The Formation of Acetylenic Bond by the Elimination Reaction of Some Enol-esters. I. Syntheses of Enol-esters

By Masazumi NAKAGAWA, Gen NAKAMINAMI, Fumio OGURA and Hiroshi ONO

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In recent years the wide distribution of various kinds of polyacetylenic compounds in the plant kingdom was well recognized[1], and considerable attention has been directed towards the mode of the formation of such a labile molecule containing a large amount of energy in a living cell. The most plausible one among the proposed several hypotheses[2] seems to be the dehydration mechanism of an enol of a β-dicarbonyl compound by way of a suitable

$$RCOCH_2COR' \rightarrow RC(OX)=CHCOR' \rightarrow RC\equiv CCOR'$$

enol derivative. This hypothesis has been supported indirectly by recent biochemical evidence which was obtained by the ^{14}C tracer technique[3].

Quite recently, Jones 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[4], and the mechanism has been supported experimentally by the formation of phenylpropiolic acid from enol-brosylate of diethyl benzoylmalonate in an alkaline medium[5]. But the full explanation of the Jones' hypothesis and the detail of the experimental support are not ready for our hands.

Independently we have carried out the experimental confirmation of the formation of triple bond by simple elimination reaction of several enol-esters. The present paper deals with the synthesis of some enol-esters and the formation of acetylenic compounds from them will be reported in the following papers.

1) For review on this field, see, F. Bohlmann, *Angew. Chem.*, **67**, 389 (1955); E. R. H. Jones, *Proc. Chem. Soc.*, **1960**, 199; N. A. Sörensen, ibid., **1961** 98.
2) J. D. Bu'Lock, *Quart. Revs.*, **10**, 371 (1956).
3) J. D. Bu'Lock and H. Gregory, *Biochem. J.*, **72**, 322 (1959); J. D. Bu'Lock, D. C. Allport and W. B. Turner, *J. Chem. Soc.*, **1961**, 1654.
4) *Chem. & Ind. News*, **39**, No. 12, 46 (1961).
5) I. Fleming and J. Harey-Mason, *Proc. Chem. Soc.*, **1961**, 245.

$$RC(OX)=CHCOR'$$

I : R, R′=C_6H_5
a : X=$PO(OC_6H_5)_2$
b : X=COC_6H_5

II : R=C_6H_5, R′=OCH_3
a : X=$PO(OC_6H_5)_2$
b : X=$SO_2C_6H_4$-*p*-CH_3

III : R=CH_3, R′=OC_2H_5
a : X=$PO(OC_6H_5)_2$
b : X=$SO_2C_6H_4$-*p*-CH_3

IV : R, R′=CH_3, X=$PO(OC_6H_5)_2$

$$[RCOCHCOR']Na + ClPO(OC_6H_5)_2 \quad (V)$$
$$\rightarrow RC(OPO(OC_6H_5)_2)=CHCOR'$$

The following seven enol-esters were synthesized in the present work. These hitherto unknown enol-phosphates were obtained in good yield by the reaction of the sodium derivatives of the corresponding β-dicarbonyl compounds with diphenyl phosphorochloridate (V). Diphenyl 1, 3-diphenyl-2-propen-1-on-3-yl phosphate (Ia) and diphenyl β-methoxycarbonyl-α-styryl phosphate (IIa) were obtained in crystalline form, while diphenyl 1-ethoxycarbonyl-1-propen-2-yl phosphate (IIIa) and diphenyl 3-penten-2-on-4-yl phosphate (IV) were obtained in liquid form. The last one could not be purified owing to the decomposition in the attempted distillation even under a high vacuum. The structures of these compounds were confirmed by analyses except in the case of the phosphate IV, and also by the fact that all of these were insoluble in a dilute aqueous alkali solution and gave no coloration with ferric chloride. As will be reported later, elimination reaction was successfully realized in the cases of Ia and IIa affording the correspoding acetylenic compounds.

It has long been known that *C*-acylated products are mainly obtained, when sodium derivatives of various β-dicarbonyl compounds are treated with acyl halides. However, exclusive *O*-acylation was observed in the abovementioned phosphorylation, and no *C*-acylated product was detected. The usual method of *O*-acylation with acyl halides in pyridine gave no satisfactory result for the synthesis of phosphate Ia. No reaction appeared to occur, when the copper complex of methyl benzoylacetate was treated with phosphorochloridate (V).

Although many investigations were carried out until now about the reaction of the sodium derivatives of β-dicarbonyl compounds with various sulfonyl chlorides[6], the corresponding enol-sulfonates could not be obtained except at one instance. Kohler and MacDonald[6a], and Findeisen[6b] obtained sodium *p*-toluenesulfinate, ethyl chloroacetoacetate and ethyl diacetosuccinate, when the sodium derivative of ethyl acetoacetate was treated with *p*-toluenesulfonyl chloride in dry ether. The present authors carried out the reaction in acetone and obtained 4, 4′-dimethyldiphenyldisulfone[7] together with an oil. The oily material could be distilled under a high vacuum, but a small amount of chlorine containing impurity could not be removed. The distillate was insoluble in a dilute alkali solution and gave a negative test against ferric chloride and it is likely to consist mainly of enol-tosylate of ethyl acetoacetate (IIIb). The formation of the disulfone, in the present case, is attributable to the reaction of sulfonyl chloride with the sulfinate which is produced at the first stage[7].

The sodium derivative of methyl benzoylacetate was treated with *p*-toluenesulfonyl chloride in ether, yielding crude methyl *p*-toluenesulfonyloxycinnamate (IIb) in crystals. The pure material was obtained in only a few per cent yield owing to the difficulty in the removal of a considerable amount of contaminant. The assigned structure of the tosylate IIb was supported by analysis and the fact that the substance is insoluble in aqueous alkali and gives a negative test against ferric chloride*.

Treatment of dibenzoylmethane and methyl benzoylacetate with *p*-toluenesulfonyl chloride in pyridine did not afford the desired tosylates. Also the reaction of the copper complex of the above ketoester with the sulfonyl chloride gave unsatisfactory result.

β-Benzoyloxychalcone (Ib) was prepared according to the literature[8].

Experimental**

Diphenyl 1, 3-Diphenyl-2-propen-1-on-3-yl Phosphate (Ia).—A solution of dibenzoylmethane[9] (17.3 g., 0.077 mol.) in absolute ethanol (340 ml.) was added dropwise at room temperature to a stirred solution of sodium ethoxide (from 1.8 g., 0.078 g. atom, of sodium and 175 ml. of absolute ethanol).

Ethanol was evaporated (below 40°C) under reduced pressure, and the residual yellow solid was collected on a funnel, and washed with ether. A further crop was obtained from the filtrate and washings. The well dried solid was pulverized, suspended in dry ether (150 ml.), and a solution

6) a) E. P. Kohler and M. B. MacDonald, *Am. Chem. J.*, **22**, 227 (1899); b) T. v. Findeisen, *J. prakt. Chem.*, [2] **65**, 529 (1902); c) H. Böhme and H. Fischer, *Ber.*, **76**, 92, 99 (1943); d) E. M. Philbin, E. R. Stuart, R. F. Timoney and T. S. Wheeler, *J. Chem. Soc.*, **1957**, 2338.

7) E. P. Kohler and M. B. MacDonald, *Am. Chem. J.*, **22**, 219 (1899).

* In a preliminary experiment, the tosylate (IIb) afforded phenylpropiolic acid by the action of sodium *tert*-butoxide. This also supports the assignment.

8) L. Claisen and E. Haase, *Ber.*, **36**, 3674 (1903).

** All melting points and boiling points are uncorrected.

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

of diphenyl phosphorochloridate[10] (V) (19.7 g., 0.074 mol.) in dry ether (150 ml.) was added dropwise with stirring at room temperature to this suspension during 30 min. The mixture was stirred for 3 1/4 hr., refluxed with stirring for 13 hr., and was then left at room temperature for 79 hr. After addition of water (90 ml.), the insoluble solid was filtered, washed with water and ether and recrystallized from ethanol to give the fairly pure phosphate Ia (20.7 g., 59% based on dibenzoylmethane), m. p. 112.5~115°C, which was further recrystallized twice from the same solvent to yield the analytical sample, light yellow cubes, m. p. 113.5~115°C.

Found: C, 70.64; H, 4.53. Calcd. for $C_{27}H_{21}O_5P$: C, 71.05; H, 4.64%.

Dibenzoylmethane (4.2 g.) was recovered from the ethereal layer of the above-mentioned filtrate and washings.

Diphenyl β-Methoxycarbonyl-α-styryl Phosphate (IIa).—The sodium compound prepared from methyl benzoylacetate[11] (10.0 g., 0.056 mol.) was mixed with diphenyl phosphorochloridate (V) (15.0 g., 0.056 mol.) according to the same manner as described above. The reaction mixture was stirred at room temperature for 6.5 hr., allowed to stand overnight and then refluxed with stirring for 4 hr. Water (90 ml.) was added to the ice-cooled reaction mixture, and the solid phosphate was filtered and washed successively with water and ether. A further crop was obtained from the ethereal solution. Recrystallization of the combined crops from light petroleum (b. p. 60~80°C) afforded almost pure material (14.2 g., 62%), m. p. 74~76°C, which was further recrystallized from the same solvent as colorless needles, m. p. 75~76°C.

Found: C, 64.75; H, 4.69; P, 7.27. Calcd. for $C_{22}H_{19}O_6P$: C, 64.39; H, 4.67; P, 7.55%.

Diphenyl 1-Ethoxycarbonyl-1-propen-2-yl Phosphate (IIIa).—The sodium derivative (10.7 g., 0.07 mol.) of ethyl acetoacetate was mixed with diphenyl phosphorochloridate (V) (18.9 g., 0.07 mol.) as described above. The mixture was stirred for 13 hr., and kept at room temperature for several hr. Water was added and the ethereal layer was washed successively with a 5% sodium hydroxide solution and a sodium chloride solution, and dried (Na_2SO_4). After evaporation of the solvent, the residue was distilled under reduced pressure to give the phosphate IIIa (16.1 g., 63.5%) as a colorless liquid, b. p.167~172°C/2×10^{-3} mmHg, n_D^{20} 1.5336.

Found: C, 59.79; H, 5.32; P, 8.48. Calcd. for $C_{18}H_{19}O_6P$: C, 59.67; H, 5.29; P, 8.56%.

Diphenyl 3-Penten-2-on-4-yl Phosphate (IV).—The sodium compound, prepared from acetylacetone (23.6 g., 0.24 mol.), and diphenyl phosphorochloridate (V) (63.2 g., 0.24 mol.) were mixed as above. The reaction mixture was stirred at room temperature for 9 hr., left overnight, and was then treated as in the case of the phosphate IIIa affording an orange oil (54.0 g., 69%). An attempt to distill the oil was unsuccessful even under a high vacuum (3×10^{-4} mmHg) because of its slow decomposition at a bath-temperature above 150°C.

Methyl β-p-Toluenesulfonyloxycinnamate (IIb).—A mixture of methyl sodiobenzoylacetate (prepared from 3.6 g., 0.02 mol. of the ester) and *p*-toluenesulfonyl chloride (3.8 g., 0.02 mol.) obtained in the manner as used for the phosphate, was stirred at room temperature for 9 hr., refluxed for 23 hr., and left at room temperature about 100 hr. After addition of water, the ethereal solution separated was washed successively with dilute aqueous sodium hydroxide and water, and dried (Na_2SO_4). Removal of the ether afforded a solid, which was separated from a concomitant oil by filtration, washed with ether, and recrystallized from methanol to give the tosylate IIb as colorless plates (0.5 g., 7.5%), m. p. 103~104°C.

Found: C, 61.26; H, 4.83; S, 9.71. Calcd. for $C_{17}H_{16}O_5S$: C, 61.43; H, 4.85; S, 9.65%.

Ethyl β-p-Toluenesulfonyloxycrotonate (IIIb).—*p*-Toluenesulfonyl chloride (38.0 g., 0.2 mol.) in anhydrous acetone was added to a suspension of sodium compound prepared from ethyl acetoacetate (26.0 g., 0.2 mol.) in the same solvent. The reaction mixture was stirred at room temperature for 6 hr., refluxed for 5.5 hr., and then allowed to stand at room temperature for 2 days. After a large amount of water was added to the reaction mixture, a white crystalline material and an oil separated which were extracted repeatedly with benzene. The combined benzene extracts were washed with a 5% sodium hydroxide solution and with a sodium chloride solution, and dried. Evaporation of benzene gave a crystalline material together with an oil. The oil was distilled under a high vacuum affording the tosylate IIIb as light yellow viscous oil (21.9 g., 38.5%), b. p. 126~128°C/4×10^{-4} mmHg, $n_D^{20.5}$ 1.5270.

Found: C, 54.12; H, 5.55. Calcd. for $C_{13}H_{16}O_5S$: C, 54.57; H, 5.97%.

The crystals were recrystallized twice from benzene yielding 4, 4'-dimethyldiphenyldisulfone as colorless needles (2.1 g.), m. p. 208.5~209.5°C (decomp.), [lit.[7], m. p. 212°C (decomp.)].

Found: C, 54.31; H, 4.54; S, 20.36. Calcd. for $C_{14}H_{14}O_4S_2$: C, 54.17; H, 4.55; S, 20.66%.

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Department of Chemistry
Faculty of Science
Osaka University
Nakanoshima, Osaka

10) E. Baer, "Biochemical Preparations", Vol. 2, John Wiley and Sons, Inc., New York (1952), p. 97.
11) A. Wahl, *Compt. rend.*, **147**, 72 (1908).