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# Cobalt(II)-Catalyzed Aerobic Oxidation of Terminal-Capped Alkynyl α-Cyano Alkanone Systems. An Oxygen-Mediated Radical Chain Reaction

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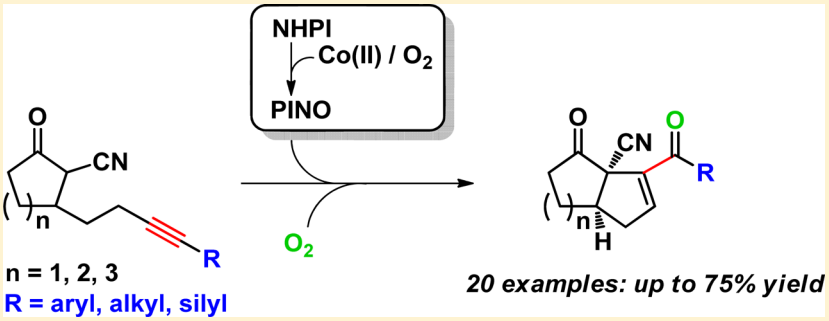
Supporting Information

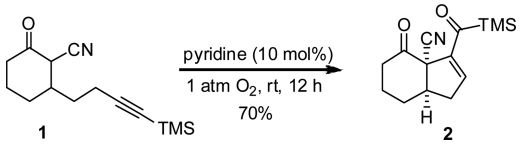



**ABSTRACT:** A new *N*-hydroxyphthalimide (NHPI)/Co(II)-catalyzed protocol, mechanistically involving a sequence of α-hydrogen abstraction, 5-*exo*-*dig* cyclization, oxygen capture, hydrogen transfer, and 1,4-dehydration, has been developed to facilitate aerobic oxidation of aryl-, silyl-, and alkyl-capped alkynyl α-cyano alkanone systems to the corresponding highly functionalized products in an effective manner, thus turning this novel chain reaction, originally occurring spontaneously in low yields, into a practical methodology.

## INTRODUCTION

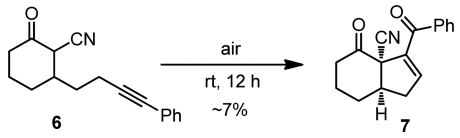
Since compound **1** was discovered to undergo aerobic oxidation spontaneously to afford α,β-unsaturated acylsilane **2** in ca. 30% yield upon exposure to air, attempts have been made to optimize reaction conditions, leading to findings that substrate **1** could convert to product **2** more effectively under catalysis with pyridine at 1 atm of oxygen (Scheme 1).[1]

**Scheme 1. Trimethylsilyl-Capped Aerobic Oxidation**

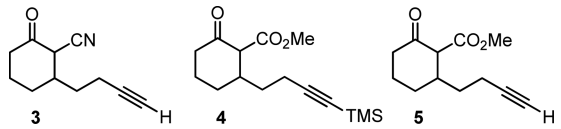



The generality of the autoxidative reaction has been verified by a variety of silyl-capped alkynyl α-cyano cycloalkanones as reported previously.[1] However, we found that the TMS-free α-cyano cyclohexanone **3** and its α-ester counterparts **4** and **5** were rather stable under air, suggesting that both the α-cyano group and TMS functionality are required to induce the observed autoxidation. To expand the scope of this interesting type of reaction, attempts to cap the terminal acetylene with various functionalities were then made. In one approach, when the acetylene was capped with a phenyl group, the expected transformation of substrate **6** to enone **7** was found to proceed spontaneously in ca. 7% yield under air (Scheme 2). Even if

**Scheme 2. Phenyl-Capped Aerobic Oxidation**




reactant **6** stood on the bench or was dissolved in a commonly used solvent, including ethyl acetate, dichloromethane, or dimethylformamide, for more than 2 days under air, its conversion rate into **7** was maintained at this level and starting material was recovered intact at 90%. When optimal reaction conditions developed previously (Scheme 1) were applied to substrate **6**, a complex mixture was obtained and the yield of product **7** was barely improved as analyzed by $^1$H NMR.




Screening of reaction conditions was then extensively carried out. Consequently, a commonly effective procedure was developed to realize the desired aerobic oxidation, wherein the terminal acetylene unit of the titled systems allowed it to be

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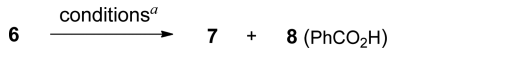
capped with either an aryl, silyl, or alkyl functionality. Results and discussion are presented as follows.

## RESULTS AND DISCUSSION

Given that aforementioned aerobic reactions are triggered via a free radical cascade process, metal catalysts or oxidants reported to serve as useful radical initiators in air, including CuO/dibenzoyl peroxide (DBP), Mn(III)/Co(II)/$O_2$, di-*tert*-butyl peroxide, TBAI/TBHP, CuI, $Mn(OAc)_3$, $I_2$, CAN, and *N*-hydroxyphthalimide (NHPI),[2−8] are first examined. Using substrate **6** as an initial model, screening results are listed in Table 1. Though the desired product **7**, except for treatment with $Mn(OAc)_3$ (entry 4), was mainly obtained in all cases examined, a side product, benzoic acid **8**, was accompanied in 17−45% yields. In fact, the direct oxidative cleavage of alkynes into carboxylic acids under metal catalysis has been well-documented,[9] which might account for the low yield of product **7**. As indicated in entry 9, the reaction system (10 mol % of $Co(OAc)_2$/20 mol % of NHPI/PhH/air), giving rise to product **7** in 61% yield, is tentatively considered the system of choice and is applied to an array of substrates to verify its synthetic generality.

**Table 1. Screening of Reaction Conditions**

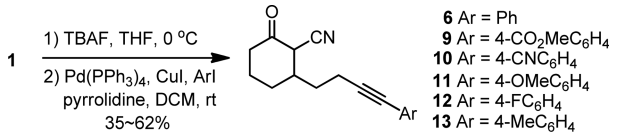



| entry | reagent | solvent | time (h) | 7/8 yield (%)[b] |
|---|---|---|---|---|
| 1 | | PhH | 24 | ~7/− |
| 2 | 10% TBAI/1.0 equiv of TBHP | PhH | 48 | 51/45 |
| 3 | 20% CuI | DMF | 12 | 20/17 |
| 4 | 2.0 equiv of $Mn(OAc)_3$ | PhH | 12 | 27/37 |
| 5 | 10% $I_2$ | PhH | 48 | 9/− |
| 6 | 2.0 equiv of CAN | MeOH | 12 | 33/17 |
| 7 | 20% NHPI | PhH | 40 | 50/35 |
| 8 | 10% $Cu(acac)_2$/20% NHPI | PhH | 12 | 39/27 |
| **9** | **10% $Co(OAc)_2$/20% NHPI** | **PhH** | **12** | **61/30** |
| 10 | 10% $Co(OAc)_2$/20% NHPI | DMF | 12 | 42/25 |

[a]All reactions were performed using substrate **6** (0.35 mmol) and 10−20 mol % of catalyst in 1 mL of solvent as indicated above; the resulting mixture was vigorously stirred at room temperature under air. [b]Yields are for isolated, chromatographically pure products.

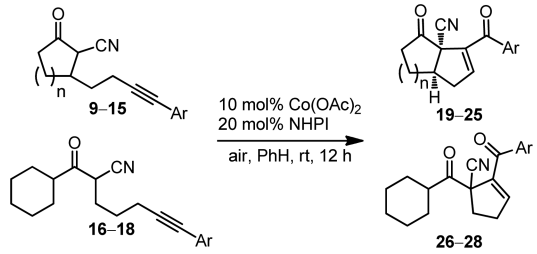
As shown in Scheme 3, compound **6** and various aryl-capped substrates **9**−**13** were readily prepared from compound **1** via a two-step sequence, involving deprotection of the trimethylsilyl group followed by Sonogashira coupling with an aryl iodide, in an overall yield of 35−62%.[10,11]

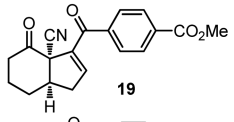
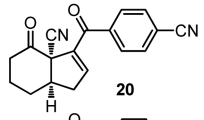
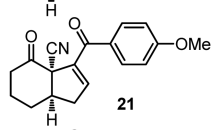
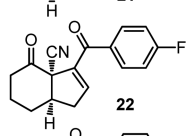
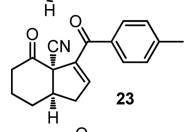
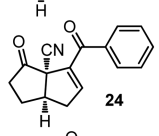
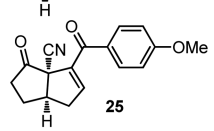
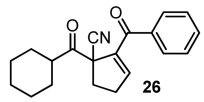
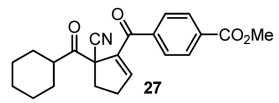
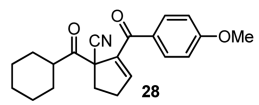
**Scheme 3. Preparation of Aryl-Capped Alkynes**




As compiled in Table 2, the present methodology is applicable for the acetylene unit capped with various aryls, irrespective of the stereoelectronic nature of the *para* substituent, affording the corresponding products in 35−61% yields (entries 1−7). Product **20** was unambiguously determined by the X-ray analysis,[12] lending strong support to the structural elucidation for this series of compounds by the use of conventional spectroscopic methods ($^1H$, $^{13}C$, IR, and HRMS). Similarly, acyclic substrates **16**−**18**, readily prepared in good to excellent yields according to synthetic procedures reported in the literature,[4b,5b,13] were also subjected to this newly developed protocol. As a result, desired products **26**−**28** were obtained in 28−40% yields, structures of which were fully confirmed by the X-ray analysis.[14,15] It is noteworthy that different from cyclic substrates (e.g., compound **1**), the

**Table 2. Autoxidation of Aryl-Capped Alkynyl α-Cyano Alkanones**




| entry | substrate | product | yield (%)[a] |
|---|---|---|---|
| 1 | **9** n = 2, Ar = 4-$CO_2MeC_6H_4$ |  **19** | 61 |
| 2 | **10** n = 2, Ar = 4-$CNC_6H_4$ |  **20** | 50[b] |
| 3 | **11** n = 2, Ar = 4-$OMeC_6H_4$ |  **21** | 42 |
| 4 | **12** n = 2, Ar = 4-$FC_6H_4$ |  **22** | 40 |
| 5 | **13** n = 2, Ar = 4-$MeC_6H_4$ |  **23** | 40 |
| 6 | **14** n = 1, Ar = Ph |  **24** | 38 |
| 7 | **15** n = 1, Ar = 4-$OMeC_6H_4$ |  **25** | 35 |
| 8 | **16** Ar = Ph |  **26** | 40 |
| 9 | **17** Ar = 4-$MeCO_2C_6H_4$ |  **27** | 36[b] |
| 10 | **18** Ar = 4-$MeOC_6H_4$ |  **28** | 28[b] |

[a]Yields were for isolated, chromatographically pure products. [b]The structure was confirmed by X-ray crystallographic analysis.



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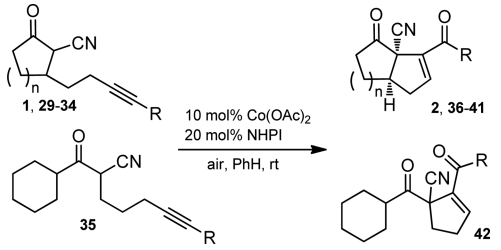
spontaneous conversion rate of acyclic substrates **16**–**18** are thoroughly undetectable by $^1$H NMR analysis. Though above autoxidative products seem to be isolated in low to moderate yields (28–61%), however, unlike a regular reaction with a simple mechanistic insight, the inherent reactivity of this unique reaction comprises a five-step domino transformation, including $\alpha$-hydrogen abstraction, 5-*exo*-*dig* cyclization, oxygen capture, hydrogen transfer, and 1,4-dehydration. Even if 28% is the lowest reaction yield in all cases examined in Table 2, the average yield of each transformation is as high as 78%. In general, the corresponding side products, benzoic acids, were obtained in 25–40% for the current procedure.

Since the acetylene unit capped with an aryl group was found to be prone to oxidative cleavage, we assumed that a trialkylsilyl group providing more steric hindrance might retard the approach of active oxygen radical species (e.g., M–O–O•) to lessen the side effect. As such, this newly developed protocol was also employed to reinvestigate trialkylsilyl-capped counterparts containing a TMS,[1] TES, or TBDMS functionality. Results are listed in Table 3. As TMS-capped $\alpha$-cyano ketones **1**, **29**, **30**, and **35** were treated with Co(II)-catalyzed conditions, corresponding acylsilanes **2** (entry 2; 68% vs 70%), **36** (entry 1; 55% vs 59%), **37a**/**37b** (entry 3; 46% vs 28%), and **42** (entry 8; 44% vs 21%) were produced in almost equal or better yields compared to those obtained by previous reaction conditions (10 mol % of pyridine/1 atm $O_2$/rt), thus demonstrating that this newly developed method is more efficient and practical. Moreover, when the TMS group of substrate **1** was replaced with a bulkier TES or TBDMS group, the similar aerobic oxidation could proceed with equal facility, affording the corresponding products **39** (entry 5; 73%) and **41** (entry 7; 75%), respectively, in yields slightly higher than that of their TMS counterpart **2** (entry 2; 68%). These results seem to reflect our argument that the steric hindrance of the terminal silyl group might hamper active oxygen radicals to access the acetylene unit, thus lessening its oxidative cleavage and resulting in higher yields. In addition, acylsilane products containing a bulkier TES or TBDMS group are much more stable than those containing a TMS group because, upon long-term exposure to light, the former remain intact but the latter are slowly decomposed to the corresponding $\alpha,\beta$-unsaturated aldehydes, presumably due to Norrish type I cleavage.[1,16]

Using the transformation of compound **17** into **27** as a typical example, the proposed mechanism is depicted in Scheme 4. The chain reaction is initiated by abstracting hydrogen $\alpha$ to the cyano and ketone group of **17** via a phthalimide *N*-oxyl (PINO) radical, generated under catalysis with Co(II)/NHPI in the presence of oxygen,[8a] to form radical intermediate **A**, which could immediately undergo 5-*exo*-*dig* addition to produce vinyl radical **B**.[17−19] Subsequently, an oxygen molecule is captured by vinyl radical **B** to provide vinyl peroxyl radical **C** by which the hydrogen of NHPI is abstracted to form hydroperoxide **D** followed by 1,4-dehydration to give product **27** and restart the catalytic cycle (pathway A). Alternatively, radical **C** might take pathway B to form dioxetane radical **E**, which could decompose to furnish 1,3-diketone **I**, leading to carboxylic acid **J** via hydrolysis, and acyl radical **F**, leading to benzoic acid **G** via oxygenation.[6,9,23] 2-Cyano-1,3-diketone **I**, a coproduct of benzoic acid **G**, appeared unstable and prone to hydrolysis in the presence of moisture to afford the corresponding acid **J** as detected by LC-MS (see S37 and S38 in Supporting Information).

**Table 3. Autoxidation of Silyl-capped Alkynyl $\alpha$-Cyano Alkanones**




| entry | substrate | product | t (h) | yield (%)[a] |
|---|---|---|---|---|
| 1 | **29** n = 1 R = TMS | **36** | 12 | 55(59)[b] |
| 2 | **1** n = 2 R = TMS | **2** | 18 | 68(70)[b] |
| 3 | **30** n = 3 R = TMS | **37a** / **37b** | 48 | **37a**/**37b** 46(28)[b] |
| 4 | **31** n = 1 R = TES | **38** | 6 | 62 |
| 5 | **32** n = 2 R = TES | **39** | 12 | 73[c] |
| 6 | **33** n = 1 R = TBDMS | **40** | 12 | 69[c] |
| 7 | **34** n = 2 R = TBDMS | **41** | 24 | 75[c] |
| 8 | **35** R = TMS | **42** | 48 | 44(21)[b] |

[a]Yields were for isolated, chromatographically pure products. [b]The yields in the parentheses are those of the reaction carried out under previous conditions in ref 1 (10 mol % of pyridine/1 atm $O_2$/rt). [c]The structure was confirmed by X-ray crystallographic analysis.[20−22]

To confirm the mechanism, authentic sample **I** was then prepared according to Scheme 5. Intermediate **H** was synthesized via a modified procedure of Knoevenagel condensation followed by deprotection with TsOH in 80% over two steps.[4b,5b] Hydroxyl **H** was then oxidized with PCC to afford cyclic $\beta$-hydroxyl ketone, which without purification was further oxidized with DMP to afford the desired 2-cyano-1,3-diketone **I** in 39% over two steps. Compound **I** thus obtained was found to be hydrolyzed in $CDCl_3$ in a couple of hours to form the corresponding carboxylic acid **J** as verified by $^1$H and $^{13}$C spectra shown in Figure S1 in the Supporting Information. Neverthless, the clean $^1$H and $^{13}$C spectra of **I** could be



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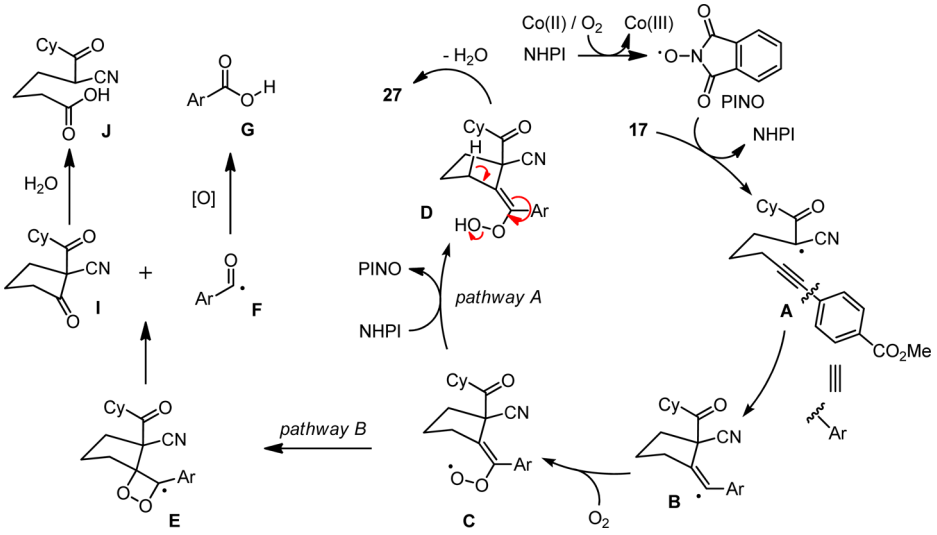
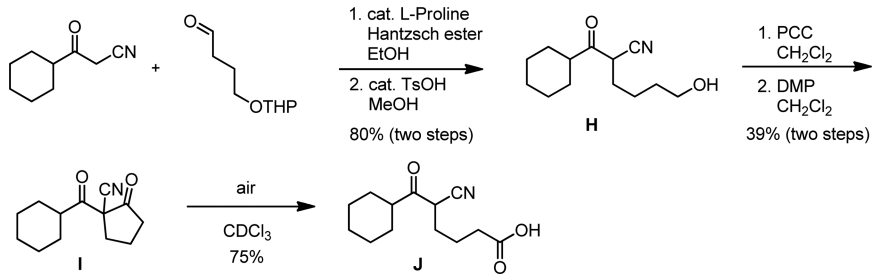
**Scheme 4. Proposed Mechanism for Aerobic Oxidation with NHPI/Co(II) Acetate**



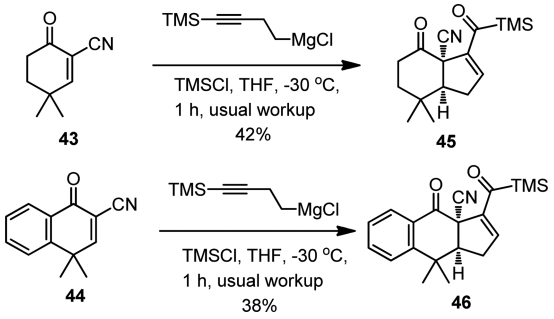

**Scheme 5. Preparation of Authentic Sample 2-Cyano-1,3-diketone I**




recorded timely (see S34 in Supporting Information). The above results lend strong support to the mechanism proposed in Scheme 4.

More intriguingly, when substrates **43** and **44** (Scheme 6) were designed to make the pendant acetylene unit get closer to

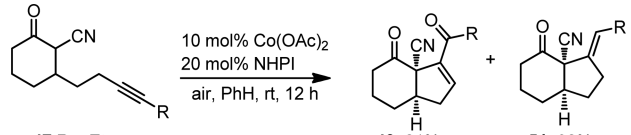
**Scheme 6. Reaction Rate Enhanced by Thorpe−Ingold Effect**




the reacting $\alpha$-carbon center via the Thorpe−Ingold effect, the expected chain reaction occurred almost instantly after a usual workup of 1,4-conjugate addition of the Grignard reagent, furnishing desired products **45** and **46** in 42 and 38% yields in one pot, respectively, structures of which were unambiguously confirmed by the X-ray crystallographic analysis.[24,25] Obviously, a *gem*-dimethyl group installed at the $\gamma$ position could force the acetylene-containing linker to adopt a constrained conformation like intermediate **A** (Scheme 4), thus accelerating the chain reaction in an efficient fashion.

When the above optimal reaction system was further extended to substrates capped with an alkyl group such as **47** and **48** (Scheme 7), readily prepared by 1,4-conjugate addition

**Scheme 7. Unexpected Conia-Ene Reactions in Alkyl-Capped Series**




of an appropriate Grignard reagent to 2-cyano-2-cyclohexenone in good yields,[26] the corresponding products **49** and **50** were obtained in 21 and 26% yields, respectively. Also emphasized is the fact that, upon exposure to air over 2 days, not a trace of substrates **47** and **48** was spontaneously converted into products **49** and **50** as determined by $^1$H NMR analysis. These results suggest that the new methodology is synthetically more useful than the previous one in that it can activate the latent autoxidative reaction rather than just enhance it. However, the formation of products **51** and **52** is somewhat unexpected because similar products are not observed in both silyl-capped and aryl-capped series. In light of stereochemistry, they are tentatively assigned as *trans* isomers based on our previous studies on Conia-ene reactions with the same substrates in the presence of Lewis acids such as $ZnI_2$.[26b]



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The above outcomes might be rationalized as follows. As illustrated in Figure 1, based on a Hartree−Fock quantum

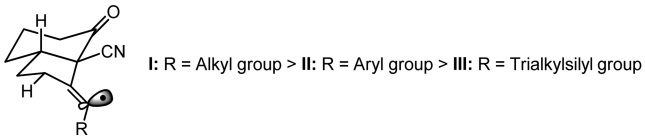


**Figure 1.** Relative energy of vinyl radicals **I**, **II**, and **III** based on Hartree−Fock quantum mechanic calculation.

mechanic calculation (see S39 in Supporting Information),[27] vinyl radical **I** with the relatively highest energy is supposed to be more reactive than its counterparts **II** and **III** and thus could randomly capture either an oxygen molecule to continue the chain reaction or abstract a hydrogen atom from the reaction environment to terminate it.

We also observed that the trialkylsilyl-capped series usually afforded the corresponding products in higher yields than their aryl- and alkyl-capped counterparts. An explanation could be that, in addition to the steric hindrance of the silyl group making oxidative cleavage of the alkyne unit more difficult, a unique stabilizing force provided by the Si element through delocalization with its d orbital or low-lying $\sigma^*$ (Si−C) antibonding orbital might render trialkylsilyl vinyl radicals that exist longer, thus trapping oxygen more efficiently.[1,18,23] For comparison purposes, $\alpha$-cyano ester **53** and $\beta$-keto ester **54**, structurally analogous to $\alpha$-cyano ketone **35** (Table 3, entry 8, 44%), were also synthesized and subjected to the same reaction conditions. As a result, both substrates **53** and **54** (Figure 2)

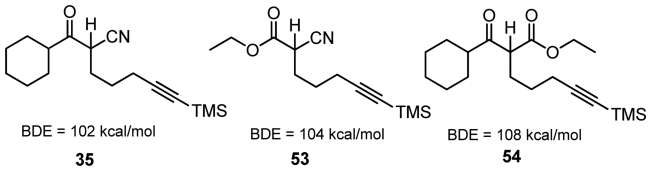


**Figure 2.** Bond dissociation energy of substrates **35**, **53**, and **54**.

were recovered intact over a period of 24 h at room temperature or under heating in refluxing benzene for 10 h, of which the poor reactivity might be ascribed to higher bond dissociation energy (BDE) compared with that of substrate **35**.

## CONCLUSION

Our continued investigation on terminal-capped alkynyl $\alpha$-cyano alkanone systems has culminated in a legitimate protocol (10 mol % of $Co(OAc)_2$/20 mol % NHPI/PhH/air), by which an aerobic chain reaction, regardless of whether its spontaneous conversion rate is detectable, can be promoted in an effective fashion. Also demonstrated is the fact that the substituent capped on the terminal acetylene of the titled systems is structurally variable and not restricted to the trialkylsilyl group, originally recognized to be one of the essential elements. Nevertheless, there is no doubt that the Si element of the trialkylsilyl group may play an extraordinary role in inducing the radical chain reaction although the underlying cause remains to be determined.

## EXPERIMENTAL SECTION

**General Experimental Procedure.** All reactions were performed under air unless otherwise stated. All solvents and reagents were employed as received without further purification. Analytical thin layer chromatography was performed on $SiO_2$ 60 F-254 plates, and flash column chromatography was carried out using $SiO_2$ 60 (particle size 0.040−0.055 mm, 230−400 mesh). Visualization was performed under UV irradiation at 254 nm followed by staining with aqueous potassium permanganate ($KMnO_4$ (3 g) and $K_2CO_3$ (20 g) in 300 mL of $H_2O$ containing 5 mL of an aqueous solution of NaOH (5%, w/v)) and charring by a heat gun. Infrared spectra were recorded on a Fourier transform infrared spectrometer and expressed in $cm^{-1}$. $^1H$ NMR spectra were recorded at 400 MHz and $^{13}C$ NMR spectra at 100 MHz. Chloroform-*d* was used as the solvent and TMS ($\delta$ = 0.00 ppm) as an internal standard. Chemical shifts are reported as $\delta$ values in parts per million as referenced to TMS. Multiplicities are recorded as s (singlet), d (doublet), t (triplet), q (quartet), quint (quintet), dd (doublet of doublets), dt (doublet of triplets), td (triplet of doublets), qd (quartet of doubles), tt (triplet of triplets), ddd (doublet of doublet of doublets), m (multiplet), br (broad). Coupling constants ($J$) are expressed in hertz. HRMS was obtained on a triple quadrupole mass analysis system using an electrospray ionization (ESI) source or a double quadrupole mass analysis system using an electron impact (EI) source, and spectral data were recorded as $m/z$ values. Melting points were measured using an electrothermal instrument.

**Preparation of Substrates.** The general procedure for 1,4-conjugate addition in the synthesis of compounds **1**, **31**−**34**, **45**, and **46** is demonstrated as follows using **1** as a typical example.[1]

*2-Oxo-6-(4-(trimethylsilyl)but-3-ynyl)-cyclohexanecarbonitrile (**1**).* To a stirred solution of $\alpha$-cyano-2-cyclohexenone (302 mg, 2.50 mmol) in THF (5 mL) was added freshly prepared (4-buty-1-nyl)trimethylsilane magnesium chloride solution (6.0 mL, 0.92 M in THF, 5.50 mmol) dropwise at −30 °C. After being stirred for 10 min at the same temperature, TMSCl (0.95 mL, 7.50 mmol) was introduced in one portion. The resulting mixture was stirred for another 1 h at −30 °C. Saturated $NH_4Cl$ solution (8 mL) was added to quench the reaction. The aqueous layer was separated and extracted with diethyl ether (3 × 15 mL). The combined organic extracts were washed with brine, dried over $MgSO_4$, filtered, and concentrated to give the crude residue, which was purified by flash chromatography on silica gel using EtOAc/*n*-hexane (1:9) as eluant to afford substrate **1** (476 mg, 77% yield, a mixture of keto isomers in a ratio of 1:2 (*cis*/*trans*)) as a yellowish oil: $^1H$ NMR (600 MHz, $CDCl_3$) major isomer $\delta$ 3.33 (d, $J$ = 11.6 Hz, 1H), 2.56−2.52 (m, 1H), 2.38−1.80 (m, 6H), 1.74−1.33 (m, 4 H), 0.08 (s, 9H); minor isomer $\delta$ 3.52 (d, $J$ = 4.5 Hz, 1H); $^{13}C$ NMR (150 MHz, $CDCl_3$) major isomer $\delta$ 200.0, 115.7, 105.1, 86.0, 49.6, 42.2, 40.3, 32.9, 27.0, 22.7, 16.8, −0.1 (3C); minor isomer $\delta$ 200.9, 115.4, 104.7, 86.2, 47.5, 40.9, 38.8, 30.4, 28.8, 22.6, 17.0, −0.3 (3C); IR (neat) 2249, 2174, 1728 $cm^{-1}$; HRMS (EI) $m/z$ calcd for $C_{14}H_{21}NOSi$ 247.1392 $[M]^+$; found 247.1391.

*2-Oxo-5-(4-(triethylsilyl)but-3-ynyl)-cyclopentanecarbonitrile (**31**).* A mixture of keto isomers in a ratio of 1:5 (*cis*/*trans*) was obtained as a yellowish oil: 372 mg, 54% yield; $^1H$ NMR (400 MHz, $CDCl_3$) major isomer $\delta$ 2.93 (d, $J$ = 12.4 Hz, 1H), 2.58−2.27 (m, 4H), 2.17−1.86 (m, 2H), 1.73−1.64 (m, 2H), 1.59−1.49 (m, 1H), 0.94 (t, $J$ = 8.0 Hz, 9H), 0.54 (q, $J$ = 8.0 Hz, 6H); minor isomer $\delta$ 3.38 (d, $J$ = 7.6 Hz, 1H); $^{13}C$ NMR (100 MHz, $CDCl_3$) major isomer $\delta$ 205.9, 116.0, 106.1, 83.3, 45.9, 41.7, 37.1, 32.7, 27.0, 17.5, 7.4 (3C), 4.3 (3C); minor isomer $\delta$ 206.3, 114.2, 105.9, 83.8, 44.2, 38.4, 36.1, 29.6, 26.4, 17.9, 7.3 (3C), 4.2 (3C); IR (neat) 2955, 2875, 2245, 2173, 1759, 1459, 726; HRMS (EI) $m/z$ calcd for $C_{16}H_{25}NOSi$ 275.1705 $[M]^+$; found 275.1709.

*2-Oxo-6-(4-(triethylsilyl)but-3-ynyl)-cyclohexanecarbonitrile (**32**).* A mixture of keto isomers in a ratio of 1:1.5 (*cis*/*trans*) was obtained as a yellowish oil: 441 mg, 61% yield; $^1H$ NMR (400 MHz, $CDCl_3$) major isomer $\delta$ 3.32 (d, $J$ = 11.2 Hz, 1H), 2.76−2.68 (m, 1H), 2.63−2.57 (m, 1H), 2.46−1.99 (m, 5H), 1.90−1.55 (m, 4H), 0.95 (t, $J$ = 8.0 Hz, 9H), 0.55 (q, $J$ = 8.0 Hz, 6H); minor isomer $\delta$ 3.51 (d, $J$ = 4.4 Hz, 1H); $^{13}C$ NMR (100 MHz, $CDCl_3$) major isomer $\delta$ 200.0, 115.7, 106.0, 83.3, 49.6, 42.2, 40.3, 33.0, 28.8, 24.7, 16.9, 7.3 (3C), 4.3 (3C); minor isomer $\delta$ 200.8, 115.4, 105.7, 83.4, 47.5, 40.8, 38.8, 30.5, 27.0, 24.6, 17.0, 7.3 (3C), 4.3 (3C); IR (neat) 2955, 2877, 2241, 2173, 1728,


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1458, 1239, 740 $cm^{-1}$; HRMS (EI) $m/z$ calcd for $C_{15}H_{22}NOSi$ 260.1471 $[M - Et]^+$; found 260.1477.

*2-(4-(tert-Butyldimethylsilyl)but-3-ynyl)-5-oxocyclopentanecarbonitrile (**33**).* A mixture of keto isomers in a ratio of 1:4 (*cis*/*trans*) was obtained as a yellowish oil: 241 mg, 35% yield; $^1H$ NMR (400 MHz, $CDCl_3$) major isomer $\delta$ 2.92 (d, $J$ = 12.4 Hz, 1H), 2.60−2.30 (m, 4H), 2.06−1.83 (m, 2H), 1.74−1.64 (m, 2H), 1.59−1.49 (m, 1H), 0.89 (s, 9H), 0.05 (s, 6H); minor isomer $\delta$ 3.38 (d, $J$ = 7.6 Hz, 1H); $^{13}C$ NMR (100 MHz, $CDCl_3$) major isomer $\delta$ 205.9, 116.0, 105.6, 84.2, 45.9, 41.7, 37.1, 32.7, 27.0, 25.9 (3C), 17.4, 16.3, −4.6 (2C); minor isomer $\delta$ 206.2, 114.2, 105.5, 83.8, 44.2, 40.5, 36.1, 29.6, 26.4, 25.9 (3C), 17.8, 16.6, −4.6 (2C); IR (neat) 2954, 2858, 2242, 2173, 1759, 1463, 776; HRMS (EI) $m/z$ calcd for $C_{12}H_{16}NOSi$ 218.1001 $[M - {}^tBu]^+$; found 218.0991.

*2-(4-(tert-Butyldimethylsilyl)but-3-ynyl)-6-oxocyclohexanecarbonitrile (**34**).* A mixture of keto isomers in a ratio of 1:3 (*cis*/*trans*) was obtained as a yellowish oil: 239 mg, 33% yield; $^1H$ NMR (400 MHz, $CDCl_3$) major isomer $\delta$ 3.31 (d, $J$ = 11.2 Hz, 1H), 2.68−2.56 (m, 2H), 2.46−1.99 (m, 5H), 1.90−1.55 (m, 4H), 0.89 (s, 9H), 0.05 (s, 6H); minor isomer $\delta$ 3.51 (d, $J$ = 4.8 Hz, 1H); $^{13}C$ NMR (100 MHz, $CDCl_3$) major isomer $\delta$ 199.9, 115.7, 105.6, 84.4, 49.7, 42.3, 40.4, 33.0, 28.9, 26.0 (3C), 24.8, 17.0, 16.4, −5.7 (2C); minor isomer $\delta$ 200.8, 115.5, 105.2, 84.5, 47.5, 41.0, 38.9, 30.7, 27.1, 26.0 (3C), 24.9, 17.1, 16.2, −5.3 (2C); IR (neat) 2952, 2858, 2248, 2173, 1730, 1463, 1251, 776 $cm^{-1}$; HRMS (EI) $m/z$ calcd for $C_{13}H_{18}NOSi$ 232.1158 $[M - {}^tBu]^+$; found 232.1148.

*7,7-Dimethyl-4-oxo-3-((trimethylsilyl)carbonyl)-3a,4,5,6,7,7a-hexahydro-1H-indene-3a-carbonitrile (**45**).* Compound **45** was obtained directly after a usual workup of 1,4-conjugate addition: yellow solid; 304 mg, 42% yield; mp 95−96 °C; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 6.93 (t, $J$ = 2.4 Hz, 1H), 3.02 (m, 1H), 2.89 (ddd, $J$ = 10.0, 8.0, 1.6 Hz, 1H), 2.72 (ddd, $J$ = 18.4, 8.0, 3.2 Hz, 1H), 2.42−2.30 (m, 2H), 1.94−1.81 (m, 2H), 1.47 (s, 3H), 0.98 (s, 3H), 0.30 (s, 9H); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ 229.7, 201.7, 146.2, 145.7, 118.8, 59.5, 54.5, 36.5, 34.8, 34.6, 32.4, 28.4, 27.9, −1.9 (3C); IR ($CH_2Cl_2$) 2962, 2240, 1731, 1595, 1250, 848 $cm^{-1}$; HRMS (EI) $m/z$ calcd for $C_{16}H_{23}NO_2Si$ 289.1498 $[M]^+$; found 289.1489.

*9,9-Dimethyl-4-oxo-3-((trimethylsilyl)carbonyl)-3a,4,9,9a-tetrahydro-1H-cyclopenta[b]naphthalene-3a-carbonitrile (**46**).* Compound **46** was obtained directly after a usual workup of 1,4-conjugate addition: yellow solid; 321 mg, 38% yield; mp 136−137 °C; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 7.80 (dd, $J$ = 7.6, 1.2 Hz, 1H), 7.56 (td, $J$ = 7.6, 1.2 Hz, 1H), 7.36 (d, $J$ = 7.6 Hz, 1H), 7.30 (td, $J$ = 7.6, 1.2 Hz, 1H), 6.81 (dd, $J$ = 3.2, 2.4 Hz, 1H), 3.22 (t, $J$ = 9.0 Hz, 1H), 2.88 (ddd, $J$ = 19.2, 9.2, 3.2 Hz, 1H), 2.19 (ddd, $J$ = 19.2, 9.2, 2.4 Hz, 1H), 1.48 (s, 6H), 0.21 (s, 9H); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ 229.3, 187.2, 149.2, 148.7, 144.3, 134.5, 132.2, 129.2, 127.0, 125.3, 120.0, 56.0, 55.0, 37.0, 36.8, 33.6, 25.4, −2.0 (3C); IR ($CH_2Cl_2$) 2966, 2903, 2239, 1685, 1599, 1377, 1250, 849 $cm^{-1}$; HRMS (EI) $m/z$ calcd for $C_{20}H_{23}NO_2Si$ 337.1498 $[M]^+$; found 337.1499.

The general procedure for Sonogashira coupling in the synthesis of substrates **6** and **9**−**15** is demonstrated as follows using **9** as a typical example.

*Methyl 4-(4-(2-Cyano-3-oxocyclohexyl)but-1-ynyl)benzoate (**9**).* A mixture of 2-oxo-6-(4-(trimethylsilyl)but-3-ynyl)-cyclohexanecarbonitrile **1** (1.0 g, 4.0 mmol) was treated with TBAF (4.8 mL, 1 M in THF) in THF (20 mL) at 0 °C for 1 h and then cooled to room temperature and quenched with water. The aqueous phase was extracted with ethyl acetate (2 × 30 mL). The combined organic extracts were washed with water and brine, dried over anhydrous $Na_2SO_4$, filtered, and concentrated under reduced pressure to give the crude residue which, without purification, was further treated with methyl 4-iodobenzoate (1.25 g, 4.8 mmol), CuI (76 mg, 0.40 mmol), $Pd(PPh_3)_4$ (462 mg, 0.40 mmol), and pyrrolidine (0.67 mL, 8.0 mmol) in $CH_2Cl_2$ (15 mL) under nitrogen at room temperature for 6 h. The mixture was filtered through a pad of Celite and silica gel followed by being washed with $CH_2Cl_2$ (50 mL). The organic solution was concentrated under reduced pressure to give the crude residue, which was subjected to purification by flash chromatography on silica gel using 30% EtOAc in *n*-hexane as eluant to afford a mixture of keto isomers in a ratio of 1:3 (*cis*/*trans*) as a yellowish oil (630 mg, 51% yield): $^1H$ NMR (400 MHz, $CDCl_3$) major isomer $\delta$ 7.93 (d, $J$ = 8.4 Hz, 2H), 7.41 (d, $J$ = 8.4 Hz, 2H), 3.88 (s, 3H), 3.32 (d, $J$ = 11.6 Hz, 1H), 2.64−2.47 (m, 2H), 2.33−2.03 (m, 4H), 1.90−1.67 (m, 5H); minor isomer $\delta$ 3.55 (d, $J$ = 4.4 Hz, 1H); $^{13}C$ NMR (100 MHz, $CDCl_3$) major isomer $\delta$ 200.0, 166.4, 131.3 (2C), 129.2 (2C), 128.9, 128.0, 115.7, 91.4, 81.0, 52.0, 49.6, 42.1, 40.1, 33.1, 28.8, 24.6, 16.4; IR (neat) 2950, 2248, 1721, 1606, 1437, 1279, 1110 $cm^{-1}$; HRMS (ESI) $m/z$ calcd for $C_{19}H_{20}NO_3$ 310.1443 $[M + H]^+$; found 310.1438.

The general procedure for Knoevenagel condensation using Hantzsch ester as a reducing agent in the synthesis of substratess **16**−**18** and **35** is demonstrated as follows using **16** as a typical example.[13]

*2-(Cyclohexanecarbonyl)-7-phenylhept-6-ynenitrile (**16**).* To a stirred solution of 3-oxohexanenitrile (755 mg, 6.8 mmol) and 5-phenylpent-4-ynal (1.3 g, 8.2 mmol) in EtOH (100 mL) were added L-proline (312 mg, 2.7 mmol) and Hantzsch ester (1.7 g, 6.8 mmol) sequentially in one portion. The resulting mixture was stirred at 25 °C for 16 h. The reaction solution was concentrated under reduced pressure, which was purified by flash chromatography on silica gel using 33% $CH_2Cl_2$ in *n*-hexane as eluant to afford substrate **16** as a pale-yellow oil: 1.40 g, 70% yield; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 7.38−7.36 (m, 2H), 7.27−7.25 (m, 3H), 3.60 (dd, $J$ = 8.4, 5.6 Hz, 1H), 2.73 (tt, $J$ = 11.2, 3.6 Hz, 1H), 2.48 (t, $J$ = 6.8 Hz, 2H), 2.13−1.65 (m, 8H), 1.42−1.17 ppm (m, 6H); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ 203.5, 131.4, 128.2, 127.7, 123.4, 117.3, 88.2, 81.7, 49.1, 41.7, 28.5, 28.3, 27.8, 25.7, 25.4, 25.2, 25.1, 18.7; IR (neat) 2934, 2242, 1722, 1450 $cm^{-1}$; HRMS (ESI) $m/z$ calcd for $C_{20}H_{24}NO$ 294.1858 $[M + H]^+$; found 294.1845.

*Methyl 4-(6-Cyano-7-cyclohexyl-7-oxohept-1-ynyl)benzoate (**17**):* Yellow oil; 1.39 g, 58% yield; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 7.94 (d, $J$ = 8.8 Hz, 2H), 7.42 (d, $J$ = 8.8 Hz, 2H), 3.89 (s, 3H), 3.58 (dd, $J$ = 8.4, 6.0 Hz, 1H), 2.74 (tt, $J$ = 10.8, 3.2 Hz, 1H), 2.50 (t, $J$ = 6.8 Hz, 2H), 2.12−1.65 (m, 8H), 1.43−1.17 ppm (m, 6H); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ 203.3, 166.4, 131.3, 129.3, 129.0, 128.1, 117.2, 91.6, 81.1, 52.0, 49.1, 41.6, 28.4, 28.2, 27.7, 25.5, 25.3, 25.2, 25.1, 18.8; IR (neat) 2934, 2241, 1731, 1715, 1607, 1436, 1308, 1109 $cm^{-1}$; HRMS (EI) $m/z$ calcd for $C_{22}H_{25}NO_3$ 351.1834 $[M]^+$; found 351.1830.

*2-(Cyclohexanecarbonyl)-7-(4-methoxyphenyl)hept-6-ynenitrile (**18**):* Yellow oil; 1.21 g, 55% yield; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 7.29 (d, $J$ = 8.8 Hz, 2H), 6.79 (d, $J$ = 8.8, Hz, 2H), 3.77 (s, 3H), 3.60 (dd, $J$ = 8.4, 5.6 Hz, 1H), 2.72 (tt, $J$ = 10.8, 3.2 Hz, 1H), 2.45 (t, $J$ = 6.8 Hz, 2H), 2.10−1.93 (m, 2H), 1.89−1.86 (m, 2H), 1.79−1.63 (m, 4H), 1.41−1.15 ppm (m, 6H); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ 203.5, 159.1, 132.8, 117.3, 115.5, 113.8, 81.5, 56.6, 55.1, 49.1, 41.7, 28.5, 28.3, 27.8, 25.7, 25.4, 25.2, 25.1, 18.7; IR (neat) 2934, 2241, 1720, 1606, 1510, 1450, 1247, 834 $cm^{-1}$; HRMS (ESI) $m/z$ calcd for $C_{21}H_{26}NO_2$ 324.1958 $[M + H]^+$; found 324.1952.

*2-(Cyclohexanecarbonyl)-7-(trimethylsilyl)hept-6-ynenitrile (**35**):* Colorless oil; 1.42g, 72% yield; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 3.57 (dd, $J$ = 8.8, 5.6 Hz, 1H), 2.72 (tt, $J$ = 11.2, 3.6 Hz, 1H), 2.28 (t, $J$ = 6.8 Hz, 2H), 2.01−1.86 (m, 4H), 1.81−1.61 (m, 4H), 1.41−1.18 (m, 6H), 0.12 ppm (s, 9H); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ 203.5, 117.3, 105.3, 86.0, 49.2, 41.8, 28.6, 28.4, 27.7, 25.5, 25.3, 25.2, 19.1, 0.0; IR (neat) 2935, 2176, 1723, 1451, 1250, 844 $cm^{-1}$; HRMS (EI) $m/z$ calcd for $C_{17}H_{27}NOSi$ 289.1862 $[M]^+$; found 289.1867.

**Synthesis of Products.** The general procedure for autoxidative annulation in the synthesis of products **7**, **19**−**28**, **38**−**42**, and **49**−**52** was demonstrated as follows using **7** as a typical example.

*3-Benzoyl-4-oxo-3a,4,5,6,7,7a-hexahydro-1H-indene-3a-carbonitrile (**7**).* A mixture of 2-oxo-6-(4-phenylbut-3-ynyl)-cyclohexanecarbonitrile **6** (125 mg, 0.50 mmol), $Co(OAc)_2$ (7 mg, 0.04 mmol), and *N*-hydroxyphthalimide (13 mg, 0.08 mmol) in benzene (1 mL) was stirred under air at room temperature for 12 h. The mixture was filtered through a pad of Celite and silica gel followed by being washed with $CH_2Cl_2$ (2 × 20 mL). The organic layer was concentrated under reduced pressure to give the residue, which was subjected to purification by flash chromatography on silica gel using


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EtOAc/*n*-hexane = 2/5 as eluant to afford product **7** (81 mg, 61% yield) as a colorless oil: $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.74 (d, $J$ = 7.2 Hz, 2H), 7.56 (t, $J$ = 7.2 Hz, 1H), 7.44 (t, $J$ = 7.2 Hz, 2H), 6.83 (t, $J$ = 2.8 Hz, 1H), 3.29−3.23 (m, 1H), 2.98 (ddd, $J$ = 18.4, 6.8, 2.8 Hz, 1H), 2.77 (dt, $J$ = 13.6, 6.0 Hz, 1H), 2.48−2.40 (m, 2H), 2.14−2.06 (m, 1H), 2.02−1.94 (m, 2H), 1.68−1.59 (m, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 201.1, 190.2, 149.1, 140.0, 137.2, 132.7, 128.9, 128.4, 117.8, 59.7, 50.4, 38.4, 38.2, 27.0, 24.0; IR (neat) 2929, 2238, 1726, 1646, 1343 cm$^{-1}$; HRMS (EI) $m/z$ calcd for $C_{17}H_{15}NO_2$ 265.1103 [M]$^+$; found 265.1098.

*Methyl 4-(3a-Cyano-4-oxo-3a,4,5,6,7,7a-hexahydro-1H-indene-3-carbonyl)benzoate* (**19**): Colorless oil; 99 mg, 61% yield; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.10 (d, $J$ = 8.8 Hz, 2H), 7.77 (d, $J$ = 8.8 Hz, 2H), 6.81 (t, $J$ = 2.8 Hz, 1H), 3.93 (s, 3H), 3.28 (quint, $J$ = 6.4 Hz, 1H), 2.97−2.90 (m, 1H), 2.86−2.78 (m, 1H), 2.48−2.39 (m, 2H) 2.19−1.92 (m, 3H), 1.69−1.61 (m, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 201.2, 189.7, 166.0, 150.1, 140.8, 140.0, 133.4, 129.6, 128.7, 117.7, 59.1, 52.4, 50.5, 38.2, 38.1, 26.6, 23.9; IR (neat) 2953, 2234, 1725, 1651, 1282, 1109 cm$^{-1}$; HRMS (ESI) $m/z$ calcd for $C_{19}H_{18}NO_4$ 324.1236 [M + H]$^+$; found 324.1227.

*3-(4-Cyanobenzoyl)-4-oxo-3a,4,5,6,7,7a-hexahydro-1H-indene-3a-carbonitrile* (**20**): White solid; 73 mg, 50% yield; mp 149−150 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.82 (d, $J$ = 8.0 Hz, 2H), 7.75 (d, $J$ = 8.0 Hz, 2H), 6.80 (t, $J$ = 2.8 Hz, 1H), 3.31 (quint, $J$ = 6.4 Hz, 1H), 2.92 (ddd, $J$ = 18.8, 7.6, 2.8 Hz, 1H), 2.87−2.80 (m, 1H), 2.49−2.39 (m, 2H), 2.23−2.16 (m, 1H), 2.15−2.06 (m, 1H), 2.00−1.92 (m, 1H), 1.71−1.63 (m, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 201.2, 188.8, 149.9, 140.8, 139.8, 132.3, 129.3, 117.8, 117.5, 115.9, 58.7, 50.6, 38.1, 37.8, 26.2, 23.9; IR ($CH_2Cl_2$ cast) 2941, 2232, 1731, 1651, 1250 cm$^{-1}$; HRMS (ESI) $m/z$ calcd for $C_{18}H_{15}N_2O_2$ 291.1134 [M + H]$^+$; found 291.1129.

*3-(4-Methoxybenzoyl)-4-oxo-3a,4,5,6,7,7a-hexahydro-1H-indene-3a-carbonitrile* (**21**): Colorless oil; 62 mg, 42% yield; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.75 (d, $J$ = 8.0 Hz, 2H), 6.90 (d, $J$ = 8.0 Hz, 2H), 6.78 (t, $J$ = 2.8 Hz, 1H), 3.88 (s, 3H), 3.21 (quint, $J$ = 6.4 Hz, 1H), 3.00 (ddd, $J$ = 18.4, 7.2, 2.8 Hz, 1H), 2.71−2.64 (m, 1H), 2.47−2.40 (m, 2H), 2.05−1.81 (m, 3H), 1.64−1.56 (m, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 201.2, 188.7, 163.5, 147.2, 139.9, 131.5, 129.8, 117.9, 113.8, 60.3, 55.5, 50.4, 38.5, 38.4, 27.3, 24.0; IR (neat) 2960, 2239, 1727, 1599, 1261, 1026 cm$^{-1}$; HRMS (ESI) $m/z$ calcd for $C_{18}H_{18}NO_3$ 296.1287 [M + H]$^+$; found 296.1281.

*3-(4-Fluorobenzoyl)-4-oxo-3a,4,5,6,7,7a-hexahydro-1H-indene-3a-carbonitrile* (**22**): Colorless oil; 57 mg, 40% yield; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.78 (dd, $J$ = 8.8, 5.6 Hz, 2H), 7.12 (t, $J$ = 8.8 Hz, 2H), 6.79 (t, $J$ = 2.8 Hz, 1H), 3.26 (quint, $J$ = 6.0 Hz, 1H), 2.96 (ddd, $J$ = 18.4, 7.2, 2.8 Hz, 1H), 2.80−2.73 (m, 1H), 2.48−2.39 (m, 2H), 2.15−2.07 (m, 1H), 2.00−1.93 (m, 2H), 1.67−1.59 (m, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 201.3, 188.7, 165.5 (d, $^1J_{C-F}$ = 253.1 Hz), 148.8, 139.7, 133.4 (d, $^4J_{C-F}$ = 3.0 Hz), 131.6 (d, $^3J_{C-F}$ = 9.2 Hz), 117.8, 115.6 (d, $^2J_{C-F}$ = 22.2 Hz), 59.6, 50.4, 38.2 (2C), 26.8, 23.9; IR (neat) 2945, 2239, 1726, 1648, 1598, 1230 cm$^{-1}$; HRMS (EI) $m/z$ calcd for $C_{17}H_{14}FNO_2$ 283.1009 [M]$^+$; found 283.1012.

*3-(4-Methylbenzoyl)-4-oxo-3a,4,5,6,7,7a-hexahydro-1H-indene-3a-carbonitrile* (**23**): Colorless oil; 56 mg, 40% yield; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.68 (d, $J$ = 8.4 Hz, 2H), 7.25 (d, $J$ = 8.4 Hz, 2H); 6.85 (t, $J$ = 2.4 Hz, 1H), 3.28−3.22 (m, 1H), 3.02 (ddd, $J$ = 18.4, 6.8, 2.4 Hz, 1H), 2.78−2.70 (m, 1H), 2.52−2.43 (m, 2H), 2.42 (s, 3H), 2.13−2.03 (m, 1H), 2.02−1.90 (m, 2H), 1.69−1.60 (m, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 201.2, 189.8, 148.4, 143.7, 140.0, 134.5, 129.2, 129.1, 117.9, 59.9, 50.4, 38.5, 38.3, 27.2, 24.0, 21.6 ; IR (neat) 2949, 2238, 1725, 1643 cm$^{-1}$; HRMS (EI) $m/z$ calcd for $C_{18}H_{17}NO_2$ 279.1259 [M]$^+$; found 279.1261.

*4-Benzoyl-3-oxo-1,2,3,3a,6,6a-hexahydropentalene-3a-carbonitrile* (**24**): Colorless oil; 48 mg, 38% yield; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.73 (d, $J$ = 7.2 Hz, 2H), 7.56 (t, $J$ = 7.2 Hz, 1H), 7.44 (t, $J$ = 7.2 Hz, 2H), 6.74 (t, $J$ = 2.4 Hz, 1H), 3.51−3.45 (m, 1H), 3.21 (ddd, $J$ = 19.6, 8.0, 2.4 Hz, 1H), 2.68 (dt, $J$ = 19.6, 2.4 Hz, 1H), 2.62−2.48 (m, 2H), 2.46−2.37 (m, 1H), 1.85−1.76 (m, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 204.1, 189.6, 148.8, 137.3, 137.1, 132.9, 128.9, 128.4, 117.4, 58.6, 46.3, 40.1, 36.3, 26.7; IR (neat) 2958, 2239, 1750, 1652 cm$^{-1}$; HRMS (EI) $m/z$ calcd for $C_{16}H_{13}NO_2$ 251.0946 [M]$^+$; found 251.0948.

*4-(4-Methoxybenzoyl)-3-oxo-1,2,3,3a,6,6a-hexahydropentalene-3a-carbonitrile* (**25**): Colorless oil; 49 mg, 35% yield; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.78 (d, $J$ = 7.2 Hz, 2H), 6.93 (d, $J$ = 7.2 Hz, 2H), 6.65 (t, $J$ = 2.4 Hz, 1H), 3.86 (s, 3H), 3.48−3.43 (m, 1H), 3.20 (ddd, $J$ = 19.2, 7.6, 2.4 Hz, 1H), 2.66 (dt, $J$ = 19.2, 2.4 Hz, 1H), 2.64−2.36 (m, 3H), 1.83−1.74 (m, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 204.3, 188.2, 163.6, 146.3, 137.3, 131.5, 129.7, 117.4, 113.7, 59.1, 53.5, 46.3, 40.0, 36.4, 26.8; IR (neat) 2920, 2241, 1753, 1641 cm$^{-1}$; HRMS (ESI) $m/z$ calcd for $C_{17}H_{16}NO_3$ 282.1152 [M + H]$^+$; found 282.1125.

*2-Benzoyl-1-(cyclohexanecarbonyl)cyclopent-2-enecarbonitrile* (**26**): Colorless oil; 62 mg, 40% yield; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.45 (d, $J$ = 7.6 Hz, 2H), 7.58 (t, $J$ = 7.6 Hz, 1H), 7.46 (t, $J$ = 7.6 Hz, 2H), 6.89 (t, $J$ = 2.4 Hz, 1H), 3.36 (tt, $J$ = 11.2, 3.2 Hz, 1H), 2.95−2.80 (m, 2H), 2.63−2.56 (m, 1H), 2.40−2.32 (m, 1H), 2.10−1.69 (m, 4H), 1.52−1.17 ppm (m, 6H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 206.4, 190.1, 150.1, 143.2, 137.0, 132.7, 128.8, 128.4, 120.1, 57.6, 48.7, 36.1, 33.5, 29.1, 28.7, 27.9, 25.6, 25.6, 24.9; IR (neat) 2933, 2856, 2237, 1719, 1643, 1449 cm$^{-1}$; HRMS (EI) $m/z$ calcd for $C_{20}H_{21}NO_2$ 307.1572 [M]$^+$; found 307.1585.

*Methyl 4-(5-Cyano-5-(cyclohexanecarbonyl)cyclopent-1-enecarbonyl)benzoate* (**27**): White solid; 66 mg, 36% yield; mp 124−126 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.10 (d, $J$ = 8.0 Hz, 2H), 7.77 (d, $J$ = 8.0 Hz, 2H), 6.86 (t, $J$ = 2.8 Hz, 1H), 3.93 (s, 3H), 3.35 (tt, $J$ = 11.2, 3.2 Hz, 1H), 2.95−2.82 (m, 2H), 2.65−2.59 (m, 1H), 2.41−2.34 (m, 1H), 2.10−2.04 (m, 2H), 1.84−1.70 (m, 3H), 1.49−1.20 ppm (m, 5H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 206.3, 189.5, 166.0, 151.0, 143.1, 140.6, 133.5, 129.6, 128.7, 119.9, 57.5, 52.4, 48.7, 36.1, 33.6, 29.2, 27.9, 25.6, 25.6, 24.9; IR ($CH_2Cl_2$ cast) 2935, 2856, 2237, 1723, 1646, 1283, 1108 cm$^{-1}$; HRMS (EI) $m/z$ calcd for $C_{22}H_{23}NO_4$ 365.1627 [M]$^+$; found 365.1643.

*1-(Cyclohexanecarbonyl)-2-(4-methoxybenzoyl)cyclopent-2-enecarbonitrile* (**28**): White solid; 47 mg, 28% yield; mp 118−120 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.76 (d, $J$ = 9.2 Hz, 2H), 6.91 (d, $J$ = 9.2 Hz, 2H), 6.81 (t, $J$ = 2.4 Hz, 1H), 3.85 (s, 3H), 3.35 (tt, $J$ = 10.8, 3.2 Hz, 1H), 2.89−2.84 (m, 2H), 2.61−2.54 (m, 1H), 2.39−2.32 (m, 1H), 2.11−2.02 (m, 2H), 1.83−1.69 (m, 4H), 1.49−1.19 ppm (m, 4H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 206.6, 188.6, 163.4, 148.5, 143.3, 131.3, 129.7, 120.3, 113.7, 57.9, 55.5, 48.8, 36.1, 33.5, 29.2, 27.9, 25.7, 25.6, 24.9; IR ($CH_2Cl_2$ cast) 2934, 2855, 2237, 1720, 1634, 1600, 1259, 1028 cm$^{-1}$; HRMS (ESI) $m/z$ calcd for $C_{21}H_{24}NO_3$ 338.1756 [M + H]$^+$; found 338.1746.

*3-Oxo-4-((triethylsilyl)carbonyl)-1,2,3,3a,6,6a-hexahydropentalene-3a-carbonitrile* (**38**): Yellow oil; 90 mg, 62% yield; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 6.89 (t, $J$ = 2.8 Hz, 1H), 3.40−3.34 (m, 1H), 3.19 (ddd, $J$ = 19.6, 8.4, 2.8 Hz, 1H), 2.59 (dt, $J$ = 19.6, 2.8 Hz, 1H), 2.43−2.39 (m, 2H), 2.36−2.26 (m, 1H), 1.77−1.69 (m, 1H), 0.93 (t, $J$ = 8.0 Hz, 9H), 0.77 (q, $J$ = 8.0 Hz, 6H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 230.1, 203.7, 148.1, 144.7, 117.3, 57.3, 45.8, 40.5, 35.7, 26.4, 7.2 (3C), 3.1 (3C); IR (neat) 2919, 2238, 1754, 1590, 1460, 737 cm$^{-1}$; HRMS (EI) $m/z$ calcd for $C_{16}H_{23}NO_2Si$ 289.1498 [M]$^+$; found 289.1494.

*4-Oxo-3-((triethylsilyl)carbonyl)-1,4,5,6,7,7a-hexahydroindene-3a-carbonitrile* (**39**): Yellow solid; 111 mg, 73% yield; mp 59−60 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.01 (t, $J$ = 2.8 Hz, 1H), 3.13−3.06 (m, 1H), 2.96 (ddd, $J$ = 18.8, 6.8, 2.8 Hz, 1H), 2.68−2.62 (m, 1H), 2.43 (ddd, $J$ = 18.4, 4.8, 2.8 Hz, 1H), 2.23−2.16 (m, 1H), 2.06−2.00 (m, 1H), 1.92−1.85 (m, 2H), 1.56−1.50 (m, 1H), 0.96 (t, $J$ = 8.0 Hz, 9H), 0.80 (q, $J$ = 8.0 Hz, 6H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 230.3, 201.0, 148.0, 147.5, 117.8, 58.4, 49.9, 38.8, 38.1, 27.1, 24.3, 7.2 (3C), 3.1 (3C); IR ($CH_2Cl_2$ cast) 2955, 2875, 2235, 1733, 1576, 1457, 1239, 850 cm$^{-1}$; HRMS (EI) $m/z$ calcd for $C_{17}H_{25}NO_2Si$ 303.1655 [M]$^+$; found 303.1644.

*4-((tert-Butyldimethylsilyl)carbonyl)-3-oxo-1,2,3,3a,6,6a-hexahydropentalene-3a-carbonitrile* (**40**): Yellow solid; 100 mg, 69% yield; mp 85−86 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 6.92 (t, $J$ = 2.8 Hz, 1H), 3.41−3.35 (m, 1H), 3.21 (ddd, $J$ = 19.6, 8.4, 2.8 Hz, 1H), 2.62 (dt, $J$ = 19.6, 2.8 Hz, 1H), 2.45−2.41 (m, 2H), 2.37−2.30 (m, 1H), 1.78−1.70 (m, 1H), 0.90 (s, 9H), 0.27 (s, 3H), 0.26 (s, 3H); $^{13}$C NMR


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(100 MHz, $CDCl_3$) $\delta$ 229.4, 203.6, 148.4, 145.1, 117.3, 57.4, 45.8, 40.5, 35.8, 26.5 (3C), 26.4, 16.8, −5.4, −5.7; IR ($CH_2Cl_2$ cast) 2954, 2858, 2242, 2174, 1759, 1589, 1251, 839 $cm^{-1}$; HRMS (ESI) $m/z$ calcd for $C_{16}H_{24}NO_2Si$ 290.1576 $[M + H]^+$; found 290.1568.

*3-((tert-Butyldimethylsilyl)carbonyl)-4-oxo-3a,4,5,6,7,7a-hexahydro-1H-indene-3a-carbonitrile (**41**):* Yellow solid; 114 mg, 75% yield; mp 93−94 °C; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 7.01 (t, $J$ = 2.8 Hz, 1H), 3.12−3.06 (m, 1H), 2.95 (ddd, $J$ = 18.8, 6.8, 2.8 Hz, 1H), 2.67 (dt, $J$ = 13.2, 6.4 Hz, 1H), 2.43 (ddd, $J$ = 18.8, 5.2, 2.8 Hz, 1H), 2.24−2.17 (m, 1H), 2.07−2.00 (m, 1H), 1.93−1.87 (m, 2H), 1.57−1.48 (m, 1H), 0.93 (s, 9H), 0.29 (s, 3H), 0.26 (s, 3H); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ 229.6, 201.0, 148.6, 147.9, 117.9, 58.5, 49.9, 38.8, 38.1, 27.0, 26.4 (3C), 24.3, 16.7, −5.4, −5.7; IR ($CH_2Cl_2$ cast) 2931, 2239, 1728, 1583, 1251, 840 $cm^{-1}$; HRMS (EI) $m/z$ calcd for $C_{17}H_{25}NO_2Si$ 303.1655 $[M]^+$; found 303.1643.

*1-(Cyclohexanecarbonyl)-2-((trimethylsilyl)carbonyl)cyclopent-2-enecarbonitrile (**42**):* Yellow oil; 67 mg, 44% yield; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 7.06 (t, $J$ = 2.8 Hz, 1H), 3.34 (t, $J$ = 10.8, 3.2 Hz, 1H), 2.94−2.81 (m, 2H), 2.52−2.45 (m, 1H), 2.30−2.22 (m, 1H), 2.19−1.97 (m, 2H), 1.83−1.73 (m, 4H), 1.54−1.36 (m, 4H), 0.28 ppm (s, 9H); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ 229.7, 206.5, 150.0, 148.5, 120.3, 56.1, 48.70, 35.6, 33.7, 29.7, 29.3, 27.8, 25.7, 24.9, −2.05 (3C); IR (neat) 2935, 2235, 1719, 1585, 1250, 846 $cm^{-1}$; HRMS (EI) $m/z$ calcd for $C_{17}H_{25}NO_2Si$ 303.1655 $[M]^+$; found 303.1650.

*4-Oxo-3-propionyl-3a,4,5,6,7,7a-hexahydro-1H-indene-3a-carbonitrile (**49**):* Colorless oil; 23 mg, 21% yield; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 7.06 (t, $J$ = 2.4 Hz, 1H), 3.19 (quint, $J$ = 6.8 Hz, 1H), 2.92 (ddd, $J$ = 18.4, 7.2, 2.8 Hz, 1H), 2.80−2.67 (m, 3H), 2.45−2.38 (m, 1H), 2.35−2.28 (m, 1H), 2.12−2.04 (m, 1H), 2.02−1.92 (m, 2H), 1.65−1.56 (m, 1H), 1.13(t, $J$ = 7.2 Hz, 3H); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ 201.4, 196.1, 146.4, 141.5, 117.8, 58.5, 50.6, 38.0, 37.9, 31.8, 26.7, 24.2, 7.7; IR (neat) 2940, 2238, 1729, 1671, 1369 $cm^{-1}$; HRMS (ESI) $m/z$ calcd for $C_{13}H_{16}NO_2$ 218.1176 $[M + H]^+$; found 218.1177.

*3-Butyryl-4-oxo-3a,4,5,6,7,7a-hexahydro-1H-indene-3a-carbonitrile (**50**):* Colorless oil; 30 mg, 26% yield; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 7.05 (t, $J$ = 2.4 Hz, 1H), 3.19 (quint, $J$ = 6.4 Hz, 1H), 2.92 (ddd, $J$ = 18.4, 6.8, 2.4 Hz, 1H), 2.76−2.63 (m, 3H), 2.42 (ddd, $J$ = 18.4, 5.6, 2.8 Hz, 1H), 2.35−2.28 (m, 1H), 2.12−2.01 (m, 1H), 1.98−1.92 (m, 2H), 1.73−1.56 (m, 3H), 0.96 (t, $J$ = 7.2 Hz, 3H); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ 201.3, 195.7, 146.3, 141.9, 117.8, 50.6, 40.5, 38.1, 37.9, 26.7, 24.2, 17.5, 13.7; IR (neat) 2956, 2932, 2242, 1729, 1669, 1375 $cm^{-1}$; HRMS (ESI) $m/z$ calcd for $C_{14}H_{18}NO_2$ 232.1332 $[M + H]^+$; found 232.1333.

*(E)-4-Oxo-3-propylideneoctahydro-1H-indene-3a-carbonitrile (**51**):*[26b] Colorless oil; 33 mg, 32% yield; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 5.65 (tt, $J$ = 7.6, 20 Hz, 1H), 2.90−2.84 (m, 1H), 2.65−2.52 (m, 3H), 2.50−2.41 (m, 1H), 2.11 (quint, $J$ = 7.6 Hz, 1H), 2.03−1.94 (m, 3H), 1.93−1.84 (m, 2H), 1.69−1.55 (m, 2H), 0.98 (t, $J$ = 7.2 Hz, 3H); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ 202.4, 134.1, 133.0, 118.9, 57.3, 52.5, 38.5, 30.7, 28.7, 25.8, 24.9, 22.1, 13.4; IR (neat) 2940, 2234, 1714, 1458, 1240 $cm^{-1}$; HRMS (ESI) $m/z$ calcd for $C_{13}H_{18}NO$ 204.1383 $[M + H]^+$; found 204.1384.

*(E)-3-Butylidene-4-oxooctahydro-1H-indene-3a-carbonitrile (**52**):*[26b] Colorless oil; yield: 30 mg, 28%; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 5.69 (tt, $J$ = 7.6, 2.0 Hz, 1H), 2.90−2.84 (m, 1H), 2.65−2.49 (m, 3H), 2.48−2.41 (m, 1H), 2.11−1.84 (m, 6H), 1.68−1.55 (m, 2H), 1.43−1.35 (m, 2H), 0.90 (t, $J$ = 7.2 Hz, 3H); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ 202.5, 134.7, 131.6, 118.9, 57.5, 52.6, 38.5, 30.8, 30.6, 28.8, 26.0, 25.0, 22.3, 13.7; IR (neat) 2960, 2932, 2234, 1716, 1453, 1235 $cm^{-1}$; HRMS (ESI) $m/z$ calcd for $C_{14}H_{20}NO$ 218.1539 $[M + H]^+$; found 218.1540.

**Synthesis of the Authentic Sample I.** *2-(Cyclohexanecarbonyl)-6-hydroxyhexanenitrile (**H**).* To a stirred solution of 3-cyclohexyl-3-oxopropanenitrile (1.51 g, 10 mmol) and 4-((tetrahydro-2*H*-pyran-2-yl)oxy)butanal (1.72 g, 10 mmol) in EtOH (50 mL) were added L-proline (230 mg, 2 mmol) and Hantzsch ester (2.54 g, 10 mmol) sequentially in one portion. The resulting mixture was stirred at 25 °C for 16 h. The reaction solution was concentrated under reduced pressure followed by rapid chromatography on silical gel ($CH_2Cl_2$) to afford the crude product. To a stirred solution of the crude product in methanol (50 mL) was added *p*-TsOH (380 mg, 2 mmol) in one portion. The resulting mixture was stirred at 25 °C for 10 h. The reaction solution was concentrated under reduced pressure to give the crude residue, which was purified by chromatography on silica gel using EtOAc/*n*-hexane = 1/3 to 1/1 as eluant to afford compound **H** (1.78 g, 80% yield over two steps) as a colorless oil: $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 3.68 (t, $J$ = 6.0 Hz, 2H), 3.52 (dd, $J$ = 8.0, 6.0 Hz, 1H), 2.75 (tt, $J$ = 10.8, 3.2 Hz, 1H), 1.95−1.15 (m, 16H); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ 203.8, 117.3, 61.4, 48.8, 41.9, 31.4, 28.1, 28.0, 25.2, 24.9, 23.1; IR (neat) 3422, 2934, 2858, 2243, 2198, 1719, 1450 $cm^{-1}$; LRMS (ESI) $m/z$ = 224 $[M + H]^+$, 246 $[M + Na]^+$, 469 $[2M + Na]^+$; HRMS (ESI) $m/z$ calcd for $C_{13}H_{22}NO_2$ 224.1645 $[M + H]^+$; found 224.1651.

*1-(Cyclohexanecarbonyl)-2-oxocyclopentanecarbonitrile (**I**).* To a stirred solution of 2-(cyclohexanecarbonyl)-6-hydroxyhexanenitrile **H** (447 mg, 2 mmol) in dry $CH_2Cl_2$ (20 mL) were added Celite (2 g) and PCC (1.08 g, 5 mmol) sequentially in one portion at 0 °C. The resulting mixture was stirred at 25 °C for 3 h. The reaction mixture was filtered with a pad of silica gel, and then the filtrate was concentrated under reduced pressure to give the crude $\beta$-hydroxy ketone. To the solution of the $\beta$-hydroxy ketone in dry $CH_2Cl_2$ (20 mL) was added DMP (848 mg, 2 mmol) in one portion at 0 °C. The resulting mixture was stirred at 25 °C for 1 h. The reaction mixture was quenched with 10% $Na_2S_2O_{3(aq)}$ solution (10 mL) at 0 °C for 30 min. The organic layer was washed with saturated $NaHCO_{3(aq)}$ solution and brine, dried over $MgSO_{4(s)}$, filtered, and concentrated to give the crude residue, which was purified by chromatography on silica gel using EtOAc/*n*-hexane (3/20) as eluant to afford 2-cyano-1,3-diketone **I** (171 mg, 39% yield over two steps) as a colorless oil: $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 3.15 (tt, $J$ = 10.8, 3.6 Hz, 1H), 2.74 (quint, $J$ = 6.8 Hz, 1H), 2.47 (t, $J$ = 7.6 Hz, 2H), 2.43 (quint, $J$ = 6.8 Hz, 1H); 2.19−2.06 (m, 2H), 2.04−1.96 (m, 1H), 1.87−1.69 (m, 4H), 1.45−1.16 (m, 5H); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ 204.1, 201.3, 116.5, 60.3, 48.9, 36.9, 32.9, 29.2, 28.1, 25.2, 25.0, 24.8, 19.6; IR (neat) 2934, 2857, 2239, 1761, 1715, 1450 $cm^{-1}$; LRMS (ESI) $m/z$ = 220 $[M + H]^+$, 242 $[M + Na]^+$.

*5-Cyano-6-cyclohexyl-6-oxohexanoic acid (**J**).* 2-Cyano-1,3-diketone **I** (22 mg, 0.1 mmol) was hydrolyzed to acid **J** upon exposure to air in $CDCl_3$ over 48 h at roon temperature. The solution was concentrated to give the crude residue, which was purified by chromatography on silica gel using EtOAc as eluant to afford acid **J** (18 mg, 75% yield) as a colorless oil: $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 3.54 (dd, $J$ = 8.0, 6.0 Hz, 1H), 2.49 (tt, $J$ = 10.8, 3.2 Hz, 1H), 2.44 (t, $J$ = 6.8 Hz, 2H) 2.15−1.69 (m, 8H), 1.49−1.16 (m, 7H); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ 203.3, 178.6, 117.2, 49.2, 41.8, 33.0, 28.5, 28.3, 27.8, 25.4, 25.3, 25.1, 21.9; LRMS (ESI) $m/z$ = 260 $[M + Na]^+$; HRMS (ESI) $m/z$ calcd for $C_{13}H_{18}NO_3$ 236.1292 $[M - H]^-$; found 236.1284.

## ■ ASSOCIATED CONTENT

### Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b01837.

$^1H$ and $^{13}C$ NMR spectra of all new compounds including compounds **I** and **J**; X-ray crystallographic analysis of products **20**, **27**, **28**, **39**−**41**, **45**, and **46**; geometries of vinyl radicals **I**, **II**, and **III** and compounds **35**, **53**, and **54** along with Cartesian atom coordinates, absolute energies, and BDE (PDF)

X-ray data for **20** (CIF)

X-ray data for **27** (CIF)

X-ray data for **28** (CIF)

X-ray data for **39** (CIF)

X-ray data for **40** (CIF)

X-ray data for **41** (CIF)

X-ray data for **45** (CIF)

X-ray data for **46** (CIF)



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### Notes

The authors declare no competing financial interest.

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(12) Crystallographic data for **20** (CCDC 971512): $C_{18}H_{14}N_2O_2$, $M_w$ = 290.31, triclinic, $a$ = 7.729(15) Å, $b$ = 7.756(14) Å, $c$ = 12.50(3) Å, $V$ = 730(2) Å$^3$, space group $P\bar{1}$, $Z$ = 2, a total of 4725 reflections were collected in the range 1.67 to 25.03°. Of these, 2465 were independent; for the observed data, $wR2$ = 0.2474, $R1$ = 0.1106.

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(15) Crystallographic data for **28** (CCDC 968701): $C_{21}H_{23}NO_3$, $M_w$ = 337.40, triclinic, $a$ = 7.7230(3) Å, $b$ = 21.7910(10) Å, $c$ = 10.8617(4) Å, $V$ = 1809.62(13) Å$^3$, space group $P21/n$, $Z$ = 4, a total of 12 081 reflections were collected in the range 2.82 to 25.03°. Of these, 3183 were independent; for the observed data, $wR2$ = 0.0952, $R1$ = 0.0381.

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(20) Crystallographic data for **39** (CCDC 883936): $C_{17}H_{25}NO_2Si$, $M_w$ = 303.47, triclinic, $a$ = 17.6278(10) Å, $b$ = 8.0278(5) Å, $c$ = 12.3398(7) Å, $V$ = 1693.79(17) Å$^3$, space group $P21/c$, $Z$ = 4, a total of 11 381 reflections were collected in the range 2.80 to 25.24°. Of these, 3008 were independent; for the observed data, $wR2$ = 0.1027, $R1$ = 0.0579.

(21) Crystallographic data for **40** (CCDC 971513): $C_{16}H_{23}NO_2Si$, $M_w$ = 289.44, triclinic, $a$ = 7.1377(10) Å, $b$ = 12.3260(18) Å, $c$ = 18.630(3) Å, $V$ = 1634.6(4) Å$^3$, space group $P21/n$, $Z$ = 4, a total of 8759 reflections were collected in the range 1.98 to 25.15°. Of these, 2915 were independent; for the observed data, $wR2$ = 0.1830, $R1$ = 0.0815.

(22) Crystallographic data for **41** (CCDC 966268): $C_{17}H_{25}NO_2Si$, $M_w$ = 303.47, triclinic, $a$ = 19.146(14) Å, $b$ = 7.452(6) Å, $c$ = 12.716(9) Å, $V$ = 1755(2) Å$^3$, space group $Cc$, $Z$ = 4, a total of 4110 reflections were collected in the range 2.95 to 25.02°. Of these, 2443 were independent; for the observed data, $wR2$ = 0.0922, $R1$ = 0.0564.

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(24) Crystallographic data for **45** (CCDC 885581): $C_{16}H_{23}NO_2Si$, $M_w$ = 289.44, triclinic, $a$ = 11.211(10) Å, $b$ = 12.349(11) Å, $c$ = 12.562(11) Å, $V$ = 1607(3) Å$^3$, space group $P\bar{1}$, $Z$ = 4, a total of 6252 reflections were collected in the range 1.86 to 27.38°. Of these, 6252 were independent; for the observed data, $wR2$ = 0.2574, $R1$ = 0.1046.

(25) Crystallographic data for **46** (CCDC 886563): $C_{20}H_{23}NO_2Si$, $M_w$ = 337.48, triclinic, $a$ = 26.426(12) Å, $b$ = 26.426(12) Å, $c$ = 7.039(4) Å, $V$ = 7.039(4) Å$^3$, space group $R3$, $Z$ = 9, a total of 8174 reflections were collected in the range 1.54 to 25.00°. Of these, 2311 were independent; for the observed data, $wR2$ = 0.0799, $R1$ = 0.0744.

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