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A Convenient Synthesis of 3,4-Dialkyl-5-carbomethoxy-2-pyrone

Shosuke YAMAMURA, Shuichi IWADARE, Shusi UEDA and Yoshimasa HIRATA
Chemical Institute, Nagoya University, Chikusa, Nagoya

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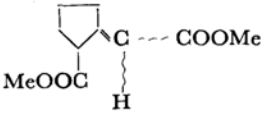
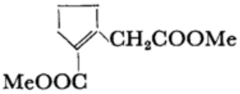
In general, it is difficult to make 3,4-dialkyl-2-pyrone derivatives. We here describe a three-step synthesis of 3,4-dialkyl-5-carbomethoxy-2-pyrone from the β-keto ester.[1]

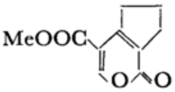
When heated with carbomethoxymethylene-triphenyl-phosphorane at 100—110°C for 15 hr under nitrogen, and then submitted to silica gel chromatography (Mallinckrodt, 100 Mesh), 2-carbomethoxy-cyclopentanone did not afford a condensation product (I), but it did afford, in a 62% yield, an isomer (II), bp 101—102°C/4 mmHg; $\nu_{\max}^{\text{film}}$ 1748, 1713 and 1650 cm^{-1}; NMR spectrum (in benzene): 1.65 (2H, near q, J=7.5 cps), 2.1–2.8 (4H, br), 3.37 (3H, s), 3.40 (3H, s) and 3.73 ppm (2H, s).*[1] In the presence of sodium methoxide,*[2] II was treated with methyl formate at room temperature for 40 hr to afford a brown solution;[2] this solution was then cooled at 0°C and reacted with hydrogen chloride gas at 0°C for 30 min. The reaction mixture was then allowed to stand at room temperature overnight to afford, in a 41% yield, the desired pyrone (III), mp 95—96°C, the structure of which was supported by the following physical data: $\nu_{\max}^{\text{KBr}}$ 1726 br, 1624 and 1548 cm^{-1}; $\lambda_{\max}^{\text{MeOH}}$ 291 and 265 mμ (ε, 4550 and 8025 respectively); NMR spectrum: 2.10 (2H, near q, J=7.5 cps), 2.83 (2H, t, J=7.5 cps), 3.21 (2H, t, J=7.5 cps), 3.87 (3H, s) and 8.25 ppm (1H, s).



(I)



(II)



(III)

Experimental

The melting point was uncorrected. The IR and UV spectra were recorded with JASCO IR-S and Hitachi-124 spectrometers respectively. The NMR spectra were obtained on a Varian Associates A-60 spectrometer. Chemical shifts for all the NMR spectra are given in ppm from an internal TMS standard, with $CDCl_3$ used as the solvent unless otherwise stated. The mass spectra were measured with a Hitachi RMU-6D mass spectrometer with an ionization energy of 70 eV.

Condensation of 2-Carbomethoxy-cyclopentanone with Carbomethoxymethylene - triphenyl - phosphorane. A mixture of the keto ester (20 g) and carbomethoxymethylene - triphenyl - phosphorane (26 g) was stirred at 100—110°C for 15 hr under nitrogen, and then cooled at room temperature to give a brown solid which was extracted with a large amount of carbon tetrachloride. The solvent was removed under reduced pressure to give a brown oil, which was then chromatographed on silica gel (200 g) and eluted with CCl_4-$CHCl_3$ (4 : 1) to afford 9.6 g of a colourless liquid (II), bp 101—102°C/4 mmHg; *m/e* 198 (M+); NMR spectrum: 1.95 (2H, near q, J=7.5 cps), 2.4—2.9 (4H, br), 3.71 (3H, s) 3.74 ppm (5H, s) (Found: C, 60.00; H, 7.11%. Calcd for $C_{10}H_{14}O_4$: C, 60.59; H, 7.12%).

Formation of 3,4 - Dialkyl-5-carbomethoxy - 2 - pyrone. A mixture of II (14 g) and methyl formate (14 g) was slowly stirred into 400 m*l* of dry ether containing fresh sodium methoxide (7.0 g) at 0°C. After having been kept at 0°C for 3 hr, the reaction mixture was allowed to stand at room temperature for 40 hr with stirring; then it was cooled at 0°C and saturated with hydrogen chloride gas at 0°C for 30 min. The reaction mixture was allowed to stand again at room temperature overnight, and then extracted with a large amount of ether. The ethereal solution was successively washed with water, 5% $NaHCO_3$, and water saturated with NaCl. Finally, the solution was dried over Na_2SO_4 and the solvent was removed under reduced pressure to afford a brown solid, which was chromatographed on silica gel (100 g) and eluted with CCl_4-$CHCl_3$ (4 : 1) to give pale yellow crystals. Recrystallization from methanol afforded 5.6 g of white crystals, mp 95—96°C; *m/e* 194 (M+) (Found: C, 62.05; H, 5.11%. Calcd for $C_{10}H_{10}O_4$: C, 61.85; H, 5.19%).

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1) S. Iwadare, S. Ueda, Y. Hirata and S. Yamamura, Preprints for the 21st Annual Meeting of the Chemical Society of Japan (march 31, 1968), p. 1726.

*[1] An exocyclic double bond of I migrated to a more stable position, as is shown in II.

*[2] Sodium methoxide should be used immediately after preparation.

2) G. H. Coleman and D. Craig, "Organic Syntheses," Coll. Vol. II, p. 179 (1943).