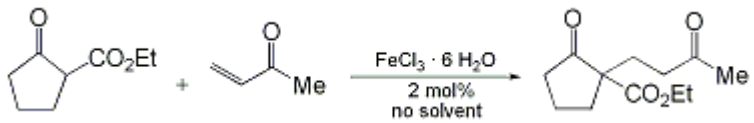
DOI:10.15227/orgsyn.078.0249

Organic Syntheses, Coll. Vol. 10, p.588 (2004); Vol. 78, p.249 (2002).

2-(3-OXOBUTYL)CYCLOPENTANONE-2-CARBOXYLIC ACID ETHYL ESTER

[Cyclopentanecarboxylic acid, 2-oxo-1-(3-oxobutyl)-, ethyl ester]



Submitted by Jens Christoffers[1]
Checked by Richard Heid and Edward J. J. Grabowski.

1. Procedure

A 50-mL, round-bottomed flask (Note 1), equipped with a magnetic stirring bar, is charged with cyclopentanone-2-carboxylic acid ethyl ester (25.0 g, 160 mmol) (Note 2) and iron(III)chloride hexahydrate (865 mg, 3.20 mmol). The flask is kept in a water bath at room temperature (external temperature) (Note 3), and methyl vinyl ketone (MVK) (15.0 mL, 12.7 g, 182 mmol) (Notes 4 and 5) is added within 1 hr using a syringe pump. The resulting mixture is stirred for 12 hr at room temperature, then all volatile materials are removed under reduced pressure from the reaction mixture (Note 6) at room temperature for 3 hr with continued stirring. Subsequently, the flask is equipped with a Claisen top and condenser and the product is distilled under high vacuum (Note 7). The distillate is collected in a single receiver flask to afford 33.3-33.7 g (91-93%) of analytically pure 2-(3-oxobutyl) cyclopentanone-2-carboxylic acid ethyl ester (Notes 8 and 9).

2. Notes

1. The reaction flask must be wide-necked to facilitate rapid distillation.
2. All starting materials were purchased from the Aldrich Chemical Company, Inc. , and used without further purification.
3. A water cooling bath is required to prevent the volatile MVK from being evolved, since the reaction is slightly exothermic.
4. MVK is a hazardous and toxic material. All operations must be carried out in a hood.
5. A little excess of MVK (1.1 equiv) is required, since this starting material is very volatile. To obtain a very pure product, it is easier to remove an excess of the Michael acceptor instead of the donor.
6. An excess of MVK is removed as well as small amounts of decomposition (by hydrolysis) product cyclopentanone.
7. The bp of the product is 130°C at 1 mm. An oil bath temperature of 160-170°C is necessary to achieve rapid distillation. Temperatures above 190°C lead to decomposition, although a bath temperature of 200°C and the use of a heat gun at the end might be necessary to transfer the distillate completely into one receiver flask. Moreover, vigorous stirring during distillation is advisable, since the compound tends to delayed boiling.
8. The distillate is pure by elemental analysis and is free from solvent contamination. The physical properties are as follows: $C_{12}H_{18}O_4$ (226.27): Anal. Calcd for C, 63.70; H, 8.02. Found C, 63.48; H, 7.93; Mol. mass calcd. 226.1205, found 226.1207 (HRMS). Spectral data: IR (ATR) cm^{-1}: 2976 (m), 1748 (vs), 1717 (vs), 1448 (m), 1406 (m), 1367 (m), 1318 (m), 1260 (s), 1232 (s), 1165 (s), 1116 (m), 1029 (m), 861 (m) ; ^1H NMR (400 MHz, $CDCl_3$) δ: 1.23 (t, 3 H, J = 7.2), 1.82 - 2.03 (m, 4 H), 2.03 - 2.13 (m, 1 H), 2.12 (s, 3 H), 2.24 - 2.49 (m, 4 H), 2.69 (ddd, 1 H, J = 18, J = 9.6, J = 6.0), 4.14 (q, 2 H, J = 7.1) ; ^{13}C NMR (50 MHz, $CDCl_3$) δ: 13.29 (CH_3), 18.84 (CH_2), 26.24 (CH_2), 29.00 (CH_3), 33.22 (CH_2), 37.07 (CH_2), 38.01 (CH_2), 58.23 (C), 60.23 (OCH_2), 170.47 (C=O), 206.61 (C=O), 213.75 (C=O) .
9. As an alternative to distillation and in accord with the observations of the submitter, the checkers have shown that the reaction mixture can be diluted with 100 mL of methyl t-butyl ether (MTBE), and filtered through a column of 150 g of silica gel with sufficient flushing by MTBE to remove all product.

Concentration of the MTBE on a rotary evaporator followed by keeping the resulting oil at 1 mm/25o for 24 hr affords product of comparable purity, except for traces of MTBE, and slightly improved yield.

Waste Disposal Information

All toxic materials were disposed of in accordance with "Prudent Practices in the Laboratory"; National Academy Press; Washington, DC, 1995.

3. Discussion

Transition metal catalysis of the Michael reaction of 1,3-dicarbonyl compounds with acceptor activated alkenes has been known since the early 1980's.[2,3] It is a valuable alternative to the classic base catalysis of the reaction. Because of the mild and neutral conditions, the chemoselectivity of these reactions is superior to that provided by base catalysis, since the latter suffers from various unwanted side or subsequent reactions, such as aldol cyclizations, ester solvolyses or retro-Claisen type decompositions. A number of transition metal and lanthanide compounds have been reported to catalyze the Michael reaction, but $FeCl_3 \cdot 6\ H_2O$ is one of the most efficient systems to date. A number of β-diketones or β-oxo esters and MVK are cleanly converted to the corresponding Michael reaction products within a few hours at room temperature, with quantitative yields being achieved in most cases.[4] No significant excess of the Michael acceptor is required, and the amount of catalyst employed can be as low as 1 mol%. Importantly, as long as the product and starting materials are liquid at room temperature, solvents are unnecessary. Moreover, the reaction can be performed without any need for anhydrous or inert conditions. Since no side reactions are observed, work-up and purification are very simple: either direct distillation of the product from the reaction mixture (as in the representative example shown here), or, if the volatility of the compound does not allow this, filtration through a short column of silica gel, which removes all iron-containing materials. There are of course also a number of other very efficient and mild systems for the catalysis of the Michael reaction.[5] However, $FeCl_3 \cdot 6\ H_2O$ is the most readily available catalyst in this area, and also with respect to economical and ecological considerations, it is the transition metal compound of choice. Moreover, the procedure introduced here comes very close to an "ideal synthesis",[6] since starting materials are converted stoichiometrically and atom-economically without need of any reagents or even solvents and without generation of any stoichiometric by-product.

References and Notes

1. Institut für Organische Chemie der Technischen Universität Berlin, Strabe des 17. Juni 135, D-10623 Berlin, Germany. Present address: Institut für Organische Chemie, Universität Stuttgart, Pfaffenwaldring 55, D-70569 Stuttgart, Germany.
2. (a) Nelson, J. H.; Howells, P. N.; DeLullo, G. C.; Landen, G. L.; Henry, R. A. *J. Org. Chem.* **1980**, *45*, 1246-1249; (b) Watanabe, K.; Miyazu, K.; Irie, K. *Bull. Chem. Soc. Jpn.* **1982**, *55*, 3212-3215.
3. Review: Christoffers, J. *Eur. J. Org. Chem*. **1998**, 1259-1266.
4. (a) Christoffers, J. *J. Chem. Soc., Chem. Commun.* **1997**, 943-944; (b) Christoffers, J. *J. Chem. Soc., Perkin Trans. 1* **1997**, 3141-3149.
5. (a) Macquarrie, D. J. *Tetrahedron Lett.* **1998**, *39*, 4125-4128; (b) Boruah, A.; Baruah, M.; Prajapati, D.; Sandu, J. S. *Synth. Commun.* **1998**, *28*, 653-658; (c) see Ref. 3 for literature of 1997 or earlier.
6. Curran, D. P. *Angew. Chem., Int. Ed. Engl.* **1998**, *37*, 1175-1196.

Appendix
Chemical Abstracts Nomenclature (Collective Index Number); (Registry Number)

2-(3-Oxobutyl)cyclopentanone-2-carboxylic acid ethyl ester:
Cyclopentanecarboxylic acid, 2-oxo-1-(3-oxobutyl)-, ethyl ester (10); (61771-81-1)

Cyclopentanone-2-carboxylic acid ethyl ester: Aldrich:
Ethyl 2-oxocyclopentanecarboxylic acid:
Cyclopentanecarboxylic acid, 2-oxo-, ethyl ester (8,9); (611-10-9)

Iron(III) chloride hexahydrate:
Iron chloride, hexahydrate (8,9); (10025-77-1)

Methyl vinyl ketone:
3-Buten-2-one (8,9); (78-94-4)