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Studies on Elimination

VI *. A New Route to Vinyl Ketones

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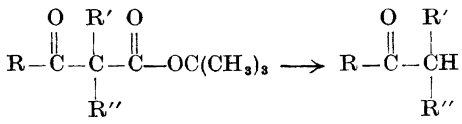
The reactions between *t*-butyl acetoacetate and different aliphatic, aromatic and heterocyclic aldehydes, according to Knoevenagel, give the 1:1 adducts, I, which after spontaneous elimination of water give α,β-unsaturated β-ketoesters, II. By heating II with catalytic amounts of *p*-toluenesulphonic acid carbon dioxide and isobutylene are eliminated to give the corresponding vinyl ketones, III. Our procedure seems to be general for the preparation of ketones of vinyl-type. In one case the adduct was isolated at the aldole stage (I, R = C_6H_5), which has not been previously observed; decomposition of the named aldol yielded the corresponding vinyl ketone.

Our studies on the synthetic application of tertiary β-ketoesters [1–7] in organic chemistry have shown that the smooth elimination of the carbo-*t*-butoxygroup by heating the β-ketoesters in the presence of catalytic amounts of *p*-toluenesulphonic acid offers some advantages, especially as sensitive functional groups generally are not attacked during the elimination



(R = OC_2H_5, CH_3CO; R′, R″ = different groups)

In connection with our investigation of the preparation of 1-methyl-cyclohexene-1-one-3 and related compounds, we observed that *t*-butyl acetoacetate gave the 1:1 product, II, with *i*-butyraldehyde and that the subsequent Michael-addition with another molecule of *t*-butyl acetoacetate did not meet with success under the conditions chosen. This means that the reaction stopped at the Knoevenagel stage, II.

* Part V: Ref.[6]

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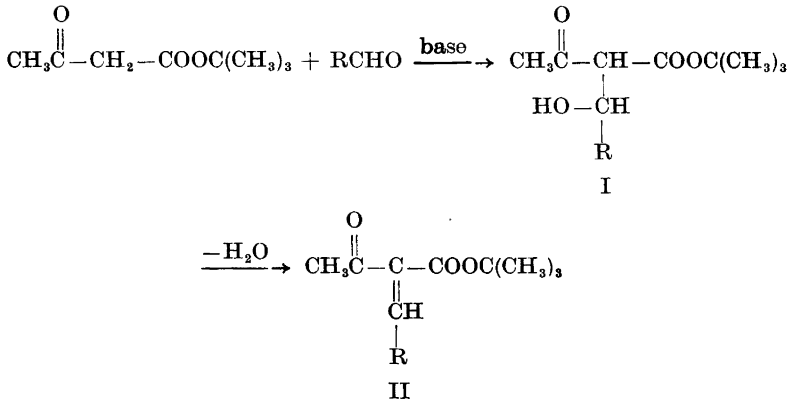
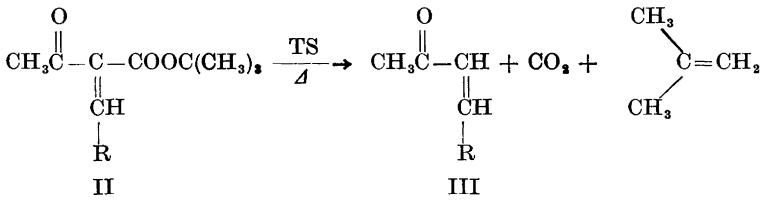


II a: R = CH_3
II b: R = n-C_3H_7
II c: R = i-C_3H_7
II d: R = 2-thienyl
II e: R = p-tolyl
II f: R = 2-furyl

We have therefore prepared a series of condensation products, II, with piperidine as base, following the method of Knoevenagel (for pertinent references, see Ref.[8]). Generally the preparations were made at a low temperature, but for R = isopropyl it was necessary to heat to obtain reasonable yields of II. For R = H we could not isolate either I or II in a pure state; the comparable ethyl methyleneacetoacetate has only been isolated as a polymer and is not distillable even at high vacuum.[10] In one case, however, we were able to isolate the aldol-intermediate I (R = C_6H_5); to our knowledge this is the first instance known of a case where 1,2-elimination of water could have occurred. There are known cases,[9] however, where lactonization has occurred before water-elimination and by which the aldol-stage has been preserved.

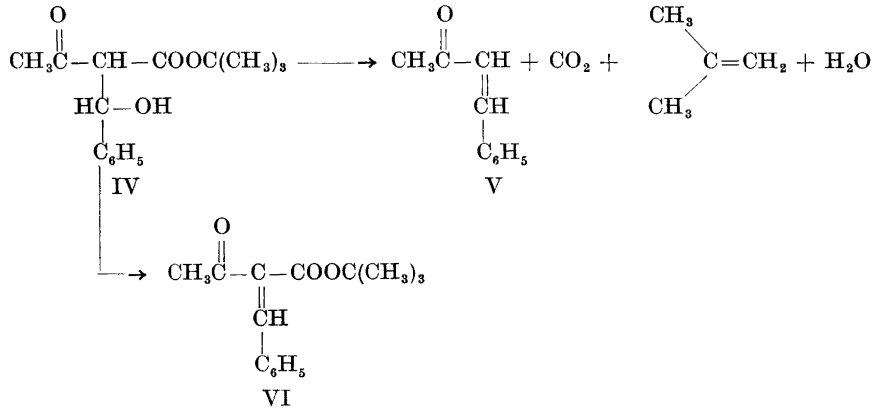
When II was heated to about 150°C in the presence of catalytic amounts of p-toluenesulphonic acid, carbon dioxide and isobutylene were eliminated and the corresponding vinyl ketone was isolated in high yield.



(TS = p-toluenesulphonic acid)

II, III a: R = CH_3
II, III b: R = n-C_3H_7
II, III c: R = i-C_3H_7
II, III d: R = 2-thienyl
II, III e: R = p-tolyl

For II (R = 2-furyl) no ketone III was isolated, but only a tar was formed. Also IV, (I: R = C_6H_5) gave the corresponding α,β-unsaturated ketone, V, (benzalacetone) on heating with *p*-toluenesulphonic acid:



When IV was kept at room temperature and in a closed vial for some time, the melting point decreased from 120° to 84° and the infrared spectrum of a dried sample showed no hydroxyl-absorption, analyses also gave correct values for the normal Knoevenagel 1:1 product VI. Water had been eliminated and any drastic treatment of the aldol IV is thus not necessary to bring about dehydration.

EXPERIMENTAL

t-Butyl acetoacetate was prepared according to Lawesson, Grönwall and Sandberg.[11] Analyses were made at the Analytical Department of Uppsala University, Uppsala, Sweden, and by Dr. Alfred Bernhardt, Mülheim (Ruhr), Germany. Boiling and melting points are uncorrected.

Preparation of II a. In a 250 ml three-necked flask, fitted with a mechanical stirrer, a reflux condenser and a dropping funnel, were placed 79.0 g (0.5 mole) of *t*-butyl acetoacetate and 22.0 g (0.5 mole) of acetaldehyde. The flask was then cooled to about −5°C and during cooling 1.5 g of piperidine in 2−3 ml of absolute ethanol were added dropwise to the solution; the solution was stirred at −5°C for another 24 h and was then left standing for 19 h at about −15°C. The mixture was then dissolved in ether, washed with water until neutral and dried over sodium sulphate. The ether was removed and fractionation of the rest gave a yellow liquid with b.p. 95−96°C/9 mm Hg, n_D^{20} 1.4457. Yield: 56.7 g (62 %) (Found: C 65.19; H 8.80. Calc: C 65.19; H 8.75).

Preparation of II b. From 36.0 g (0.5 mole) of butyraldehyde and 79 g (0.5 mole) of *t*-butyl acetoacetate. Kept for 3 h at −5°C and 45 h at about −15°C. A yellow liquid with b.p. 115°C/10 mm Hg, n_D^{20} 1.4482. Yield: 69.6 g (66 %) (Found: C 67.26; H 9.49. Calc: C 67.89; H 9.50).

Preparation of II c. 31.6 g (0.2 mole) of *t*-butyl acetoacetate and 19.32 g (0.3 mole) of 95 % *i*-butyraldehyde were allowed to react with each other at −8°C for 30 min in the presence of 1 g of piperidine dissolved in 1.5 ml of ethanol. Thereafter, the reaction mixture was heated to 70−80°C for another 30 min. The work-up was carried out as above and a faintly yellow liquid was obtained with b.p. 104−106°C/10 mm Hg, n_D^{20} 1.4466. Yield: 33 g (78 %) (Found: C 67.67; H 9.50. Calc: 67.89; H 9.50).

Preparation of II d. From 31.6 g (0.2 mole) of *t*-butyl acetoacetate and 28 g (0.25 mole) of 2-thiophenecarboxaldehyde at −10°C for 48 h. After the usual work-up, distillation

gave a yellow liquid with b.p. 140–150°C/0.1 mm Hg. On leaving in a refrigerator, it solidified giving – after recrystallization from ethanol – white crystals with m.p. 84–85°C. Yield: 34.2 g (68 %) (Found: C 62.14; H 6.40. Calc: C 61.89; H 6.39).

Preparation of II e. From 31.6 g (0.2 mole) of *t*-butyl acetoacetate and 30 g (0.25 mole) of *p*-tolylaldehyde. 1 g of piperidine in 1.5 ml ethanol was added (reaction temp. –25°) and after 36 h at –10°C the reaction was worked up. White crystals (from ethanol) with m.p. 58–59°C. Yield 40.5 g (78 %) (Found: C 74.01; H 7.71. Calc: C 73.82; H 7.74).

Preparation of II f. From 63.2 g (0.4 mole) of *t*-butyl acetoacetate and 39.2 g (0.4 mole) of redistilled furfural. The reaction mixture was kept at –8° for 6 h and at –15° for 40 h. White crystals (from ethanol) with m.p. 91–93°C. Yield: 60.5 g (64 %) (Found: C 66.08; H 6.90. Calc: C 66.08; H 6.83).

Preparation of IV. 15.8 g (0.1 mole) of *t*-butyl acetoacetate and 15.9 g (0.15 mole) of benzaldehyde were allowed to react at –5°C in the presence of 1 g of piperidine dissolved in 1.5 ml of anhydrous ethanol and were then placed in a deep-freezer at –10°C for 48 h. A solid precipitated, which was recrystallized from ethanol. M.p. 126–127.5°C. Yield: 18.2 g (70 %) (Found: C 68.27; H 8.03. Calc: C 68.16; H 7.63). After standing for one month IV had been converted to VI by dehydration. White crystals with m.p. 84–85° (from ethanol). (Found: C 72.88; H 7.21; Calc: C 73.14; H 7.37).

Preparation of methyl vinylketones. As the procedure is the same for all preparations only one example is given. All other data are recorded in Table 1. 63.2 g (0.4 mole) of *t*-butyl acetoacetate and 12 g (0.4 mole) of formaldehyde were placed in a three-necked flask fitted with a sealed stirrer, a dropping funnel and an addition tube, one arm of which bears a reflux condenser and the other a thermometer. The flask was cooled to –5°C, and a mixture of 2 g of piperidine in 2–3 ml of absolute ethanol was added. The stirring was continued for 5 h and then the reaction mixture was placed in a cooling room for 44 h at about –15°C. Then the mixture was dissolved in ether and the organic phase was shaken until neutral and dried over sodium sulphate. The ether was stripped off and the excess of *t*-butyl acetoacetate (5.8 g) was distilled off. With attempted further frac-

Table 1. Preparation of vinylketones: $CH_3COCH = CH(R)$.

R	B.p.		n_D^{20}	Yield %
	C°	mm Hg		
H	81– 83	752	1.4091 [a]	46
CH_3 [b]	118–120	750	1.4344	87
n-C_3H_7 [c]	70– 73	9	1.4328	93
i-C_3H_7 [d]	155–156	760	1.4360	92
2-Thienyl [e]	90	0.6	–	72
p-Tolyl [f]	80– 85	2	–	71

a: Lit.[12] $n_D^{22} = 1.4095$.
b: The semicarbazone: m.p. 125–126°C (from ethanol) (lit.[13] m.p. 126°C).
c: The semicarbazone: m.p. 150–152°C (from ethanol) (lit.[14] m.p. 152°C).
d: The semicarbazone: m.p. 162–164°C (from ethanol) (lit.[15] m.p. 161–163°C).
e: M.p. 32–35°C (from pet. ether) (lit.[16] m.p. 30–35°C).
f: M.p. 34–35°C (from pet. ether) (lit.[17] m.p. 34–35°C).

tionation, the product began to decompose. However, after addition of 0.1 g of *p*-toluenesulphonic acid to the residue, the distillation vessel was connected to a water pump and warmed on an oil-bath maintained at a temperature of about 130–140°C. When the decomposition was complete (constant pressure) the product was distilled. A colourless liquid with a pungent odour was obtained. B.p. 81–83°C/752 mm Hg, n_D^{20} 1.4091. (lit.[12]: n_D^{20} = 1.4095) Yield: 13.0 g (46 %).

Preparation of V. 11.6 g (0.047 mole) of IV were decomposed at 155–160°C. The residue solidified and after recrystallization from ethanol gave crystals with m.p. 39–41°C. (Lit.[18], m.p. 40°C). Yield: 5.9 g (86 %). The infrared spectrum of the product and that of authentic benzalacetone were superimposable.

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