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Aqueous-phase, thermal Pauson–Khand reactions in the presence of surfactants

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Abstract—Efficient stoichiometric Pauson–Khand reactions were realized in water as the only solvent, and in the presence of surfactants as additives. Use of the cationic surfactant CTAB provided good yields of cyclopentenones from the thermal reactions of pre-formed dicobalthexacarbonyl complexes of enynes and alkynes. The water-CTAB medium was found to be less effective with $Co_4(CO)_{12}$ as the promoter of the reaction. Incidentally, these results have provided a strictly water-based PKR protocol under very mild and convenient conditions. © 2003 Elsevier Science Ltd. All rights reserved.

The development of water-based organic transformations has been of great interest among chemists since water is undeniably a suitable reaction solvent for realizing safe, harmless and environmentally friendly processes in the production of fine chemicals.[1] Due to its distinctive properties, namely hydrogen bonding, small molecular size, and hydrophobic/hydrophilic interactions, water is capable of improving the association of molecules in a particular reaction.[2] These characteristics, in addition to its natural abundance, make water unique in comparison to organic solvents. Although solubility issues of organic compounds in aqueous media can arise, a variety of organometallic reactions have now been shown to proceed smoothly under aqueous conditions, e.g. the Suzuki reaction, Heck-type reactions, olefin metathesis reactions, hydroformylations, hydrogenations and alkyne trimerization.[1c,d,3]

In the case of the Pauson–Khand reaction (PKR), only a few accounts of this organometallic reaction being carried out in the presence of water, either as an additive, co-solvent or solvent, have been reported. Sugihara has demonstrated a catalytic PKR in toluene at 120°C at 7 atm CO pressure, using water as an additive.[4] A stoichiometric variant has also been reported by the same laboratories, where cyclizations of enyne–$Co_2(CO)_6$ complexes are carried out in a mixture of 1,4-dioxane and 2 M aqueous NH_4OH (1:3, v/v) at 100°C.[5] Recently, Chung has established a strictly aqueous protocol, i.e. water as the sole solvent, where colloidal cobalt nanoparticles catalyzed the PKR at 130°C at 20 atm CO pressure.[6] The catalyst was produced via the reduction of an aqueous solution of cobalt acetate with sodium borohydride in the presence of sodium dodecyl sulfate. In our laboratory, when the thermal PKR was conducted in water as the sole solvent, the dicobalthexacarbonyl complex of the enyne remained as an immiscible oily mass at the bottom of the flask although the cyclopentenone product was isolated after extraction and purification. After consideration of these factors, we thought it would be intriguing to examine the possibility of conducting the PKR in water as the solvent and in the presence of surfactants or detergents as additives. Herein we report that this strategy has allowed the strictly water-based PKR to proceed in good yields under much milder conditions compared to previous reports.

In our preliminary experiments summarized in Table 1, the thermally promoted cyclization of the dicobalthexacarbonyl complex of enyne **1** in water led to a low yield of enone **2**, which is presumably due to the low miscibility of the organometallic complex in water (entry 1).[7] Hence, we turned to the use of surfactants, detergents and other additives in our target aqueous PKR protocol to improve the miscibility of the organic materials, and possibly enhance reaction efficiency in water. Surfactants and detergents are amphiphilic surface-active agents that assemble in aqueous or nonpolar media forming supramolecular assemblies, such as micelles and vesicles.[1c] Due to the very high polarity gradient between the surface and the core, encapsulation of reactants in micelles often enhances the reaction rates. Furthermore, micelle-forming surfactants also solubilize organic compounds.

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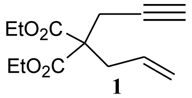
Table 1. Preliminary aqueous Pauson–Khand reactions with additives[a]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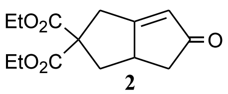
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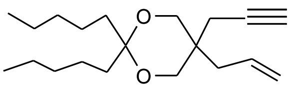
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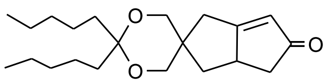
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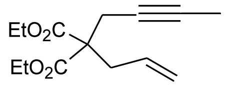
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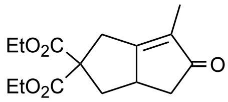
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Entry	Substrate[b,d]	Additive	Equiv.	Enone	Yield (%)
1[c]	**1**	–	–	**2**	36
2[c]	**1**	β-CD	0.25	**2**	52
3	**1**	β-CD	1	**2**	42
4	**1**	γ-CD	1	**2**	40
5	**3**	–	–	**4**	44
6	**3**	β-CD	1	**4**	24
7	**3**	γ-CD	1	**4**	35
8	**3**	Triton X-100	1	**4**	43
9	**3**	Triton X-100 (reduced)	1	**4**	57
10	**5**	Tween 40	0.6	**6**	74
11	**5**	Brij 35	0.6	**6**	74
12	**5**	CTAHS	0.6	**6**	82
13	**5**	CTAB	0.6	**6**	83

[a] Reactions were carried out at concentrations of 0.05 M in water at 70°C under a nitrogen atmosphere and were complete in 18 h.

[b] Enyne was converted to dicobalthexacarbonyl complex and then concentrated.

[c] 0.01 M in water, Ar atmosphere.

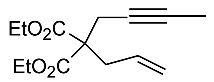
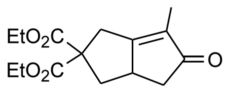
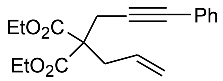
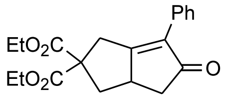
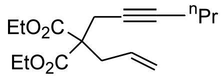
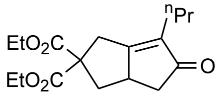
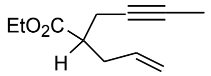
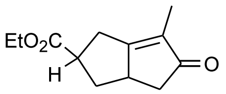
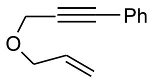
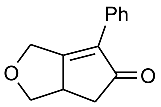
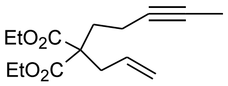
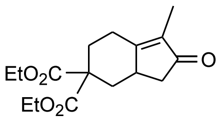
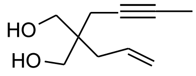
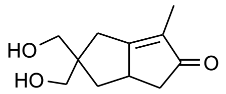
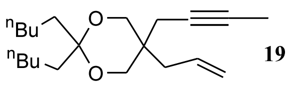
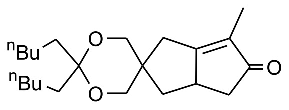
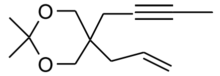
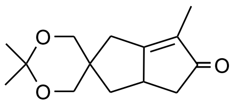
[d] Reactions in entries 10–13 were run with small amount of Celite.

Addition of β-cyclodextrin (β-CD),[8] either in less than stoichiometric or stoichiometric quantities, only resulted in a slight improvement in the yields (entries 2 and 3). The corresponding reaction using 1 equiv. of γ-CD furnished a similar result (entry 4). Nonetheless, we proceeded by modifying the substrate to contain a six-membered cyclic ketal, such as enyne **3**, in an effort to possibly enhance its interaction with the slightly non-polar cyclodextrin cavity and secondarily, to increase its rigidity. Unexpectedly, addition of β-CD to the reaction mixture bearing enyne **3** resulted in lower yields (entry 6) compared to when the reaction was carried out in the absence of this additive (entry 5). Since the yields observed in these preliminary experiments were mostly below the 50% range, it became apparent that the substrates did not interact effectively with the cyclodextrin. Kobayashi has demonstrated a very efficient palladium-catalyzed allylic alkylation of a β-ketoester with allyl acetate using polyoxyethylene(10) isooctylcyclohexyl ether (Triton® X-100) in water.[9] We speculated that this neutral surfactant might also serve to enhance the yield of the aqueous Pauson–Khand reaction. Thus, when Triton® X-100 was used in these reactions the reduced form was observed to furnish an improved yield of the PKR product (entry 5 versus 9). The unreduced form yielded results similar to those obtained in reactions of **3** with cyclodextrins (entry 8).

We then proceeded to evaluate the effect of other additives, such as Tween 40, Brij 35, cetyl trimethylammonium hydrogen sulfate (CTAHS), and cetyltrimethylammonium bromide (CTAB)[9] in the thermal PKR under aqueous conditions. Gratifyingly, cyclization of the dicobalthexacarbonyl complex of enyne **5**, in the presence of these additives furnished good yields of yield of enone **6** (entries 10–13). It is noteworthy that superior yields were obtained from reactions using CTAB and CTAHS as additives.

Having observed an improved efficiency of the thermal PKR in water as the sole solvent, in the presence of CTAB, a variety of substrates were screened to verify the generality of this strategy (Table 2). Enone products were isolated in yields higher than 80% for enynes **5**, **7** and **9** (entries 1–4) although a marginal decrease in the yield was observed from the cyclization of an enyne with one ester group in the tether (entry 5). It is noteworthy that the reaction of 1,7-enyne **15** provided a good yield of a 5,6-bicyclononenone **16** (entry 7). A dihydroxylated substrate, such as enyne **17** cyclized smoothly to furnish a good yield of enone **18** (entry 8). Reactions of enynes **19** and **21** bearing ketal groups, for increased solubility in a water–surfactant medium, resulted in the formation of moderate yields of the desired enones (entries 9 and 10). The ketal moieties in

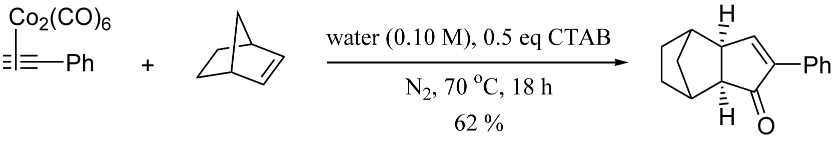
Table 2. Aqueous Pauson–Khand reactions with cetyltrimethylammonium bromide[a]

Entry	Substrate[b]			Enone	Yield (%)
1		**5**	**6**		83
2[c]					84
3		**7**	**8**		88
4		**9**	**10**		85
5		**11**	**12**		78
6		**13**	**14**		74
7		**15**	**16**		65
8		**17**	**18**		65
9		**19**	**20**		58
10		**21**	**22**		40

(a) Reactions were carried out at concentrations of 0.05 M in water at 70°C with a small amount of Celite and 0.6 eq. of CTAB under N_2 and were complete in 18 hours.

(b) Enynes were converted to their corresponding alkyne dicobalthexacarbonyl complexes and then concentrated. (c) No Celite was added.

these substrates remained intact under these conditions unlike reactions of enyne **21** that were carried out with Brij 35 and CTAHS, in which 56% and 62% yields of enone **18** were obtained, respectively. Finally, it is worth noting that an intermolecular PKR, depicted by the cyclization of the dicobalthexacarbonyl complex of phenylacetylene and norbornene, proceeded efficiently in a water–CTAB medium to provide a good yield of enone **23** (Eq. (1)).



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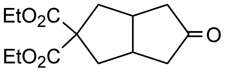
(1)

Table 3. Aqueous Pauson–Khand reactions with $Co_4(CO)_{12}$ and surfactants[a]



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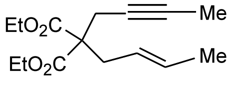

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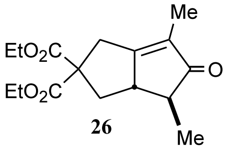

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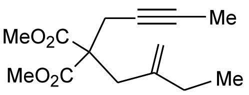

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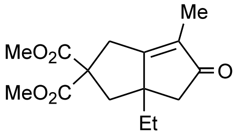

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Entry	Substrate	Surfactant	Equiv.	$Co_4(CO)_{12}$ (equiv.)	Product	Yield (%)
1	**1**	Triton X-100	1	2	**24**	59
2	**1**	Triton X-100	2	2	**24**	61
3	**1**	Fisher detergent	1 g	2	**24**	49
4	**1**	CTAB	1.3	2	**24**	66
5	**13**	CTAB	0.6	1	**14**	36
6	**25**	CTAB	0.6	1	**26**	34
7	**27**	CTAB	0.6	1	**28**	60

[a] Reactions were carried out under N_2 at concentrations of 0.05 M in water at 70°C, with a small amount of Celite present, and were complete in 18 h.

Armed with the positive outcome of cyclization reactions of preformed cobalt complexes, the reactivity of tetracobalt dodecacarbonyl under aqueous PKR conditions was also investigated with several surfactants and detergents (Table 3).[10] Reaction of enyne **1** in water with Triton® X-100 (entries 1 and 2), Fisher detergent (entry 3), and CTAB (entry 4) all led to the significant formation of bicyclooctanone **24**, the product derived from **1** undergoing a reductive PKR.[11] In the absence of an additive, the reaction of **1** using 1 equiv. of $Co_4(CO)_{12}$ furnished 44% of bicyclooctanone **24** along with 9% of the bicyclooctenone **2**. Substrates bearing internal alkynes that are less prone to reductive PKR, depicted by enynes **13** and **25**, were not efficiently converted to their corresponding enones under these conditions (entries 5 and 6). However, a good yield of the PKR adduct **28** was obtained from the reaction of enyne **27** (entry 7).

In summary, the dicobalthexacarbonyl complexes of enynes and alkynes underwent the thermal PKR in aqueous media, in which the apparent sluggishness of the reactions in water alone was circumvented by the use of surfactants. Among the surface-active agents investigated in these studies the surfactants CTAB and CTAHS were determined to be most effective, although the latter was observed to lead to the hydrolysis of ketals in the substrates. Cyclodextrins and Triton® X-100, both reduced and non-reduced forms, provided variable results. Cyclizations in water using $Co_4(CO)_{12}$ with CTAB only provided variable results. Although organic solvent was still required for the extraction process, it is noteworthy that the stoichiometric PKR successfully ensued in a water–surfactant medium as illustrated by numerous examples. Finally, these studies provided the first strictly water-based PKR protocol under very mild and convenient conditions.[12]

Acknowledgements

This work was generously supported by the National Science Foundation and the MDS Research Foundation.

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7. $\mathrm{Co_2(CO)_8}$ and $\mathrm{Co_4(CO)_{12}}$ (Strem Chemicals, Inc.) were stored in a freezer and used without purification. All reactions were performed in base-washed glassware.
Preparation of enyne dicobalthexacarbonyl complexes. To a solution of enyne **3** (65 mg, 0.21 mmol) in $\mathrm{CH_2Cl_2}$ (1 mL) was added $\mathrm{Co_2(CO)_8}$ (82.4 mg, 0.241 mmol). The reaction mixture was then stirred at room temperature under $\mathrm{N_2}$ for 1 h. Concentration under reduced pressure provided the corresponding enyne–$\mathrm{Co_2(CO)_6}$ complex in quantitative yield.
Typical experimental procedure for aqueous PKR with enyne dicobalthexacarbonyl complexes (Tables 1 and 2). To a round-bottomed flask containing the enyne–$\mathrm{Co_2(CO)_6}$ complex of **3** (0.21 mmol) was added water (3 mL) followed by Triton® X-100 (145 mg, 0.224 mmol) and a small amount of Celite. The reaction mixture was then placed under an atmosphere of nitrogen and heated at 70°C for 18 h. Upon completion of the reaction, the mixture was filtered through a filter paper on a Büchner funnel, extracted with diethyl ether, and dried over $\mathrm{MgSO_4}$. Subsequent concentration and purification by flash column chromatography ($\mathrm{SiO_2}$, 25% EtOAc in hexanes) afforded 32 mg of enone **4** (43% yield). In the reactions depicted in Table 2, CTAB was added directly to the enyne–$\mathrm{Co_2(CO)_6}$ complex before the introduction of water. A small amount of Celite was added into these reaction mixtures to facilitate stirring and to adsorb cobalt residues after the reaction. Insignificant differences in the yields were observed when Celite was not added to the reaction mixture.
8. Cyclodextrins are cyclic oligosaccharides consisting of six (α-CD), seven (β-CD), and eight (γ-CD) glucopyranose units and possessing both hydrophilic and hydrophobic sites. For a background on cyclodextrins, see: Szejtli, J. *Chem. Rev.* **1998**, *98*, 1743.
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10. *Typical experimental procedure for aqueous PKR's with* $\mathrm{Co_4(CO)_{12}}$ (Table 3). To a round-bottomed flask containing enyne **1** (53 mg, 0.22 mmol) and $\mathrm{Co_4(CO)_{12}}$ (254 mg, 0.444 mmol) was added water (5 mL) followed by Triton® X-100 (144 mg, 0.222 mmol). The reaction mixture was then placed under an atmosphere of nitrogen and heated at 70°C for 18 h. Upon completion of the reaction, the mixture was filtered through a filter paper on a Büchner funnel, extracted with ethyl acetate, dried over $\mathrm{MgSO_4}$, and filtered through a short pad of Celite. Subsequent concentration and purification by flash column chromatography ($\mathrm{SiO_2}$, 25% EtOAc in hexanes) provided 35 mg of ketone **23** (59% yield).
11. Chung observed that enyne **1** bearing a terminal alkyne moiety provided minor amounts of the ketone **24** using colloidal cobalt nanoparticles in aqueous media. See Ref. 6 and also: (a) Krafft, M. E.; Boñaga, L. V. R.; Wright, J. A.; Hirosawa, C. *J. Org. Chem.* **2002**, *67*, 1233; (b) Krafft, M. E.; Boñaga, L. V. R. *Angew. Chem., Int. Ed.* **2000**, *39*, 3676.
12. *Spectral information for studied compounds*:
Enyne **3**: ^{1}H NMR ($\mathrm{CDCl_3}$, 300 MHz): δ 5.81 (ddt, $J=16.8$, 10.1, 7.4 Hz, 1H, $\mathrm{CH_2C}H\mathrm{{=}CH_2}$), 5.08 (dm, $J=16.8$ Hz, 1H, $\mathrm{CH_2CH{=}CH}H$), 5.05 (dm, $J=10.1$ Hz, 1H, $\mathrm{CH_2CH{=}C}H\mathrm{H}$), 3.38 (t, $J=6.7$ Hz, 4H, $\mathrm{(CH_3(CH_2)_4C}H_2\mathrm{OCH_2)\times 2}$), 3.28 (AB, $J_{\mathrm{AB}}=9.4$ Hz, 2H, $\mathrm{CH_3(CH_2)_4CH_2OC}H_2$), 3.24 (AB, $J_{\mathrm{AB}}=9.4$ Hz, 2H, $\mathrm{CH_3(CH_2)_4CH_2OC}H_2$), 2.21 (d, $J=2.7$ Hz, 2H, $\mathrm{C}H_2\mathrm{CCH}$), 2.17 (d, $J=7.4$ Hz, 2H, $\mathrm{C}H_2\mathrm{CH{=}CH_2}$), 1.94 (t, $J=2.7$ Hz, 1H, $\mathrm{CH_2CC}H$), 1.46–1.60 (m, 4H, $\mathrm{(CH_3(CH_2)_3C}H_2\mathrm{CH_2OCH_2)\times 2}$), 1.22–1.40 (m, 12H, $\mathrm{(CH_3(C}H_2\mathrm{)_3(CH_2)_2OCH_2)\times 2}$), 0.88 (t, $J=7.4$ Hz, 6H, $\mathrm{(C}H_3\mathrm{(CH_2)_5OCH_2)\times 2}$). Anal. calcd for $\mathrm{C_{21}H_{38}O_2}$: C, 78.20; H, 11.87. Found: C, 78.44; H, 11.99.
Enone **4**: ^{1}H NMR ($\mathrm{CDCl_3}$, 300 MHz): δ 5.84 (s, 1H, $\mathrm{CH_2C{=}C}H\mathrm{C{=}O}$), 3.44 (obscured t, $J=6.6$ Hz, 2H, $\mathrm{CH_3(CH_2)_4C}H_2\mathrm{OCH_2C}$), 3.42 (obscured AB, $J_{\mathrm{AB}}=8.7$ Hz, 1H, $\mathrm{CH_3(CH_2)_5OC}H\mathrm{HC}$), 3.39 (obscured AB, $J_{\mathrm{AB}}=8.7$ Hz, 1H, $\mathrm{CH_3(CH_2)_5OCH}H\mathrm{C}$), 3.37 (obscured t, $J=6.6$ Hz, 2H, $\mathrm{CH_3(CH_2)_4C}H_2\mathrm{OCH_2C}$), 3.25 (AB, $J_{\mathrm{AB}}=8.7$ Hz, 1H, $\mathrm{CH_3(CH_2)_5OC}H\mathrm{HC}$), 3.20 (AB, $J_{\mathrm{AB}}=8.7$ Hz, 1H, $\mathrm{CH_3(CH_2)_5OCH}H\mathrm{C}$), 3.12 (obscured m, 1H, $\mathrm{CH_2C}H\mathrm{CH_2C{=}O}$), 2.59 (dd, $J=18.1$, 6.6 Hz, 1H, $\mathrm{CH_2CHC}H\mathrm{HC{=}O}$), 2.53 (s, 2H, $\mathrm{C}H_2\mathrm{C{=}CHC{=}O}$), 2.11 (obscured m, 1H, $\mathrm{C}H\mathrm{HCHCH_2C{=}O}$), 2.03 (dm, $J=18.1$ Hz, 1H, $\mathrm{CH_2CHCH}H\mathrm{C{=}O}$), 1.45–1.62 (m, 4H, $\mathrm{(CH_3(CH_2)_3C}H_2\mathrm{CH_2OCH_2C)\times 2}$), 1.18–1.40 (m, 12H, $\mathrm{(CH_3(C}H_2\mathrm{)_3CH_2CH_2OCH_2C)\times 2}$), 1.07 (dd, $J=12.8$, 12.8 Hz, 1H, $\mathrm{CH}H\mathrm{CHCH_2C{=}O}$), 0.88 (t, $J=7.0$ Hz, 6H, $\mathrm{(C}H_3\mathrm{(CH_2)_5OCH_2C)\times 2}$). Anal. calcd for $\mathrm{C_{22}H_{38}O_3}$: C, 75.38; H, 10.93. Found: C, 75.39; H, 11.00.
Enyne **11**: ^{1}H NMR ($\mathrm{CDCl_3}$, 300 MHz): δ 5.73 (ddt, $J=16.8$, 10.1, 7.4 Hz, 1H, $\mathrm{CH_2C}H\mathrm{{=}CH_2}$), 5.09 (dd, $J=17.5$, 1.3 Hz, 1H, $\mathrm{CH_2CH{=}CH}H$), 5.04 (dm, $J=10.1$ Hz, 1H, $\mathrm{CH_2CH{=}C}H\mathrm{H}$), 4.16 (q, $J=6.7$ Hz, 2H, $\mathrm{CH_3C}H_2\mathrm{O_2C}$), 2.58 (tt, $J=7.4$, 6.7 Hz, 1H, $\mathrm{CH_3CH_2O_2CC}H$), 2.28–2.49 (m, 4H, $\mathrm{C}H_2\mathrm{CCCH_3}$, $\mathrm{C}H_2\mathrm{CH{=}CH_2}$), 1.76 (t, $J=2.7$ Hz, 3H, $\mathrm{CH_2CCC}H_3$), 1.25 (t, $J=6.7$ Hz, 3H, $\mathrm{C}H_3\mathrm{CH_2O_2C}$). Anal. calcd for $\mathrm{C_{11}H_{16}O_2}$: C, 73.30; H, 8.95. Found: C, 73.14; H, 9.02.
Enone **12**: ^{1}H NMR ($\mathrm{CDCl_3}$, 300 MHz): δ 4.19 (q, $J=7.4$ Hz, 2H, $\mathrm{CH_3C}H_2\mathrm{O_2C}$), 3.20 (dddd, $J=8.7$, 8.7, 4.7, 1.3 Hz, 1H, $\mathrm{CH_3CH_2O_2CC}H$), 2.91–3.03 (br m, 1H, $\mathrm{CH_2C}H\mathrm{CH_2C{=}O}$), 2.91 (obscured ABm, $J_{\mathrm{AB}}=17.5$ Hz, 1H, $\mathrm{C}H\mathrm{HC{=}CCH_3C{=}O}$), 2.80 (ABd, $J_{\mathrm{AB}}=18.1$ Hz, $J=8.7$ Hz, 1H, $\mathrm{CH}H\mathrm{C{=}CCH_3C{=}O}$), 2.65 (dd, $J=18.1$, 6.7 Hz, 1H, $\mathrm{CH_2CHC}H\mathrm{HC{=}O}$), 2.44 (dd, $J=12.8$, 8.1 Hz, 1H, $\mathrm{C}H\mathrm{HCHCH_2C{=}O}$), 2.02 (dd, $J=18.1$, 2.7 Hz, 1H, $\mathrm{CH_2CHCH}H\mathrm{C{=}O}$), 1.71 (s, 3H, $\mathrm{CH_2C{=}CC}H_3\mathrm{C{=}O}$), 1.40 (ddd, $J=12.8$, 12.8, 9.4 Hz, 1H, $\mathrm{CH}H\mathrm{CHCH_2C{=}O}$), 1.29 (t, $J=7.4$ Hz, 3H, $\mathrm{C}H_3\mathrm{CH_2O_2C}$. Anal. calcd for $\mathrm{C_{12}H_{16}O_3}$: C, 69.21; H, 7.74. Found: C, 69.03; H, 7.77.
Enyne **15**: ^{1}H NMR ($\mathrm{C_6D_6}$, 500 MHz): δ 5.72 (ddt, $J=17.1$, 10.3, 7.3 Hz, 1H, $\mathrm{CH_2C}H\mathrm{{=}CH_2}$), 4.99 (dd, $J=16.6$, 1.5 Hz, 1H, $\mathrm{CH_2CH{=}CH}H$), 4.95 (dm, $J=10.3$ Hz, 1H, $\mathrm{CH_2CH{=}C}H\mathrm{H}$), 3.93 (ABq, $J_{\mathrm{AB}}=18.1$, $J=7.3$ Hz, 2H, $\mathrm{CH_3C}H_2\mathrm{O_2C}$), 3.90 (ABq, $J_{\mathrm{AB}}=18.1$, $J=7.3$ Hz, 2H, $\mathrm{CH_3C}H_2\mathrm{O_2C}$), 2.82 (d, $J=7.3$ Hz, 2H, $\mathrm{C}H_2\mathrm{CH{=}CH_2}$), 2.41–2.47 (m, 2H, $\mathrm{C}H_2\mathrm{CH_2CCCH_3}$), 2.29 (tq, $J=7.3$, 2.4 Hz, 2H, $\mathrm{CH_2C}H_2\mathrm{CCCH_3}$), 1.51 (t, $J=2.4$ Hz, 3H, $\mathrm{CH_2CH_2CCC}H_3$), 0.87 (t, $J=7.3$ Hz, 6H, $\mathrm{(C}H_3\mathrm{CH_2O_2C)\times 2}$). Anal. calcd for $\mathrm{C_{15}H_{22}O_4}$: C, 67.65; H, 8.33. Found: C, 67.43; H, 8.36.
Enone **16**: ^{1}H NMR ($\mathrm{CDCl_3}$, 300 MHz): δ 4.28 (ABq, $J_{\mathrm{AB}}=14.1$ Hz, $J=7.4$ Hz, $\mathrm{CH_3C}H\mathrm{HO_2C}$), 4.27 (ABq, $J_{\mathrm{AB}}=14.1$ Hz, $J=7.4$ Hz, $\mathrm{CH_3CH}H\mathrm{O_2C}$), 4.17 (q, $J=7.4$ Hz, 2H, $\mathrm{CH_3C}H_2\mathrm{O_2C}$), 2.82 (ddd, $J=14.1$, 4.7, 2.7 Hz, 1H, $\mathrm{CH_2C}H\mathrm{HC{=}CH_3C{=}O}$), 2.74 (ddd, $J=14.1$, 4.7, 2.7 Hz, 2H, $\mathrm{C}H\mathrm{HCHCH_2C{=}O}$), 2.71–2.76 (obscured m, 1H,

CH$_2$C*H*CH$_2$C=O), 2.62 (ddd, *J*=14.1, 4.7, 2.7 Hz, 1H, C*H*HCH$_2$C=CCH$_3$C=O), 2.59 (dd, *J*=18.8, 6.7 Hz, 1H, CH$_2$CHC*H*HC=O), 2.37 (ddd, *J*=14.1, 14.1, 5.4 Hz, 1H, CH$_2$CH*H*C=CCH$_3$C=O), 1.96 (dd, *J*=18.8, 2.0 Hz, 1H, CH$_2$CHCH*H*C=O), 1.74 (ddd, *J*=13.4, 13.4, 4.7 Hz, 1H, CH*H*CH$_2$C=CCH$_3$C=O), 1.68 (s, 3H, CH$_2$CH$_2$C=CC*H*$_3$C=O), 1.48 (dd, *J*=14.1, 14.1 Hz, 1H, CH*H*CHCH$_2$C=O), 1.30 (t, *J*=7.4 Hz, 3H, C*H*$_3$CH$_2$O$_2$C), 1.23 (t, *J*=7.4 Hz, 3H, C*H*$_3$CH$_2$O$_2$C). Anal. calcd for C$_{16}$H$_{22}$O$_5$: C, 65.29; H, 7.53. Found: C, 65.00; H, 7.54.

Enyne **17**: ^{1}H NMR (CDCl$_3$, 300 MHz): δ 5.82 (ddt, *J*=16.8, 10.1, 7.4 Hz, 1H, CH$_2$C*H*=CH$_2$), 5.12 (dm, *J*=16.8 Hz, 1H, CH$_2$CH=CH*H*), 5.10 (dm, *J*=10.7 Hz, 1H, CH$_2$CH=C*H*H), 3.66 (AB, J_{AB}=11.4 Hz, 2H, HOC*H*$_2$C), 3.61 (AB, J_{AB}=11.4 Hz, 2H, HOC*H*$_2$C), 2.23 (br s, 2H, (*H*OCH$_2$C)×2), 2.18 (q, *J*=2.7 Hz, 2H, C*H*$_2$CCCH$_3$), 2.13 (d, *J*=7.4 Hz, 2H, C*H*$_2$CH=CH$_2$), 1.79 (t, *J*=2.7 Hz, 3H, CH$_2$CCC*H*$_3$. Anal. calcd for C$_{10}$H$_{16}$O$_2$·0.1 H$_2$O: C, 70.64; H, 9.48. Found: C, 70.46; H, 9.75. HRMS (CI) calcd for C$_{10}$H$_{17}$O$_2$: 169.1229, Found: 169.1225.

Enone **18**: ^{1}H NMR (CDCl$_3$, 300 MHz): δ 3.81 (AB, J_{AB}=10.7 Hz, 1H, HOC*H*HC), 3.75 (AB, J_{AB}=10.7 Hz, 1H, HOCH*H*C), 3.66 (AB, J_{AB}=10.7 Hz, 1H, HOC*H*HC), 3.58 (AB, J_{AB}=10.7 Hz, 1H, HOCH*H*C), 2.90–3.02 (m, 1H, CH$_2$C*H*CH$_2$C=O), 2.64 (dd, *J*=18.1, 6.7 Hz, 1H, CH$_2$CHC*H*HC=O), 2.52 (AB, J_{AB}=18.8 Hz, 1H, C*H*HC=CCH$_3$C=O), 2.41 (AB, J_{AB}=18.8 Hz, 1H, CH*H*C=CCH$_3$C=O), 2.23 (br s, 2H, (*H*OCH$_2$C)×2), 2.12 (dd, *J*=12.8, 8.0 Hz, 1H, C*H*HCHCH$_2$C=O), 2.03 (dd, *J*=18.1, 2.7 Hz, 1H, CH$_2$CHCH*H*C=O), 1.69 (s, 3H, CH$_2$C=CC*H*$_3$C=O), 0.91 (dd, *J*=12.8, 12.8 Hz, 1H, CH*H*CHCH$_2$C=O). HRMS (EI) calcd for C$_{11}$H$_{16}$O$_3$: 196.1100, Found: 196.1093.

Enyne **19**: ^{1}H NMR (CDCl$_3$, 300 MHz): δ 5.75 (ddt, *J*=16.8, 10.7, 7.4 Hz, 1H, CH$_2$C*H*=CH$_2$), 5.11 (dm, *J*=16.8 Hz, 1H, CH$_2$CH=CH*H*), 5.10 (dm, *J*=10.7 Hz, 1H, CH$_2$CH=C*H*H), 3.64 (AB, J_{AB}=11.4 Hz, 2H, (COC*H*$_2$C), 3.59 (AB, J_{AB}=11.4 Hz, 2H, (COC*H*$_2$C), 2.27 (q, *J*=2.7 Hz, 2H, C*H*$_2$CCCH$_3$), 2.15 (br d, *J*=8.1 Hz, 2H, C*H*$_2$CH=CH$_2$), 1.79 (t, *J*=2.7 Hz, 3H, CH$_2$CCC*H*$_3$), 1.59–1.73 (m, 4H, (CH$_3$(CH$_2$)$_3$C*H*$_2$COCH$_2$)×2), 1.20–1.42 (m, 12H, (CH$_3$(C*H*$_2$)$_3$CH$_2$COCH$_2$)×2), 0.90 (t, *J*=6.7 Hz, 3H, (C*H*$_3$(CH$_2$)$_3$CH$_2$COCH$_2$), 0.89 (t, *J*=7.4 Hz, 3H, (C*H*$_3$(CH$_2$)$_3$CH$_2$COCH$_2$. Anal. calcd for C$_{21}$H$_{36}$O$_2$: C, 78.70; H, 11.32. Found: C, 78.69; H, 11.38.

Enone **20**: ^{1}H NMR (CDCl$_3$, 300 MHz): δ 3.78 (AB, J_{AB}=11.4 Hz, 1H, COC*H*HC), 3.69 (AB, J_{AB}=11.4 Hz, 1H, COCH*H*C), 3.63 (AB, J_{AB}=11.4 Hz, 1H, COC*H*HC), 3.50 (AB, J_{AB}=11.4 Hz, 1H, COCH*H*C), 2.80–2.97 (br m, 1H, CH$_2$C*H*CH$_2$C=O), 2.63 (dd, *J*=18.1, 6.7 Hz, 1H, CH$_2$CHC*H*HC=O), 2.55 (obscured AB, J_{AB}=21.5 Hz, 1H, C*H*HC=CCH$_3$C=O), 2.48 (AB, J_{AB}=21.5 Hz, 1H, CH*H*C=CCH$_3$C=O), 2.13 (dd, *J*=12.8, 8.1 Hz, 1H, C*H*HCHCH$_2$C=O), 2.01 (dd, *J*=18.1, 2.7 Hz, 1H, CH$_2$CHC*H*HC=O), 1.58–1.76 (m, 7H, (CH$_3$(CH$_2$)$_3$C*H*$_2$C)×2, CH$_2$C=CC*H*$_3$C=O), 1.20–1.44 (m, 12H, (CH$_3$(C*H*$_2$)$_3$CH$_2$C)×2), 0.90 (t, *J*=7.4 Hz, 3H, C*H*$_3$(CH$_2$)$_4$C), 0.89 (t, *J*=7.4 Hz, 3H, C*H*$_3$(CH$_2$)$_4$C), 0.87 (obscured m, 1H, CH*H*CHCH$_2$C=O. HRMS (FAB) calcd for C$_{22}$H$_{36}$O$_3$Na: 371.2562, Found: 371.2557.

Enone **22**: ^{1}H NMR (CDCl$_3$, 300 MHz): δ 3.82 (AB, J_{AB}=11.4 Hz, 1H, COC*H*HC), 3.73 (ABd, J_{AB}=11.4 Hz, *J*=1.3 Hz, 1H, COCH*H*C), 3.67 (AB, J_{AB}=11.4 Hz, 1H, COC*H*HC), 3.54 (ABd, J_{AB}=11.4 Hz, *J*=1.3 Hz, 1H, COCH*H*C), 2.83–2.98 (br m, 1H, CH$_2$C*H*CH$_2$C=O), 2.64 (dd, *J*=18.1, 6.7 Hz, 1H, CH$_2$CHC*H*HC=O), 2.59 (obscured AB, J_{AB}=18.8 Hz, 1H, C*H*HC=CCH$_3$C=O), 2.51 (AB, J_{AB}=18.8 Hz, 1H, CH*H*C=CCH$_3$C=O), 2.14 (dd, *J*=12.8, 8.1 Hz, 1H, C*H*HCHCH$_2$C=O), 2.02 (dd, *J*=18.1, 3.4 Hz, 1H, CH$_2$CHCH*H*C=O), 1.70 (s, 3H, CH$_2$C=CC*H*$_3$C=O), 1.45 (s, 3H, C*H*$_3$COCH$_2$C), 1.44 (s, 3H, C*H*$_3$COCH$_2$C), 0.89 (dd, *J*=12.8, 12.8 Hz, 1H, CH*H*CHCH$_2$C=O. Anal. calcd for C$_{14}$H$_{20}$O$_3$: C, 71.16; H, 8.53. Found: C, 70.93; H, 8.72.

Enyne **27**: ^{1}H NMR (CDCl$_3$, 300 MHz): δ 4.90 (dm, *J*=2.0 Hz, 1H, CH$_2$C=CH*H*CH$_2$CH$_3$), 4.83 (br s, 1H, CH$_2$C=C*H*HCH$_2$CH$_3$), 3.72 (s, 6H, (C*H*$_3$O$_2$C)×2), 2.83 (s, 2H, C*H*$_2$C=CH$_2$CH$_2$CH$_3$), 2.76 (q, *J*=2.7 Hz, 2H, C*H*$_2$CCH$_3$), 1.91 (q, *J*=7.4 Hz, 2H, CH$_2$C=CH$_2$C*H*$_2$CH$_3$), 1.76 (t, *J*=2.7 Hz, 3H, CH$_2$CC*H*$_3$), 1.00 (t, *J*=7.4 Hz, 3H, CH$_2$C=CH$_2$CH$_2$C*H*$_3$). ^{13}C NMR (CDCl$_3$, 75 MHz): δ 170.95, 145.79, 113.36, 79.00, 73.51, 56.86, 52.40, 37.47, 29.14, 22.76, 12.18, 3.17. IR (cm^{-1}): 3082, 2956, 2880, 1732, 1644, 1436, 1376, 1330, 1292, 1204, 1150, 1120, 1084, 1060, 1042, 1012, 974, 958, 940, 904, 862, 820, 800. Anal. calcd for C$_{14}$H$_{20}$O$_4$: C, 66.65; H, 7.99. Found: C, 66.82; H, 8.07.

Enone **28**: ^{1}H NMR (CDCl$_3$, 300 MHz): δ 3.80 (s, 3H, C*H*$_3$O$_2$C), 3.72 (s, 3H, C*H*$_3$O$_2$C), 3.26 (AB, J_{AB}=17.4 Hz, 1H, C*H*HC=CCH$_3$C=O), 3.18 (AB, J_{AB}=17.4 Hz, 1H, CH*H*C=CCH$_3$C=O), 2.73 (AB, J_{AB}=14.1 Hz, 1H, C*H*HC(CH$_2$CH$_3$)CH$_2$C=O), 2.45 (AB, J_{AB}=17.5 Hz, 1H, CH$_2$C(CH$_2$CH$_3$)C*H*HC=O), 2.17 (AB, J_{AB}=17.5 Hz, 1H, CH$_2$C(CH$_2$CH$_3$)CH*H*C=O), 2.02 (AB, J_{AB}=14.1 Hz, 1H, CH*H*C(CH$_2$CH$_3$)CH$_2$C=O), 1.72 (s, 3H, CH$_2$C=CC*H*$_3$C=O), 1.49 (dq, *J*=14.1, 7.4 Hz, 1H, CH$_2$C(C*H*HCH$_3$)CH$_2$C=O), 1.22 (dq, *J*=14.1, 7.4 Hz, 1H, CH$_2$C(CH*H*CH$_3$)CH$_2$C=O), 0.77 (t, *J*=7.4 Hz, 3H, CH$_2$C(CH$_2$C*H*$_3$)CH$_2$C=O). Anal. calcd for C$_{15}$H$_{20}$O$_5$: C, 64.27; H, 7.19. Found: C, 64.06; H, 7.24.

For compounds **5**–**8**, **13**, **14**, **24**–**26**, see: Krafft, M. E.; Bonaga, L. V. R.; Wright, J. A.; Hirosawa, C. *J. Org. Chem.* **2002**, *67*, 1233. For compounds **1** and **2**, see: Krafft, M. E.; Bonaga, L. V. R.; Hirosawa, C. *J. Org. Chem.* **2001**, *66*, 3004. For compounds **9** and **10**, see: Kondo, T.; Suzuki, N.; Okada, T.; Mitsudo, T. *J. Am. Chem. Soc.* **1997**, *119*, 6187.