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# Convenient preparation of *tert*-butyl esters

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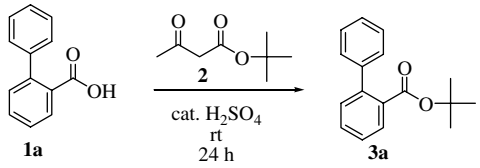
**Abstract**—A general method is presented for the preparation of *tert*-butyl esters by the gentle warming of the carboxylic acid in the presence of excess of *tert*-butyl acetoacetate and a catalytic amount of acid. This method generates only low pressures, and is therefore suitable for laboratory scale pressure glassware.


We present here a convenient method (Scheme 1) for the preparation of *tert*-butyl esters through the in situ generation of isobutylene from *tert*-butyl acetoacetate using catalytic sulfuric acid in the presence of carboxylic acid.

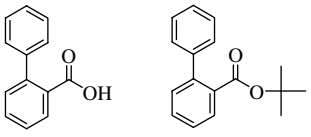
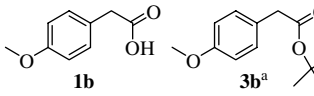
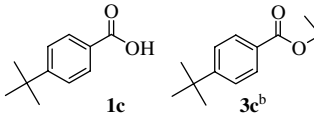
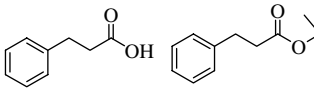
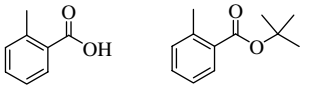
Several methods for the preparation of *tert*-butyl esters from carboxylic acids have been developed. These reactions can be separated into two classes. The first are methods that use irreversible reagents such as alkyl halides, S-pyridyl-thiolates in the presence of $CuBr_2$, *tert*-butyl 2,2,2-trichloroacetimidate, *N*,*N*-dimethylformamide-di-*tert*-butyl acetal or EDCI/DMAP/*tert*-butanol.[1] We find these methods to be undesirable because they require reagents that are too expensive for general use in large-scale work.[2,3]

The second class of approaches employ isobutylene. This gaseous reagent is volatile and its use can generate high pressures, making use of isobutylene as a reagent in the laboratory problematic. Recent work has been directed toward the alleviation of some of these issues by generating isobutylene in situ. These methods use *tert*-butyl alcohol as the isobutylene source with catalysis by acid and heat to form the desired esters.[4] Such processes




**Scheme 1.**

**Table 1.** Preparation of *tert*-butyl esters using *tert*-butyl acetoacetate[5]

| Entry # | Starting material | Product | % Yield | Reaction notes |
|---|---|---|---|---|
| 1 |  **1a** | **3a** | 82 | $H_2SO_4$, 24 h, rt |
| 2 |  **1b** | **3b**[a] | 90 | $H_2SO_4$, 48 h, 50 °C |
| 3 |  **1c** | **3c**[b] | 91 | $H_2SO_4$, 48 h, rt |
| 4 |  **1d** | **3d**[c] | 95 | $H_2SO_4$, 48 h, rt |
| 5 |  **1e** | **3e**[d] | 91 | $H_2SO_4$, 8 h, 50 °C |

[a] Refs. 2a,4a,4b.
[b] Ref. 3b.
[c] Refs. 3a,3b.
[d] Ref. 1e.

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require a method for driving the reaction to completion by removal of water.

We envisioned using *tert*-butyl acetoacetate as the source of isobutylene since it could offer several advantages. This procedure does not call for the use of expensive reagents, the handling of gaseous isobutylene, or harsh conditions. Further, the only byproducts would be acetone and $CO_2$, so it would not be necessary to remove water in order to drive the reaction to acceptable conversions.

Our initial target for optimization was compound **1a**. We examined several acids including sulfuric acid, methanesulfonic acid and *p*-toluenesulfonic acid as potential catalysts. We found that sulfuric acid gave us the highest conversions. Using excess of *tert*-butyl acetoacetate and catalytic amounts of sulfuric acid at room temperature, we were able to obtain the desired *tert*-butyl esters, across a range of substrates, in acceptable yields (Table 1).

We believe that the procedure outlined here is a convenient and scalable method for the conversion of preparative quantities of carboxylic acids to their corresponding *tert*-butyl esters.

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## References and notes

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2. For procedures for the acid catalyzed esterification with isobutylene, see: (a) Altschul, R. *J. Am. Chem. Soc.* **1948**, *70*, 2604; (b) Altschul, R. *J. Am. Chem. Soc.* **1946**, *68*, 2569.
3. *tert*-Butyl esters can also be formed by the exchange of methyl esters with *tert*-butyl acetate. For descriptions of these reactions, see: (a) Stanton, M. G.; Gagne, M. R. *J. Org. Chem.* **1997**, *62*, 8240; (b) Stanton, M. G.; Allen, C. B.; Kissling, R. M.; Lincoln, A. L.; Gagne, M. R. *J. Am. Chem. Soc.* **1998**, *120*, 5981.
4. For esterifications using the in situ generation of isobutylene, see: (a) Karmakar, D.; Das, P. J. *Synth. Commun.* **2001**, *31*, 535; (b) Wright, S. W.; Hagemon, D. L.; Wright, A. S.; McClure, L. D. *Tetrahedron Lett.* **1997**, *38*, 7345.
5. Representative procedure for the preparation of esters: Carboxylic acid **1a** (0.49 g, 2.48 mmol, 1 mol equiv), 0.02 g (0.20 mmol, 0.08 mol equiv) of concd $H_2SO_4$, and 2.62 g (16.24 mmol, 6.5 mol equiv) of *tert*-butyl acetoacetate were charged to a 15 mL glass pressure tube equipped with a threaded Teflon plug. The reaction was sealed and held at rt for 24 h. After 24 h, the reaction vessel was cooled in a dry/ice acetone bath to reduce any pressure that might have been generated during the reaction. Once the contents were frozen, the cap was cautiously removed. The contents were transferred to a separatory funnel and partitioned between ether and, sequentially, 1.25% aqueous NaOH and saturated brine. The organic extract was dried ($Na_2SO_4$) and concentrated. The NaOH phase was acidified and extracted with ether to recover 0.10 g (80% conversion) of unreacted acid. The yellow oily organic residue was chromatographed to give 0.42 g (82% yield) of **3a** as a clear oil. TLC $R_f = 0.29$ (EtOAc/hexanes, 5:95). IR (neat, $cm^{-1}$) 2978 (s), 1705 (s), 1597 (m), 1475 (m); $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$: 1.2 (s, 9H), 7.3 (m, 7H), 7.5 (qd, $J = 1.5$, 7.5 Hz 1H), 7.7 (dd, $J = 1.4$, 7.6 Hz 1H); $^{13}C$ NMR (300 MHz, $CDCl_3$) $\delta$: 130.7, 130.5, 129.7, 128.7, 128.0, 127.1, 127.0, 27.6; HRMS calcd for $C_{17}H_{18}O_2$ (M+Na) 277.1204, found 277.1417.