*CCA-503*

547.461.3.07

*Note*

# Synthesis of 1,1-di-*tert*-Butyl-2-ethyl ethanetricarboxylate and 1,1-di-*tert*-Butyl-3-ethyl propanetricarboxylate

*S. Pavlov and V. Arsenijević*

*Laboratory of Organic Chemistry, Faculty of Pharmacy, University of Belgrade, Belgrade, Serbia, Yugoslavia*

Received April 9, 1968

The synthesis of 1,1-di-*tert*-butyl-2-ethyl ethanetricarboxylate (I) and 1,1-di-*tert*-butyl-3-ethyl propanetricarboxylate (II) is described. The reaction of di-*tert*-butyl malonate with ethyl bromoacetate gives I, and the Michael condensation between di-*tert*-butyl malonate and ethyl acrylate gives II. In both cases the yields are very good.

The use of *tert*-butyl ethyl malonate as a starting material in the general synthesis of $\beta$-keto esters is well known. However, in spite of comparatively good yields in the preparation of keto esters, the method could not be widely employed because the starting mixed ester is rather inaccessible.[1,2]

The ease with which *tert*-butyl ester groups undergo acidolysis under mild conditions[1,3–5], whilst the carbethoxy group remains intact, permits these compounds to be employed. as starting materials in the syntheses of $\gamma$ and $\delta$-keto esters and the corresponding keto acids.

In this note the preparation of 1,1-di-*tert*-butyl-2-ethyl ethanetricarboxylate[6] (I) and 1,1-di-*tert*-butyl-3-ethyl propanetricarboxylate (II) is described. In the synthesis of I, the sodioderivative of di-*tert*-butyl malonate is treated with ethyl bromoacetate in dry *tert*-butanol. The yield of the mixed tricarboxylic ester is 75—80%*, while the by-product, the mixed tetracarboxylic ester is obtained in a small quantity (10—12%). The use of ethyl chloroacetate decreased the yield of I (51%), while the amount of the mixed tetraester was increased. Similar behaviour was found by the condensation of di-ethylmalonate with $\alpha$-halogenoacetates[7].

The ester II was obtained by Michael condensation between di-*tert*-butyl malonate and ethyl acrylate, in the presence of a catalytic amount of sodium hydride; *tert*-butyl malonate should be taken in excess in order to avoid the condensation of two molecules of ethyl acrylate. The excess of *tert*-butyl malonate which did not react, can be easily regenerated by distillation. If di-*n*-butyl malonate and ethyl acrylate are taken in equimolar amounts[8], the yield of the tricarboxylic ester is decreased (49%).

---

* In an earlier preparation[6] of the mixed ester I, in which the sodioderivative of di-*tert*-butyl malonate was treated with ethyl chloroacetate in boiling tetrahydrofurane, the yield was only 47%.

## EXPERIMENTAL

### *di*-tert-*Butyl malonate*

This ester was prepared from malonyl dichloride and *tert*-butanol by method described[9], but instead of being distilled the crude malonyl dichloride was used*, yield 60—65% (based on malonic acid).

### *1,1-di*-tert-*Butyl-2-ethyl ethanetricarboxylate* (I)

To a solution of di-*tert*-butyl sodiomalonate, prepared from 26.5 g. (0.12 mole) of di-*tert*-butyl malonate and 2.4 g. (0.1 mole) of sodium hydride in 70 ml. of dry *tert*-butanol a solution of 15 g. (0.09 mole) of ethyl bromoacetate in 25 ml. of dry *tert*-butanol was added. After stirring for 1.5 hours at about 70° the mixture was diluted with saturated sodium chloride. The organic layer was separated and the aqueous layer was extracted with ether. The combined extracts and the organic layer were dried and after removal of ether and *tert*-butanol by distillation at atmospheric pressure, three drops of quinoline were added (to prevent decomposition of the *tert*-butyl ester groups), and the liquid was distilled in an ammonia-flushed apparatus. The first fraction consisted of 3.5 g. of di-*tert*-butyl malonate, b. p. 66—68°/1 mm. After an intermediate fraction (2.1 g.), I is distilled at 116—119°/0.5 mm. (Lit. 104—106°/0.4 mm.)[6]. The yield was 20.4—22 g. (75—80% based on ethyl bromoacetate). The residue was distilled at 148—152°/0.5 mm.; yield 3.5—4.2 g. The analysis of the redistilled product corresponds to the mixed ester of 1,3,3,5-pentanetetracarboxylic acid.

### *1,1-di*-tert-*Butyl-3-ethyl propanetricarboxylate* (II)

In a 250 ml. two-necked flask fitted with a reflux condenser and a dropping funnel, which were protected by soda lime tubes, 43.2 g. (0.2 mole) of di-*tert*-butyl malonate and about 50 mg. of sodium hydride were placed. The magnetic stirrer was started, and after 15 minutes a solution of 20 g. (0.2 mole) of ethyl acrylate in 21 g. of di-*tert*-butyl malonate was added dropwise, over a period of 30 minutes. During the addition, the reaction mixture was kept at 40° and then stirred overnight, at room temperature. After this period, the pungent odour of ethyl acrylate disappeared, and the mixture was poured onto 200 ml. of water. The layers were separated, and the aqueous layer was extracted twice with ether. The extracts were combined with the organic layer, washed with saturated sodium chloride solution and dried over magnesium sulfate. After removal of ether, 2—3 drops of quinoline were added, and the residual liquid was fractionally distilled under reduced pressure, in an ammonia-flushed apparatus. There was obtained 18—19 g. of di-*tert*-butyl malonate b. p. 111—114°/30 mm. and 45—50 g. (72—80%) of the mixed triester II, b. p. 123—125°/0.4 mm., $n_D^{19} = 1.4329$

*Anal.* $C_{16}H_{28}O_6$ (316.38) calc'd.: C 60.74; H 8.92%
found: C 60.55; H 8.76%

## REFERENCES

1. S. Breslov, E. Baumgarten, and C. Hauser, *J. Am. Chem. Soc.* **86** (1944) 1286.
2. R. E. Bowman, *J. Chem. Soc.* **1950**, 322.
3. G. S. Fonken and W. S. Johnson, *J. Am. Chem. Soc.* **74** (1952) 831.
4. W. Puterbaugh, F. Swamer, and C. Hauser, *J. Am. Chem. Soc.* **74** (1952) 3439.
5. A. Schrecker and M. Trail, *J. Am. Chem. Soc.* **80** (1958) 6077.
6. H. Muxfeldt, *Chem. Ber.* **92** (1959) 3144.
7. F. Kay and W. Perkin, *J. Chem. Soc.* **89** (1906) 1643.

---

* Our attempts to distil malonyl dichloride at 28 mm. (as cited in *Organic Syntheses*[9]) have been almost uniformly unsuccessful, because this compound was transformed into resinous material. The resinification can be avoided if this compound is distilled under pressure at 1—3 mm. However, the undistilled chloride gave also a satisfactory result in our synthesis of di-*tert*-butyl malonate.

8. R. Evstigneeva, G. Pyshkina, O. Levanda, and N. Preobrazhenskii, *Zhur. obshch. Khim.* **33** (1963) 1841.
9. C. Raha, *Organic Syntheses,* Coll. Vol. **4**, 263.

## IZVOD

### Sinteza 1,1-di-*t*-butil-2-etil-etantrikarboksilata i 1,1-di-*t*-butil-3-etil-propantrikarboksilata

*S. Pavlov i V. Arsenijević*

Opisana je sinteza 1,1-di-*t*-butil-2-etil-etantrikarboksilata (I) i 1,1-di-*t*-butil-3-etil-propantrikarboksilata (II). Reakcijom di-*t*-butil-malonata sa etil-bromoacetatom dobija se estar I dok Michaelova kondenzacija di-*t*-butil-malonata sa etil-akrilatom daje estar II. U oba slučaja prinos je vrlo dobar. Ovi mešoviti triestri poseduju dve t-butil-estarske grupe koje, kao što je poznato, lako podležu acidolizi pod blagim uslovima, dok karbetoksi grupa, pod istim uslovima ostaje nepromenjena. Zbog ovakvih osobina ovi mešoviti estri bi mogli da nađu primenu u sintezi. na pr. za dobijanje γ i δ-keto-estara i keto-kiselina.

ZAVOD ZA ORGANSKU HEMIJU
FARMACEUTSKI FAKULTET
BEOGRAD

Primljeno 9. travnja 1963.