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Hydroxy Chalcogenide-Promoted Morita–Baylis–Hillman Alkylation Reaction: Intermolecular Applications with Alkyl Halides as Electrophiles

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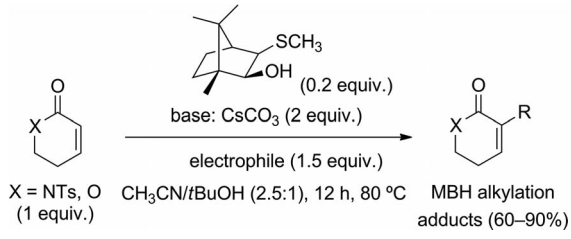
Hydroxysulfides acted as catalysts to promote the Morita–Baylis–Hillman alkylation reaction of cyclohexenones and dihydropyridinones. The procedure worked efficiently with a variety of halides as electrophiles. Side reactions were in competition with the MBH alkylation, but fine-tuning the reaction conditions minimized their occurence.

Introduction

The Morita–Baylis–Hillman reaction (MBH) is an important carbon–carbon bond-forming transformation, in which a reaction occurs between the α-position of an activated alkene and an electrophile under the influence of a catalyst to provide a densely functionalized molecule.[1] In recent years, many groups have expanded the utility of this process with respect to the three essential components.[2] With regard to the substrates, these include acyclic and cyclic alkenes, alkynes, and allenes that are activated by ketone, ester, amide, nitrile, nitro, sulfonate, and phosphate functional groups. Electrophiles are generally aldehydes, activated ketones, and imines (aza-MBH).[3] Activated alkenes can also act as electrophiles to result in dimerization and cross-coupling reactions (Rauhut–Courrier reaction).[4] A few reports account for the use of a limited number of alkyl halides,[5] and there are two instances of the use of epoxides as electrophiles.[6] All of these latter reagents imply that there is an alkylation version of MBH chemistry that is underdeveloped, especially the intermolecular version, as most examples reported to date involve cyclizations of halogen-containing MBH substrates. With regard to the catalyst, the vast majority of published reactions use tertiary amines or phosphines. The chalcogenide-mediated Morita–Baylis–Hillman reaction is an alternative procedure, which mainly involves sulfides and selenides in combination with $TiCl_4$.[7] The use of chiral sulfinylimines in the asymmetric aza-Morita–Baylis–Hillman reaction has also been reported,[8] and cysteine was shown to catalyze a Rauhut–Courier reaction.[9]

In the course of our studies of the MBH reaction, we were interested in exploring alternatives such as the employment of unusual substrates and new organic catalysts. In particular, we believe that the MBH-type alkylation process deserves more attention, as it is an attractive way to produce functionalized molecules that are not attainable by classical MBH methodology. We recently published the unprecedented use of hydroxylsulfides as catalysts to perform the MBH alkylation reaction efficiently under basic conditions.[10] In that work, we used α,β-unsaturated lactams and lactones as the activated alkenes (see Scheme 1).[11]



Scheme 1. MBH reaction of α,β-unsaturated lactams and lactones with different electrophiles.

However, the need for a noncommercial, chiral catalyst was superfluous in this reaction because no stereogenic centers were created. In the present communication, the potential use of other hydroxysulfides as viable catalysts in this intriguing reaction is studied, and the method is applied to cyclohexenones and dihydropyridinones.

Results and Discussion

As starting materials for the present study, we selected cyclohexenones **1a** and **1b** and *N*-protected 2,3-dihydro-4-pyridinones **2a** and **2b**, which were prepared by using a reported procedure.[12] We and others have shown the positive outcome of having hydroxy groups situated at an appropriate distance within the catalyst molecule to accelerate the MBH reaction.[13] Thus, we selected a group of hydroxysulfides for the purpose of comparing their catalytic behavior in the MBH process (see Figure 1). In addition to the cam-

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phor-derived hydroxysulfides **3** and **4**, which were used previously by us[10] and other groups,[14] we employed simple commercial compounds such as **5**–**9**.

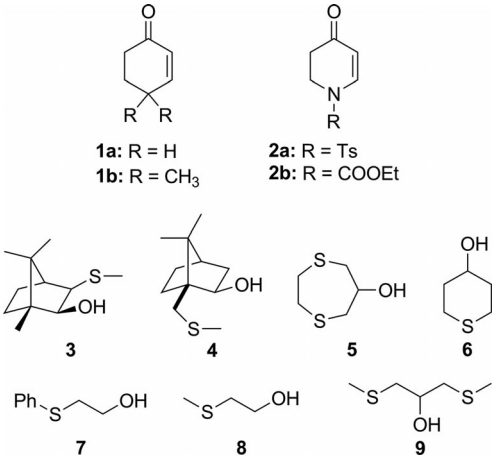
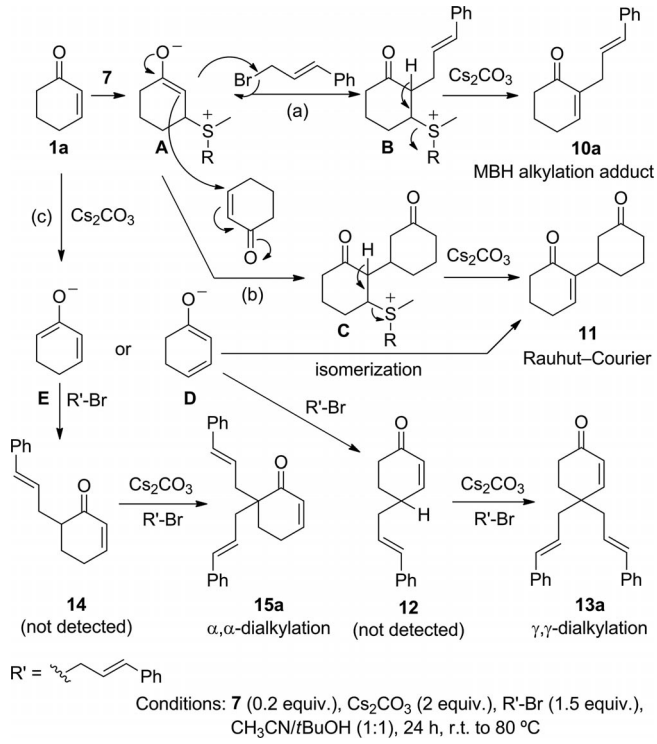


Figure 1. Substrates and catalysts selected for this study.

The first step was to perform the MBH alkylation reaction with 2-cyclohexenone (**1a**) and all of the different hydroxysulfides. In the first attempt, we used catalyst **7** and cinnamyl bromide, which revealed a wide array of secondary reactions (see Scheme 2). Three processes were in competition with each other, and their products were isolated and characterized. Thus, the MBH alkylation reaction gave product **10a** (50%) upon displacement of the bromide atom by **A** to give intermediate **B** and then elimination of the catalyst. In addition, the reaction of intermediate **A** with a second molecule of **1a** gave Rauhut–Courier product **11** (20%) through intermediate **C**. The formation of enolate **D** allowed for a double alkylation at C-4 of the substrate to give **13** (15%) through monoalkylated product **12**, which was not detected (see Table 1, Entry 1). As previously described in the literature, **11** could also be formed from enolate **D** through a conjugate addition to 2-cyclohexenone and shift of the double bond.[15] We checked this possibility by carrying out the reaction of **1a** with Cs_2CO_3 in the absence of the other reagents, and **11** was produced in 99% yield (see Table 1, Entry 2). The dimerization of unsaturated ketones is not a trivial process and has recently received attention.[16] In addition, trace amounts of a different dialkylation product were observed in the spectrum of crude products, which could possibly correspond to compound **15** as a result of the formation of the less favored enolate **E**. After the first attempt, the main conclusion was that we were able to perform the MBH alkylation reaction by using hydroxysulfides, but the conditions needed fine-tuning to improve the yields. We then increased the reaction time and the amount of electrophile to 1.5 equiv. to increase the yield of **10a** to 70% (see Table 1, Entry 4). This attempt also showed the result of performing the reaction from the start at 80 °C as well as employing a 1:1 mixture of CH_3CN/*t*BuOH as the solvent. Under these conditions we reached a 70% yield of **10a** and obtained only a small amount of the dimer **11**. An evaluation of the effect of changing the solvent was carried out (see Table 1, Entries 5–8), in which we showed that by using *t*BuOH, tetrahydrofuran (THF), acetone, or CH_3CN, the MBH product yield was below the one achieved by using the CH_3CN/*t*BuOH (1:1) mixture. When the reaction was extended to 4,4-dimethyl-2-cyclohexenone (**1b**), in which the 4-position was blocked from enolization by the two geminal methyl groups, we were unable to detect the desired MBH product, which was probably because of the steric effects associated with this hindered enone.

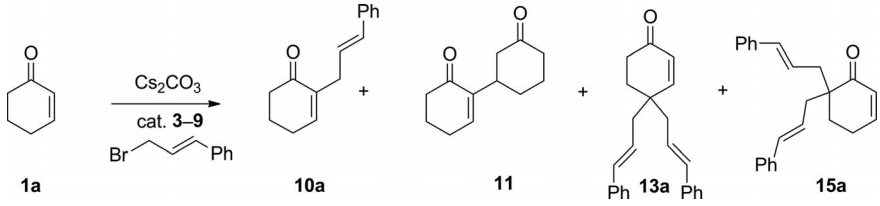


Scheme 2. MBH alkylation and side reactions of cyclohexenone **1a** with cinnamyl bromide.

The conditions that were employed in Entry 4 were then used with the other catalysts (see Table 1, Entries 9–14). Phenylthioethanol (**7**) was the best catalyst among the commercial compounds tested. The performance of compound **3** was slightly below that of **7**, but good results were still obtained (see Table 1, Entry 9). This is the first time that a simple sulfide catalyzed a MBH reaction without the assistance of other additives.

Other electrophiles were then employed to expand the scope of the process (for reaction conditions, see Table 2, Entries 1 and 2). Thus, allyl bromide gave **10b** in good yields of 75–83% (see Table 2, Entries 3–5,) along with small amounts of dimer **11**. In addition, 1-bromo-2-butyne gave a 63% yield of **10c** and 15% of α,α-dialkylated derivative **15c** along with 10% of **11** (see Table 2, Entry 6). The reaction of 2-cyclohexenone with ethyl 2-(bromomethyl)-prop-2-enoate gave product **10d** in 60% yield (see Table 2, Entry 7). Finally, the reactions with methyl iodide and benzyl bromide gave **10e** and **10f** in 65 and 45% yield, respectively (see Table 2, Entries 8 and 9).

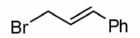
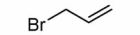
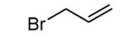
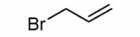
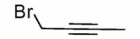
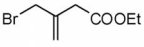
Table 1. Reaction conditions of **1a** with cinnamyl bromide.[a]



Entry	Cat.	R′–Br [equiv.]	Solvent[b]	Temp. [°C]	Time [h]	% Yield[c] 1a	10a	11	13a	15a
1	7	1	2.5:1	r.t.–80	12	10	50	15	15	<5
2	–	–	2.5:1	r.t.–80	12	–	–	99	–	–
3	–	1.5	2.5:1	r.t.–80	12	10	–	60	25	<5
4	7	1.5	1:1	80	24	<5	70	11	10	–
5	7	1.5	*t*BuOH	82	24	10	40	45	–	–
6	7	1.5	THF	67	24	25	30	25	15	<5
7	7	1.5	acetone	57	24	10	55	30	5	–
8	7	1.5	CH_3CN	80	24	10	60	25	5	–
9	3	1.5	1:1	80	24	10	65	11	<5	<5
10	4	1.5	1:1	80	24	10	60	15	<5	<5
11	5	1.5	1:1	80	24	20	–	45	10	<5
12	6	1.5	1:1	80	24	25	–	40	10	<5
13	8	1.5	1:1	80	24	10	58	12	10	<5
14	9	1.5	1:1	80	24	15	–	40	10	<5

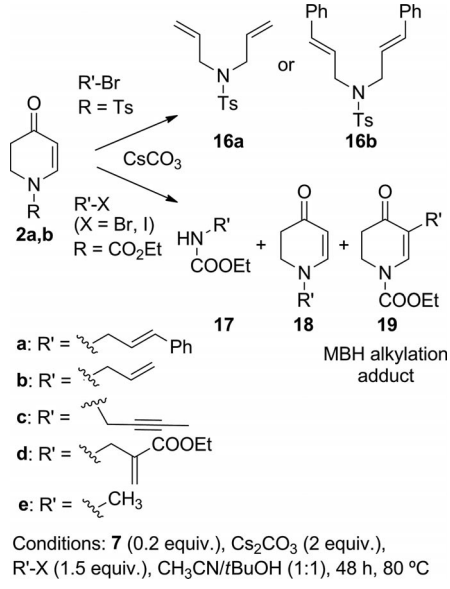
[a] Reagents and conditions for all reactions: Cat. (catalyst, 0.2 equiv.), Cs_2CO_3 (2 equiv.). [b] Ratios correspond to mixtures of CH_3CN/*t*BuOH mixtures. [c] Yield of pure product.

Table 2. Reactions of **1a** with different halides.[a]

Entry	Cat.	R–X	Time [h]	Yield (%)[b] 1a	10	11	13	15
1	7		24	<5	70	11	10	<5
2	**3**		24	10	65	11	<5	<5
3	**3**		24	<5	83	12	–	–
4	**4**		24	<5	80	12	–	–
5	7		24	<5	75	15	–	–
6	7		24	10	63	10	–	15
7	7		24	15	60	15	–	–
8	7	CH_3I	24	<5	65	20	–	–
9	7	$PhCH_2Br$	48	25	45	10	–	–

[a] Reagents and conditions for all reactions: catalyst (0.2 equiv.), Cs_2CO_3 (2 equiv.), CH_3CN/*t*BuOH (1:1), R–X (1.5 equiv.), 80 °C. [b] Yield of pure product.

The second part of the present study involves the use of dihydropyridinones as substrates. These interesting heterocycles have the advantage of avoiding the side reactions that result from enolization. However, our first reaction between compound **2a** and allyl bromide was disappointing, as the only detected reaction product was **16a** (90%), whereas **16b** (89%) was isolated as the only product of the parent reaction with cinnamyl bromide (see Scheme 3). We have not studied in detail a plausible reaction pathway to explain the formation of **16**, but the instability of **2a** under the basic reaction conditions surely causes the ring opening of the dihydropyridinone and a subsequent cascade process to lead to the diallylation of the tosylamide. Thus, we envisioned that changing the protecting group at the nitrogen would possibly reduce the occurrence of these processes and allow for the desired MBH-type reaction. In fact, when **2b** was submitted to the reaction under the optimal conditions (see Table 2, Entry 1) with cinnamyl bromide as the electrophile, most of unreacted starting material **3b** was recovered, so the reaction time was extended to 48 hours, thereby increasing the yield of **19a** to 45% (see Table 3, Entry 1). For byproducts of this reaction, we isolated **18** in 20% yield and



Scheme 3. MBH alkylation reactions of dihydropyridinones **2a** and **2b**.

the open-chain product **17** in 15% yield. The reaction with allyl bromide (see Table 3, Entry 2) gave MBH adduct **19b** in 65% yield, and the amounts of the side products were reduced. The reaction with 1-bromo-2-butyne (see Table 3, Entry 3) afforded **19c** in only 40% yield. On the other hand, ethyl 2-(bromomethyl)prop-2-enoate was not reactive under the conditions (see Table 3, Entry 4). Finally, methyl iodide gave the best results with the isolation of **19e** in 70% yield along with a 25% yield of the side product **18e** (see Table 3, Entry 5). From these results, it is clear that dihydropyridinones are less reactive toward a 1,4-addition than other enones such as cyclohexenones, and this has already been noted by other groups.[17] The carbamate protecting group, which was revealed as critical for the reaction, has the drawback of being unstable under the employed basic conditions, and nucleophilic alkylation products such as **18** are produced.

Table 3. MBH alkylation reaction of **2b** with different electrophiles.[a]

Entry	R′–X [equiv.]	% Yield[b] **2b**	**17**	**18**	**19**
1	**a** (1.5)[c]	10	15	20	45
2	**b** (1.5)[d]	<5	10	15	65
3	**c** (1.5)[e]	20	<5	25	40
4	**d** (1.5)[f]	40	<5	–	–
5	**e** (1.5)[g]	<5	<5	25	70

[a] Reagents and conditions for all reactions: catalyst **7** (0.2 equiv.), Cs_2CO_3 (2 equiv.). CH_3CN/*t*BuOH (1:1), 80 °C, 48 h. [b] Yield of pure product. [c] Cinnamyl bromide. [d] Allyl bromide. [e] 1-Bromo-2-butyne. [f] Ethyl 2-(bromomethyl)prop-2-enoate. [g] Methyl iodide.

Conclusions

In summary, the reactions of a variety of cyclic enones with different electrophiles and hydroxysulfides under MBH conditions have been explored for the first time. This study reveals that hydroxysulfides can be successfully employed as effective catalysts to promote MBH alkylation reactions of cyclic enones. Different side reactions can be avoided by selecting the best reaction conditions for each substrate.

Experimental Section

General Methods: Products **10e**,[18] **10f**,[19] **11**,[20] **16a**,[21] **16b**,[22] **17a**,[23] **17b**,[24] and **18e**.[25] were characterized by comparison with the literature data.

General Procedure: To a stirred mixture of the cyclic enone (1 equiv.) and catalyst **7** (0.2 equiv.) in a mixture of CH_3CN/*t*BuOH (1:1 v/v, 6 mL) were added Cs_2CO_3 (2 equiv.) and the corresponding electrophile (1.5 equiv.). The resulting suspension was stirred at 80 °C. Upon completion of the reaction (as monitored by TLC), the mixture was quenched by filtration through Celite, which was washed with AcOEt (15 mL). The combined organic layers were then concentrated under reduced pressure, and the resulting crude oil was purified by column chromatography on silica gel to afford the desired product.

2-[(2*E*)-3-Phenylprop-2-en-1-yl]cyclohex-2-en-1-one (10a): Following the general procedure (see Table 1, Entry 4), **1a** (100 mg, 1.04 mmol), the catalyst 2-(phenylsulfanyl)ethanol (**7**, 31 mg, 0.20 mmol), Cs_2CO_3 (678 mg, 2.08 mmol), and cinnamyl bromide (307 mg, 1.56 mmol) gave the crude product that was purified by column chromatography (hexane/ethyl acetate, 9:1) to afford **10a** (155 mg, 70%) as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.98–2.02 (m, 2 H, CH_2), 2.35–2.37 (m, 2 H, CH_2), 2.44–2.48 (m, 2 H, CH_2), 3.10 (d, J = 7.0 Hz, 2 H, CH_2), 6.16–6.26 (dt, J = 15.8 Hz, J = 7.0 Hz, 1 H, =CH), 6.40 (d, J = 15.8 Hz, 1 H, =CH), 6.78 (t, J = 4.1 Hz, 1 H, =CH), 7.17–7.36 (m, 5 H, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 23.1 (CH_2), 26.1 (CH_2), 32.8 (CH_2), 38.5 (CH_2), 126.1 (CH), 127.1 (CH), 128.5 (CH), 131.6 (CH), 137.5 (C), 138.4 (C), 146.0 (CH), 199.0 (CO) ppm. IR (NaCl): $\tilde{\nu}$ = 3110, 1680 (C=O) cm^{-1}. MS (ESI): m/z = 213 [M + H]$^+$. $C_{15}H_{16}O$ (212.29): calcd. C 84.87, H 7.60; found C 85.06, H 7.71.

4,4-Bis[(2*E*)-3-phenylprop-2-en-1-yl]cyclohex-2-en-1-one (13a): Following the general procedure (see Table 1, Entry 4), **1a** (100 mg, 1.04 mmol), catalyst **7** (31 mg, 0.20 mmol), Cs_2CO_3 (678 mg, 2.08 mmol), and cinnamyl bromide (307 mg, 1.56 mmol) gave the crude product that was purified by column chromatography (hexane/ethyl acetate, 9:1) to afford **13a** (34 mg, 10%) as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.29–2.41 (m, 6 H, CH_2), 2.64–2.71 (m, 2 H, CH_2), 5.65 (d, J = 10.0 Hz, 1 H, =CH), 6.02–6.10 (m, 3 H, =CH), 6.37 (d, J = 15.8 Hz, 2 H, =CH), 7.17–7.38 (m, 10 H, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 24.5 (CH_2), 38.8 (CH_2), 42.4 (CH_2), 53.6 (C), 125.3 (CH), 126.2 (CH), 127.2 (CH), 127.8 (CH), 128.5 (CH), 132.6 (C), 133.2 (C), 137.4 (CH), 213.9 (CO) ppm. IR (NaCl): $\tilde{\nu}$ = 3065, 3027, 2900, 1707 (C=O) cm^{-1}. $C_{24}H_{24}O$ (328.45): calcd. C 87.76, H 7.37; found C 87.67, H 7.49.

2-Allyl-cyclohex-2-en-1-one (10b): Following the general procedure (see Table 2, Entry 5), **1a** (100 mg, 1.04 mmol), catalyst **7** (31 mg, 0.20 mmol), Cs_2CO_3 (678 mg, 2.08 mmol), and allyl bromide (189 mg, 1.56 mmol) gave the crude product that was purified by column chromatography (hexane/ethyl acetate, 9:1) to afford **10b** (106 mg, 75%) as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.97–2.02 (m, 2 H, CH_2), 2.36–2.37 (m, 2 H, CH_2), 2.42–2.47 (m, 2 H, CH_2), 2.95 (dd, J = 6.7 Hz, J = 1.4 Hz, 2 H, CH_2), 5.05 (dd, J = 14.8 Hz, J = 1.4 Hz, 2 H, CH=CH_2), 5.77–5.86 (m, 1 H, CH=CH_2), 6.74 (t, J = 4.2 Hz, 1 H, =CH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 23.1 (CH_2), 26.1 (CH_2), 33.5 (CH_2), 38.5 (CH_2), 116.2 (CH_2), 135.9 (CH), 138.1 (C), 145.8 (CH), 199.1 (CO) ppm. IR (NaCl): $\tilde{\nu}$ = 2944, 1687 (C=O) cm^{-1}. $C_9H_{12}O$ (136.19): calcd. C 79.37, H 8.88; found C 79.54, H 8.74.

2-(But-2-yn-1-yl)cyclohex-2-en-1-one (10c): Following the general procedure (see Table 2, Entry 6), **1a** (100 mg, 1.04 mmol), catalyst **7** (31 mg, 0.20 mmol), Cs_2CO_3 (678 mg, 2.08 mmol), and 1-bromo-2-butyne (207 mg, 1.56 mmol) gave the crude product that was purified by column chromatography (hexane/ethyl acetate, 20:1) to afford **10c** (97 mg, 63%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.84 (t, J = 2.5 Hz, 3 H, CH_3), 1.99–2.03 (m, 2 H, CH_2), 2.41–2.46 (m, 4 H, CH_2), 3.08–3.10 (m, 2 H, CH_2), 7.13–7.16 (m, 1 H, =CH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 3.5 (CH_3), 19.3 (CH_2), 23.0 (CH_2), 26.0 (CH_2), 38.3 (CH_2), 75.4 (C), 79.3 (C), 135.1 (C), 146.0 (CH), 198.5 (CO) ppm. IR (NaCl): $\tilde{\nu}$ = 3334, 2920, 2218, 1669 (C=O) cm^{-1}. $C_{10}H_{12}O$ (148.20): calcd. C 81.04, H 8.16; found C 80.44, H 8.06.

6,6-Di(but-2-yn-1-yl)cyclohex-2-en-1-one (15c): Following the general procedure (see Table 2, Entry 6), **1a** (100 mg, 1.04 mmol), catalyst **7** (31 mg, 0.20 mmol), Cs_2CO_3 (678 mg, 2.08 mmol), and 1-bromo-2-butyne (207 mg, 1.56 mmol) gave the crude product that was purified by column chromatography (hexane/ethyl acetate,

20:1) to afford **15c** (27 mg, 15%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.76 (t, J = 2.6 Hz, 6 H, CH_3), 2.43 (dd, J = 4.5 Hz, J = 2.4 Hz, 4 H, CH_2), 2.47–2.50 (m, 2 H, CH_2), 2.59–2.60 (m, 2 H, CH_2), 5.78 (dt, J = 9.9 Hz, J = 1.6 Hz, 1 H, =CH), 6.04 (dt, J = 9.9 Hz, J = 3.9 Hz, 1 H, =CH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 3.5 (CH_3), 25.4 (CH_2), 27.7 (CH_2), 37.9 (CH_2), 51.2 (C), 74.8 (C), 78.6 (C), 128.1 (CH), 131.5 (CH), 212.1 (CO) ppm. IR (NaCl): $\tilde{\nu}$ = 3028, 2924, 2861, 2236, 1718 (C=O) cm^{-1}. $C_{14}H_{16}O$ (200.28): calcd. C 83.96, H 8.05; found C 84.16, H 8.15.

Ethyl 2-[(2-Oxocyclohex-3-en-1-yl)methyl]prop-2-enoate (10d): Following the general procedure (see Table 2 Entry 7), **1a** (100 mg, 1.04 mmol), catalyst **7** (31 mg, 0.20 mmol), Cs_2CO_3 (678 mg, 2.08 mmol), and ethyl 2-(bromomethyl)prop-2-enoate (301 mg, 1.56 mmol) gave the crude product that was purified by column chromatography (hexane/ethyl acetate, 20:1) to afford **10d** (130 mg, 60%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.28 (t, J = 7.1 Hz, 3 H, CH_3), 1.96–2.02 (m, 2 H, CH_2), 2.34–2.37 (m, 2 H, CH_2), 2.42–2.46 (m, 2 H, CH_2), 3.22 (s, 2 H, CH_2), 4.18 (q, J = 7.2 Hz, 2 H, CH_2), 5.55 (d, J = 1.4 Hz, 1 H, =CH), 6.21 (t, J = 0.6 Hz, 1 H, =CH), 6.76 (t, J = 4.2 Hz, 1 H, =CH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.2 (CH_3), 23.0 (CH_2), 26.1 (CH_2), 31.3 (CH_2), 38.4 (CH_2), 60.6 (CH_2), 126.5 (CH_2), 137.1 (C), 138.4 (C), 146.8 (CH), 166.9 (COO), 198.5 (CO) ppm. IR (NaCl): $\tilde{\nu}$ = 2924, 1718 (C=O), 1682 (C=O) cm^{-1}. $C_{12}H_{16}O_3$ (208.26): calcd. C 69.21, H 7.74; found C 69.46, H 7.87.

2-Methylcyclohex-2-en-1-one (10e):[18] Following the general procedure (see Table 2, Entry 8), **1a** (100 mg, 1.04 mmol), catalyst **7** (31 mg, 0.20 mmol), Cs_2CO_3 (678 mg, 2.08 mmol), and methyl iodide (221 mg, 1.56 mmol) gave the crude product that was purified by column chromatography (hexane/ethyl acetate, 9:1) to afford **10e** (96 mg, 65%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.69 (d, J = 1.8 Hz, 3 H, CH_3), 1.91 (q, J = 6.5 Hz, 2 H, CH_2), 2.19–2.31 (m, 2 H, CH_2), 2.39 (t, J = 6.5 Hz, 2 H, CH_2), 6.71–6.73 (m, 1 H, =CH) ppm. Compound **10e** is a known compound.[18]

2-Benzylcyclohex-2-en-1-one (10f):[19] Following the general procedure (see Table 2, Entry 9), **1a** (100 mg, 1.04 mmol), catalyst **7** (31 mg, 0.20 mmol), Cs_2CO_3 (678 mg, 2.08 mmol), and benzyl bromide (267 mg, 1.56 mmol) gave the crude product that was purified by column chromatography (hexane/ethyl acetate, 9:1) to afford **10f** (75 mg, 45%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.95–2.01 (m, 2 H, CH_2), 2.33–2.40 (m, 2 H, CH_2), 2.47–2.50 (m, 2 H, CH_2), 3.51 (br. d, J = 1.3 Hz, 2 H, CH_2), 6.55 (t, J = 4.2 Hz, 1 H, =CH), 7.10–7.22 (m, 3 H, ArH), 7.25–7.35 (m, 2 H, ArH) ppm. Compound **10f** is a known product.[19]

Ethyl 3,4-Dihydro-4-oxo-5-[(2*E*)-3-phenylprop-2-en-1-yl]-2*H*-pyridine-1-carboxylate (19a): Following the general procedure (see Table 3, Entry 1) **2b** (90 mg, 0.53 mmol), catalyst **7** (17 mg, 0.11 mmol), Cs_2CO_3 (345 mg, 1.06 mmol), and cinnamyl bromide (158 mg, 0.80 mmol) gave the crude product that was purified by column chromatography (hexane/ethyl acetate, 9:1) to afford **19a** (68 mg, 45%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.34 (t, J = 7.1 Hz, 3 H, CH_3), 2.59 (t, J = 7.2 Hz, 2 H, CH_2), 3.10 (d, J = 6.9 Hz, 2 H, CH_2), 4.01 (t, J = 7.2 Hz, 2 H, CH_2), 4.28 (q, J = 7.1 Hz, 2 H, CH_2), 6.21 (dt, J = 15.8 Hz, J = 7.0 Hz, 1 H, =CH), 6.43 (d, J = 15.8 Hz, 1 H, =CH), 7.20–7.35 (m, 5 H, ArH), 7.75 (s, 1 H, =CH) ppm. ^{13}C NMR [100 MHz, deuterated dimethyl sulfoxide ([D$_6$]DMSO)]: δ = 14.2 (CH_3), 29.7 (CH_2), 35.3 (CH_2), 42.2 (CH_2), 62.8 (CH_2), 116.2 (C), 125.9 (CH_2), 127.0 (CH), 128.3 (CH), 128.5 (CH), 130.4 (CH), 137.0 (C), 140.8 (CH), 152.5 (COO), 192.4 (CO) ppm. IR (NaCl): $\tilde{\nu}$ = 2965, 2929, 1727 (N-CO-O), 1628 (C=O), 1547 (C=C) cm^{-1}. MS (ESI): m/z = 286 [M + H]$^+$, 287 [M + 2H]$^{2+}$. $C_{17}H_{19}NO_3$ (285.34): calcd. C 71.56, H 6.71, N 4.91; found C 71.74, H 6.61, N 5.01.

2,3-Dihydro-1-[(2*E*)-3-phenylprop-2-en-1-yl]-1*H*-pyridin-4-one (18a): Following the general procedure (see Table 3, Entry 1), **2b** (90 mg, 0.53 mmol), catalyst **7** (17 mg, 0.11 mmol), Cs_2CO_3 (345 mg, 1.06 mmol), and cinnamyl bromide (158 mg, 0.80 mmol) gave the crude product that was purified by column chromatography [gradient of hexane/ethyl acetate (9:1) to ethyl acetate] to afford **18a** (23 mg, 20%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.51 (t, J = 8.0 Hz, 2 H, CH_2), 3.49 (t, J = 7.7 Hz, 2 H, CH_2), 3.95 (dd, J = 1.3 Hz, J = 11.7 Hz, 2 H, CH_2), 5.01 (d, J = 7.4 Hz, 1 H, =CH), 6.17 (dt, J = 6.5 Hz, J = 15.7 Hz, 1 H, =CH), 6.59 (d, J = 15.8 Hz, 1 H, =CH), 7.1 (d, J = 7.5 Hz, 1 H, =CH), 7.29–7.40 (m, 5 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 35.6 (CH_2), 46.9 (CH_2), 58.0 (CH_2), 98.7 (CH), 123.4 (CH), 126.6 (CH), 128.3 (CH), 128.8 (CH), 134.5 (CH), 135.8 (C), 153.9 (CH), 191.7 (CO) ppm. IR (NaCl): $\tilde{\nu}$ = 3029, 2935, 2840, 1637 (C=O), 1588 (C=C) cm^{-1}. MS (ESI): m/z = 214 [M + H]$^+$, 215 [M + 2H]$^{2+}$. $C_{14}H_{15}NO$ (213.28): calcd. C 78.84, H 7.09, N 6.57; found C 78.78, H 7.00, N 6.32.

Ethyl 5-Allyl-3,4-dihydro-4-oxo-2*H*-pyridine-1-carboxylate (19b): Following the general procedure (see Table 3, Entry 2), **2b** (90 mg, 0.53 mmol), catalyst **7** (17 mg, 0.11 mmol), Cs_2CO_3 (345 mg, 1.06 mmol), and allyl bromide (97 mg, 0.80 mmol) gave the crude product that was purified by column chromatography (hexane/ethyl acetate, 9:1) to afford **19b** (72 mg, 65%) as a colorless oil. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 1.26 (t, J = 7.1 Hz, 3 H, CH_3), 2.51 (t, J = 7.2 Hz, 2 H, CH_2), 2.85 (dd, J = 6.5 Hz, J = 1.0 Hz, 2 H, CH_2), 3.92 (t, J = 7.2 Hz, 2 H, CH_2), 4.22 (q, J = 7.1 Hz, 2 H, CH_2), 4.98–5.06 (m, 2 H, CH_2), 5.73–5.84 (m, 1 H, =CH), 7.68 (s, 1 H, =CH) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 14.2 (CH_3), 30.4 (CH_2), 35.3 (CH_2), 42.2 (CH_2), 62.8 (CH_2), 106.0 (C), 115.8 (CH_2), 136.3 (CH), 140.5 (CH), 152.4 (COO), 192.2 (CO) ppm. IR (NaCl): $\tilde{\nu}$ = 2965, 2929, 2857, 1727 (N-CO-O), 1678 (C=O), 1624 (C=C) cm^{-1}. $C_{11}H_{15}NO_3$ (209.24): calcd. C 63.14, H 7.23, N 6.69; found C 63.29, H 7.13, N 6.82.

1-Allyl-2,3-dihydro-1*H*-pyridin-4-one (18b): Following the general procedure (see Table 3, Entry 2), **2b** (90 mg, 0.53 mmol), catalyst **7** (17 mg, 0.11 mmol), Cs_2CO_3 (345 mg, 1.06 mmol), and allyl bromide (97 mg, 0.80 mmol) gave the crude product that was purified by column chromatography [gradient of hexane/ethyl acetate (9:1) to ethyl acetate] to afford **18b** (11 mg, 15%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.50 (t, J = 7.9 Hz, 2 H, CH_2), 3.44 (t, J = 7.9 Hz, 2 H, CH_2), 3.78 (d, J = 5.7 Hz, 2 H, CH_2), 4.98 (d, J = 7.5 Hz, 1 H, =CH), 5.27–5.31 (m, 2 H, =CH_2), 5.78–5.86 (m, 1 H, =CH), 7.03 (d, J = 7.5 Hz, 1 H, =CH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 35.6 (CH_2), 46.8 (CH_2), 58.3 (CH_2), 98.5 (CH), 119.1 (CH_2), 132.5 (CH), 154.0 (CH), 191.6 (CO) ppm. IR (NaCl): $\tilde{\nu}$ = 2966, 2921, 2850, 1646 (C=O), 1597 (C=C) cm^{-1}. MS (ESI): m/z = 138 [M + H]$^+$. $C_8H_{11}NO$ (137.18): calcd. C 70.04, H 8.08, N 10.21; found C 70.15, H 7.99, N 10.05.

Ethyl 5-(But-2-ynyl)-3,4-dihydro-4-oxo-2*H*-pyridine-1-carboxylate (19c): Following the general procedure (see Table 3, Entry 3), **2b** (90 mg, 0.53 mmol), catalyst **7** (17 mg, 0.11 mmol), Cs_2CO_3 (345 mg, 1.06 mmol), and 1-bromo-2-butyne (106 mg, 0.80 mmol) gave the crude product that was purified by column chromatography (hexane/ethyl acetate, 9:1) to afford **19c** (47 mg, 40%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.36 (t, J = 7.1 Hz, 3 H, CH_3), 1.84 (t, J = 2.6 Hz, 3 H, CH_3), 2.58 (t, J = 7.4 Hz, 2 H, CH_2), 3.11 (dd, J = 1.4 Hz, J = 3.8 Hz, 2 H, CH_2), 4.01 (t, J = 7.3 Hz, 2 H, CH_2), 4.31 (dd, J = 7.1 Hz, J = 21.4 Hz, 2 H, CH_2), 8.06 (s, 1 H, =CH) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ =

3.1 (CH_3), 14.1 (CH_3), 16.3 (CH_2), 35.1 (CH_2), 42.1 (CH_2), 62.9 (CH_2), 75.9 (C), 78.6 (C), 113.2 (C), 140.6 (CH), 152.2 (COO), 191.7 (CO) ppm. IR (NaCl): $\tilde{\nu}$ = 2965, 2920, 2852 (C), 1732 (N-CO-O), 1673 (C=O), 1619 (C=C) cm^{-1}. $C_{12}H_{15}NO_3$ (221.26): calcd. C 65.14, H 6.83, N 6.33; found C 65.20, H 6.93, N 6.55.

1-(But-2-yn-1-yl)-2,3-dihydro-1*H*-pyridin-4-one (18c): Following the general procedure (see Table 3, Entry 3), **2b** (90 mg, 0.53 mmol), catalyst **7** (17 mg, 0.11 mmol), Cs_2CO_3 (345 mg, 1.06 mmol), and 1-bromo-2-butyne (106 mg, 0.80 mmol) gave the crude product that was purified by column chromatography [gradient of hexane/ethyl acetate (9:1) to ethyl acetate] to afford **18c** (20 mg, 25%) as a colorless oil. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.86 (t, J = 2.4 Hz, 3 H, CH_3), 2.52 (t, J = 8.0 Hz, 2 H, CH_2), 3.48 (t, J = 8.0 Hz, 2 H, CH_2), 3.89 (dd, J = 2.4 Hz, J = 7.16 Hz, 2 H, CH_2), 5.05 (d, J = 7.6 Hz, 1 H, =CH), 7.09 (d, J = 7.6 Hz, 1 H, =CH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 3.5 (CH_3), 35.7 (CH_2), 45.3 (CH_2), 47.1 (CH_2), 100.0 (CH), 153.4 (CH), 191.9 (CO) ppm. IR (NaCl): $\tilde{\nu}$ = 2971, 2926, 2854, 1660 (C=O), 1597 (C=C) cm^{-1}. $C_9H_{11}NO$ (149.19): calcd. C 72.46, H 7.43, N 9.39; found C 72.78, H 7.05, N 9.11.

Ethyl 3,4-Dihydro-5-methyl-4-oxo-2*H*-pyridine-1-carboxylate (19e): Following the general procedure (see Table 3, Entry 5), **2b** (90 mg, 0.53 mmol), catalyst **7** (17 mg, 0.11 mmol), Cs_2CO_3 (345 mg, 1.06 mmol), and methyl iodide (114 mg, 0.80 mmol) gave the crude product that was purified by column chromatography (hexane/ethyl acetate, 9:1) to afford **19e** (68 mg, 70%) as a colorless oil. ^1H NMR (400 MHz, [D$_6$]DMSO): δ = 1.19 (t, J = 7.1 Hz, 3 H, CH_3), 1.58 (d, J = 1.1 Hz, 3 H, CH_3), 2.41 (t, J = 7.3 Hz, 2 H, CH_2), 3.83 (t, J = 7.2 Hz, 3 H, CH_2), 4.13 (q, J = 7.1 Hz, 2 H, CH_2), 7.67 (s, 1 H, =CH) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 12.6 (CH_3), 14.2 (CH_3), 35.3 (CH_2), 42.2 (CH_2), 62.7 (CH_2), 113.6 (C), 140.0 (CH), 152.4 (COO), 193.2 (CO) ppm. IR (NaCl): $\tilde{\nu}$ = 2960, 2924, 1718 (N-CO-O), 1669 (C=O), 1619 (C=C) cm^{-1}. MS (ESI): m/z = 184 $[M + H]^+$. $C_9H_{13}NO_3$ (183.21): calcd. C 59.00, H 7.15, N 7.65; found C 59.11, H 7.05, N 7.55.

Supporting Information (see footnote on the first page of this article): NMR spectra for MBH products.

Supporting Information (see footnote on the first page of this article): ^1H and ^{13}C NMR spectra for **10a**–**d**, **13a**, **15c**, **18a**–**c**, **19a**–**c** and **19e**.

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