4-Chloro-3-methylcrotonic Acid Derivatives and Phosphonates

By Kazuyoshi FUJIWARA, Hidetaka TAKAHASHI and Masaki OHTA

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3-Methylcrotonic acid derivatives are important intermediates for the synthesis of Vitamin A or of carotenoid. The present authors have found a very convenient procedure for the preparation of 4-chloro-3-methylcrotonic acid derivatives by the use of phosphonates. Recently, Wadsworth and Emmons[1] described how carbonyl compounds reacted with phosphonates by the action of sodium hydride to give olefinic compounds. In this study, ethyl

1) W. S. Wadsworth and W. D. Emmons, *J. Am. Chem. Soc.*, **83**, 1733 (1962).

4-chloro-3-methylcrotonate and 4-chloro-3-methylcrotononitrile were obtained from chloroacetone and appropriate phosphonate by the aid of sodium amide or of hydride in dry ether or tetrahydrofuran.

$$ClCH_2\overset{CH_3}{\overset{|}{C}}O + (EtO)_2\overset{O}{\overset{\|}{P}}CH_2R \rightarrow ClCH_2\overset{CH_3}{\overset{|}{C}}{=}CHR \quad (I)$$

(R, CO_2Et or CN)

Phosphonate in dry ether or tetrahydrofuran was stirred into a slurry of sodium amide or hydride in the same solvent at about 20°C. After this addition, the solution was stirred at room temperature while the evolved gas was removed under a slow stream of nitrogen. To the yellow solution, maintained below 25°C, chloroacetone in the same solvent was added drop by drop, a gummy precipitate appearing. After the reaction mixture had been stirred at room temperature for 1 hr., much excess water was added and then the product was extracted with ether. The ether, after being dried over sodium sulfate, was removed and the residue distilled under reduced pressure. I, R=CO_2Et; yield, 58%; b. p., 83~84°C/15 mmHg. Found: C, 51.38; H, 6.47; Cl, 21.41. Calcd. for $C_7H_{11}ClO_2$: C, 51.70; H, 6.82; Cl, 21.81%. I, R=CN; yield, 72%; b. p., 89~90°C/22 mmHg. Found: C, 51.92; H, 5.31; N, 12.09. Calcd. for C_5H_6ClN: C, 51.96; H, 5.23; N, 12.12%.

The 4-chloro-3-methylcrotonic acid derivatives condensed with triethyl phosphite at 180~200°C to give phosphonates. II, R=CO_2Et; yield, 81%; b. p., 157~158°C/8 mmHg. Found: C, 49.68; H, 8.11. Calcd. for $C_{11}H_{21}O_5P$: C, 49.99; H, 8.01%. II, R=CN; yield, 89%; b. p., 135~136°C/4 mmHg. Found: C, 49.58; H, 7.44; N, 6.44. Calcd. for $C_9H_{16}NO_3P$: C, 49.76; H, 7.43; N, 6.45%.

$$ClCH_2\overset{CH_3}{\overset{|}{C}}{=}CHR + (EtO)_3P \rightarrow (EtO)_2\overset{O}{\overset{\|}{P}}CH_2\overset{CH_3}{\overset{|}{C}}{=}CHR \quad (II)$$

Further investigation into the reaction between haloketones and phosphonates is now in progress; details will be presented elsewhere.

Laboratory of Organic Chemistry
Tokyo Institute of Technology
Meguro-ku, Tokyo