H), 1.26 (s, 6H), 1.11−0.99 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 162.6, 148.6, 134.0, 127.2, 125.5, 114.2, 55.1, 46.9, 33.7, 30.4, 25.9, 25.8, 25.6, 23.9. Minor isomer (32%): ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.14−7.13 (m, 4H), 4.54 (s, 2H), 3.62 (s, 2H), 3.52−3.45 (m, 1H), 2.89 (heptet, J = 7.2 Hz, 1H), 1.78 (d, J = 9.3 Hz, 4H), 1.64 (d, J = 11.1 Hz, 1H), 1.53−1.29 (m, 4H), 1.22 (d, J = 7.2 Hz, 6H), 1.10−1.00 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 161.7, 147.5, 135.4, 126.9, 126.4, 114.1, 59.1, 45.3, 31.9, 25.5, 25.3, 25.0, 23.9. IR (DCM) ν (cm^{-1}): 2258 (CN), 1655 (C═O). HRMS (ESI) calcd for $C_{19}H_{27}N_2O$ $[M + H]^+$ m/z 299.2118, found 299.2120.

*2-Cyano-N-cyclohexyl-N-(4-methoxybenzyl)acetamide (**1p**).* 1.66 g, 58% yield. Colorless crystals, mp 82−83 °C. Exists as two different conformational isomers in solution. Major isomer (61%): ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.11 (d, J = 8.5 Hz, 2H), 6.90 (d, J = 8.5 Hz, 2H), 4.49−4.37 (m, 3H), 3.81 (s, 3H), 3.33 (s, 2H), 1.83−1.71 (m, 4H), 1.64 (d, J = 11.2 Hz, 1H), 1.52−1.24 (m, 4H), 1.12−1.00 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 162.5, 159.1, 128.4, 126.7, 114.5, 114.2, 55.3, 55.1, 46.6, 30.4, 25.9, 25.7, 25.5. Minor isomer (39%): ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.16 (d, J = 8.4 Hz, 2H), 6.82 (d, J = 8.4 Hz, 2H), 4.52 (s, 2H), 3.78 (s, 3H), 3.62 (s, 2H), 3.50−3.42 (m, 1H), 1.75 (t, J = 11.5 Hz, 4H), 1.64 (d, J = 11.2 Hz, 1H), 1.52−1.25 (m, 4H), 1.12−1.00 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 161.8, 158.5, 130.3, 128.5, 114.1, 113.7, 59.0, 55.2, 44.9, 31.9, 25.5, 25.2, 24.9. IR (DCM) ν (cm^{-1}): 2258 (CN), 1651 (C═O). HRMS (ESI) calcd for $C_{17}H_{23}N_2O_2$ $[M + H]^+$ m/z 287.1754, found 287.1758.

*2-Cyano-N-cyclohexyl-N-(4-(methylthio)benzyl)acetamide (**1q**).* 1.23 g, 67% yield. Colorless crystals, mp 95−96 °C. Exists as two different conformational isomers in solution. Major isomer (57%): ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.25 (d, J = 8.1 Hz, 2H), 7.11 (d, J = 8.1 Hz, 2H), 4.50−4.38 (m, 3H), 3.32 (s, 2H), 2.49 (s, 3H), 1.78 (dd, J = 30.4, 14.5 Hz, 4H), 1.64 (d, J = 10.6 Hz, 2H), 1.50−1.26 (m, 4H), 1.10−0.99 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 162.5, 135.2, 133.4, 127.0, 126.1, 114.1, 55.1, 46.8, 30.4, 25.9, 25.7, 25.5, 15.6. Minor isomer (43%): ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.18 (d, J = 8.4 Hz, 2H), 7.14 (d, J = 8.4 Hz, 2H), 4.53 (s, 2H), 3.62 (s, 2H), 3.50−3.45 (m, 1H), 2.46 (s, 3H), 1.76 (t, J = 14.5 Hz, 4H), 1.64 (d, J = 10.6 Hz, 1H), 1.50−1.25 (m, 4H), 1.11−0.99 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 161.9, 138.4, 137.0, 127.6, 126.7, 114.1, 59.1, 45.1, 31.9, 25.5, 25.2, 24.9, 15.9. IR (DCM) ν (cm^{-1}): 2258 (CN), 2227 (CN), 1651 (C═O). HRMS (ESI) calcd for $C_{17}H_{23}N_2OS$ $[M + H]^+$ m/z 303.1526 found 303.1529.

*2-Cyano-N-cyclohexyl-N-(2-methylbenzyl)acetamide (**1r**).* 0.85 g, 32% yield. Colorless crystals, mp 135−136 °C. Exists as two different conformational isomers in solution. Major isomer (70%): ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.22−7.19 (m, 2H), 7.14−7.10 (m, 2H), 4.54−4.48 (m, 1H), 4.38 (s, 2H), 3.30 (s, 2H), 2.31 (s, 3H), 1.86−1.74 (m, 4H), 1.69−1.60 (m, 1H), 1.44−1.25 (m, 4H), 1.13−0.99 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 162.6, 134.5, 134.4, 130.8, 127.5, 126.6, 124.3, 114.1, 55.0, 45.0, 30.2, 25.6, 25.5, 25.3, 19.0. Minor isomer (30%): ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.22−7.19 (m, 2H), 7.14−7.10 (m, 1H), 7.01−6.98 (m, 1H), 4.51 (s, 2H), 3.66 (s, 2H), 3.61−3.54 (m, 1H), 2.31 (s, 3H), 1.78 (s, 4H), 1.69−1.60 (m, 1H), 1.44−1.25 (m, 4H), 1.13−0.99 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 162.6, 135.1, 134.3, 130.1, 126.6, 125.9, 125.2, 114.1, 59.0, 43.2, 31.5, 25.7, 25.5, 24.9, 19.1. IR (DCM) ν (cm^{-1}): 2259 (CN), 1652 (C═O). HRMS (ESI) calcd for $C_{17}H_{23}N_2O$ $[M + H]^+$ m/z 271.1805, found 271.1803.

*2-Cyano-N-cyclohexyl-N-(3-methylbenzyl)acetamide (**1s**).* 1.61 g, 60% yield. Colorless crystals, mp 78−79 °C. Exists as two different conformational isomers in solution. Major isomer (65%): ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.26 (dd, J = 7.5 Hz, 1H), 7.11 (d, J = 7.5 Hz, 1H), 7.04−6.97 (m, 2H), 4.52−4.46 (m, 1H), 4.45 (s, 2H), 3.31 (s, 2H), 2.36 (s, 3H), 1.84−1.73 (m, 4H), 1.66−1.62 (m, 1H), 1.50−1.26 (m, 4H), 1.10−1.00 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 162.6, 139.0, 136.8, 129.0, 128.5, 126.1, 122.5, 114.1, 55.0, 47.1, 31.9, 30.4, 25.9, 25.6, 25.3, 21.4. Minor isomer (35%): ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.17 (dd, J = 7.5 Hz, 1H), 7.04−6.97 (m, 3H), 4.55 (s, 2H), 3.63 (s, 2H), 3.52−3.44 (m, 1H), 2.32 (s, 3H), 1.83−1.73 (m, 4H), 1.67−1.62 (m, 1H), 1.48−1.26 (m, 4H), 0.90−0.85 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 161.8, 138.1, 138.0, 128.3, 127.7, 127.5, 123.9, 114.1, 59.1, 45.4, 31.5, 25.8, 25.5, 25.0, 22.6, 14.1. IR (DCM) ν (cm^{-1}): 2259 (CN), 1653 (C═O). HRMS (ESI) calcd for $C_{17}H_{23}N_2O$ $[M + H]^+$ m/z 271.1805, found 271.1806.

*N,N-Bis(4-chlorobenzyl)-2-cyanoacetamide (**1t**).* 1.23 g, 51% yield. Colorless crystals, mp 79−80 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.37 (d, J = 8.3 Hz, 2H), 7.30 (d, J = 8.3 Hz, 2H), 7.15 (d, J = 8.2 Hz, 2H), 7.07 (d, J = 8.2 Hz, 2H), 4.56 (s, 2H), 4.40 (s, 2H), 3.54 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 162.43, 134.31, 134.24, 133.96, 133.03, 129.78, 129.55, 129.02, 127.63, 113.63, 50.19, 48.75, 25.27. IR (DCM) ν (cm^{-1}): 2259 (CN), 1651 (C═O). HRMS (ESI) calcd for $C_{17}H_{15}Cl_2N_2O$ $[M + H]^+$ m/z 333.0556 found 333.0556.

*2-Cyano-N,N-bis(4-methoxybenzyl)acetamide (**1u**).* 1.36 g, 42% yield. Colorless crystals, mp 70−71 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.16 (d, J = 8.5 Hz, 2H), 7.04 (d, J = 8.5 Hz, 2H), 6.90 (d, J = 8.5 Hz, 2H), 6.85 (d, J = 8.5 Hz, 2H), 4.54 (s, 2H), 4.34 (s, 2H), 3.81 (s,

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3H), 3.79 (s, 3H), 3.52 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 162.3, 159.4, 159.2, 129.8, 128.1, 127.5, 126.7, 114.6, 114.1, 114.0, 114.0, 55.3, 55.2, 49.9, 48.6, 25.3. IR (DCM) ν (cm^{-1}): 2259 (CN), 1651 (C═O). HRMS (ESI) calcd for $C_{19}H_{21}N_2O_3$ $[M + H]^+$ m/z 325.1547 found 325.1544.

*N-Benzyl-2-cyano-N-isopropylacetamide (**1v**).* 0.86 g, 40% yield. Colorless oil. Major isomer (63%): ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.40−7.37 (m, 1H), 7.32−7.27 (m, 2H), 7.21−7.19 (m, 2H), 4.82 (hept, J = 6.8 Hz, 1H), 4.46 (s, 2H), 3.32 (s, 2H), 1.17 (d, J = 6.8 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 162.5, 136.6, 129.2, 127.8, 125.5, 114.1, 47.1, 46.5, 25.9, 20.0. Minor isomer (39%): ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.40−7.37 (m, 1H), 7.33−7.27 (m, 2H), 7.24−7.22 (m, 2H), 4.56 (s, 2H), 4.01 (hept, J = 6.8 Hz, 1H), 3.64 (s, 2H), 1.21 (d, J = 6.8 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 161.7, 138.1, 128.4, 126.9, 126.9, 114.1, 50.3, 44.5, 25.4, 21.3. IR (DCM) ν (cm^{-1}): 2259 (CN), 1654 (C═O). HRMS (ESI) calcd for $C_{13}H_{17}N_2O$ $[M + H]^+$ m/z 217.1335, found: 217.1338.

General Procedure for the Chemoselective Intramolecular Buchner Reactions Using Iodonium Ylides Generated in Situ as Carbene Precursors. A suspension of *N*-benzyl-2-cyanoacetamide **1** (1 mmol), $PhI(OAc)_2$ (386 mg, 1.2 mmol), KOH pellets (2−4 pellets, 151 mg in total, 2.7 mmol), and $Cu(OAc)_2{\cdot}H_2O$ (5 mg, 0.025 mmol) in DCM (20 mL) was refluxed for 8 h. After the reaction mixture was cooled to room temperature, it was washed with water (20 mL) and 1 mol/L HCl (20 mL). The organic layer was dried over anhydrous Na_2SO_4 and then evaporated. The resulting residue was purified by silica gel chromatography (petroleum ether/EtOAc, v/v 5:1−1:1) to give the 5,7-bicyclic product **2**.

*9-Aza-9-benzyl-1-cyanobicyclo[5.3.0]deca-2,4,6-trien-10-one (**2a**).* 220 mg, 84% yield. Colorless crystals, mp 172−174 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.38−7.32 (m, 3H), 7.27−7.25 (m, 2H), 6.75−6.68 (m, 2H), 6.46−6.42 (m, 1H), 6.33−6.32 (m, 1H), 5.15 (d, J = 8.8 Hz, 1H), 4.59 (s, 2H), 4.16 (dd, J = 14.8, 1.2 Hz, 1H), 3.93 (dd, J = 14.8, 1.2 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 167.3, 134.8, 130.3, 129.5, 129.0, 128.4, 128.2, 128.2, 122.5, 114.0, 107.5, 49.6, 47.2, 41.9. IR (DCM) ν (cm^{-1}): 2235 (CN), 1708 (C═O). HRMS (ESI) calcd for $C_{17}H_{15}N_2O[M + H]^+$ m/z 263.1179, found 263.1176.

*9-Aza-1-cyano-9-methylbicyclo[5.3.0]deca-2,4,6-trien-10-one (**2b**).* 74 mg, 40% yield. Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 6.78−6.71 (m, 2H), 6.46−6.41 (m, 2H), 5.17 (d, J = 8.8 Hz, 1H), 4.34 (d, J = 14.9 Hz, 1H), 4.09 (d, J = 14.9 Hz, 1H), 3.02 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 167.2, 130.3, 129.5, 128.5, 122.4, 115.2, 114.1, 109.4, 52.1, 42.4, 30.2. IR (DCM) ν (cm^{-1}): 2235 (CN), 1712 (C═O). HRMS (ESI) calcd for $C_{11}H_{10}N_2NaO$ $[M + Na]^+$ m/z 209.0685, found 209.0680.

*9-Aza-1-cyano-9-cyclohexylbicyclo[5.3.0]deca-2,4,6-trien-10-one (**2c**).* 152 mg, 60% yield. Colorless crystals, mp 162−163 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 6.76−6.70 (m, 2H), 6.45−6.40 (m, 2H), 5.12 (d, J = 8.8 Hz, 1H), 4.27 (d, J = 14.9 Hz, 1H), 4.08−4.05 (m, 2H), 1.88−1.78 (m, 3H), 1.72−1.69 (m, 2H), 1.49−1.30 (m, 4H), 1.19−1.07 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 166.6, 130.2, 129.5, 128.3, 122.4, 114.6, 114.2, 108.4, 51.8, 46.3, 42.7, 30.1, 30.0, 25.3, 25.2, 25.2. IR (DCM) ν (cm^{-1}): 2234 (CN), 1697 (C═O). HRMS (ESI) calcd for $C_{16}H_{19}N_2O$ $[M + H]^+$ m/z 255.1492, found 255.1495.

*9-Aza-9-(2,6-dichlorobenzyl)-1-cyanobicyclo[5.3.0]deca-2,4,6-trien-10-one (**2d**).* 166 mg, 50% yield. Colorless crystals, mp 168−170 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.40−7.35 (m, 2H), 7.28−7.23 (m, 1H), 6.74−6.66 (m, 2H), 6.45−6.39 (m, 1H), 6.33−6.28 (m, 1H), 5.05 (d, J = 8.8 Hz, 1H), 5.01 (d, J = 14.4 Hz, 1H), 4.94 (d, J = 14.3 Hz, 1H), 4.08 (dd, J = 14.6, 1.8 Hz, 1H), 3.79 (dd, J = 14.6, 1.2 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 166.7, 136.6, 130.4, 130.1, 129.9, 129.3, 129.2, 128.9, 128.7, 128.1, 122.4, 113.8, 52.1, 48.8, 42.2. IR (DCM) ν (cm^{-1}): 2236 (CN), 1715 (C═O). HRMS (ESI) calcd for $C_{17}H_{13}Cl_2N_2O[M + H]^+$ m/z 331.0399, found 331.0398.

*9-Aza-1-cyano-9-neopentylbicyclo[5.3.0]deca-2,4,6-trien-10-one (**2e**).* 111 mg, 46% yield. Colorless crystals, mp 124−126 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 6.77−6.70 (m, 2H), 6.47−6.41 (m, 1H), 6.39−6.35 (m, 1H), 5.09 (d, J = 8.8 Hz, 1H), 4.42 (dd, J = 14.9, 1.5 Hz, 1H), 4.20 (dd, J = 14.9, 1.5 Hz, 1H), 3.23 (d, J = 13.8 Hz, 1H), 3.18 (d, J = 13.8 Hz, 1H), 1.00 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 168.3, 130.2, 129.4, 128.2, 122.2, 114.1, 107.0, 55.8, 53.3, 41.2, 33.9, 28.2. IR (DCM) ν (cm^{-1}): 2236 (CN), 1710 (C═O). HRMS (ESI) calcd for $C_{15}H_{19}N_2O[M + H]^+$ m/z 243.1492, found 243.1495.

*9-Aza-9-benzyl-1-cyano-2,4,6-trimethylbicyclo[5.3.0]deca-2,4,6-trien-10-one (**2i**).* 152 mg, 50% yield. Colorless crystals, mp 132−134 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.39−7.27 (m, 5H), 6.39 (s, 1H), 5.98 (s, 1H), 4.80 (d, J = 14.5 Hz, 1H), 4.47 (d, J = 14.5 Hz, 1H), 4.05 (d, J = 14.8 Hz, 1H), 3.87 (d, J = 14.8 Hz, 1H), 2.10 (s, 3H), 2.01 (s, 3H), 1.77 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 166.9, 139.0, 135.2, 129.8, 129.4, 128.9, 128.4, 128.1, 128.0, 124.4, 115.6, 114.5, 49.1, 48.5, 47.2, 24.2, 19.9, 17.9. IR (DCM) ν (cm^{-1}): 2235 (CN), 1709 (C═O). HRMS (ESI) calcd for $C_{20}H_{21}N_2O[M + H]^+$ m/z 305.1648, found 305.1650.

*2-Cyclohexyl-2,3,3a,3b-tetrahydro-3-oxo-1H-naphtho[1′,2′:1,3]-cyclopropa[1,2-c]pyrrole-3a-carbonitrile (**2j**).* 228 mg, 75% yield. Colorless crystals, mp 242−245 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.56 (d, J = 7.1 Hz, 1H), 7.43−7.32 (m, 3H), 6.82 (d, J = 9.6 Hz, 1H), 6.24 (dd, J = 9.6, 5.1 Hz, 1H), 4.34 (d, J = 10.9 Hz, 1H), 3.99−3.90 (m, 1H), 3.43 (d, J = 10.9 Hz, 1H), 2.68 (d, J = 5.1 Hz, 1H), 1.95−1.78 (m, 3H), 1.72−1.63 (m, 2H), 1.55−1.24 (m, 4H), 1.17−1.05 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 166.9, 131.2, 130.5, 129.4, 128.7, 128.5, 126.1, 125.9, 119.8, 112.1, 51.3, 45.2, 37.5, 36.4, 30.7, 29.9, 25.3, 25.3, 25.2, 18.3. IR (DCM) ν (cm^{-1}): 2241 (CN), 1692 (C═O). HRMS (ESI) calcd for $C_{20}H_{21}N_2O$ $[M + H]^+$ m/z 305.1648, found 305.1651.

*2-Cyclohexyl-1,2,3,3a-tetrahydro-3-oxodibenzo[3,4:6,7]cyclo-hepta[1,2-c]pyrrole-3a-carbonitrile (**2k**).* 301 mg, 85% yield. Colorless crystals, mp 172−174 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.15 (d, J = 7.7 Hz, 1H), 7.89 (d, J = 7.8 Hz, 1H), 7.81 (d, J = 7.8 Hz, 1H), 7.59−7.37 (m, 6H), 4.69 (d, J = 19.4 Hz, 1H), 4.60 (s, 1H), 4.30−4.21 (m, 2H), 2.05−2.00 (m, 1H), 1.93−1.86 (m, 3H), 1.78−1.72 (m, 1H), 1.62−1.48 (m, 4H), 1.25−1.16 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 168.3, 146.9, 133.8, 132.8, 131.0, 129.8, 128.1, 128.0, 127.8, 125.7, 125.6, 124.4, 118.0, 50.9, 47.3, 43.0, 40.3, 31.7, 31.4, 25.6, 25.5, 25.5. IR (DCM) ν (cm^{-1}): 2243 (CN), 1673 (C═O). HRMS (ESI) calcd for $C_{24}H_{23}N_2O[M + H]^+$ m/z 355.1805, found 355.1806.

*9-Aza-4-bromo-1-cyano-9-cyclohexylbicyclo[5.3.0]deca-2,4,6-trien-10-one (**2l**).* 112 mg, 34% yield. Colorless crystals, mp 178−179 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.12 (d, J = 7.1 Hz, 1H), 6.57 (d, J = 9.3 Hz, 1H), 6.29 (d, J = 7.1 Hz, 1H), 5.13 (d, J = 9.3 Hz, 1H), 4.25 (d, J = 15.3 Hz, 1H), 4.09−3.99 (m, 2H), 1.92−1.81 (m, 3H), 1.76−1.66 (m, 2H), 1.49−1.29 (m, 4H), 1.19−1.06 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 165.6, 132.1, 131.8, 124.2, 122.2, 117.4, 113.8, 111.6, 52.0, 46.2, 43.2, 30.0, 30.0, 25.2, 25.2, 25.1. IR (DCM) ν (cm^{-1}): 2243 (CN), 2238 (CN), 1700 (C═O). HRMS (ESI) calcd for $C_{16}H_{18}BrN_2O[M + H]^+$ m/z 333.0597, found 333.0602.

*9-Aza-1,4-dicyano-9-cyclohexylbicyclo[5.3.0]deca-2,4,6-trien-10-one (**2m**).* 98 mg, 35% yield. Colorless crystals, mp 169−170 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.28 (d, J = 6.6 Hz, 1H), 6.60 (d, J = 9.0 Hz, 1H), 6.55 (d, J = 6.6 Hz, 1H), 5.30 (d, J = 9.0 Hz, 1H), 4.35 (d, J = 16.0 Hz, 1H), 4.13 (d, J = 16.0 Hz, 1H), 4.08−4.00 (m, 1H), 1.89−1.82 (m, 3H), 1.75−1.69 (m, 2H), 1.48−1.31 (m, 4H), 1.18−1.06 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 165.0, 138.0, 128.4, 121.9, 121.4, 118.0, 115.2, 112.8, 111.3, 52.2, 46.7, 42.4, 30.1, 30.0, 25.2, 25.2, 25.1. IR (DCM) ν (cm^{-1}): 2243 (CN), 2230 (CN), 1766 (C═O). HRMS (ESI) calcd for $C_{17}H_{18}N_3O$ $[M + H]^+$ m/z 280.1444, found 280.1449.

*9-Aza-1-cyano-9-cyclohexyl-4-methylbicyclo[5.3.0]deca-2,4,6-trien-10-one (**2n**).* 132 mg, 52% yield. Colorless crystals, mp 145−147 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 6.48 (d, J = 7.1 Hz, 1H), 6.25 (d, J = 7.1 Hz, 1H), 6.18 (d, J = 8.2 Hz, 1H), 4.67 (d, J = 8.2 Hz, 1H), 4.15 (d, J = 13.9 Hz, 1H), 4.05−3.97 (m, 1H), 3.92 (d, J = 13.9 Hz, 1H), 2.12 (s, 3H), 1.88−1.80 (m, 3H), 1.70 (d, J = 11.2 Hz, 2H), 1.48−1.30 (m, 4H), 1.16−1.05 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 166.7, 138.9, 128.2, 127.7, 122.2, 114.2, 96.5, 51.6, 46.4, 30.1, 29.9, 25.2, 25.2, 25.2, 23.6. IR (DCM) ν (cm^{-1}): 2237 (CN), 1702 (C═O). HRMS (ESI) calcd for $C_{17}H_{21}N_2O$ $[M + H]^+$ m/z 269.1648, found 269.1651.

*9-Aza-1-cyano-9-cyclohexyl-4-isopropylbicyclo[5.3.0]deca-2,4,6-trien-10-one (**2o**).* 115 mg, 39% yield. Colorless crystals, mp 168−169

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°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 6.50 (d, J = 7.5 Hz, 1H), 6.26 (d, J = 7.9 Hz, 1H), 6.24 (d, J = 7.5 Hz, 1H), 4.60 (d, J = 7.9 Hz, 1H), 4.12 (d, J = 13.7 Hz, 1H), 4.05−3.98 (m, 1H), 3.89 (d, J = 13.7 Hz, 1H), 2.60 (hept, J = 7.4 Hz, 1H), 1.87−1.79 (m, 3H), 1.69 (d, J = 11.3 Hz, 2H), 1.47−1.27 (m, 4H), 1.17 (d, J = 7.4 Hz, 3H), 1.15 (d, J = 7.5 Hz, 3H), 1.20−1.05 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 166.9, 149.3, 125.3, 125.1, 122.3, 113.8, 93.4, 51.6, 46.5, 35.7, 30.3, 30.0, 25.3, 25.2, 25.2, 22.5, 22.1. IR (DCM) ν (cm^{-1}): 2236 (CN), 1699 (C═O). HRMS (ESI) calcd for $C_{19}H_{25}N_2O$ $[M + H]^+$ m/z 297.1961, found 297.1965.

*9-Aza-1-cyano-9-cyclohexyl-4-methoxybicyclo[5.3.0]deca-2,4,6-trien-10-one (**2p**).* 145 mg, 51% yield. Colorless crystals, mp 179−180 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 6.28 (d, J = 8.0 Hz, 1H), 6.01 (d, J = 8.0 Hz, 2H), 4.86 (s, 1H), 4.15 (d, J = 13.6 Hz, 1H), 4.05−3.98 (m, 1H), 3.92 (d, J = 13.6 Hz, 1H), 3.70 (s, 3H), 1.87−1.80 (m, 3H), 1.70 (d, J = 11.1 Hz, 2H), 1.47−1.32 (m, 4H), 1.16−1.06 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 166.5, 158.6, 122.1, 118.4, 114.2, 109.0, 55.0, 51.7, 46.4, 42.0, 30.2, 30.0, 25.3, 25.2, 25.2. IR (DCM) ν (cm^{-1}): 2232 (CN), 1701 (C═O). HRMS (ESI) calcd for $C_{17}H_{21}N_2O_2$ $[M + H]^+$ m/z 285.1598, found 285.1601.

*9-Aza-1-cyano-9-cyclohexyl-4-methylthiobicyclo[5.3.0]deca-2,4,6-trien-10-one (**2q**).* 103 mg, 33% yield. Colorless crystals, mp 133−134 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 6.59 (d, J = 7.0 Hz, 1H), 6.31 (d, J = 7.6 Hz, 1H), 6.29 (d, J = 6.7 Hz, 1H), 5.03 (d, J = 7.6 Hz, 1H), 4.21 (d, J = 14.5 Hz, 1H), 4.01 (d, J = 14.5 Hz, 1H), 4.06−3.98 (m, 1H), 2.39 (s, 3H), 1.87−1.80 (m, 3H), 1.70 (d, J = 12.1 Hz, 2H), 1.47−1.30 (m, 4H), 1.15−1.06 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 166.2, 140.9, 127.4, 125.4, 121.9, 114.0, 105.0, 51.8, 46.3, 41.2, 30.1, 30.0, 25.2, 25.2, 25.2, 16.0. IR (DCM) ν (cm^{-1}): 2237 (CN), 1702 (C═O). HRMS (ESI) calcd for $C_{17}H_{21}N_2OS$ $[M + H]^+$ m/z 301.1369, found 301.1376.

*9-Aza-1-cyano-9-cyclohexyl-6-methylbicyclo[5.3.0]deca-2,4,6-trien-10-one (**2r**).* 162 mg, 64% yield. Colorless crystals, mp 155−157 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 6.69−6.62 (m, 2H), 6.36 (ddd, J = 9.1, 4.5, 2.1 Hz, 1H), 5.36 (d, J = 9.1 Hz, 1H), 4.18 (d, J = 15.0 Hz, 1H), 4.11−4.05 (m, 1H), 4.01 (d, J = 15.0 Hz, 1H), 1.92 (s, 3H), 1.89−1.81 (m, 3H), 1.77−1.69 (m, 2H), 1.50−1.38 (m, 4H), 1.18−1.08 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 167.0, 134.1, 130.5, 129.6, 128.1, 115.0, 51.9, 45.9, 44.7, 30.1, 30.1, 25.3, 25.3, 25.3, 18.4. IR (DCM) ν (cm^{-1}): 2237 (CN), 1702 (C═O). HRMS (ESI) calcd for $C_{17}H_{21}N_2O$ $[M + H]^+$ m/z 269.1648, found 269.1651.

*9-Aza-1-cyano-9-cyclohexyl-2-methylbicyclo[5.3.0]deca-2,4,6-trien-10-one and 9-aza-1-cyano-9-cyclohexyl-5-methylbicyclo-[5.3.0]deca-2,4,6-trien-10-one (**2sa** and **2sb**, 1:1).* These two isomers cannot be separated from each other by silica gel column chromatography). 154 mg, 60% yield. Colorless crystals, mp 155−157 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 6.55−6.44 (m, 3H), 6.32 (t, J = 7.8 Hz, 1H), 6.18−6.15 (m, 2H), 4.70 (d, J = 8.2 Hz, 1H), 4.16 (d, J = 14.2 Hz, 1H), 4.11−4.00 (m, 3H), 3.96 (d, J = 14.2 Hz, 1H), 3.84 (d, J = 13.4 Hz, 1H), 2.13 (s, 3H), 2.03 (s, 3H), 1.83 (d, J = 17.4 Hz, 6H), 1.73−1.68 (m, 4H), 1.45−1.31 (m, 8H), 1.17−1.07 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 167.0, 166.9, 138.3, 135.6, 129.2, 128.6, 128.0, 127.5, 123.6, 120.7, 114.3, 113.7, 51.8, 51.6, 46.9, 46.6, 30.4, 30.2, 30.0, 30.0, 25.3, 25.3, 25.3, 23.8, 22.4. IR (DCM) ν (cm^{-1}): 2237 (CN), 1702 (C═O). HRMS (ESI) calcd for $C_{17}H_{21}N_2O$ $[M + H]^+$ m/z 269.1648, found 269.1651.

*9-Aza-4-chloro-9-(4-chlorobenzyl)-1-cyanobicyclo[5.3.0]deca-2,4,6-trien-10-one (**2t**).* 231 mg, 70% yield. Colorless crystals, mp 119−122 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.34 (d, J = 8.4 Hz, 2H), 7.20 (d, J = 8.4 Hz, 2H), 6.87 (d, J = 7.3 Hz, 1H), 6.46 (d, J = 9.1 Hz, 1H), 6.29 (d, J = 7.3 Hz, 1H), 5.20 (d, J = 9.1 Hz, 1H), 4.58 (d, J = 14.7 Hz, 1H), 4.53 (d, J = 14.7 Hz, 1H), 4.17 (d, J = 15.2 Hz, 1H), 3.92 (d, J = 15.2 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 166.6, 135.4, 134.4, 133.1, 129.8, 129.6, 129.3, 128.7, 121.9, 113.5, 109.3, 49.4, 46.6, 42.0. IR (DCM) ν (cm^{-1}): 2240 (CN) 1716 (C═O). HRMS (ESI) calcd for $C_{17}H_{13}Cl_2N_2O$ $[M + H]^+$ m/z 331.0399, found 331.0401.

*9-Aza-1-cyano-4-methoxy-9-(4-methoxybenzyl)bicyclo[5.3.0]-deca-2,4,6-trien-10-one (**2u**).* 264 mg, 82% yield. Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.18 (d, J = 8.4 Hz, 2H), 6.88 (d, J = 8.4 Hz, 2H), 6.19 (d, J = 8.0 Hz, 1H), 5.98 (d, J = 6.8 Hz, 2H), 4.85 (s, 1H), 4.49 (s, 2H), 4.02 (d, J = 13.8 Hz, 1H), 3.80 (s, 3H), 3.76 (d, J = 13.8 Hz, 1H), 3.69 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 167.2, 159.5, 158.7, 129.9, 129.7, 127.5, 127.0, 122.2, 114.7, 114.3, 114.1, 77.3, 77.0, 76.7, 55.3, 55.1, 49.6, 46.6. IR (DCM) ν (cm^{-1}): 2238 (CN), 1716 (C═O). HRMS (ESI) calcd for $C_{19}H_{19}N_2O_3$ $[M + H]^+$ m/z 323.1390, found 323.1392.

*9-Aza-1-cyano-9-isopropylbicyclo[5.3.0]deca-2,4,6-trien-10-one (**2v**) and 1-Benzyl-4,4-dimethylazetidin-2-one-3-carbonitrile (**3**).* These two products cannot be separated from each other by silica gel column chromatography. Combined yield: 141 mg, 66%. Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ for **2v** (47%): 6.76−6.69 (m, 2H), 6.45−6.40 (m, 2H), 5.10 (d, J = 8.8 Hz, 1H), 4.51−4.42 (m, 1H), 4.26 (dd, J = 14.8, 1.5 Hz, 1H), 4.04 (d, J = 14.8 Hz, 1H), 1.26 (d, J = 6.8 Hz, 3H), 1.18 (d, J = 6.8 Hz, 3H); δ for **3** (53%): 7.34−7.27 (m, 5H), 4.33 (s, 2H), 3.76 (s, 1H), 1.39 (s, 3H), 1.32 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ for 2v:: 166.5 (C═O for **3**), 157.1 (C═O for **2v**), 135.3, 130.2, 129.4, 128.9, 128.3, 128.1, 122.5, 114.2, 113.5, 108.2, 59.0, 49.5, 45.3, 44.0, 43.9, 25.2, 23.0, 19.7, 19.5. IR (DCM) ν (cm^{-1}): 2234 (CN), 1772 (C═O for **3**), 1701 (C═O for **2v**),. HRMS (ESI) calcd for $C_{13}H_{15}N_2O$ $[M + H]^+$ m/z 215.1179, found 215.1182.

Preparation of Diazo Compound 4. Sodium azide (2.34 g, 36 mmol) was dissolved in a mixture of H_2O (10 mL) and CH_2Cl_2 (5 mL), and the resulting solution was cooled to 0 °C in an ice−water bath. To this vigorously stirred solution was added triflic anhydride (1 mL, 6 mmol) dropwise through a syringe in 10 min. After being stirred at 0 °C for 2 h, the organic phase was separated and the aqueous phase was extracted with 5 mL of CH_2Cl_2. The combined organics were washed with 10 mL of aqueous $NaHCO_3$, dried over Na_2SO_4, and then used in the next step immediately. Amide **1v** (1.08 g, 5 mmol) was dissolved in 10 mL of CH_3CN, and then a freshly prepared solution of triflic azide in CH_2Cl_2 was added under N_2 at 0 °C in an ice−water bath. After addition of triethylamine, the resulting mixture was stirred at room temperature for 18 h. The solution was concentrated under reduced pressure. The resulting residue was purified by silica gel column chromatography (petroleum ether/EtOAc, v/v 5:1) to give pure product **4**.

*N-Benzyl-2-cyano-2-diazo-N-isopropylacetamide (**4**).* 1.13 g, 93% yield. Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.37−7.32 (m, 2H), 7.28−7.22 (m, 3H), 4.58 (s, 2H), 4.46 (heptet, J = 6.4 Hz, 1H), 1.22 (d, J = 6.4 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 159.7, 137.6, 128.6, 127.3, 126.6, 109.8, 49.9, 46.4, 20.9. IR (DCM) ν (cm^{-1}): 2213 (CN), 2120 (CN_2), 1766 (C═O). HRMS (ESI) calcd for $C_{13}H_{15}N_4O$ $[M + H]^+$ m/z 243.1240, found: 243.1240.

Procedure for the Cu(acac)$_2$-Catalyzed Decomposition of Diazo Compound 3. A solution of **3** (242 mg, 1 mmol) in 5 mL of dried solvent was added dropwise to a solution of catalyst in 5 mL of solvent at reflux via a syringe during 40 min under N_2. The reaction was monitored by thin layer chromatography (TLC). After the raw material was consumed completely, the resulting solution was concentrated at reduced pressure and the residue was purified by silica gel column chromatography (petroleum ether/EtOAc, v/v 4:1) to afford a mixture of **2v** and **3** (these two products cannot be separated from each other by silica gel column chromatography). Combined yield: 139 mg, 65%. Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ for **2v** (45%): 6.76−6.69 (m, 2H), 6.45−6.40 (m, 2H), 5.10 (d, J = 8.8 Hz, 1H), 4.51−4.42 (m, 1H), 4.26 (dd, J = 14.8, 1.5 Hz, 1H), 4.04 (d, J = 14.8 Hz, 1H), 1.26 (d, J = 6.8 Hz, 3H), 1.18 (d, J = 6.8 Hz, 3H); δ for **3** (55%): 7.34−7.27 (m, 5H), 4.33 (s, 2H), 3.76 (s, 1H), 1.39 (s, 3H), 1.32 (s, 3H).

Preparation of *N,N*-Dibenzyl-2-(phenylsulfonyl)acetamide (5). A solution of sodium benzenesulfinate (2.46 g, 15 mmol) and *N,N*-dibenzyl-2-chloroacetamide (4.11 g, 15 mmol) in 50 mL of DMF was stirred at room temperature for 3 h. Water (50 mL) was added, following by addition of ethyl acetate (50 mL). Then the organic layer was washed three times with water (50 mL) and dried over sodium sulfate. After removal of solvent under reduced pressure, the afforded crude product was recrystallized with ethyl acetate/petroleum ether to give **5** (5.07 g, 89% yield) as colorless crystals, mp 98−100 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.90 (d, J = 7.8 Hz, 2H), 7.66 (t, J = 7.3

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Hz, 1H), 7.53 (dd, J = 7.8, 7.3 Hz, 2H), 7.38−7.30 (m, J = 14.6, 7.8 Hz, 6H), 7.25 (d, J = 7.1 Hz, 2H), 7.13 (d, J = 7.3 Hz, 2H), 4.68 (s, 2H), 4.59 (s, 2H), 4.26 (s, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 162.1, 138.7, 136.2, 135.5, 134.2, 129.1, 129.1, 128.7, 128.5, 128.1, 127.9, 127.6, 126.2, 59.9, 50.9, 49.1. HRMS (ESI) calcd for $C_{22}H_{22}NO_3S$ $[M + H]^+$ m/z 380.1315, found: 380.1312.

Preparation of *N,N*-Dibenzyl-3-oxobutanamide (6).[21] A mixture of 2,2,6-trimethyl-4*H*-1,3-dioxin-4-one (2.84 g, 20 mmol) and *N,N*-dibenzylamine was heated to 90 °C and stirred overnight. The residue was purified by silica gel column chromatography (silica gel, petroleum ether/EtOAc, v/v 5:1) to afford *N,N*-dibenzyl-3-oxobutanamide (**6**) (5.07 g, 90% yield) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 14.81 (s, 0.25 H, enol form, 25%), 7.39−7.23 (m, 8H), 7.18−7.12 (m, 2H), 5.20 (s, 0.25 H, enol form, 25%), 4.62 (s, 2H), 4.41 (s, 2H), 3.62 (s, 1.5 H, ketone form, 75%), 2.28 (s, 2.25H, ketone form, 75%), 1.93 (s, 0.75H, enol form, 25%).[22] ^{13}C NMR (101 MHz, $CDCl_3$) δ: 202.3, 175.8, 172.5, 167.3, 137.1, 136.6, 136.3, 135.9, 129.0, 128.8, 128.6, 128.6, 128.3, 128.0, 128.0, 127.8, 127.6, 127.5, 127.4, 126.5, 126.3, 86.8, 50.5, 49.9, 49.6, 48.3, 47.7, 30.3, 22.0.

■ ASSOCIATED CONTENT

Supporting Information

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

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Notes

The authors declare no competing financial interest.

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