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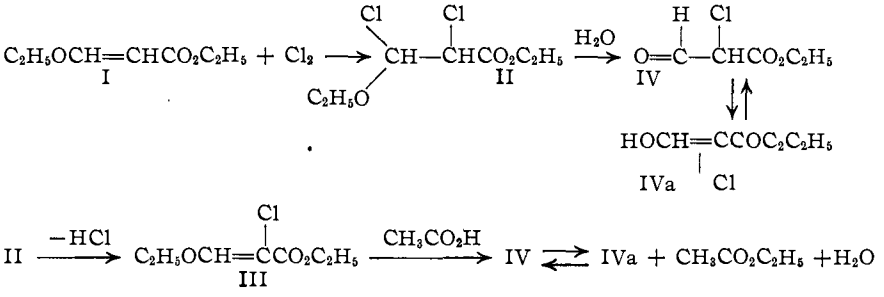
Chlorine Derivatives of Certain β-Ethoxy Esters[1]

BY W. J. CROXALL AND MARIAN F. FEGLEY

During the course of investigations concerned with the chemistry of ethyl β-ethoxyacrylate (I),[2] the addition of chlorine to this ester was examined and certain reactions of the various chlorine derivatives were studied. The results of these experiments are herein reported. The chlorination of ethyl ethoxymaleate was also studied.

The addition of chlorine to the acrylate (I) yields ethyl α,β-dichloro-β-ethoxypropionate (II). As would be expected this ester, which contains an α-chloro ether structure, could not be distilled and was sensitive to moisture. Pyrolysis of the dichloropropionate (II) or dehydrohalogenation with triethylamine gave ethyl α-chloro-β-ethoxyacrylate (III) in good yield whereas treatment with water produced ethyl α-formyl-α-chloroacetate (IV) in only fair yield. The formyl derivative (IV) was also obtained from the α-chloroacrylate (III) by refluxing with glacial acetic acid using *p*-toluenesulfonic acid as a catalyst; the yield however was poor. The over-all reactions may be summarized as

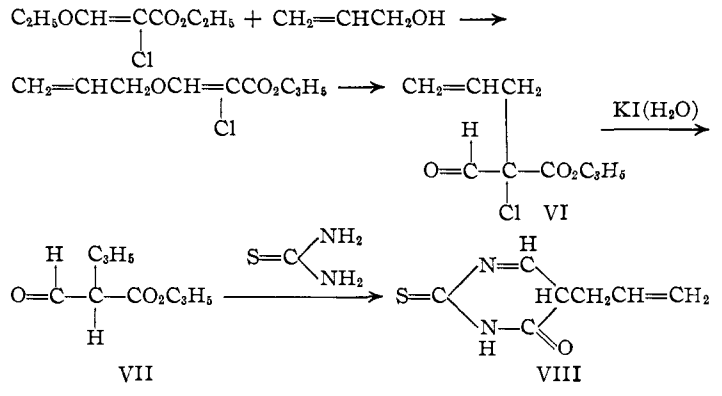


As indicated in the equations, the formylacetate (IV) is represented as existing in both the aldehyde (IV) and enol (IVa) forms[3] since the ester produced a deep purple coloration with alcoholic ferric chloride. Undoubtedly IVa exists as a "conjugated chelated" ring structure.[4]

Ethyl α-chloro-β-ethoxyacrylate (III) upon treatment with ethanol in the presence of a catalytic amount of sodium ethoxide is readily converted to ethyl α-chloro-β,β-diethoxypropionate (V).[5] Conversely, the propionate (V) may be cleaved to ethanol and the acrylate (III) by distillation from small quantities of sodium bisulfate.[5]

Application of a transetherification–transesterification reaction[5] with the chloroacrylate (III) was carried out using allyl alcohol and *p*-toluenesulfonic acid catalyst. However, the expected intermediate, allyl α-chloro-β-alloxyacrylate, could not be isolated in pure form, all samples being contaminated with its rearranged product, allyl α-chloro-α-allyl-α-formylacetate (VI). Accordingly the ester was completely rearranged to the formylacetate (VI).[4] Characterization of VI was accomplished by conversion with aqueous potassium iodide to allyl α-allyl-α-formylacetate (VII)[4] which in turn was treated with thiourea in the presence of sodium ethoxide to give 5-allyl-2-thiouracil (VIII). An independent synthesis of the uracil (VIII), utilizing ethyl α-allyl-α-formylacetate (IX)[4] and thiourea, gave identical material. These transformations may be represented as shown below.

Addition of chlorine to ethyl α-chloro-β-ethoxyacrylate (III) produced the stable ethyl α,α,β-trichloro-β-ethoxypropionate (X). Reaction of the trichloropropionate (X) with ethanol yielded ethyl α,α-dichloro-β,β-diethoxypropionate



(XI) while phenol and 2,4-dichlorophenol gave ethyl α,α-dichloro-β-phenoxy-β-ethoxypropionate (XII) and ethyl α,α-dichloro-β-(2,4-dichlorophenoxy)-β-ethoxypropionate (XIII), respectively

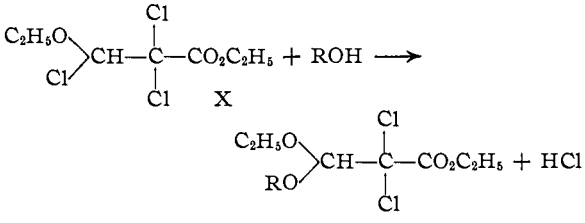
(1) For the previous paper of this series see, Croxall and Fegley, THIS JOURNAL, **72**, 970 (1950).

(2) Croxall and Schneider, *ibid.*, **71**, 1257 (1949).

(3) Wislicenus, *Ber.*, **43**, 3530 (1910).

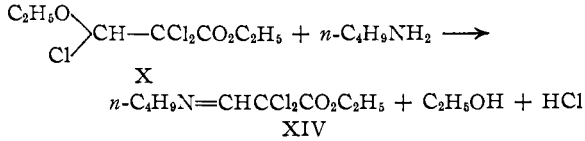
(4) Croxall and Van Hook, THIS JOURNAL, **72**, 803 (1950).

(5) Croxall, Van Hook and Luckenbaugh, *ibid.*, **71**, 2736 (1949).



R = C_2H_5— (XI), C_6H_5— (XII), 2,4-$Cl_2C_6H_3$— (XIII)

With *n*-butylamine the trichloropropionate (X) gave the Schiff base ethyl α,α-dichloro-β-(*n*-butylimino)-propionate (XIV).



Ethyl ethoxymaleate (XV)[2] reacted with chlorine to give the unstable ethyl α,β-dichloro-β-ethoxysuccinate (XVI), which was converted to ethyl α-chloro-β-ethoxymaleate (XVII) by treatment with triethylamine. Addition of chlorine to XVII then produced ethyl α,α,β-trichloro-β-ethoxysuccinate (XVIII).

Acknowledgment.—The analyses were carried out under the direction of Dr. E. L. Stanley and Mr. C. W. Nash. Mrs. J. P. Glatfelter performed a number of the experiments. Dr. J. O. Van Hook converted the formyl ester (IX) to the uracil (VIII).

Experimental

Ethyl α,β-Dichloro-β-ethoxypropionate (II).—To a stirred solution of 216 g. (1.5 moles) of ethyl β-ethoxyacrylate (I) in 200 g. of chloroform, maintained at 5–10°, there was introduced chlorine gas until the solution became slightly yellow in color. This point corresponded to 1.5 moles of chlorine being absorbed. Removal of excess chloroform at reduced pressures resulted in a liquid residue which fumed in the air and was unstable. Attempts to distill the residue resulted in liberation of hydrogen chloride. Reactions that were conducted with the dichloropropionate (II) utilized the chloroform solution or the freshly prepared solvent free residue. Chlorination of the acrylate (I) in the absence of solvent at 5–10° also gave the dichloropropionate (II) in a satisfactory manner.

Ethyl α-Chloro-β-ethoxyacrylate (III).—A solution of the dichloropropionate (II) (1.5 moles in 200 g. of chloroform) as prepared above was distilled at atmospheric pressure to remove chloroform. The resulting residue was heated to 185° during which time hydrogen chloride was evolved. Fractionation then gave 199 g. (75%) of the chloroacrylate (III), b. p. 137–140° (31 mm.); $n^{20}D$ 1.4728. *Anal.* Calcd. for $C_7H_{11}O_3Cl$: Cl, 19.85. Found: Cl, 20.11.

In another experiment, 1.28 moles of acrylate (I) was chlorinated, the excess chloroform removed by distillation under reduced pressure and the resulting ethyl α,β-dichloro-β-ethoxypropionate (II) taken up in 400 ml. of ether. To the stirred ether solution, 137 g. (1.35 moles) of triethylamine was added slowly. The amine hydrochloride was removed by filtration and washed with additional ether. Distillation gave, after removal of ether, a 78% yield of the chloroacrylate (III).

Ethyl α-Chloro-α-formylacetate (IV).—To 100 ml. of water there was added with stirring 122 g. (0.5 mole plus 13 g. chloroform) of the dichloropropionate (II) over a one-hour period. The organic layer was separated, the aqueous layer extracted with ether, the extracts combined with the organic layer and dried over anhydrous sodium sulfate. Fractionation gave, after removal of ether, chloroform and ethanol, 6 g. of forerun, b. p. to 68° (20 mm.) and 36 g. (48%) of the formylacetate (IV), b. p. 68–70° (20 mm.); $n^{20}D$ 1.4576. *Anal.* Calcd. for $C_5H_7O_3Cl$: Cl, 23.55. Found: Cl, 23.41. There was 23 g. of higher boiling material which was not characterized, b. p. to 130° (20 mm.). Upon standing the material partially solidified. Treatment with alcoholic ferric chloride produced a deep purple color.[3] Preparation of a phenylhydrazine derivative according to the method of Wislicenus[3] gave a derivative, m. p. 221–222° (from benzene). A 2,4-dinitrophenylhydrazine derivative was prepared, m. p. 238° (from benzene). *Anal.* Calcd. for $C_{17}H_{14}O_{10}N_8$: N, 22.85. Found: N, 22.59.

In a 500-ml. flask equipped with a Stark–Dean trap, a mixture of 156 g. (0.88 mole) of ethyl α-chloro-β-ethoxyacrylate (III), 100 g. of toluene, 53 g. (0.88 mole) of glacial acetic acid and 1 g. of *p*-toluenesulfonic acid was refluxed for seven hours. There was collected 3.5 g. of water in the trap. Fractionation gave 153 g. of forerun, b. p. 72° (760 mm.)–68° (25 mm.); 39 g. (29%) of the formylacetate (IV), b. p. 68–74° (20 mm.), $n^{20}D$ 1.4577; and 51 g. of higher boiling material which was unchanged chloroacrylate (III).

Ethyl α-Chloro-β,β-diethoxypropionate (V).—To a solution of 119 g. (0.66 mole) of ethyl α-chloro-β-ethoxyacrylate (III) in 100 g. of anhydrous ethanol there was added 1 g. of sodium dissolved in 40 g. of anhydrous ethanol. During the addition of the sodium ethoxide solution the temperature rose from 25 to 42°. The mixture was warmed to 60° and held at 50–60° for one hour. The sodium ethoxide was neutralized with glacial acetic acid and filtered. The excess ethanol was removed by distillation under reduced pressure and the residue washed with 35 ml. of water. The organic layer was separated, dried over anhydrous sodium sulfate and distilled. There was obtained 102 g. (69.7%) of the propionate (V), b. p. 98–99° (6 mm.), $n^{20}D$ 1.4273.[6] In another experiment a 77% yield was obtained. Distillation of the propionate (V) (40 g., 0.18 mole) from 0.1 g. of sodium bisulfate gave ethanol and 21 g. (66.5%) of ethyl α-chloro-β-ethoxyacrylate (III).

Allyl α-Chloro-α-allyl-α-formylacetate (VI).—A mixture of 269 g. (1.5 moles) of ethyl α-chloro-β-ethoxyacrylate (III), 200 g. (3.45 moles) of allyl alcohol and 4 g. of *p*-toluenesulfonic acid was fractionated through a three-foot packed column equipped with a partial take off head to give 138 g. of ethanol, b. p. 78–80°. The residue was transferred to a Claisen flask, 2 g. of β-naphthol (polymerization inhibitor) added, and then distilled. After removal of excess allyl alcohol there was obtained 268 g. of material, b. p. 50–116° (2 mm.), $n^{20}D$ 1.4707–1.4883. There was 19 g. of residue. All attempts to fractionate the distillate to obtain pure allyl α-chloro-β-alloxyacrylate were unsuccessful.

Accordingly, the distillate (416 g. obtained from other experiments and 5 g. of β-naphthol) was slowly fractionated through a one-foot packed column equipped with a partial take off head. After twenty hours of fractionation there was obtained 359 g. of crude formylacetate (VI), b. p. 48–55° (1 mm.) and 44 g. of higher boiling material, b. p. 55–70° (1 mm.). Redistillation gave a main fraction as the pure material, b. p. 46–50 (1 mm.), $n^{20}D$ 1.4580. *Anal.* Calcd. for $C_9H_{11}O_3Cl$: Cl, 17.50. Found: Cl, 17.56.

Allyl α-Allyl-α-formylacetate (VII).—To 10 g. (0.05 mole) of the formylacetate (VI) there was added 10 ml. of an aqueous 20% potassium iodide solution and 15 ml. of glacial acetic acid to effect solution. The mixture was allowed to stand one hour and then heated to 95°. The iodine, as liberated in the mixture, was titrated with a saturated solution of sodium thiosulfate. During the titration it was necessary to add additional glacial acetic

(6) Oroshnik and Spoerri, THIS JOURNAL, **67**, 721 (1945).

acid to maintain solution. When no more iodine was liberated, the mixture was diluted with water, the oil separated, extracted with ether and dried over anhydrous sodium sulfate. Distillation gave, after removal of ether, 2.5 g. of the formylacetate (VII), b. p. 80° (1 mm.), $n^{20}D$ 1.4715.

5-Allyl-2-thiouracil (VIII).—There was mixed 2.5 g. of the formylacetate (VII), 1.3 g. of thiourea and 30 ml. of anhydrous ethanol. The mixture was warmed to effect solution and 0.5 g. of sodium dissolved in 15 ml. of ethanol added. After refluxing for five hours, the mixture was cooled, neutralized with concd. hydrochloric acid, filtered hot and the volume reduced to one-half by evaporation on the hot-plate. The crude uracil (VIII) separated on cooling and was collected on a filter, m. p. 178–182°. After two recrystallizations from ethanol it melted at 185–186°.

A sample of the uracil (VIII) prepared from ethyl α-allyl-α-formylacetate (IX)[4] in a similar manner melted at 184–186° and gave no depression when mixed with the uracil (VIII) from above. *Anal.* Calcd. for $C_7H_8N_2OS$: C, 50.00; H, 4.82; S, 19.0. Found: C, 49.46; H, 5.12; S, 18.9.

Ethyl α,α,β-Trichloro-β-ethoxypropionate (X).—A solution of 268 g. (1.5 moles) of ethyl α-chloro-β-ethoxyacrylate (III) in 100 g. of chloroform was cooled to 10° and chlorine gas introduced until a faint yellow color persisted. Distillation gave, after removal of chloroform, 340 g. (91%) of the trichloropropionate (X), b. p. 86–90° (2 mm.); $n^{20}D$ 1.4605. *Anal.* Calcd. for $C_7H_{11}O_3Cl_3$: Cl, 42.7. Found: Cl, 42.5.

Ethyl α,α-Dichloro-β,β-diethoxypropionate (XI).—A mixture of 18 g. (0.07 mole) of the trichloropropionate (X), 40 g. of ethanol and 2 drops of concd. hydrochloric acid was refluxed for eight hours. Fractionation gave, after removal of excess ethanol and 2 g. of forerun, 13 g. (67.5%) of the dichloropropionate (XI), b. p. 85–92° (2 mm.), $n^{20}D$ 1.4488. *Anal.* Calcd. for $C_9H_{16}O_4Cl_2$: Cl, 27.6. Found: Cl, 27.6.

Ethyl α,α-Dichloro-β-ethoxy-β-phenoxypropionate (XII).—A mixture of 40 g. (0.161 mole) of the trichloropropionate (X) and 16.5 g. (0.164 mole) of phenol was heated on a steam-bath under reduced pressure (70–20 mm.) for six hours during which time hydrogen chloride was evolved. Distillation gave 33 g. (67.5%) of the phenoxypropionate (XII), b. p. 119–122° (1 mm.); $n^{20}D$ 1.5037; d^{20}_{20} 1.239. *Anal.* Calcd. for $C_{13}H_{16}O_4Cl_2$: Cl, 23.08; *MR* 73.31. Found: Cl, 22.73; *MR* 73.37.

Ethyl α,α-Dichloro-β-ethoxy-β-(2,4-dichlorophenoxy)-propionate (XIII).—In a similar experiment using 2,4-dichlorophenol, the 2,4-dichlorophenoxypropionate (XIII) was obtained in 49% yield, b. p. 171–172° (5 mm.), $n^{20}D$ 1.5221. *Anal.* Calcd. for $C_{13}H_{14}O_4Cl_4$: Cl, 37.7. Found: Cl, 37.4.

Ethyl α,α-Dichloro-β-(n-butylimino)-propionate (XIV).—With cooling there was added to 50 g. (0.2 mole) of the trichloropropionate (X), 29 g. of *n*-butylamine. The temperature was maintained below 50°. To the mixture consisting of a slurry of amine hydrochloride was added 100 g. of methanol to effect solution. Gaseous ammonia was passed into the solution and the ammonium chloride removed on the filter. The filtrate was treated successively with ammonia gas and filtered until no more ammonium chloride precipitated. Distillation gave, after removal of methanol and excess amine, 28.5 g. (60%) of the imine (XIV), b. p. 122–129° (3 mm.), $n^{20}D$ 1.4705. *Anal.* Calcd. for $C_9H_{15}O_2Cl_2N$: Cl, 29.53; N, 5.8. Found: Cl, 30.07; N, 6.0.

Ethyl α-Chloro-β-ethoxymaleate (XVII).—Ethyl ethoxymaleate (XV) (108 g., 0.5 mole) dissolved in 200 g. of chloroform was cooled to 10–12° and maintained at this temperature while chlorine gas (0.5 mole) was introduced. The chloroform was removed by distillation under reduced pressure to give a residue which was treated with triethylamine by the same procedure used for III. Fractionation gave 87 g. (69.5%) of the chloromaleate (XVII), b. p. 118–122° (3 mm.), $n^{20}D$ 1.4678.[7] *Anal.* Calcd. for $C_{10}H_{15}O_5Cl$: Cl, 14.2. Found: Cl, 14.2.

Ethyl α,α,β-Trichloro-β-ethoxysuccinate (XVIII).—Chlorination of 70 g. (0.31 mole) of the chloromaleate (XVII) dissolved in 250 g. of chloroform at 10° gave 69 g. (70%) of the chlorosuccinate (XVIII), b. p. 107–110° (2 mm.), $n^{20}D$ 1.4660. *Anal.* Calcd. for $C_{10}H_{15}O_5Cl_3$: Cl, 33.1. Found: Cl, 31.9.

Summary

The addition of chlorine to ethyl β-ethoxyacrylate (I) and ethyl ethoxymaleate (XV) yields the unstable dichlorides which are readily converted to the stable ethyl α-chloro-β-ethoxyacrylate (III) and ethyl α-chloro-β-ethoxymaleate (XVII). Treatment of III and XVII with chlorine produces the stable ethyl α,α,β-trichloro-β-ethoxypropionate (X) and ethyl α,α,β-trichloro-β-ethoxysuccinate (XVIII). Various reactions of these chlorine derivatives are presented.

(7) Cope, THIS JOURNAL, **58**, 570 (1936).

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, DUQUESNE UNIVERSITY]

Hydrazones and Azines of Diaryl Ketones

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In this paper we wish to report convenient procedures for the preparation of hydrazones and azines of diaryl ketones. We also wish to consider the reasons for the distinctive behavior of diaryl ketones in reactions with the common reagents for the carbonyl group when compared to other types of carbonyl compounds.

The reaction of hydrazine with carbonyl compounds proceeds with increasing difficulty as the carbonyl compound varies in the order aldehyde < dialkyl ketone < alkaryl ketone < diaryl ketone. Aldehydes and dialkyl ketones on shaking with hydrazine in a water or alcoholic medium form the hydrazone or azine.[1] When necessary the conversion of the hydrazone to the azine is brought about by the addition of a drop of acid (acetic or hydrochloric) during the crystallization process. The preparation of hydrazones and azines of alkaryl ketones requires heating and, in the case of azine formation, acid catalysis.[2] Examination of the literature reveals that even more vigorous conditions are required to prepare hydrazones and

(1) (a) Blout and Gofstein, THIS JOURNAL, **67**, 13 (1945); (b) Gerhardt, *Monatsh.*, **41**, 199 (1920); (c) Curtius, *J. prakt. Chem.*, [2] **44**, 161 (1891).

(2) (a) Blout, Eager and Gofstein, THIS JOURNAL, **68**, 1983 (1946); (b) Bruining, *Rec. trav. chim.*, **41**, 655 (1922).