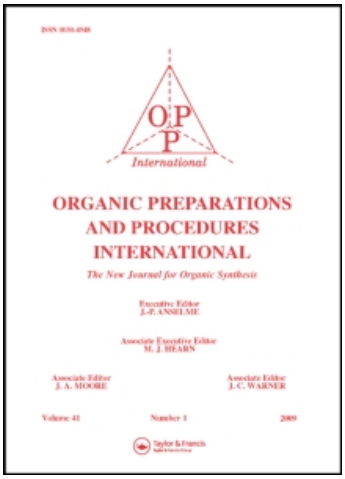


**Organic Preparations and Procedures International**
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t902189982

# A CONVENIENT SYNTHESIS OF β-KETOESTERS

Edward C. Taylor[a]; Ignatius J. Turchi[a]
[a] Department of Chemistry, Princeton University, Princeton, New Jersey

**To cite this Article** Taylor, Edward C. and Turchi, Ignatius J.(1978) 'A CONVENIENT SYNTHESIS OF β-KETOESTERS', Organic Preparations and Procedures International, 10: 5, 221 — 224
**To link to this Article: DOI:** 10.1080/00304947809355043
**URL:** http://dx.doi.org/10.1080/00304947809355043

ORGANIC PREPARATIONS AND PROCEDURES INT. 10(5), 221-224 (1978)

# A CONVENIENT SYNTHESIS OF β-KETOESTERS

Edward C. Taylor* and Ignatius J. Turchi
Department of Chemistry, Princeton University
Princeton, New Jersey 08540



In connection with other projects being carried out in our laboratories, we had need for a convenient and general synthesis of β-ketoesters. Pichat and Beaucourt[1] have prepared γ,δ-unsaturated-β-ketoesters by acylation of the lithium enolate of ethyl trimethylsilylmalonate 1 (4-5 fold excess), followed by aqueous hydrolysis and decarboxylation of the intermediate 3. We report herein our extensions of this method[2] to the preparation of a broad variety of β-ketoesters 4 (see Table). Using the same procedure we have also obtained the bis-β-ketoesters 5 and 6 in good yield.

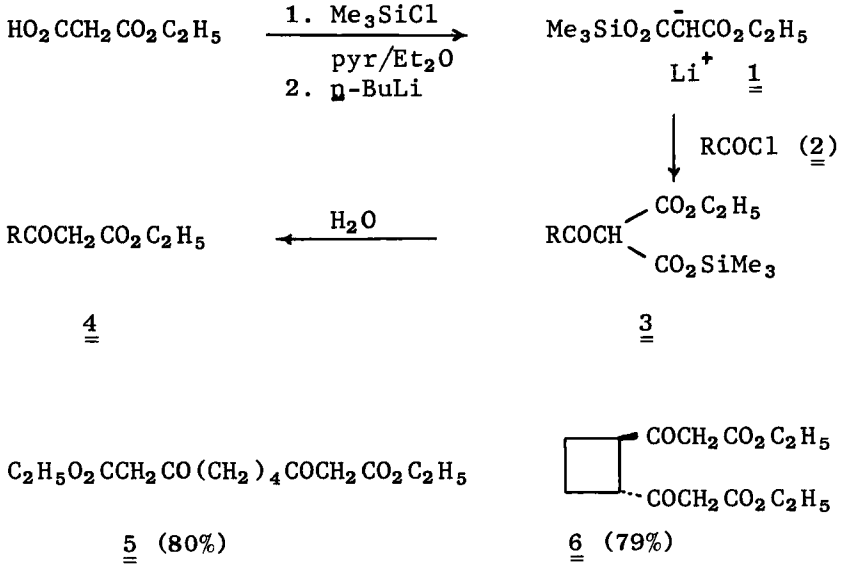

Table 1. β-Ketoesters ($RCOCH_2CO_2C_2H_5$)

| R | bp °C (torr) | Yield[3], % | Ref. |
|---|---|---|---|
| t-Bu | 43-45 (0.03) | 84 | 4 |
| t-$BuCH_2$ | 45-48 (0.03) | 93 | 5 |
| $C_5H_9CH_2$(cyclopentyl-methyl) | 80-81 (0.03) | 85 | 6 |
| $C_3H_5$(cyclopropyl) | 42-43 (0.03) | 86 | 7 |
| $C_6H_{11}$ | 74-76 (0.02) | 79 | 8 |
| 1-Adamantyl | 118-120 (0.05) | 81 | - |
| $C_6H_5CH_2$ | 74-76 (0.03) | 84 | 8 |
| $C_6H_5(CH_2)_2$ | 80-82 (0.03) | 90 | 9 |
| $C_6H_5$ | 68-69 (0.03) | 88 | 10 |
| $C_6F_5$ | 63-64 (0.01) | 81 | 11 |
| 2-Furyl | 76-78 (0.01) | 89 | 8 |
| $CH_3OCH_2$ | 47-48 (0.03) | 72 | 12 |
| $Cl_3C$ | 48-50 (0.03) | 58 | 13 |
| $FCH_2$ | 63-65 (5.0) | 33 | 14 |

The procedure outlined here offers a particularly attractive route to β-ketoesters because of its simplicity and versatility, and it complements the recently reported method of Kellogg involving displacement of bromide ion from the sodio enolate of ethyl γ-bromoacetoacetate by nucleophiles.[12]

## EXPERIMENTAL

General Procedure.- To a solution of monoethyl malonate[15] (0.16 mol, 21.1 g) and pyridine (0.19 mol, 14.7 g) in dry ether (300 mL) under nitrogen was added dropwise with stirring chlorotrimethylsilane (0.21 mol, 22.3 g). After 4 hours at

room temperature, the mixture was filtered to remove pyridine hydrochloride which was washed with several portions of dry ether. The solution was then transferred to a 500-mL three-neck round-bottom flask and cooled to -78° under a $N_2$ atmosphere. To this solution was then added n-butyl lithium (2.2 mmol/mL in hexane, 40 mL) dropwise with stirring.[16] The mixture was allowed to remain an additional 20 minutes at -78° and then a solution of the acid chloride (0.035 mol; 0.018 mol for the diacid chlorides) in 1,2-dimethoxyethane (150 mL) was added dropwise over a 30-minute period. The mixture was allowed to warm to room temperature and stand for 17 hours. Water (30 mL) was added and the mixture was stirred until a clear solution resulted. The solvents were removed under reduced pressure, the residue dissolved in a minimum amount of water and extracted with two 50-mL portions of ether. The ether extracts were washed with dilute hydrochloric acid, water and sodium bicarbonate solution, dried ($Na_2SO_4$), the solvent removed and the residue distilled under reduced pressure.



4, R = 1-Adamantyl. Nmr ($CDCl_3$): δ 1.25 (t,3,$CH_3$), 1.78 (m,12 adamantyl $CH_2$), 2.05 (m,3,adamantyl CH), 3.48 (s,∿2, $COCH_2CO$), 4.16 (q,2,$OCH_2CH_3$), 4.93 (s,CH enol). Ir (neat): 2970w, 2880s, 2845s, 1740s, 1700s, 1635s, 1615s, 1445m, 1230s, 1025m, 1010m $cm^{-1}$.

Anal: Calcd for $C_{15}H_{22}O_3$: C, 71.97; H, 8.86. Found: C, 72.20; H, 8.78.

5. Nmr ($CDCl_3$): δ 1.22 (t,6,$CH_3$), 1.58 (m,4,$CH_2CH_2$), 2.52 (m,4,$CH_2CO$), 3.37 (s,∿4,$COCH_2CO$), 4.23 (q,4,$OCH_2CH_3$), 4.93 (s,CH enol). Ir (neat): 2970m, 2920m, 1735s, 1705s, 1630w, 1310s, 1250s, 1020m $cm^{-1}$. mp 176-179° (0.01 torr).

Anal. Calcd for $C_{14}H_{22}O_6$: C, 58.73; H, 7.75. Found: C, 58.92; H, 7.89.

6. Nmr ($CDCl_3$): δ 1.23 (t,6,$CH_3$), 2.10 (m,4,cyclobutane $CH_2$), 3.37 (s,∿4,$COCH_2CO$), 3.63 (m,2,cyclobutane CH), 4.12

(q,4,$OC\underline{H}_2CH_3$), 4.93 (s,CH enol). Ir (neat): 2980m, 2940m, 1735s, 1705s, 1630w, 1310s, 1245s, 1160s, 1020s $cm^{-1}$. bp 178-180° (0.02 torr).

Anal. Calcd for $C_{14}H_{20}O_6$: C, 59.14; H, 7.09. Found: C, 59.36; H, 7.27.

## REFERENCES


1. L. Pichat and J.-P. Beaucourt, Synthesis, 537 (1973).
2. See also (a) B. M. Trost and R. A. Kunz, J. Org. Chem., 39, 2648 (1974); (b) E. W. Colvin, Chem. Soc. Rev., 7, 15 (1978).
3. Based on acid chloride.
4. G. Renner, I. Boie, and Q. Scheben, Ger. Offen. 2,412,784 (1975); Chem. Abstr., 84, 43341p (1976).
5. E. B. Reid and R. B. Fortenbaugh, J. Org. Chem., 16, 33 (1951).
6. M. Jackman, A. J. Bergman, and S. Archer, J. Am. Chem. Soc., 70, 497 (1948).
7. R. Jacquier, C. Petrus, F. Petrus, and J. Verducci, Bull. Soc. Chim. Fr., 3694 (1969).
8. D. S. Breslow, E. Baumgartner, and C. R. Hauser, J. Am. Chem. Soc., 66, 1286 (1944).
9. Y.-L. Chen and W. F. Barthel, ibid., 75, 4287 (1953).
10. J. B. Dorsch and S. M. McElvain, ibid., 54, 2962 (1932).
11. N. N. Vorozhtsov, V. A. Barkhash, A. T. Prudchenko, and G.S. Shchegoleva, Zh. Obshch. Khim., 35, 1501 (1965); Chem. Abstr., 63, 14742f (1965).
12. C. B. Troostwijk and R. M. Kellogg, Chem. Commun., 932 (1977).
13. D. K. Wald and M. M. Joullie, J. Org. Chem., 31, 3369 (1966).
14. E. D. Bergmann, S. Cohen, and I. Shahak, J. Chem. Soc., 3278 (1959).
15. R. E. Strube, Org. Syn. Coll. Vol. 4, 417 (1963).
16. For reasons which are not understood, higher yields and purer products are obtained when a large excess of n-butyl lithium is employed.


(Received June 26, 1978; in revised form August 18, 1978)