Efficient and Reusable PdCl₂(MeCN)₂/CuCl₂/PEG-400 System for Cyclization of Alkenyl β -Keto Esters and Amides

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Supporting Information

List of Contents

(A) Materials	S2
(B) Typical experimental procedures	S2
(C) Analytical data for 2	S2-4
(D) References	S4
(E) Spectra	S5-15

(A) Materials

Alkene β -keto esters **1a–1i** and amines **1j–1k** were prepared from reaction of corresponding acetoacetates and acetoacetamides with unsaturated bromides, respectively.¹

(B) Typical experimental procedures

Typical experimental procedures for the palladium-catalyzed hydroalkylation cyclization reaction in PEG-400. A mixture of **1** (0.5 mmol), PdCl₂(MeCN)₂ (0.10 equiv), and CuCl₂ (1.0 equiv) in PEG-400 (4 g) was added to a sealed tube under N₂, and then was stirred at 55 °C for desired time until complete consumption of starting material as judged by TLC. After the mixture was extracted by dry ethyl ether (3×10 mL) and evaporated, the residue was purified by flash column chromatography (hexane/ethyl acetate) to afford the desired coupled products **2**.

The mixture of PdCl₂(MeCN)₂, CuCl₂, and PEG-400 were solidified (cooled) and subjected to a second run of the hydroalkylation cyclization reaction by charging with the same substrates (alkenyl β -keto esters and amides).

(C) Analytical data for **2**

2-Methyl-6-oxo-cyclohexanecarboxylic acid methyl ester (2a).^{2, 3}

A colorless oil, enol : keto ester = 1 : 1; ¹H NMR (CDCl₃, 300 MHz) δ : 12.32 (s, 0.37×1H), 3.77 (s, 3H), 3.05 (d, J = 11.4 Hz, 0.41×1H), 2.72–2.34 (m, 1H), 2.34–2.24 (m, 2H), 2.09–1.90 (m, 1H), 1.78–1.25 (m, 3H), 1.07 (d, J = 6.8 Hz, 0.5×3H), 1.03 (d, J = 6.5

Hz, 0.5×3H). ¹³C NMR (CDCl₃, 100 MHz) δ: 206.0, 173.2, 172.5, 103.0, 65.1, 52.0, 51.3, 40.9, 36.8, 32.3, 29.8, 29.3, 26.5, 25.0, 21.2, 21.0, 17.2.

2-Oxo-cyclohexanecarboxylic acid methyl ester (2b).^{2, 3}

A colorless oil, enol : keto ester = 4 : 1; ¹H NMR (CDCl₃, 300 MHz) δ: 12.16 (s, 0.76×1H), 3.75 (s, 3H), 3.41–3.43 (m, 0.15×1H), 2.29–2.20 (m, 4H), 1.69–1.59 (m, 4H). ¹³C NMR (CDCl₃, 75 MHz) δ: 173.4, 172.4, 97.9, 57.5, 52.4, 51.6, 41.9, 30.3, 29.4, 27.4, 23.6, 22.7, 22.2.

(Z)-Ethyl 2-(dihydro-5,5-dimethylfuran-2(3H)-ylidene)acetate (2d).³

A colorless oil; ¹H NMR (CDCl₃, 400 MHz) δ: 5.20 (s, 1H), 4.13–4.08 (m, 2H), 3.43–3.16 (m, 2H), 1.89 (t, *J* = 7.6 Hz, 2H), 1.35 (s, 6H), 1.25 (t, *J* = 6.8 Hz, 3H).

2-Ethyl-6-oxo-cyclohexanecarboxylic acid methyl ester (2e).^{2, 3}

A colorless oil, enol : keto ester = 1 : 6; ¹H NMR (CDCl₃, 300 MHz) δ: 12.33 (s, 0.2×1H), 3.77 (s, 3H), 3.15 (d, *J* = 11.0 Hz, 0.8×1H), 2.52–2.00 (m, 4H), 1.76–1.58 (m, 1H), 1.45–1.23 (m, 4H), 0.93 (t, *J* = 7.5 Hz, 3H). ¹³C NMR (CDCl₃, 100 MHz) δ: 206.3, 173.3, 172.6, 102.7, 63.4, 51.9, 51.3, 42.5, 41.1, 39.5, 33.2, 29.1, 28.4, 27.6, 27.0, 24.7, 17.0, 12.3, 10.7.

2,2-Dimethyl-6-oxo-cyclohexanecarboxylic acid methyl ester (2g).^{2, 3}

A colorless oil; ^1H NMR (CDCl_3 , 300 MHz) δ : 3.70 (s, 3H), 3.18 (s, 1H), 2.71–2.61 (m, 1H), 2.55–2.23 (m, 1H), 1.97–1.87 (m, 3H), 1.65–1.46 (m, 1H), 1.08 (s, 3H), 1.03 (s, 3H). ^{13}C NMR (CDCl_3 , 100 MHz) δ : 206.8, 169.3, 67.4, 51.7, 38.9, 36.5, 28.2, 24.9, 21.9.

N,N-dimethyl-2-oxocyclohexanecarboxamide(2j).³

A colorless oil; ^1H NMR (CDCl_3 , 300 MHz) δ : 3.59–3.55 (m, 1H), 2.99 (s, 3H), 2.93 (s, 3H), 2.55–2.53 (m, 1H), 2.49–2.45 (m, 1H), 2.19–2.05 (m, 1H), 2.14–2.00 (m, 2H), 1.72–1.70 (m, 1H), 1.26–1.23 (m, 2H). ^{13}C NMR (CDCl_3 , 75 MHz) δ : 207.8, 169.54.8, 42.3, 37.6, 36.0, 30.6, 27.4, 23.9.

(D) References

- (1) (a) Sum, P. E.; Weiler, L. *Can. J. Chem.* **1979**, *57*, 1475. (b) Vlattas, I.; Harrison, I. T.; Toskes, L.; Fried, J. H.; Cross, A. D. *J. Org. Chem.* **1968**, *33*, 4176.
- (2) Pei, T.; Widenhoefer, R. A. *Chem. Commun.* **2002**, 650.
- (3) Yang, D.; Li, J.-H.; Gao, Q.; Yan, Y.-L. *Org. Lett.* **2003**, *5*, 2869.

(E) Spectra

(2a)

(2a)

(2d)