

rock-salt cells because of the formation of insoluble reaction products.

Figures 1 and 2.—The carbon tetrachloride solution saturated with dimethylamine contained approximately 10% by weight of dimethylamine.

Figure 3.—Three ml. of pyridine was added to 3.0 millimoles (1.03 g.) of dicobalt octacarbonyl, care being taken to prevent access of air to the reaction mixture. To the reaction mixture, which according to equation 1, contained

2 millimoles of $[\text{Co}(\text{Pyr})_6][\text{Co}(\text{CO})_4]_2$, there was added two millimoles (0.17 g.) of piperidine.

The solution of piperidine in pyridine was prepared by adding two millimoles of piperidine to 3 ml. of pyridine.

The solution of $[\text{Co}(\text{Pyr})_6][\text{Co}(\text{CO})_4]_2$ in pyridine was prepared by adding 3 ml. of pyridine to 3 millimoles (1.03 g.) of dicobalt octacarbonyl as described above.

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The Preparation and Reactions of Fluorine-containing Acetoacetic Esters

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New fluorine-containing acetoacetic esters were prepared by the Claisen reaction of fluorine-containing acetate esters using sodium hydride as the condensing agent. The acetoacetic esters were found to decarboxylate in the presence of aqueous sulfuric acid to form the corresponding fluorine-containing acetones. Both the esters and ketones demonstrated a strong tendency to form addition complexes which are decomposed with difficulty.

Only two fluorine-containing acetoacetic esters have been reported previously. Ethyl γ,γ,γ -trifluoroacetoacetate^{2,3} and ethyl γ,γ -difluoroacetoacetate^{3,4} were prepared by a Claisen condensation of ethyl acetate with ethyl trifluoroacetate or ethyl difluoroacetate, respectively, using sodium ethoxide as the condensing agent. When this method was extended to the self-condensation of ethyl difluoroacetate, no acetoacetic ester was obtained.⁵

In this Laboratory, it was found that a Claisen condensation could be effected between fluorine-containing acetate esters by using sodium hydride as the condensing agent at reaction temperatures in the range of 30–70° and a comparatively short reaction time of 6–8 hours. The fluorine-containing acetoacetic esters were obtained in 75–85% yield with the exception of the pentafluoroacetoacetic ester which was formed in 65% yield. In the latter case, it was necessary to employ a reaction time of 24 hours and a higher reaction temperature (90°) which was achieved by using butyl rather than the ethyl esters. The effectiveness of sodium hydride in these reactions may be attributed, primarily, to the irreversibility of the first step of the Claisen reaction, that of conversion of the ester to a carbanion and that a stronger base is generally effective in ion formation.^{5–7}

An important observation is that only one acetoacetic ester was obtained in those cases in which two or more were possible, *i.e.*, the reaction of ethyl difluoroacetate with ethyl fluoroacetate. In this case, four possible acetoacetic esters could be formed but the only product obtained was ethyl α,γ,γ -trifluoroacetoacetate. This may be explained by the fact that the reaction was conducted

at a temperature below which ethyl difluoroacetate reacts with itself in an excess of this ester, thus favoring the formation of a carbanion from ethyl fluoroacetate in an excess of ethyl difluoroacetate. Other reactions of this type were conducted similarly and resulted in only one product.

The reaction product, in most cases, appeared to be the hemi-ketal of the acetoacetic ester rather than the ester itself. In the case of pentafluoroacetoacetic ester the addition compound with butanol was sufficiently stable to be distilled at atmospheric pressure without decomposition, but in others it was observed that the reaction product decomposed on heating, liberating the free alcohol. The effect of increased fluorine substitution should enhance the formation of such hemi-ketal structures,² and this proved to be the case.

The addition compound of ethanol with ethyl $\alpha,\alpha,\gamma,\gamma$ -tetrafluoroacetoacetate was quite acidic in aqueous solutions. A solution of the acetoacetic ester in ethanol was sufficiently acidic to liberate hydrogen from sodium borohydride and no reduction of the beta ketone could be effected under these conditions.

The fluorine-containing acetoacetic esters were hydrolyzed by refluxing in aqueous acid solutions. In strong contrast to the non-fluorinated acetoacetic acids which decompose slowly in aqueous solutions at room temperature and very fast at higher temperatures, the polyfluorinated acetoacetic acids were quite stable under these conditions. Both hydrolysis and decarboxylation of the esters took place with increasing difficulty as more fluorine was substituted in the molecule. The tetrafluoro- and pentafluoroacetoacetic acids were isolated and distilled without decomposition. It was necessary to remove the last traces of water from the acids by azeotropic distillation of the water with benzene.

By using strongly acidic solutions such as 40% sulfuric acid and refluxing the mixture, it was possible to hydrolyze and decarboxylate the fluorine-containing acetoacetic esters. The fluorine-containing acetones produced in this manner were water soluble and could be removed from the aqueous solutions by continuous extraction with ether for a

(1) Taken, in part, from the Doctoral dissertations of H. W. Kilbourne and E. R. Wilson, Purdue University. Presented before the Fluorine Symposium, Fall Meeting of the American Chemical Society, Atlantic City, N. J., 1952.

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TABLE I
 NEW COMPOUNDS

| | B.p., °C. | Analyses, % | | | | Reaction temp., °C. | Yield, % |
|--|----------------------|-------------|-------|----------|-------|---------------------|----------|
| | | Carbon | | Hydrogen | | | |
| | | Calcd. | Found | Calcd. | Found | | |
| CF ₃ COH(OC ₄ H ₉)CF ₂ CO ₂ C ₄ H ₉ ^a | 79 at 15 mm. | 44.80 | 45.01 | 5.90 | 6.05 | 90 | 65 |
| CF ₃ COCF ₂ CO ₂ C ₂ H ₅ | 130-131 | 32.75 | 33.10 | 2.27 | 2.96 | 75 | 20 |
| CHF ₂ COCF ₂ CO ₂ C ₂ H ₅ ^b | 143-144 | 35.65 | 35.60 | 2.97 | 2.99 | 70 | 81 |
| CF ₃ COCHF ₂ CO ₂ C ₂ H ₅ | 138-139 | 35.65 | 35.60 | 2.97 | 2.96 | 50 | 86 |
| CF ₃ COCH ₂ CO ₂ C ₂ H ₅ ^c | 131-132 | | | | | 50 | 84 |
| CHF ₂ COCHF ₂ CO ₂ C ₂ H ₅ | 159-160 | 39.15 | 39.30 | 3.80 | 4.01 | 30 | 68 |
| CHF ₂ COCH ₂ CO ₂ C ₂ H ₅ ^d | 162 | | | | | 40 | 83 |
| CH ₂ FCOCHF ₂ CO ₂ C ₂ H ₅ ^e | 71-72 at 3 mm. | 43.35 | 43.31 | 4.72 | 4.74 | 40 | 69 |
| CF ₃ COCHF ₂ ^f | 2-3 | | | | | Reflux | 35 |
| CHF ₂ COCHF ₂ ^g | 58 | 27.70 | 27.64 | 1.54 | 1.57 | Reflux | 62 |
| CF ₃ COCH ₂ F | 44 | 27.70 | 27.72 | 1.54 | 1.71 | Reflux | 67 |
| CHF ₂ COCH ₂ F | 73 | | | | | Reflux | 65 |
| | 146-147 ⁱ | | | | | | |
| CH ₂ FCOCH ₂ F | 101-102 | 38.29 | 38.37 | 4.25 | 4.13 | Reflux | 74 |
| CF ₃ COCF ₂ CO ₂ H ^h | 56 at 3 mm. | | | | | Reflux | 56 |
| CHF ₂ COCF ₂ CO ₂ H ⁱ | 72 at 2 mm. | | | | | Reflux | 53 |

^a n_D^{20} 1.3890. Isolated as the hemiketal. ^b n_D^{20} 1.3542. ^c See ref. 3 and 4. ^d See ref. 2. ^e In this case, ethyl mono-fluoroacetate was added dropwise to a mixture of ether and sodium hydride. ^f Calcd., mol. wt., 148; found, 149. ^g Prepared from free $\alpha,\alpha,\gamma,\gamma$ -tetrafluoroacetoacetic acid rather than the ester by a similar procedure. ^h Calcd. for C₄HF₅O₃: neut. equiv., 192.0. Found, 192.4. ⁱ Calcd. for C₄H₂F₄O₃: neut. equiv., 174.0. Found, 174.1. ^j M.p. of 2,4-dinitrophenylhydrazone. *Anal.* Calcd. for C₉H₇F₃N₄O₄: N, 19.18. Found: N, 19.18.

long period of time. The ketones were obtained in an anhydrous form by treatment with phosphoric anhydride or concentrated sulfuric acid.

The compounds prepared, their physical properties, and analyses are listed in Table I. In only one instance, that of CHF₂COCH₂F, was it possible to prepare any of the usual carbonyl group derivatives. In the case of the esters, no copper chelates were obtained.

Experimental

Starting Materials.—The various esters used were, for the most part, obtained from commercial sources and distilled and dried with calcium hydride before using. Ethyl and butyl trifluoroacetates and ethyl difluoroacetate were prepared by esterification of the corresponding acids and dried with calcium hydride before using. Butyl difluoroacetate has not been reported previously, b.p. 136.5-137°, n_D^{20} 1.3720.

Anal. Calcd. for C₈H₁₀F₂O₂: C, 47.7; H, 6.60. Found: C, 47.7; H, 6.76.

Preparation of Acetoacetic Esters.—The apparatus comprised a 500-ml., three-necked flask equipped with a reflux condenser, a sealed Hershberg stirrer, and a dropping funnel with a pressure equalizer arm. The apparatus was flame dried in a stream of dry nitrogen and a dry nitrogen atmosphere was maintained during the reaction. One mole of a fluorine-containing acetate (in the case of a mixed condensation, the ester containing the more fluorine) and 12 g. of sodium hydride were added to the flask and the mixture heated to the desired reaction temperature. The other fluorine-containing ester (0.5 mole) was added dropwise over a period of 6-8 hours. (In the case of self-conden-

sation reactions, the reactants were merely mixed and heated.) The evolution of hydrogen was noted immediately on addition and continued until the reaction was completed. The mixture was then stirred for an additional period of time and hydrolyzed by pouring into a mixture of 250 g. of crushed ice and 50 g. of concentrated sulfuric acid. The ester layer was separated and the water solution extracted with ether. The ether solutions and the ester layer were combined, dried with Drierite, and rectified using a Todd distillation assembly.

Preparation of Ketones from the Esters.—A mixture of 100 ml. of 40% sulfuric acid and 15-30 g. of the fluorine-containing acetoacetic ester was refluxed for 24 hours. After cooling to room temperature, the mixture was extracted continuously with ether for 72 hours. The ether extract was dried with Drierite and distilled to remove the ether. Phosphorus pentoxide was then added to the residue (hydrated ketone) and the mixture rectified to produce the pure ketone.

Preparation of the Acids from the Esters.—A mixture of 80-100 ml. of 10% sulfuric acid and a small amount of fluorine-containing acetoacetic ester was refluxed for 12 hours. The reaction mixture was then distilled through a short column until the alcohol formed was removed. The aqueous solution remaining was extracted continuously with ether for 48 hours. The ether extract was distilled to remove the ether and the residue dried by azeotropic distillation with benzene. After all the benzene had been removed, distillation was continued at reduced pressure to obtain the free acid.

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