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Borohydride-Mediated Radical Addition Reactions of Organic Iodides to Electron-Deficient Alkenes

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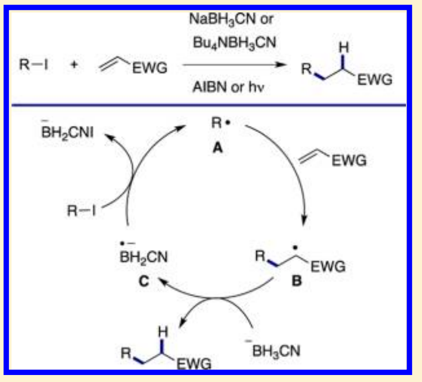
S Supporting Information

ABSTRACT: Cyanoborohydrides are efficient reagents in the reductive addition reactions of alkyl iodides and electron-deficient olefins. In contrast to using tin reagents, the reaction took place chemoselectively at the carbon−iodine bond but not at the carbon−bromine or carbon−chlorine bond. The reaction system was successfully applied to three-component reactions, including radical carbonylation. The rate constant for the hydrogen abstraction of a primary alkyl radical from tetrabutylammonium cyanoborohydride was estimated to be $<1 \times 10^4$ M^{-1} s^{-1} at 25 °C by a kinetic competition method. This value is 3 orders of magnitude smaller than that of tributyltin hydride.

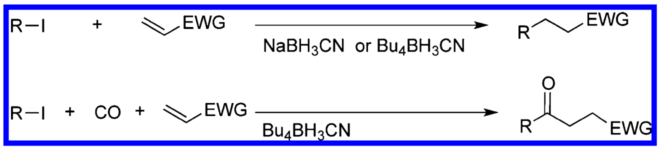


INTRODUCTION

The tremendous development of radical chemistry during the past three decades has led to some very efficient methods for the synthesis of biologically active compounds.[1] This development could not have been attained without the use of tin reagents that possess an impressively broad applicability. Recently, hydrogen atom donors for carbon radical reductions, silyl hydrides, germyl hydrides, thiols, and phosphite have been employed in reductive chain reactions.[2]

Whereas borohydrides are recognized as useful reagents for hydride sources (H^-), borohydrides are rarely used as radical hydrogen donors ($H^\bullet$). In 1973, Barltrop and Bradbury reported the photoreductions of iodobenzene, bromobenzene, and chlorobenzene by sodium borohydride via radical chain mechanisms to give benzene.[3,4] In a similar case, but with Bu_3PBH_2Ph, Roberts reported that the reaction of butyl iodide with ethyl acrylate in the presence of a radical initiator afforded the reductive addition product ethyl heptanoate in moderate yield (50%).[5,6] Later, Kurata and co-workers also reported the reductive macrocyclization of ω-iodoacrylates using sodium cyanoborohydride.[7] The total chain mechanism was not clear at that stage, but they advocated a radical mechanism in which borohydride reagents served as the hydrogen donor to an electrophilic radical. In pursuit of a potential substitute for tin hydride, we envisioned that radical methodologies based on borohydride as the hydrogen donor would have great potential and would be quite useful. In our preliminary communication,[8] we reported that the reductive addition of alkyl radicals to electron-deficient olefins[9,10] and the related carbonylation reactions proceeded in the presence of cyanoborohydride reagents as radical mediators (Scheme 1). We also reported the radical hydroxymethylation of alkyl iodides with CO[11] or HCHO.[12] In this article, we provide the full scope and limitations of reductive alkyl radical addition to electron-deficient olefins in the presence of cyanoborohydride reagents. It should be noted that recent work has shown that NHC−boranes (N-heterocyclic carbene−boranes) can act as useful radical mediators[13] and trialkylborane (alkylcatecholborane)−water (alcohol) can serve as hydrogen to carbon radicals.[14]

Scheme 1. Borohydride-Based Giese Reaction and the Related Radical Carbonylation



RESULTS AND DISCUSSION

We examined the reaction of 1-iodooctane (**1a**) with ethyl acrylate (**2a**) as a model reaction under a variety of reaction conditions (Table 1). When a mixture of **1a**, **2a** (1.5 equiv), and $NaBH_4$ in ethanol was irradiated with a 500 W xenon lamp using a Pyrex flask for 3 h under argon, the expected addition product **3aa** was obtained in 10% yield, in which the simple reduction of **1a** became a predominant reaction course (entry 1). The reaction using Bu_4NBH_4 in benzene resulted in the hydride reduction of **1a**, and no Giese product was formed (entry 2). Interestingly, however, the use of $NaBH_3CN$ and Bu_4NBH_3CN increased the yield of **3aa** (entries 3 and 4). In

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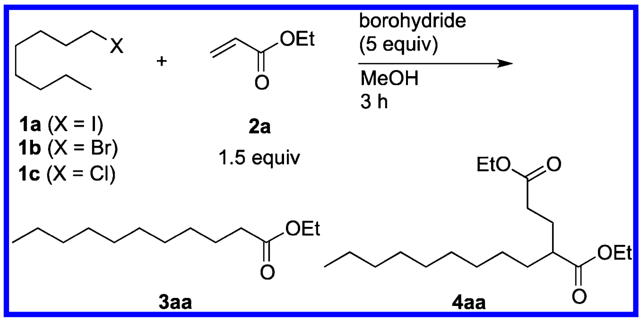
Table 1. Optimization of Reaction Conditions[a]



entry	1	borohydride	solvent	conditions	yield, %[b] 3aa	4aa
1	**1a**	$NaBH_4$	EtOH	Xe, Pyrex	10	0
2[c]	**1a**	Bu_4NBH_4	C_6H_6	Xe, Pyrex	0	0
3	**1a**	$NaBH_3CN$	MeOH	Xe, Pyrex	75	9
4	**1a**	Bu_4NBH_3CN	MeOH	Xe, Pyrex	66	16
5	**1a**	$NaBH_3CN$	MeOH	V-65, reflux	72	14
6	**1a**	$NaBH_3CN$	MeOH	AIBN, reflux	74	10
7	**1a**	$NaBH_3CN$	EtOH	V-65, flow[d]	75	12
8	**1a**	$NaBH_3CN$	THP	V-65, reflux	60	2
9	**1a**	Bu_4NBH_3CN	*i*-PrOH	Xe, Pyrex	69	15
10	**1a**	Bu_4NBH_3CN	C_6H_6	Xe, Pyrex	59	16
11	**1a**	Bu_4NBH_3CN	MeCN	Xe, Pyrex	51	18
12	**1b**	$NaBH_3CN$	MeOH	Xe, Pyrex	0	0
13	**1c**	$NaBH_3CN$	MeOH	Xe, Pyrex	0	0

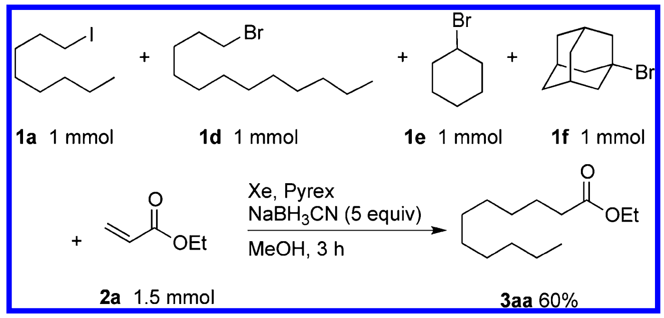
[a]The reaction was conducted on a 1 mmol scale with [**1a**] = 0.5 M, **2a** (1.5 equiv), and borohydride reagent (5.0 equiv). [b]Isolated yield after flash chromatography on SiO_2. [c]Octane was formed quantitatively. [d][**1a**] = 0.1 M, **2a** (1.6 equiv), and $NaBH_3CN$ (3 equiv); residence time 10 min. For details, see ref 8b.

this reaction, the 1:2 product **4aa** was also formed as a byproduct,[15] but the formation of reduced product was negligible. The thermal reaction conditions using a radical initiator such as V-65 (2,2′-azobis(2,4-dimethylvaleronitrile)) and AIBN (2,2′-azobis(isobutyronitrile)) also gave **3aa** in 72 and 74% yields, respectively (entries 5 and 6), whereas heating to 80 °C without a radical initiator did not allow the reaction. This strongly supported the hypothesis that a radical chain mechanism is involved in this reaction. We found that with this reaction it is possible to reduce the time and the amount of cyanoborohydride under continuous microflow conditions (entry 7).[8b] Some other solvents such as THP, *i*-PrOH, C_6H_6, and MeCN also worked well (entries 8−11).

We also tested bromoalkanes and chloroalkanes as substrates. Interestingly, no reaction took place when the corresponding 1-bromooctane (**1b**) and 1-chlorooctane (**1c**) were used (entries 12 and 13). Thus, in the present Giese-type process iodoalkanes appear to be crucial. To confirm this feature, a mixture of 1-iodooctane (**1a**) and three types of alkyl bromides, **1d−f**, were treated with ethyl acrylate (**2a**) (Scheme 2). As we expected, only **1a** gave the addition products, whereas three bromides remained unchanged.

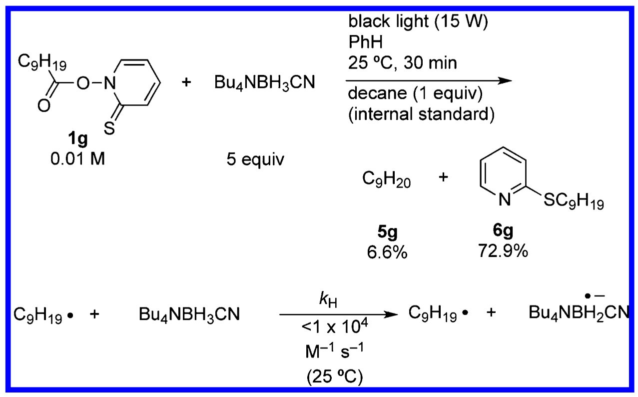
Since the Giese reaction progressed even with a high concentration of borohydride reagents, we expected that cyanoborohydride would have a low level of ability for hydrogen transfer to the alkyl radical. This led us to obtain the rate constant for the reaction of a primary alkyl radical with Bu_4NBH_3CN (k_H) via a kinetic competition method. A solution of the pyridine-2-thioneoxycarbonyl (PTOC) ester

Scheme 2. Chemoselective Reactions



1g, Bu_4NBH_3CN, which was soluble in several organic solvents, and decane (internal standard) in benzene was irradiated with a black light for 30 min. Then the yields of the nonane (**5g**; 6.6%) and 2-nonylthiopyridine (**6g**; 72.9%) were determined by GC analysis of the crude product against an internal standard (Scheme 3). To further validate the analysis, we

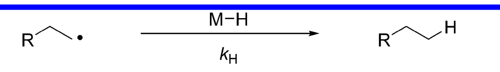
Scheme 3. Estimated Rate Constant for Hydrogen Abstraction from Bu_4NBH_3CN



conduced the control experiment without cyanoborohydride. The reduced product **5g** was obtained in 3.8% yield. The nonyl radical generated from PTOC ester has two competing equations. It can react with the starting PTOC ester to provide thio ether and another nonyl radical (self-trapping) or it can react with cyanoborohydride to provide nonane and a borane radical anion. The rate constant for H transfer (k_H) is then calculated in the usual way from the known rate constant for self-trapping (k_T)[16] and the experimentally determined product ratio, which was corrected for background reduction (3.8%). In this way, the rate constant k_H for the reaction of a primary alkyl radical with Bu_4NBH_3CN was estimated to be $<1 \times 10^4$ M^{-1} s^{-1}. This is lower than the rate constants of tributyltin hydride,[17] tris(trimethylsilyl)silicon hydride,[18] tributylgermanium hydride,[19] and an NHC−borane such as diMeImd-BH_3 (1,3-dimethylimidazol-2-ylidene−borane) (Scheme 4).[20]

Having the identified optimal conditions in hand, we then studied the generality of the borohydride-mediated Giese reaction for a variety of alkyl iodides with electron-deficient olefins (Figure 1). Primary alkyl iodides **1a,h,i,n,o** reacted with ethyl acrylate (**2a**) to give the corresponding esters in good yields (Table 1, entries 1−3, 8, and 9). Under similar conditions, secondary and tertiary iodoalkanes such as **1j−m** reacted with **2a** to give the corresponding addition products in good yields (entries 4−7). The reactions of alkyl iodides **1p,q** were chemoselective and gave the corresponding chlorine- and

Scheme 4. Rate Constants for Hydrogen Abstraction from Metal Hydrides



	Bu_3SnH	$(Me_3Si)_3SiH$	Bu_3GeH	diMeImd-BH_3	Bu_4NBH_3CN
k_H [M^{-1} s^{-1}] (25 °C)	2.3×10^6	3.8×10^5	9.3×10^4	8×10^4	$<1 \times 10^4$

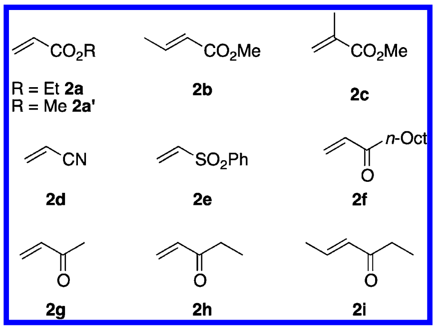


Figure 1. Electron-deficient olefins.

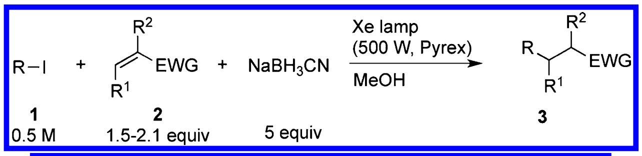
bromine-retaining products **3pa,qa**, respectively (entries 10 and 11). These products can serve as the second radical precursors when the ordinary tin hydride mediated system is applied. On the other hand, aryl iodides such as iodobenzene (**1r**) and 1-iodonaphthalene (**1s**) resulted in a lower yield, in which the reduction course preceded the addition (entries 12 and 13).[21] The reaction of **1a** with methyl crotonate (**2b**) gave the corresponding adduct **3ab** in 67% yield (entry 14), whereas methyl methacrylate (**2c**) gave a poor yield of adduct **3ac** due to the formation of significant amounts of 1:2 and 1:3 products (entry 15). The procedure using sodium cyanoborohydride/MeOH could be applied to the addition of **1a** to acrylonitrile (**2d**) and phenyl vinyl sulfone (**2e**) (entries 16 and 17) (Table 2).

Radical cascade reactions were examined by using hex-5-enyl iodide (**1t**) and cyclopropylmethyl iodide (**1u**) as the substrates (Scheme 5). When the reaction of **1u** with **2a** was carried out, **7ua**, originating from one molecule of **1u** and two molecules of **2a**, was formed as the major product (66% yield, cis/trans = 67/33) (Scheme 5).[22] The formation of **7ua** was rationally explained by the formation of cyclopropylcarbinyl radical **A** and its rapid ring opening to give homoallyl radical **B**,[23] which then undergoes addition to **2a**. The resulting radical **C** is ready to undergo 5-exo cyclization to give **D**, which adds to a second molecule of **2a** and then abstracts hydrogen from cyanoborohydride to give **7ua**.

When the procedure was applied to a radical addition reaction with *α,β*-unsaturated ketones, the reduction hampered the desired radical addition course. To elucidate the extent of the background reduction, we carried out a simple reduction of octyl vinyl ketone (**2f**). Treating **2f** with 1 equiv of $NaBH_3CN$ in MeOH at room temperature for 6 h gave a mixture of 1-undecen-3-ol (17%), 3-undecanone (31%), and 3-undecanol (5%) (Scheme 6). In contrast, Bu_4NBH_3CN did not reduce **2f** effectively under the same conditions.

Thus, the problem surrounding the addition reaction across *α,β*-unsaturated ketones was circumvented by the use of a milder reagent—Bu_4NBH_3CN instead of $NaBH_3CN$. The results are summarized in Table 3. A variety of enones, **2f–i**,

Table 2. Radical Addition Reactions of Alkyl Iodides with Electron-Deficient Olefins using $NaBH_3CN$



entry	1	2	3	yield[a]
1	1a	2a	3aa	75%
2	1h	2a	3ha	51%
3	1i	2a	3ia	71%
4	1j	2a	3ja	70%
5	1k	2a	3ka	71%
6	1l	2a	3la	68%
7	1m	2a	3ma	73%
8	1n	2a	3na	41%
9	1o	2a	3oa	70%
10	1p	2a	3pa	67%
11	1q	2a	3qa	67%
12	1r	2a	3ra	39%
13	1s	2a	3sa	21%
14	1a	2b	3ab	67%
15	1a	2c	3ac	21%[b]
16	1a	2d	3ad	69%[c]
17	1a	2e	3ae	69%

[a]Isolated yield after flash chromatography on SiO_2. [b]Products containing two and three molecules of **2c** were also formed. [c]**2d** (3 equiv), 20 h.

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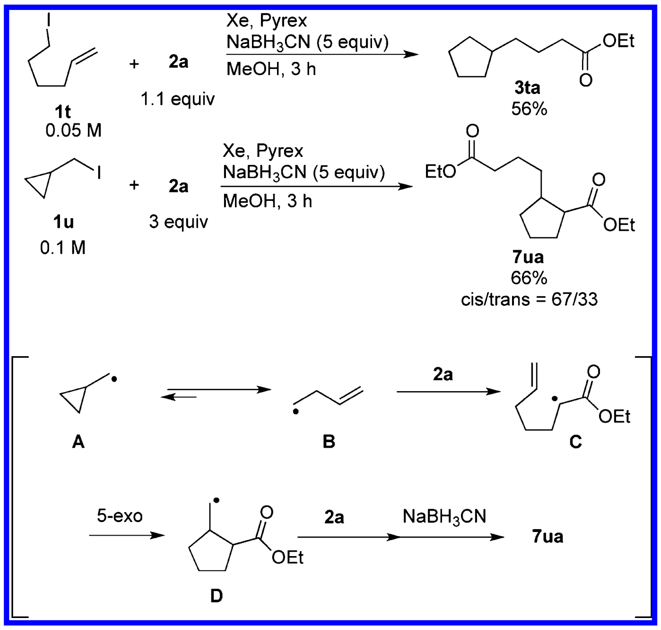
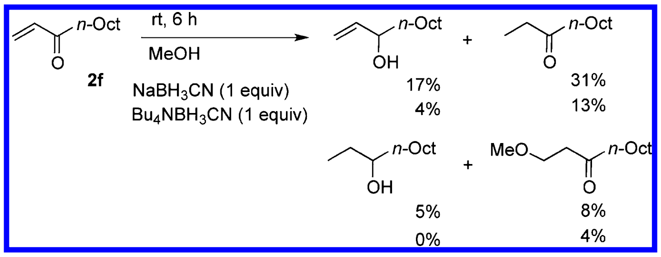
Scheme 5. Tandem Radical Processes



Scheme 6. Background Reduction

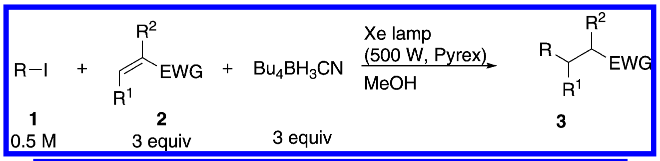


reacted with primary alkyl iodides **1a,h,p,v** smoothly to form the corresponding unsymmetrical ketones (entries 1−7). The reaction of secondary and tertiary alkyl iodides **1j**, **k**, and **m** with **2h** also worked well (entries 8−10).

We also applied a radical reaction system using Bu_4NBH_3CN−AIBN for the corresponding three-component coupling reaction with the incorporation of CO, for which tributyltin hydride or TTMSS was used in the original processes.[24] When a mixture of 1-iodooctane (**1a**), CO, and methyl acrylate (**2a′**) (2 equiv) with Bu_4NBH_3CN was subjected to the radical reaction conditions, 1,4-dicarbonyl compound **8aa′** was obtained in 62% yield (Table 4, entry 1). Similarly, the reaction of secondary and tertiary alkyl iodides, CO, and acrylate gave the corresponding three-component coupling product. The reaction using ethyl vinyl ketone (**2h**) with 1-iodoheptane (**1w**) took place to give 1,4-diketone **8wh** in 51% yield.

Mechanistic Insight. Corey employed sodium borohydride in the catalytic tin hydride reduction of various alkyl halides,[25] and Stork employed sodium cyanoborohydride as a milder reagent.[26] The role of borohydride reagent in these studies is the conversion of tributyltin halides, formed during the course of the reaction, to tributyltin hydride. In the present borohydride-mediated Giese reaction system, the generated nucleophilic alkyl radical smoothly adds to an electron-deficient olefin, such as methyl acrylate, to give an α-carbonyl radical,[27] which would abstract hydrogen directly from a cyanoborohydride anion to give the product and a cyanoborane radical anion ($BH_2CN^{\bullet-}$). In the photoreaction system using the

Table 3. Radical Addition Reactions of Alkyl Iodides with Enones using Bu_4NBH_3CN



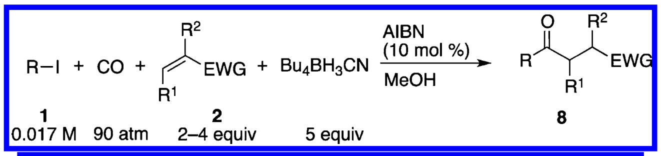
entry	1	2	3	yield[a]
1[b]	1a	2g	3ag	56%
2	1a	2h	3ah	67%
3	1v	2h	3vh	73%
4	1v	2f	3vf	67%
5	1a	2i	3ai	66%
6	1h	2h	3hh	69%
7	1p	2h	3ph	65%
8	1j	2h	3jh	48%
9	1k	2h	3kh	66%
10	1m	2h	3mh	55%

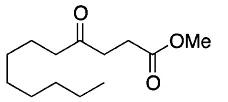
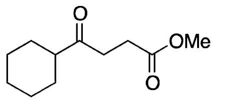
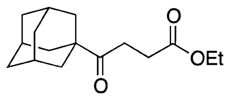
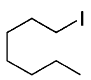
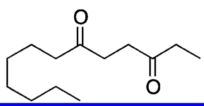
[a]Isolated yield after flash chromatography on SiO_2. [b]**2g** (10 equiv), Bu_4NBH_3CN (5 equiv).

PTOC ester **1g** and acrylonitrile in the presence of Bu_4NBH_3CN, the Giese addition product **3gd** was obtained in 9% yield along with group transfer product **9gd** (14%). As a control reaction, we tried the reduction of **9gd** in the presence of Bu_4NBH_3CN, but after 12 h, no reduction product was observed (Scheme 7). These results supported that the mechanism involves a direct hydrogen transfer to adduct radical rather than an indirect mechanism via an initially formed atom or group transfer adduct.

To gain further insight into the hydrogen delivery step, we carried out theoretical calculations using the Gaussian program. All calculations were performed at the BHandHLYP/6-311+G** level (Figure 2).[28] After complexation hydrogen abstraction of the α-ester radical ($CH_3OCOCH_2^{\bullet}$) from cyanoborohydride is quite smooth (activation energy 29.1 kJ mol^{-1}). On the other hand, the activation energy for hydrogen abstraction of ethyl radical from cyanoborohydride (60.7 kJ mol^{-1}) is twice that of the α-ester radical. This would be rationalized by the polar effect[29] that the nucleophilic cyanoborohydride anion would react with electrophilic α-ester radical more favorably. It is known that the resulting cyanoborane radical anion exhibits a nucleophilic character (Figure 3).[30]

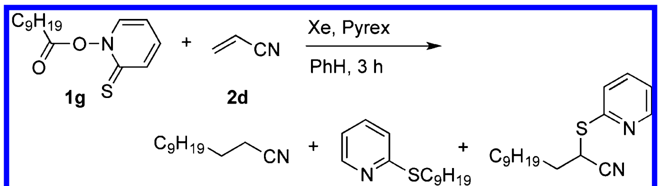
Table 4. Three-Component Coupling Reactions



entry	1	2	3		yield[a]
1	1a	2a'		8aa'	62%
2	1j	2a'		8ja'	60%
3	1m	2a		8ma	54%
4	 1w	2h		8wh	51%

[a]Isolated yield after flash chromatography on SiO_2.

Scheme 7. Control Experiment



	3gd	6g	9gd
Bu_4NBH_3CN (2 equiv)	9%	13%	14%
none	0%	12%	28%

Taking these results into consideration, we proposed a reaction mechanism for the cyanoborohydride-mediated Giese reaction (Scheme 8). Radical initiation generates the alkyl radical **A**, which adds to the electron-deficient alkene to give radical **B**. **B** abstracts hydrogen from cyanoborohydride to give the product.[31] The resulting cyanoborane radical anion **C** abstracts iodine atom to give an alkyl radical.[32] Although we do not yet know the rate constants of iodine abstraction from alkyl iodides with BH_2CN radical anion, alkyl radical formation from alkyl bromides with BH_3 radical anion is known to proceed with rate constants on the order of 10^8.[33]

■ CONCLUSION

In conclusion we have demonstrated that the Giese reaction using alkyl iodides as starting materials and cyanoborohydrides as a hydrogen source proceeds well without the use of tin hydride or its precursors. The process can be applied to carbonylative three-component coupling reactions. We have determined the rate constant of H abstraction by primary alkyl radical from tetrabutylammonium cyanoborohydride to be <1 × 10^4 M^{-1} s^{-1} at 25 °C, by the pyridine-2-thioneoxycarbonyl (PTOC) competition kinetic method at a single concentration point. DFT calculations predicted that cyanoborohydride reacts more smoothly with an electrophilic radical than with an ordinary alkyl radical, which is in good agreement with the observation that the adduct radical undergoes quick hydrogen delivery from cyanoborohydride anion, preventing radical polymerization.

■ EXPERIMENTAL SECTION

Instrumentation and Chemicals. ^1H NMR spectra were recorded at 500 or 400 MHz. ^{13}C NMR spectra were recorded at 125 or 100 MHz and referenced to the solvent peak at 77.00 ppm. Melting points were measured in capillaries. HRMS data were obtained by EI using a double-focusing mass spectrometer. Photolysis was carried out using a Pyrex round-bottomed flask and using a 500 W xenon short arc lamp. Thin-layer chromatography (TLC) was performed and visualized by fluorescence quenching under UV light or by staining with *p*-anisaldeyde/AcOH/H_2SO_4/EtOH or $12MoO_3$·H_3PO_4/EtOH. The products were purified by flash chromatography on silica gel and, if necessary, were further purified by recycling preparative HPLC equipped with GPC columns (JAIGEL-1H + JAIGEL-2H columns) using $CHCl_3$ as eluent. EtOH, MeOH, and PhH were dried and purified by standard distillation techniques. Alkyl iodides **1h,i,k,l,p,u** were prepared from the corresponding alcohol. **1o,t,v** were prepared from the corresponding bromides with sodium iodide in dry acetone. **1q** was prepared from 4-bromobenzyl alcohol and 1,5-diiodopentane by the Williamson method using sodium hydride. **2f** was prepared via 1-undecen-3-ol, which was obtained by a Grignard reaction of *n*-octylmagnesium bromide with acrolein, followed by Jones oxidation. Alkenes **2a–e,g–i** were distilled prior to use. Other reagents were commercially available and were used without further purification.

Typical Procedure A (Table 2, Entry 1). Using a magnetic stirring bar, 1-iodooctane (**1a**; 239.5 mg, 1.0 mmol), ethyl acrylate (**2a**; 150.0 mg, 1.5 mmol), $NaBH_3CN$ (311.7 mg, 5.0 mmol), and methanol (2.0 mL) were mixed in a Pyrex 10 mL round-bottomed flask, and then the mixture was irradiated by a xenon arc lamp (500 W) with stirring for 3 h under argon. A saturated ammonium chloride aqueous solution (1 mL) was added to the reaction mixture. The mixture was poured into water (20 mL) and extracted with Et_2O (20 mL × 3). The organic layer was washed with brine and dried over Na_2SO_4 and then filtered and concentrated in vacuo. The residue was purified by flash chromatography on silica gel (gradient from hexane/Et_2O 20/1 to hexane/Et_2O 10/1) to give **3aa** (160.7 mg, 75%).

Typical Procedure B (Table 3, Entry 1). Using a magnetic stirring bar, Bu_4NBH_3CN (311.7 mg, 1.5 mmol), **1a** (118.6 mg, 0.49 mmol), **2h** (127.1 mg, 1.5 mmol), and methanol (1.0 mL) were mixed in a Pyrex 10 mL round-bottomed flask, and then the mixture was irradiated by a xenon arc lamp (500 W) with stirring for 6 h under argon. The solvent was removed under reduced pressure. The residue was purified by flash chromatography on silica gel (hexane/Et_2O 20/1) to give **3ah** (64.9 mg, 67%).

Typical Procedure C (Table 4, Entry 1). Using a magnetic stirring bar, AIBN (8.7 mg, 0.053 mmol), Bu_4NBH_3CN (721.5 mg, 2.56 mmol), **1a** (120.1 mg, 0.5 mmol), **2a′** (170.1 mg, 1.98 mmol), and methanol (30 mL) were mixed in a 100 mL stainless steel autoclave. The autoclave was closed, purged three times with carbon monoxide, pressurized with 90 atm of CO, and then heated at 80 °C for 19 h. Excess CO was discharged at room temperature. A saturated ammonium chloride aqueous solution (10 mL) was added to the reaction mixture. The mixture was poured into water (50 mL) and extracted with Et_2O (3 × 50 mL). The organic layer was washed with brine and dried over Na_2SO_4 and then filtered and concentrated in vacuo. The residue was purified by flash chromatography on silica gel (hexane/AcOEt 30/1) to give **8aa′** (70.3 mg, 62%).

Spectral Data for Compounds. *Ethyl Undecanoate (**3aa**).*[22] Yield: 161 mg (75%). ^1H NMR ($CDCl_3$, 500 MHz): δ 0.88 (t, J = 6.9 Hz, 3H), 1.16–1.38 (m, 17H), 1.55–1.68 (m, 2H), 2.29 (t, J = 7.6 Hz, 2H), 4.12 (q, J = 7.2 Hz, 2H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 14.1, 14.2, 22.6, 25.0, 29.1, 29.2, 29.3, 29.4, 29.5, 31.9, 34.4, 60.1, 173.9. IR (neat): 1739 cm^{-1}. MS (EI; m/z (relative intensity)): 214 (M^+, 9), 169 (24), 101 (69), 88 (100), 73 (51), 70(49), 61 (37), 60 (35), 57 (33), 55 (48).

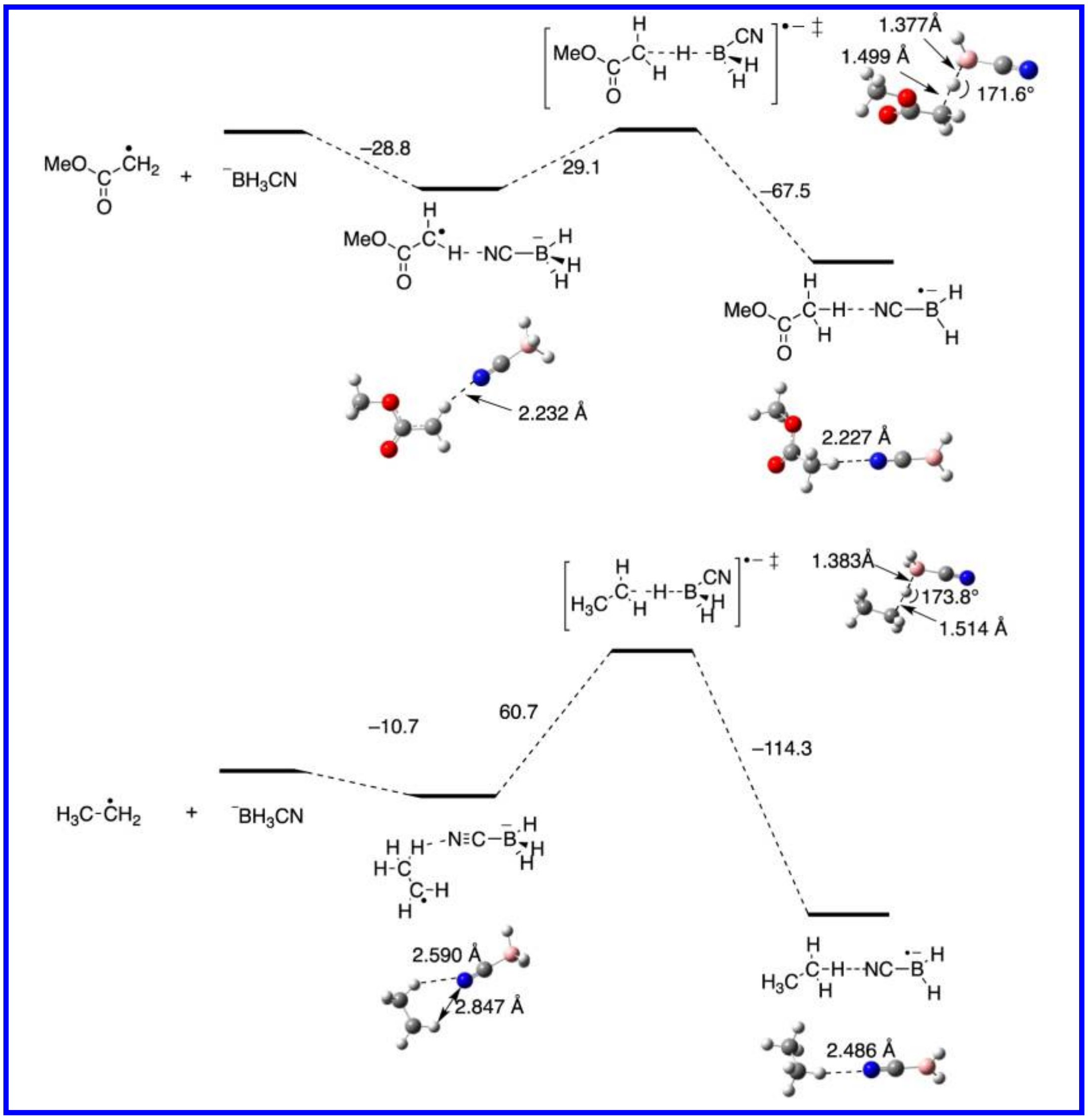


Figure 2. Optimized structures and energy barriers for hydrogen abstraction of α-carbonyl and ethyl radical from cyanoborohydride.

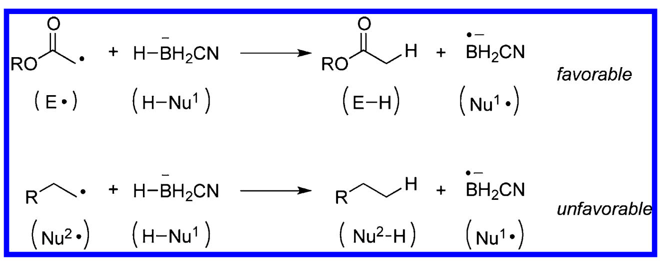
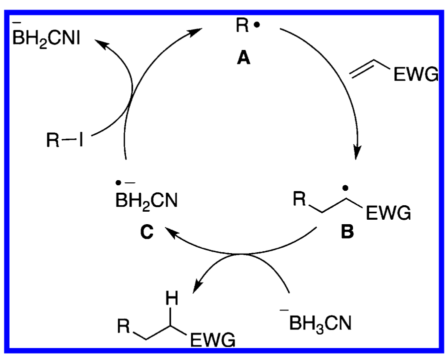


Figure 3. Polar effect for hydrogen abstraction.

*Ethyl 5-Ethylheptanoate (**3ha**).* Yield: 94 mg (51%). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 0.84 (t, J = 7.6 Hz, 6H), 1.18 (sext, J = 6.1 Hz, 1H), 1.22−1.34 (m, 9H), 1.55−1.64 (m, 2H), 2.28 (t, J = 7.6 Hz, 2H), 4.13 (q, J = 7.0 Hz, 2H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 10.8, 14.2, 22.2, 25.2, 32.1, 34.7, 40.1, 60.0, 173.7. IR (neat): 1739 cm^{-1}. MS (EI; m/z (relative intensity)): 186 (M$^+$, 0.3), 157 (12), 123 (13), 111(14), 101(15), 88 (100), 83 (40), 73 (18), 70 (33), 60 (21), 55 (47). HRMS (EI): calcd for $C_{11}H_{22}O_2$ (M$^+$) 186.1620, found 186.1612.

*Ethyl 6-Phenylhexanoate (**3la**).*[34] Yield: 146 mg (71%). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 1.25 (t, J = 7.1 Hz, 3H), 1.33−1.42 (m, 2H), 1.60−1.68 (m, 4H), 2.29 (t, J = 7.6 Hz, 2H), 2.61 (t, J = 7.8 Hz, 2H), 4.12 (q, J = 7.0 Hz, 2H), 7.15−7.31 (m, 5H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 14.1, 24.7, 28.6, 31.0, 34.1, 35.6, 60.0, 125.5, 128.08, 128.14, 142.3, 173.50. IR (neat): 1737 cm^{-1}. MS (EI; m/z (relative intensity)): 175 (M$^+$−OEt, 14), 174 (29), 130 (59), 105 (13), 101 (13), 91 (100), 88 (35), 77 (21), 65 (17).

Scheme 8. Possible Radical Chain Mechanism



*Ethyl 3-Cyclohexylpropionate (**3ja**).*[35] Yield: 130 mg (70%). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 0.81−0.91 (m, 2H), 1.05−1.29 (m, 7H), 1.48−1.55 (m, 2H), 1.60−1.74 (m, 5H), 2.30 (t, J = 8.0 Hz, 2H), 4.12 (q, J = 7.0 Hz, 2H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 14.0, 26.0, 26.3, 31.7, 32.2, 32.8, 37.0, 59.8, 173.8. IR (neat): 1735 cm^{-1}. MS (EI; m/z

(relative intensity)): 184 (M^+, 1), 139 (14), 121 (20), 101 (100), 88 (81), 73 (42), 55 (95).

*Ethyl 4-Butyloctanoate (**3ka**).* Yield: 171 mg (71%). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 0.89 (t, J = 7.1 Hz, 6H), 1.12−1.32 (m, 16H), 1.55−1.62 (m, 2H), 2.24−2.30 (m, 2H), 4.12 (q, J = 7.2 Hz, 2H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 14.0, 14.2, 23.0, 28.6, 28.7, 31.7, 32.9, 36.8, 60.0, 174.0. IR (neat): 1739 cm^{-1}. MS (EI; m/z (relative intensity)): 228 (M^+, 2), 183 (16), 141 (55), 129 (57), 101 (100), 88 (81), 85 (63), 83 (62), 73 (69), 71 (69), 70 (59), 57 (75), 55 (85). HRMS (EI): calcd for $C_{14}H_{28}O_2$ (M^+) 228.2089, found 228.2083.

*Ethyl 4-Methyl-6-phenylhexanoate (**3la**).* Yield: 169 mg (68%). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 0.95 (d, J = 5.5 Hz, 3H), 1.25 (t, J = 5.5 Hz, 3H), 1.42−1.54 (m, 3H), 1.59−1.67 (m, 1H), 1.68−1.78 (m, 1H), 2.21−2.38 (m, 2H), 2.54−2.70 (m, 2H) 4.12 (q, J = 7.2 Hz, 2H), 7.14−7.20 (m, 3H), 7.24−7.30 (m, 2H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 14.2, 19.2, 31.8, 32.0, 32.1, 33.3, 38.5, 60.2, 125.6, 128.3, 128.3, 142.7, 174.0. IR (neat): 1736 cm^{-1}. MS (EI; m/z (relative intensity)): 234 (M^+, 3), 144 (20), 105 (22), 101 (24), 91 (100), 88 (50), 73 (29). HRMS (EI): calcd for $C_{15}H_{22}O_2$ (M^+) 234.1620, found 234.1624.

*Ethyl 3-(Adamantan-1-yl)propionate (**3ma**).*[36] Yield: 173 mg (73%). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 1.26 (t, J = 7.1 Hz, 3H), 1.37−1.49 (m, 7H), 1.58−1.65 (m, 3H), 1.66−1.74 (m, 3H), 1.95 (m, 3H), 2.22−2.28 (m, 2H) 4.12 (q, J = 7.2 Hz, 2H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 14.1, 28.1, 28.4, 31.8, 37.0, 38.9, 41.9, 60.1, 174.6. IR (neat): 1738 cm^{-1}. MS (EI; m/z (relative intensity)): 236 (M^+, 34), 191 (33), 135 (100), 107 (39), 93 (51), 91 (40), 79 (54), 67 (31).

*Ethyl 4-(Trimethylsilyl)butanoate (**3na**).* Yield: 76 mg (41%). ^{1}H NMR ($CDCl_3$, 500 MHz): δ −0.01 (s, 9H), 0.48−0.54 (m, 2H), 1.26 (t, J = 7.1 Hz, 3H), 1.59−1.67 (m, 2H), 2.31 (t, J = 7.3 Hz, 2H), 4.13 (q, J = 7.2 Hz, 2H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ −1.8, 14.2, 16.4, 19.8, 38.0, 60.1, 173.7. IR (neat): 1738 cm^{-1}. MS (EI; m/z (relative intensity)): 143 (M^+−OEt, 4), 117 (45), 101 (11), 73 (100), 59 (11). HRMS (EI): calcd for $C_9H_{20}O_2Si$ (M^+) 188.1233, found 188.1232.

*Ethyl 5,5-Diethoxypentanoate (**3oa**).*[37] Yield: 153 mg (70%). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 1.20 (t, J = 7.1 Hz, 6H), 1.25 (t, J = 7.1 Hz, 3H), 1.61−1.74 (m, 4H), 2.33 (t, J = 7.3 Hz, 2H), 3.45−3.53 (m, 2H), 3.61−3.68 (m, 2H), 4.13 (q, J = 7.2 Hz, 2H), 4.49 (t, J = 5.5 Hz, 1H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 14.1, 15.1, 20.1, 32.8, 33.8, 60.0, 60.6, 102.4, 173.3. IR (neat): 1737 cm^{-1}. MS (EI; m/z (relative intensity)): 173 (M^+ − OEt, 6), 127 (11), 103 (11), 99 (16), 97 (32), 85 (100), 75 (11), 73 (13), 70 (22), 57 (46).

*Ethyl 11-Chloroundecanoate (**3pa**).* Yield: 163 mg (67%). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 1.20−1.34 (m, 10 H), 1.25 (t, J = 7.1 Hz, 3H), 1.36−1.46 (m, 2H), 1.56−1.66 (m, 2H), 1.76 (quint, J = 7.1 Hz, 2H), 2.28 (t, J = 7.6 Hz, 2H), 3.52 (t, J = 6.7 Hz, 2H), 4.12 (q, J = 7.0 Hz, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 14.2, 24.9, 26.8, 28.8, 29.0, 29.1, 29.2, 29.3, 32.5, 34.2, 45.0, 60.0, 173.7. IR (neat): 1737 cm^{-1}. MS (EI; m/z (relative intensity)): 248 (M^+, 1), 205 (12), 203 (21), 115 (14), 101 (64), 88 (100), 83 (22), 73 (41), 70 (47), 60 (45), 57 (27), 55 (68). HRMS (EI): calcd for $C_{13}H_{25}{}^{35}ClO_2$ (M^+) 248.1543, found 248.1546.

*Ethyl 8-((4-Bromobenzyl)oxy)octanoate (**3qa**).* Yield: 149 mg (67%). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 1.25 (t, J = 7.1 Hz, 3H), 1.28−1.40 (m, 6H), 1.55−1.66 (m, 4H), 2.28 (t, J = 7.6 Hz, 2H), 3.44 (t, J = 6.6 Hz, 2H), 4.12 (q, J = 7.2, 2H), 4.43 (s, 2H), 7.16−7.24 (m, 2H), 7.42−7.48 (m, 2H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 14.4, 24.8, 25.9, 28.9, 29.0, 29.5, 34.2, 60.0, 70.4, 71.9, 121.1, 129.10, 131.3, 137.6, 173.6. IR (neat): 1735 cm^{-1}. MS (EI; m/z (relative intensity)): 356 (M^+, 2), 277 (18), 207 (15), 185 (13), 171 (100), 169 (74), 125 (42), 101 (58), 97 (34), 90 (31), 88 (38), 55 (50). HRMS (EI): calcd for $C_{17}H_{25}{}^{79}BrO_3$ (M^+) 356.0987, found 356.0991.

*Methyl 3-Methylundecanoate (**3ab**).*[22] Yield: 151 mg (67%).^{1}H NMR ($CDCl_3$, 500 MHz): δ 0.88 (t, J = 6.9 Hz, 3H), 0.93 (d, J = 6.4 Hz, 3H), 1.13−1.35 (m, 14H), 1.88−1.99 (m, 1H), 2.10 (dd, J = 14.7, 7.8 Hz, 1H), 2.30 (dd, J = 14.7, 6.0 Hz, 1H), 3.66 (s, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 14.1, 19.7, 22.7, 26.9, 29.3, 29.6, 29.7, 30.3, 31.9, 36.7, 41.7, 51.3, 173.8. IR (neat): 1742 cm^{-1}. MS (EI; m/z (relative intensity)): 214 (M^+, 6), 183 (14), 157 (11), 101 (47), 74 (100), 69 (28), 59 (26).

*Methyl 2-Methylundecanoate (**3ac**).*[22] Yield: 44 mg (21%).^{1}H NMR ($CDCl_3$, 500 MHz): δ 0.88 (t, J = 7.1 Hz, 3H), 1.14 (d, J = 6.9 Hz, 3H), 1.20−1.33 (m, 14H), 1.34−1.45 (m, 1H), 1.59−1.70 (m, 1H), 2.43 (sext, J = 7.0, 7.0 Hz, 1H), 3.67 (s, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 14.1, 17.0, 22.7, 27.2, 29.3, 29.47, 29.49, 29.53, 31.9, 33.8, 39.4, 51.4, 177.4. IR (neat): 1741 cm^{-1}. MS (EI; m/z (relative intensity)): 214 (M^+, 5), 157 (17), 143 (13), 101 (57), 89 (13), 88 (100), 71 (12), 69 (23), 59 (23), 57 (48), 55 (40).

*Undecanenitrile (**3ad**).*[38] Yield: 95 mg (69%). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 0.89 (t, J = 6.9 Hz, 3H), 1.21−1.37 (m, 12H), 1.38−1.48 (m, 2H), 1.66 (quint, J = 7.5 Hz, 2H), 2.33 (t, J = 7.3 Hz, 2H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 14.0, 17.0, 22.6, 25.3, 28.6, 28.7, 29.1, 29.2, 29.4, 31.8, 119.7. IR (neat): 2926, 2247 cm^{-1}. MS (EI; m/z (relative intensity)): 152 (M^+ − CH_3, 4), 138 (21), 124 (53), 110 (78), 96 (94), 82 (100), 69 (82), 57 (89), 55 (97).

*(Decane-1-sulfonyl)benzene (**3ae**).*[36] Yield: 196 mg (69%). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 0.87 (t, J = 6.9 Hz, 3H), 1.20−1.38 (m, 14H), 1.66−1.75 (m, 2H), 3.06−3.11 (m, 2H), 7.54−7.59 (m, 2H), 7.63−7.68 (m, 1H), 7.89−7.93 (m, 2H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 13.9, 22.5, 28.1, 28.8, 29.0, 29.2, 31.7, 56.08, 56.13, 127.9, 129.06, 129.08, 133.5, 139.1.

*Ethyl 4-Cyclopentylbutyrate (**3ta**).* Yield: 54 mg (56%). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 1.01−1.13 (m, 2H), 1.26 (t, J = 7.1 Hz, 3H), 1.29−1.35 (m, 2H), 1.44−1.67 (m, 6H), 1.68−1.80 (m, 3H), 2.29 (t, J = 7.6 Hz, 2H), 4.13 (q, J = 7.2 Hz, 2H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 14.2, 24.2, 25.1, 32.6, 34.6, 35.6, 39.8, 60.1, 173.9. IR (neat): 1738 cm^{-1}. MS (EI; m/z (relative intensity)): 184 (M^+, 1), 141 (33), 121 (35), 101 (45), 88 (100), 70 (55), 60 (52), 55 (52). HRMS (EI): calcd for $C_{11}H_{20}O_2$ (M^+) 184.1463, found 184.1457.

*2-(3-(Ethoxycarbonyl)propyl)cyclopentanecarboxylic Acid Ethyl Ester (**7ua**).* Obtained as a cis/trans isomer mixture in a 67/33 ratio, as determined by GC analysis of the crude reaction mixture before being submitted to chromatographic separation. Yield: 87 mg (66%). The cis and trans isomers of **7ua** were separated using a preparative HPLC. Cis isomer: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.19−1.28 (m, 7H), 1.33−1.49 (m, 2H), 1.50−1.74 (m, 3H), 1.75−1.98 (m, 4H), 2.02−2.12 (m, 1H), 2.21−2.34 (m, 2H), 2.78−2.85 (m, 1H), 4.06−4.17 (m, 4H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 14.2, 14.3, 23.8, 24.0, 28.4, 30.6, 31.0, 34.5, 43.4, 47.5, 59.8, 60.2, 173.6, 175.4; IR (neat) 1733 cm^{-1}; MS (EI; m/z (relative intensity)) 211 (M^+ − OEt, 50), 183 (30), 169 (69), 136 (55), 119 (42), 114 (53), 95 (100), 73 (41), 67 (67), 55 (51); HRMS (EI): calcd for $C_{14}H_{24}O_4$ (M^+) 256.1675, found 256.1683. Trans isomer: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.16−1.35 (m, 8H), 1.47−1.74 (m, 5H), 1.78−1.97 (m, 3H), 2.05−2.15 (m, 1H), 2.23−2.35 (m, 3H), 4.09−4.18 (m, 4H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 14.2, 14.3, 23.6, 24.7, 30.3, 32.5, 34.5, 34.8, 44.0, 50.4, 60.18, 60.20, 173.6, 176.6; IR (neat) 1732 cm^{-1}; MS (EI; m/z (relative intensity)) 211 (M^+ − OEt, 57), 182 (58), 169 (61), 136 (100), 95 (97), 67 (72), 55 (48); HRMS (EI) calcd for $C_{14}H_{24}O_4$ (M^+) 256.1675, found 256.1669.

*2-Dodecanone (**3ag**).*[40] Yield: 65 mg (67%). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 0.88 (t, J = 6.9 Hz, 3H), 1.25−1.38 (m, 14H), 1.50−1.62 (m, 2H), 2.13 (s, 3H), 2.41 (t, J = 7.6 Hz, 2H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 14.1, 22.6, 23.8, 29.1, 29.3, 29.36, 29.43, 29.5, 29.8, 31.9, 43.8, 209.3. IR (neat): 1719 cm^{-1}. MS (EI; m/z (relative intensity)): 184 (M^+, 8), 85 (20), 82 (12), 71 (44), 58 (100), 55 (24).

*3-Tridecanone (**3ah**).*[39] Yield: 53 mg (56%). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 0.88 (t, J = 6.9 Hz, 3H), 1.05 (t, J = 7.3 Hz, 3H), 1.20−1.34 (m, 14H), 1.52−1.61 (m, 2H), 2.39 (t, J = 7.3 Hz, 2H), 2.42 (q, J = 7.3, 2H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 7.8, 14.1, 22.7, 24.0, 29.27, 29.29, 29.4, 29.5, 29.6, 31.9, 35.8, 42.4, 212.0. IR (neat): 1718 cm^{-1}. MS (EI; m/z (relative intensity)): 198 (M^+, 2), 169 (47), 95 (17), 85 (45), 72 (100), 57 (97), 55 (27).

*7-(1,3-Dioxan-2-yl)-3-heptanone (**3vh**).* Yield: 76 mg (73%). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 1.04 (t, J = 7.4 Hz, 3H), 1.30−1.43 (m, 3H), 1.55−1.63 (m, 4H), 2.01−2.12 (m, 1H), 2.37−2.44 (m, 4H), 3.71−3.79 (m, 2H), 4.06−4.12 (m, 2H), 4.5 (t, J = 5.0 Hz, 1H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 7.7, 23.5, 23.6, 25.7, 34.8, 35.7, 42.1, 66.8, 102.0, 211.5 (two signals are accidentally superimposed on each other). IR (neat): 1714 cm^{-1}. MS (EI; m/z (relative intensity)): 200

(M^+, 4), 128 (44), 113 (15), 87 (100), 67 (42), 57 (60). HRMS (EI): calcd for $C_{11}H_{20}O_3$ (M^+) 200.1412, found 200.1404.

*1-(1,3-Dioxan-2-yl)-5-tridecanone (**3vf**).* Yield: 95 mg (67%). ^1H NMR ($CDCl_3$, 500 MHz): δ 0.88 (t, J = 7.1 Hz, 3H), 1.20−1.43 (m, 13H), 1.51−1.63 (m, 6H), 2.00−2.12 (m, 1H), 2.34−2.42 (m, 4H), 3.71−3.79 (m, 2H), 4.05−4.12 (m, 2H), 4.51 (t, J = 5.3 Hz, 1H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 14.0, 22.6, 23.5, 23.6, 23.8, 25.8, 29.1, 29.2, 29.3, 31.8, 34.9, 42.6, 42.8, 66.8, 102.0, 211.3. IR (KBr): 1705 cm^{-1}. MS (EI; m/z (relative intensity)): 284 (M^+, 1), 128 (49), 110 (12), 87 (100), 57 (21). HRMS (EI): calcd for $C_{17}H_{32}O_3$ (M^+) 284.2351, found 284.2350.

*5-Methyl-3-tridecanone (**3ai**).*[41] Yield: 70 mg (66%). ^1H NMR ($CDCl_3$, 500 MHz): δ 0.83−0.92 (m, 6H), 1.05 (t, J = 7.3 Hz, 3H), 1.10−1.35 (m, 14H), 1.94−2.06 (m, 1H), 2.20 (dd, J = 15.6, 7.8 Hz, 1H), 2.34−2.48 (m, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 7.8, 14.1, 19.9, 22.6, 27.0, 29.27, 29.30, 29.6, 29.8, 31.9, 36.4, 37.0, 49.9, 211.7. IR (neat): 1716 cm^{-1}. MS (EI; m/z (relative intensity)): 212 (M^+, 1), 183 (19), 99 (28), 86 (48), 72 (47), 57 (100), 55(21).

*7-Phenyl-2-heptanone (**3hh**).* Yield: 69 mg (69%). ^1H NMR ($CDCl_3$, 500 MHz): δ 1.03 (t, J = 7.3 Hz, 3H), 1.27−1.36 (m, 2H), 1.55−1.66 (m, 4H), 2.34−2.42 (m, 4H), 2.59 (t, J = 7.8 Hz, 2H), 7.12−7.19 (m, 3H), 7.22−7.29 (m, 2H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 7.8, 23.6, 28.8, 31.2, 35.7, 35.8, 42.2, 125.6, 128.2, 128.3, 142.4, 211.6. IR (neat): 3027, 2934, 1714 cm^{-1}. MS (EI; m/z (relative intensity)): 204 (M^+, 1), 186 (23), 175 (19), 130 (23), 91 (100), 85 (26), 71 (18), 57 (76). HRMS (EI): calcd for $C_{14}H_{20}O$ (M^+) 204.1514, found 204.1513.

*13-Chloro-3-tridecanone (**3ph**).* Yield: 74 mg (65%). ^1H NMR ($CDCl_3$, 500 MHz): δ 1.05 (t, J = 7.3 Hz, 3H), 1.20−1.36 (m, 10H), 1.37−1.47 (m, 2H), 1.51−1.62 (m, 2H), 1.76 (quint, J = 7.1 Hz, 2H) 2.36−2.45 (m, 4H), 3.53 (t, J = 6.9 Hz, 2H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 7.8, 23.9, 26.8, 28.8, 29.2, 29.29, 29.31, 29.33, 32.6, 35.8, 42.4, 45.1, 211.9. IR (neat): 1715 cm^{-1}. MS (EI; m/z (relative intensity)): 232 (M^+, 2), 203 (35), 85 (36), 73 (100), 69 (29), 57 (68), 55 (49). HRMS (EI): calcd for $C_{13}H_{25}{}^{35}ClO$ (M^+) 232.1594, found 232.1601.

*1-Cyclohexyl-3-pentanone (**3jh**).*[22] Yield: 40 mg (48%). ^1H NMR ($CDCl_3$, 500 MHz): δ 0.82−0.95 (m, 2H), 1.05 (t, J = 7.3 Hz, 3H), 1.08−1.26 (m, 4H), 1.42−1.50 (m, 2H), 1.60−1.73 (m, 5H), 2.37−2.46 (m, 4H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 7.9, 26.2, 26.5, 31.3, 33.1, 35.8, 37.3, 40.0, 212.1. IR (neat): 1717 cm^{-1}. MS (EI; m/z (relative intensity)): 168 (M^+, 9), 139 (52), 121 (94), 96 (87), 85 (56), 81 (67), 72 (93), 57 (99), 55 (100).

*6-Butyl-3-decanone (**3kh**).* Yield: 70 mg (66%). ^1H NMR ($CDCl_3$, 500 MHz): δ 0.89 (t, J = 6.9 Hz, 6H), 1.05 (t, J = 7.3 Hz, 3H), 1.16−1.40 (m, 14H), 1.49−1.56 (m, 2H), 2.34−2.39 (m, 2H), 2.40 (q, J = 7.3 Hz, 2H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 7.9, 14.1, 23.1, 27.6, 28.81, 33.1, 35.8, 37.0, 39.8, 212.2. IR (neat): 1717 cm^{-1}. MS (EI; m/z (relative intensity)): 183 (M^+ − Et, 32), 165 (14), 140 (33), 109 (26), 85 (89), 72 (64), 57 (100). HRMS (EI): calcd for $C_{14}H_{28}O$ (M^+) 212.2140, found 212.2142.

*1-(Adamantan-1-yl)-3-pentanone (**3mh**).* Yield: 62 mg (55%). ^1H NMR ($CDCl_3$, 500 MHz): δ 1.04 (t, J = 7.4 Hz, 3H), 1.30−1.37 (m, 2H), 1.41−1.48 (m, 6H), 1.57−1.64 (m, 3H), 1.66−1.74 (m, 3H), 1.90−1.97 (m, 3H), 2.31−2.37 (m, 2H), 2.42 (q, J = 7.3 Hz, 2H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 8.0, 28.6, 31.8, 35.8, 36.0, 37.1, 38.0, 42.2, 212.6. IR (neat): 1715 cm^{-1}. MS (EI; m/z (relative intensity)): 220 (M^+, 3), 202 (28), 191 (67), 173 (37), 135 (100), 107 (21), 93 (39), 91 (30), 79 (48), 67 (25), 57 (41). HRMS (EI): calcd for $C_{15}H_{24}O$ (M^+) 220.1827, found 220.1830.

*Methyl 4-Oxododecanoate (**8aa′**).*[24c] Yield: 70 mg (62%). ^1H NMR ($CDCl_3$, 500 MHz): δ 0.88 (t, J = 6.9 Hz, 3H), 1.19−1.33 (m, 10H), 1.53−1.63 (m, 2H), 2.44 (t, J = 7.6 Hz, 2H), 2.59 (t, J = 6.7 Hz, 2H), 2.72 (t, J = 6.7, 2H), 3.68 (s, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 14.0, 22.6, 23.8, 27.7, 29.06, 29.14, 29.3, 31.8, 37.0, 42.8, 51.7, 173.2, 209.0.

*Methyl 4-Oxo-4-cyclohexylbutanoate (**8ja′**).*[24a] Yield: 59 mg (60%). ^1H NMR ($CDCl_3$, 500 MHz): δ 1.10−1.42 (m, 5H), 1.60−1.70 (m, 1H), 1.72−1.81 (m, 2H), 1.82−1.92 (m, 2H), 2.34−2.42 (m, 1H), 2.58 (t, J = 6.6 Hz, 2H), 2.76 (t, J = 6.4 Hz, 2H), 3.67 (s, 3H). ^{13}C NMR (CDCl3, 125 MHz): δ 25.5, 25.8, 27.6, 28.4, 34.9, 50.6, 51.6, 173.3, 211.9.

*Ethyl 4-Oxo-4-(1-adamantyl)butanoate (**8ma**).*[42] Yield: 71 mg (54%). ^1H NMR ($CDCl_3$, 500 MHz): δ 1.25 (t, J = 7.1 Hz, 3H), 1.64−1.72 (m, 3H), 1.72−1.78 (m, 3H), 1.82−1.86 (m, 6H), 2.01−2.08 (m, 3H), 2.55 (t, J = 6.7 Hz, 2H), 2.77 (t, J = 6.3 Hz, 2H), 4.12 (q, J = 7.2 Hz, 2H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 14.1, 27.9, 28.5, 31.0, 36.5, 38.2, 46.1, 60.4, 173.0, 213.7.

*3,6-Tridecanedione (**8wh**).*[43] Yield: 54 mg (51%). ^1H NMR ($CDCl_3$, 500 MHz): δ 0.88 (t, J = 7.1 Hz, 3H), 1.06 (t, J = 7.3 Hz, 3H), 1.27 (br, 8H), 1.56 (br, 2H), 2.45 (t, J = 7.4 Hz, 2H), 2.49 (q, J = 7.9 Hz, 2H), 2.68 (s, 4H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 7.8, 14.0, 22.6, 23.8, 29.0, 29.1, 31.6, 35.6, 35.9, 36.0, 42.9, 209.8, 210.1.

■ ASSOCIATED CONTENT

Supporting Information

Text and figures giving kinetic experiments and calculations, deuterium labeling experiments, DFT calculations, and ^1H and ^{13}C NMR spectra for all 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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