The Formation of Acetylenic Bond by the Elimination Reaction of Some Enol-esters. III. Formation of α, β-Acetylenic Carbonyl Compounds

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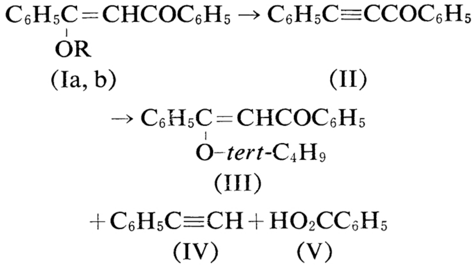
As described in the preceding paper[1], an α, β-acetylenic ketone is readily decomposed by the action of amide anion to yield the corresponding ethynyl compound and acid amide. Therefore, in order to obtain an α, β-acetylenic carbonyl compound by the elimination reaction of enol-esters, it was hoped to employ a suitable base to avoid the cleavage reaction. The nucleophilic addition of the base to a triple bond must also be avoided. The present paper deals with the studies along this line.

According to the studies of Dufraisse and his coworkers[2], primary and secondary alcohols add readily to the triple bond in acetylenic ketone II, but *tert*-alcohols were left untouched up to now. Therefore, the action of sodium *tert*-butoxide on ketone II was examined.

When ketone II was treated with sodium *tert*-butoxide in *tert*-butanol, there was obtained β-*tert*-butoxychalcone (III), as the main product, together with minor amounts of phenylacetylene (IV) and benzoic acid (V). The formation of IV and V clearly indicated that the bond-splitting reaction[1] occured subsidiarily in II.

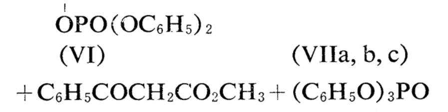


$$\underset{\text{(Ia, b)}}{C_6H_5\underset{\displaystyle OR}{C}{=}CHCOC_6H_5} \rightarrow \underset{\text{(II)}}{C_6H_5C{\equiv}CCOC_6H_5}$$

$$\rightarrow \underset{\text{(III)}}{C_6H_5\underset{\displaystyle O\text{-}tert\text{-}C_4H_9}{C}{=}CHCOC_6H_5}$$

$$+\underset{\text{(IV)}}{C_6H_5C{\equiv}CH}+\underset{\text{(V)}}{HO_2CC_6H_5}$$

a : $R=PO(OC_6H_5)_2$ b : $R=COC_6H_5$



$$\underset{\text{(VI)}}{C_6H_5\underset{\displaystyle OPO(OC_6H_5)_2}{C}{=}CHCO_2CH_3} \rightarrow \underset{\text{(VIIa, b, c)}}{C_6H_5C{\equiv}CCO_2R}$$

$$+\underset{\text{(VIII)}}{C_6H_5COCH_2CO_2CH_3}+\underset{\text{(IX)}}{(C_6H_5O)_3PO}$$

a : $R=tert\text{-}C_4H_9$ b : $R=CH_3$ c : $R=H$

The structure of III was confirmed by its analytical data and infrared spectrum, and supported also by the formation of dibenzoylmethane on heating the enol-ether under reduced pressure. These results indicate that neither the addition nor the bond-fission reaction can be suppressed by the use of sodium *tert*-butoxide in *tert*-butanol.

It was found after several experimentations

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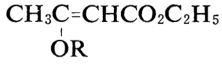
[1] M. Nakagawa, G. Nakaminami, F. Ogura and H. Ono, This Bulletin, 35, 1488 (1962).

[2] M. C. Dufraisse and P Gérald, *Bull. soc. chim. France*, [4] 31, 1285 (1922); M. C. Dufraisse and A. Gillet, *Ann. chim.*, [10] 6, 295 (1926).

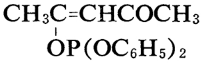
that ketone II was recovered unchanged in a fair yield, when treated with sodium *tert*-butoxide in benzene, therefore all elimination reactions in the present work were carried out in benzene as the solvent. A solution of enol-phosphate was added dropwise to a stirred suspension of sodium *tert*-butoxide in benzene, and the reaction mixture was stirred further in adequate periods. Benzoylphenylacetylene (II) was obtained from the phosphate Ia[3] and the benzoate Ib[3] in 76 and 58% respectively. Not any appreciable amount of by-product could be isolated in these cases. Similarly *tert*-butyl phenylpropiolate (VIIa) was obtained in a 24% yield from the phosphate VI[3]. The structure of VIIa was inferred from its infrared spectrum in which the characteristic absorptions ascribed to a disubstituted acetylene, an ester-carbonyl group and a *tert*-butyl group were clearly indicated. The ester VIIa was converted into methyl ester by refluxing in methanol in the presence of a small amount of sulfuric acid. The ester VIIb thus obtained was hydrolyzed to give free acid VIIc, which was readily purified by sublimation followed by recrystallization. In another experiment, the acid VIIc was isolated from the reaction mixture in a 28% yield. In the reaction of phosphate VI with sodium *tert*-butoxide, triphenylphosphate IX and methyl benzoylacetate VIII were also obtained.

The formation of keto-ester VIII and phosphate IX is probably due to ester-exchange reaction. The reaction of this type was found to be the main reaction in the case of phosphate Xa[3] by the isolation of triphenylphosphate IX and phenol from the reaction products, and no elimination reaction was observed. The elimination reaction of tosylate Xc[3] under similar conditions resulted in the formation of a small amount of a liquid, the main constituent of which was assigned to be ethyl tetrolate on the basis of the infrared spectrum. Alkaline hydrolysis of this material afforded a small amount of crystals, whose identification could not be performed owing to its minor quantity. The phosphate XI[3] gave no well-defined product on treatment with sodium *tert*-butoxide.



$$\mathrm{CH_3\underset{\underset{OR}{|}}{C}{=}CHCO_2C_2H_5}$$

(Xa, c)



$$\mathrm{CH_3\underset{\underset{OP(OC_6H_5)_2}{|}}{C}{=}CHCOCH_3}$$

(XI)

a : $R=PO(OC_6H_5)_2$

c : $R=SO_2C_6H_4\text{-}p\text{-}CH_3$

The above-mentioned results appear to provide a support for the elimination mechanism of triple bond biosynthesis through enol derivative*.

Experimental**

Action of Sodium *tert*-Butoxide on Benzoylphenylacetylene (II).—A solution of *tert*-butoxide (0.013 mol.) in dry *tert*-butanol (50 ml.) was warmed at 25∼30°C. A solution of ketone II[4] (2.0 g., 0.01 mol.) in dry ether (30 ml.) was added dropwise while stirring into the above solution during 40 min. The reaction mixture was stirred for a further 2 hr. at the same temperature, and set aside at room temperature for 16 hr. A solution of glacial acetic acid (0.8 g., 0.013 mol.) in dry ether (25 ml.) was added dropwise while stirring and cooling (ice-bath), and then water (50 ml.) was added. The aqueous solution was extracted twice with ether, and combined ethereal solutions were washed successively with sodium hydrogen carbonate solution, 5% potassium hydroxide solution and water, dried (sodium sulfate) and concentrated. The residue was dissolved in ethanol (6 ml.), and treated with mercuric chloride-potassium iodide solution in the Johnson-McEwen's procedure[5]. An oil and an amorphous solid were separated. The solid was filtered, washed with 50% aqueous ethanol, pressed on a porous plate, left overnight to remove an oily material as well as possible, and recrystallized twice from ethanol to give a mercury compound of phenylacetylene as colorless needles, m. p. 122∼123.5°C, undepressed on admixture with an authentic specimen.

On acidification (Congo Red) of the sodium hydrogen carbonate washings, an oil was separated and extracted with ether. The combined ether-extracts were washed with sodium chloride solution, dried (sodium sulfate), and evaporated. To the residue dissolved in acetic acid, water was added precipitating a solid (0.7 g., 57%), which was sublimed under reduced pressure and recrystallized twice from water to give benzoic acid as colorless plates, m. p. 121.5∼122°C. It showed no depression in the melting point on admixture with an authentic specimen.

In another experiment using 0.04 mol. of acetic acid only 0.1 g. of the crude benzoic acid was obtained, and from the neutral part crystals (0.5 g.) of *β-tert*-butoxychalcone (III) were yielded, which were treated with charcoal in methanol and recrystallized twice from the same solvent to afford light yellow plates, m. p. 97∼98°C.

Found: C, 81.54; H, 7.25. Calcd. for $C_{19}H_{20}O_2$: C, 81.39; H, 7.19%.

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3) M. Nakagawa, G. Nakaminami, F. Ogura and H. Ono, This Bulletin, **35**, 1485 (1962).

* As mentioned previously[3], quite recently, Jones [*Chem. & Ind. News*, **39**, No. 12, 46 (1961)] has suggested that the decarboxylative elimination of pyrophosphate anion from the pyrophosphate of acetylmalonyl coenzyme A is a possible route in the formation of an acetylenic bond in vivo, and the mechanism has been supported experimentally by the formation of phenylpropiolic acid from enol brosylate of diethyl benzoylmalonate in an alkaline medium (I. Fleming and J. Harey-Mason, *Proc. Chem. Soc.*, **1961**, 245.).

** All melting points and boiling points are uncorrected.

4) E. André, *Ann. chim.*, [8], **29**, 564 (1913). Cf. K. Bowden, I. M. Heilbron, E. R. H. Jones and B. C. L. Weedon, *J. Chem. Soc.*, **1946**, 39.

5) J. R. Johnson and W. L. McEwen, *J. Am. Chem. Soc.*, **48**, 471 (1926).

IR (Nujol) : $>$C=O, 1662 cm^{-1}.

The enol-ether III gave the same deep red color as dibenzoylmethane, when it was treated with ferric chloride in ethanol, but the development of the color required several minutes. A similar behavior against ferric chloride was observed also in the case of β-methoxychalcone[2].

Thermal Decomposition of β-*tert*-Butoxychalcone (III).—The enol-ether III (0.1 g.) was heated at 180~200°C (bath) under reduced pressure (aspirator) in a sublimation apparatus. Light yellow crystals adhered gradually on the cold finger, and finally only a small amount of oil was left at the bottom of the vessel. The crystals furnished dibenzoylmethane on recrystallization from methanol as light yellow needles, m. p. 77.5~78.5°C, which showed no melting point depression on admixture with an authentic specimen[6].

Found: C, 80.62; H, 5.44. Calcd. for $C_{15}H_{12}O_2$: C, 80.33; H, 5.39%.

Elimination Reaction of Diphenyl 1,3-Diphenyl-2-propen-1-on-3-yl Phosphate (Ia) by Sodium *tert*-Butoxide.—Sodium (0.95 g., 0.041 gram atom) was dissolved in hot dry *tert*-butanol (150 ml.), and the solvent was driven off at 50~55°C (bath) under reduced pressure as well as possible, affording almost colorless needles of sodium *tert*-butoxide. Dry benzene (150 ml.) was added to the crystals, and then the phosphate Ia (18.3 g., 0.04 mol.) in dry benzene (200 ml.) was added dropwise with stirring at room temperature to the resulting suspension during 1 hr. The mixture was stirred for a further 13.5 hr. at room temperature, and set aside for 28 hr. Water was added, and the benzene layer was washed successively with 5% potassium hydroxide solution and water and dried (sodium sulfate). All of the aqueous solutions were combined and extracted with ether. The combined ether-extracts were washed with water and dried (sodium sulfate). Evaporation of the solvent followed by distillation of the residue gave benzoylphenylacetylene (II) as a yellow oil (6.3 g., 76%), b. p. 142~144°C/0.5 mmHg, without affording any appreciable amount of low-boiling or high-boiling material. The oil was solidified completely, when seeded with a piece of crystal of authentic II, to give crystals melted at 42~47°C which was recrystallized twice from light petroleum (b. p. 40~60°C) to yield slightly yellow needles, m. p. 48~48.5°C, undepressed on admixture with an authentic specimen. Its infrared spectrum also showed the identity with that of the authentic specimen.

Found: C, 87.54; H, 5.04. Calcd. for $C_{15}H_{10}O$: C, 87.35; H, 4.89%.

A crystalline material which seemed to be diphenyl phosphate was obtained from the aqueous solution left after the extraction of ketone II.

Elimination Reaction of β-Benzoyloxychalcone (Ib) with Sodium *tert*-Butoxide.—A suspension of sodium *tert*-butoxide (0.022 mol.) in dry benzene (50 ml.) was prepared as above. A solution of the benzoate Ib[3] (6.6 g., 0.02 mol.) in dry benzene (50 ml.) was added dropwise with cooling (cold water) to the stirred suspension during 40 min. The mixture was stirred for 6 hr. with cooling by cold water, for a further 10 hr. at room temperature, and allowed to stand for about 30 hr. Water (150 ml.) was added with cooling by cold water, and the aqueous layer was extracted twice with benzene and twice with ether. The combined organic extracts were washed with sodium chloride solution and dried (sodium sulfate). Evaporation followed by distillation of the residue afforded ketone II as an oil (3.0 g.), b. p. 162~169°C/2.5 mmHg, which was solidified completely when seeded as described before. The solid so far obtained was dissolved in ether and washed successively with 5% potassium hydroxide solution and water. The ether was altered with benzene and the benzene solution was chromatographed on alumina (4.0 g.). Removal of the solvent from the eluate gave II (2.6 g., 58%) which was recrystallized from light petroleum (b. p. 40~60°C) as yellow plates, m. p. 46.5~49.5°C, and identified by infrared spectrum.

Elimination Reaction of Diphenyl β-Methoxycarbonyl-α-styryl Phosphate (VI) with Sodium *tert*-Butoxide.—A suspension of sodium *tert*-butoxide (0.044 mol.) in dry benzene (120 ml.) was prepared as above. A solution of the phosphate VI[3] (17.8 g., 0.043 mol.) in dry benzene (120 ml.) was added dropwise at room temperature to this stirred suspension during 1 hr. The mixture was stirred for a further 7 hr. at room temperature, left standing overnight, and then treated with water (120 ml.). The aqueous solution (solution A) was extracted twice with ether, and the combined organic solutions were washed successively with a 4% potassium carbonate solution (100 ml. × 2), ice-cooled 0.5 N sodium hydroxide solution (100 ml. × 2) and water, and dried (sodium sulfate). Evaporation followed by distillation gave a colorless liquid (product A) (2.1 g.), b. p. 93.5~96°C/1 mmHg, and an orange oily residue (product B).

The sodium hydroxide washings were acidified at 0°C, and then extracted 3 times with ether. The combined extracts were washed with sodium chloride solutionand dried (sodium sulfate). Evaporation followed by distillation afforded an oil (1.6 g., 30%), b. p. 100~101°C/1 mmHg, which was identified with methyl benzoylacetate[7] by infrared spectrum. The copper complex provided by the above oil exhibited m. p. 200~202°C and showed no melting point depression on admixture with an authentic specimen[7].

Found: C, 57.81; H, 4.42. Calcd. for $C_{20}H_{18}\cdot O_6Cu$: C, 57.48; H, 4.34%.

The above-mentioned potassium carbonate washings and the solution A afforded an oil on acidification (Congo Red) and ether-extraction. The oil appeared from its infrared spectrum as a mixture of diphenyl phosphate and a small amount of phenylpropiolic acid (VIIc), but no detailed study was taken.

Product A.—Its infrared spectrum [(liquid film) : 2215, 2250 (-C≡C-) ; 1710 ($>$C=O ester) ; 1397, 1373 (C-H *tert*-C_4H_9) ; 1300, 1150 cm^{-1} ($O{=}\overset{|}{C}{-}O{-}$)] was found to be consistent with the structure of *tert*-butyl phenylpropiolate (VIIa), although the analytical

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6) C. F. H. Allen, R. D. Abell and J. B. Normington, "Organic Syntheses", Coll. Vol. 1 (1948), p. 205.

7) A. Wahl, *Compt. rend.*, **147**, 72 (1908).

data indicated the presence of an impurity. A mixture of the product A (1.0 g.), absolute methanol (20 ml.) and concentrated sulfuric acid (4 drops) was refluxed for 12.5 hr., left to stand at room temperature for about 30 hr., and poured into ice-water. An oil was separated and extracted 3 times with ether. The combined extracts were washed successively with water, sodium hydrogen carbonate solution and water, and dried (sodium sulfate). After evaporation of the solvent, the residue was distilled giving a light yellow liquid (0.8 g., 100%), b. p. 78.5∼81°C/2 mmHg, (lit.,[8] b. p. 132∼133°C/16 mmHg), which was proved to consist mainly of methyl ester VIIb on the basis of the infrared spectrum [(liquid film): 2220 (-C≡C-); 1715 (>C=O ester); 2820 cm^{-1} (C-H CH_3O)].

A mixture of methyl ester VIIb (0.5 g.), potassium hydroxide (0.3 g., 1.5 equiv.), ethanol (8 ml.) and water (4 ml.) was refluxed for 30 min., and cooled immediately. On addition of water (10 ml.) a small amount of oil was separated. After removal of the oil by ether-extraction, the remaining aqueous solution was acidified (Congo red) with dilute sulfuric acid at 0°C. An oil was separated, and soon began to crystallize. The product was taken up in ether, washed with sodium chloride solution and dried. Evaporation of the ether afforded phenylpropiolic acid VIIc, (0.3 g., 65%) which was sublimed under reduced pressure, and recrystallized twice from carbon tetrachloride and once from water as colorless needles, m. p. 135∼137°C, (lit.[9], m. p. 137°C).

Found: C, 73.89; H, 4.22. Calcd. for $C_9H_6O_2$: C, 73.96; H, 4.14%.

IR (Nujol): 2205, 2240 (-C≡C-); 1675 (>C=O carboxyl); 3200∼2400 cm^{-1} (O-H carboxyl).

Product B.—On storage in an ice-box, product B deposited some amounts of the recovered phosphate VI, which was removed by filtration. The filtrate was distilled and the fraction, boiling at 140∼173°C/3×10^{-4} mmHg, was collected, then it was seeded with a piece of crystal of triphenyl phosphate[10] IX and stored in an ice-box. A solid was separated (1.4 g., 16%) and recrystallized from light petroleum (b. p. 40∼60°C) to give phosphate IX as colorless needles, m. p. 48.5∼50°C, which showed no melting point depresssion on admixture with an authentic specimen. Its infrared spectrum also agreed with that of the authentic specimen.

Reaction of Diphenyl 1-Ethoxycarbonyl-1-propen-2-yl Phosphate (Xa) with Sodium *tert*-Butoxide.—The phosphate[3] Xa (160.8 g., 0.44 mol.) was added dropwise at room temperature to a stirred suspension of sodium *tert*-butoxide (0.45 mol.) in dry benzene. The mixture was stirred for 20 hr., set aside for 1 day, and treated with water. The benzene layer was washed successively with 5% sodium hydroxide solution and sodium chloride solution, and dried. Benzene was removed, the residue was distilled and a fraction boiling over 130°C/3×10^{-3} mmHg, was collected. The fraction solidified, and it was recrystallized twice from light petroleum to give triphenyl phosphate (IX) as colorless needles, m. p. 49∼49.5°C, identified by infrared spectrum.

A low boiling liquid obtained above was redistilled to give a liquid, b. p. 95∼105°C/1×10^{-3} mmHg, n_D^{20} 1.4838, which was clearly different from the starting phosphate Xa, but its infrared spectrum resembled Xa. Although the product was supposed to be produced by ester-exchange reaction, the analytical value did not agree with the calculated ones for any possible compounds. Perhaps it is a mixture of various products at different stages in ester-exchange reaction.

From the sodium hydroxide extract stated above, some amount of phenol was obtained by acidification and ether-extraction.

Reaction of Ethyl *β-p*-Toluenesulfonyloxycrotonate (Xc) with Sodium *tert*-Butoxide.—The tosylate Xc[3] (13.4 g., 0.047 mol.) was added dropwise at room temperature to a stirred suspension of sodium *tert*-butoxide (0.048 mol.) in dry benzene. The mixture was stirred at room temperature for 38 hr., left standing for 75 hr., and treated with water. The aqueous layer was extracted with ether, and the combined organic layers were washed successively with 5% sodium hydroxide solution and salt solution. Evaporation followed by distillation gave ethyl tetrolate as colorless, sweet smelling liquid (0.5 g.), b. p. 63∼64°C/10 mmHg, (lit.[11], b. p. 164.5∼165.0°C/760 mmHg).

IR (liquid film): 2240 (-C≡C-); 1712 cm^{-1} (>C=O ester).

A mixture of the liquid (0.3 g.) and 0.5 N potassium hydroxide (15 ml.) was refluxed for 40 min., cooled, and extracted with ether to remove a small amount of insoluble material. Acidification and ether-extraction afforded a very small amount of crystals, which could not however be identified.

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Note added in proof (August 31, 1962).

Since this paper was submitted a short communication by J. Cymerman Craig and M. Moyle (*Proc. Chem. Soc*, **1962**, 149) has appeared in which they realized the formation of some acetylenic compounds treating the enol diethyl phosphates of the corresponding carbonyl compounds with sodium amide in liquid ammonia.

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[8] C. Moureu, *Ann. chim.*, [8] **7**, 536 (1906).

[9] F. Barisch, *J. prakt. Chem.*, [2] **20**, 173 (1879).

[10] G. Jacobson, *Ber.*, **8**, 1523 (1875); P Brigl and H. Müller, ibid., **72**, 2121 (1939).

[11] E. A. Halonen, *Acta Chem. Scand.*, **9**, 1492 (1955).