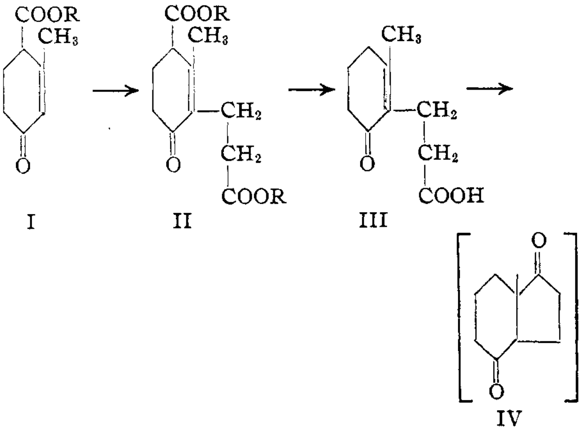
We were interested in the introduction of a side-chain bearing a carboxyl group into the ester I because the propionic acid III finally obtainable as indicated should be useful in the synthesis of cyclic diketones with an angular methyl group of the type IV. So far we have not been able to effect the ring closure.



Experimental

3-Carbomethoxy-2-methyl-6-oxo-1-cyclohexene (I, R = CH_3).—This substance was obtained by a modification of the procedure described for the corresponding ethyl ester (Hagemann ester), I, R = C_2H_5.[3]

Nine hundred and twenty grams (8 moles) of freshly distilled methyl acetoacetate and 35 cc. of piperidine were warmed to 60°. One hundred and twenty grams (4 moles) of trioxymethylene was added in small portions under stirring while keeping the temperature at 60–80°. The mixture was cooled to room temperature, 200 g. of anhydrous sodium sulfate was added and the flask left standing in the refrigerator overnight. The product was filtered from the sodium sulfate and the residue washed well with ether. The combined filtrate and washings were washed in a separatory funnel with small portions of water, 10% hydrochloric acid and again with water. The ether solution was dried over sodium sulfate, the solvent removed and the residue of crude 1,3-dicarbomethoxy-2-methyl-6-oxo-1-cyclohexene was saponified partially by refluxing for two hours in an oil-bath with a solution of 96 g. of sodium (4 moles) in 2.5 liters of absolute alcohol. After standing overnight the alcohol was removed *in vacuo*, the residue taken up in 500 cc. of ice-water and acidified under cooling with 25% sulfuric acid. The resulting oil was taken up in ether, the ether solution washed with water, dried over anhydrous sodium sulfate and the ether evaporated. The residue was distilled *in vacuo*, b. p. 135° (2 mm.), yield, 240 g. (37%). A considerable low boiling fraction was obtained (b. p. 70° (2 mm.)) consisting chiefly of 2-methyl-6-oxo-1-cyclohexene.

Anal. Calcd. for $C_9H_{12}O_3$: C, 64.3; H, 7.2. Found: C, 64.7; H, 7.2.

The semicarbazone was prepared as usual, m. p. 168–170°.

Anal. Calcd. for $C_{10}H_{15}O_3N_3$: N, 18.7. Found: N 18.7.

Methyl β-(3-Carbomethoxy-2-methyl-6-oxo-1-cyclohexen-1-yl)-propionate (II, R = CH_3).—Twenty-three grams of sodium was dissolved in 500 cc. of absolute methyl alcohol (dried over magnesium methylate) and 168 g. of 3-carbomethoxy-2-methyl-6-oxo-1-cyclohexene was added, followed by 168 g. of methyl-β-bromopropionate. The mixture was refluxed for one hour; the alcohol removed *in vacuo*, the residue taken up in ether, washed, dried over sodium sulfate and the solvent evaporated. The ether residue was distilled in vacuum. Thirty-two grams of low boiling material was obtained, consisting mostly of unchanged starting material. The main fraction boiled at 170–180° (1 mm.), yield, 170 g. (83% considering recovered starting material).

Anal. Calcd. for $C_{13}H_{18}O_5$: C, 61.4; H, 7.1. Found: C, 61.5; H, 7.4.

The semicarbazone was prepared by refluxing 1 g. of the ester with 1 g. of semicarbazide hydrochloride and 1 g. of sodium acetate; recrystallized from dilute alcohol, it melted at 145–148°.

Anal. Calcd. for $C_{14}H_{21}N_3O_5$: N, 13.5. Found: N, 13.9.

Ethyl β-(3-Carbethoxy-2-methyl-6-oxo-1-cyclohexen-1-yl)-propionate.—This ester was prepared from Hagemann's ester and ethyl-β-bromopropionate as described above; b. p. 184–186° (2 mm.), yield, 70%. No satisfactory analysis could be obtained from this material but the 2,4-dinitrophenylhydrazone obtained as usual crystallized from ethanol in orange-red prisms, m. p. 120–122°.

Anal. Calcd. for $C_{21}H_{26}O_8N_4$: N, 12.0. Found: N, 12.1.

β-(2-Methyl-6-oxo-1-cyclohexen-1-yl)-propionic Acid.—One hundred grams of II (R = CH_3) was refluxed for six hours with 200 cc. of hydriodic acid (42%). After cooling the mixture was carefully made alkaline by adding it to excess concentrated sodium carbonate solution under cooling and stirring. All neutral material was removed by repeated extraction with ether and the dark brown solution was acidified again. The acid was taken up in ether and the ether solution washed with dilute sodium thiosulfate solution and with water. After drying over anhydrous sodium sulfate the ether was evaporated and the residue was distilled *in vacuo* at about 1 mm.; yield, 40 g. The distillate crystallized on standing. Recrystallization from ligroin (b. p. 70–90°) yields the acid in long feather-shaped crystals; m. p. 79–81°. The same acid was obtained from II (R = C_2H_5).

Anal. Calcd. for $C_{10}H_{14}O_3$: C, 65.9; H, 7.7. Found: C, 65.6; H, 7.7.

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[3] Hagemann, *Ber.*, **26**, 879 (1893); Rabe and Rahm, *Ann.*, **332**, 13 (1904); *Ber.*, **38**, 969 (1905).

A New Modification of Willgerodt's Reaction

BY ERWIN SCHWENK AND EDITH BLOCH

It was first shown by Willgerodt[1] that treatment of aryl methyl ketones with yellow am-

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[1] Willgerodt, *Ber.*, **20**, 2467 (1887); **21**, 535 (1888).

monium sulfide yields the amides of arylacetic acids which by saponification with aqueous alkali give arylacetic acids. The method would probably find more use if it were not necessary to heat the reagents in a closed vessel to 150°. This disadvantage of the method has not been eliminated by recent modifications.[2,3,4,5]

We have tried to avoid the use of an autoclave by replacing the ammonium sulfide with higher boiling amines and sulfur. Morpholine[6] now made technically in very pure form and at a cheap price has been found to be most suitable. The process differs from the reaction as described by Willgerodt in that first the morpholides of

$$ArCOCH_3 \longrightarrow ArCH_2CSC_4H_8ON$$

the arylthioacetic acids are formed. The reason for this course of the reaction is probably the absence of water in the reaction mixture similar to Kindler and Tsauping Li's procedure[5], who also obtained derivatives of the arylthioacetic acids. The morpholides of the arylthioacetic acids often can be isolated in crystalline form. If that is not possible because of the oily consistency of these morpholides, even the crude oily morpholides may be submitted to a saponification with either aqueous or alcoholic alkali, which will afford the arylacetic acids after acidification of the alkaline solution.

The reaction apparently is applicable to all aryl methyl ketones in which the aryl part of the molecule is either unsubstituted or substituted by a stable group like the alkoxy group or halogen. To substances containing nitro-, amino-, hydroxy- or acetoxy- groups, the reaction seems not to be applicable in this form.

As an example, we describe the preparation of the as yet not known *o*-benzyloxyphenylacetic acid with our new method. In general, it may be said that the aryl thioacetmorpholides crystallize easily. In cases where they remained oily, we have taken the crude material and submitted it, without purification, to the saponification step. Some of the morpholides are quite difficult to saponify; we have not made an investigation of this part of the method and believe that study of the saponification in special cases may improve the final yield considerably.

Yields, melting points (not corrected) and analyses of some arylthioacetmorpholides of known arylacetic acids which we have prepared are given in the table.

TABLE I

Aryl methyl ketone	Morpholide of arylthioacetic acid		Arylacetic acid		
Aryl-	Yield, %	M. p., °C.	Yield, %	Melting point, °C. Found	Literature
Phenyl-	92[a]	79--80	75	76–77	76, 78
o-Methoxyphenyl-		oily	55	120–122	120.5, 123, 124
m-Methoxyphenyl-	85[b]	82–84	65	66–67	67
p-Bromophenyl-		oily	10	112–113	114–115
2,5-Dimethoxyphenyl-		oily	28	123–124[d]	124.5
2-Naphthyl-	87[c]	108–109	. .	140–142	137.5–139, 142
2-Phenanthryl		oily	41	179–183	181-183

[a] Calcd. for $C_{12}H_{15}NOS$: N, 6.3; S, 14.5. Found: N, 5.9; S, 14.7. [b] Calcd. for $C_{13}H_{17}NO_2S$: N, 5.6; S, 12.7. Found: N, 6.0; S, 12.5. [c] Calcd. for $C_{16}H_{17}NOS$: N, 5.0; S, 11.6. Found: N, 5.2; S, 12.0. [d] Mixed m. p. with a sample prepared from natural homogentisic acid (for which we have to thank Dr. M. Volterra, Mt. Sinai Hospital, New York City) by methylation with dimethyl sulfate and sodium hydroxide showed no depression.

Experimental

Preparation of *o*-Benzyloxyacetophenone.—Ten grams of *o*-hydroxyacetophenone, 12.5 g. of benzyl chloride and 75 cc. of 15% sodium hydroxide were refluxed for two hours. The reaction mixture was extracted, with ether, the ether extract washed and dried and distilled *in vacuo;* yield 12.5 g.; b. p. 182–184° at 11 mm. There was some unreacted material recovered from the alkaline solution.

Anal. Calcd. for $C_{15}H_{14}O_2$: C, 79.7; H, 6.3. Found: C, 79.8; H, 6.5.

2,4-Dinitrophenylhydrazone m. p. 207–209°. *Anal.* Calcd. for $C_{21}H_{18}O_5N_4$: N, 13.8. Found: N, 14.1.

Semicarbazone m. p. 175–177°. *Anal.* Calcd. for $C_{16}H_{17}O_2N_3$: N, 14.9. Found: N, 14.6.

Preparation of *o*-Benzyloxyphenylthioacetmorpholide.—11.3 grams of *o*-benzyloxyacetophenone, 4.5 g. of morpholine, and 1.6 g. of sulfur were refluxed for eight hours and then poured into ice. The morpholide was extracted with ether. The oily residue crystallized partially after standing for a day. It was several times recrystallized from dilute methanol; yield, 12 g.; m. p. 117, 118–119°. *Anal.* Calcd. for $C_{19}H_{21}O_2SN$: N, 4.3; S, 9.7. Found: N, 4.5; S, 9.5.

Preparation of *o*-Benzyloxyphenylacetic Acid.—Nine grams of *o*-benzyloxyphenylthioacetmorpholide was refluxed with 100 cc. of 10% potassium hydroxide for twelve hours. The alkaline solution was acidified, extracted with ether, and the extracts washed, dried and evaporated. The ether residue was recrystallized from benzene–petrol ether; yield 4.1 g.; m. p. 97–99°. *Anal.* Calcd. for $C_{20}H_{22}O_6$: C, 74.7; H, 5.8. Found: C, 74.7; H, 6.4.

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(2) Mosettig and van de Kamp, THIS JOURNAL, **55**, 3442 (1933).

(3) Fieser and Kilmer, *ibid.*, **62**, 1354 (1940).

(4) Bachmann and Carmack, *ibid.*, **63**, 2494 (1941).

(5) Kindler and Tsauping Li, *Ber.*, **74**, 321 (1941).

(6) Piperidine was also used in some experiments.