[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF ROCHESTER]

The Reaction of Some α-Chloroketones with Alkali

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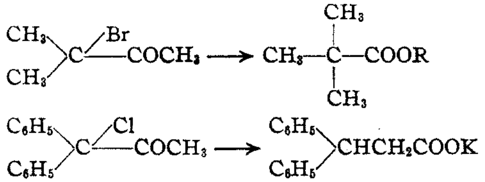
A few years ago Richard[1a] reported that under the influence of dry powdered potassium hydroxide in absolute ether, certain α-chloroketones are converted into potassium salts of straight-chained organic acids. Thus α-chloro-α-phenylacetone is transformed into potassium hydrocinnamate, α-chloro-α-benzylacetone into potassium γ-phenylbutyrate, and α-chloro-α,α-diphenylacetone (I) into potassium β,β-diphenylpropionate (II). Recently, Aston and his students[2] in a somewhat similar study have found that sodium alkoxides in dry ether bring about the rearrangement of α-bromo-secondary-alkyl ketones to esters of trialkylacetic acids.

The acids obtained by Aston and co-workers have carbon chains which are more branched than those of the starting ketones, while the acids of Richard have the same carbon skeletons as his ketones. To compare reactions of analogous ketones



$$\mathrm{(CH_3)_2C(Br)COCH_3 \longrightarrow CH_3{-}C(CH_3)_2{-}COOR}$$

$$\underset{\mathrm{I}}{\mathrm{(C_6H_5)_2C(Cl)COCH_3}} \longrightarrow \underset{\mathrm{II}}{\mathrm{(C_6H_5)_2CHCH_2COOK}}$$

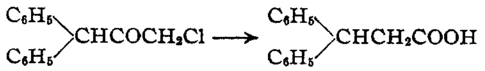
Earlier work of Richard,[3] in which it was found that desyl chloride (III) is converted into potassium diphenylacetate, gave results comparable to those of the Aston group.

$$\underset{\mathrm{III}}{\mathrm{C_6H_5CHClCOC_6H_5}} \longrightarrow \mathrm{(C_6H_5)_2CHCOOK}$$

Richard[1a] indicated that on this basis he would have expected the three ketones mentioned above to form acids with increased branching of the carbon chains. Since this is not the case, he sought to explain the facts by "synionic isomerism" of the ketones

$$\mathrm{RCHClCOCH_3 \rightleftarrows RCH_2COCH_2Cl}$$

The chloromethyl ketones, isomeric with the ketones he studied, would be expected according to his mechanism to form acids with identical structures. For example, benzhydryl chloromethyl ketone was predicted to give β,β-diphenylpropionic acid. Richard did not, however, carry out experiments to demonstrate that chloromethyl ketones react as expected.



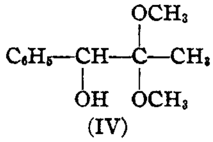
$$\mathrm{(C_6H_5)_2CHCOCH_2Cl \longrightarrow (C_6H_5)_2CHCH_2COOH}$$

In connection with Richard's prediction, it is of interest that Bergmann and Miekeley[4] treated bromoacetone with potassium methoxide in anhydrous methanol and isolated the dimethyl acetal of acetol, but mention no acid or ester. Richard did not report hydroxyacetals, although in the case of α-chloro-α-phenylacetone he isolated phenylmethylglyoxal and phenylacetone, two products which may be attributed to disproportionation.

In view of these facts, and because the experimental details are meager, especially concerning the preparation of the chloroketones, it seemed worth while to repeat the work of Richard, and to test his predictions concerning the isomeric chloromethyl ketones.

α-Chloro-α-phenylacetone (VIII), when treated with potassium hydroxide in anhydrous ether, does form potassium hydrocinnamate, identified through hydrocinnamic acid and its *p*-bromophenacyl ester. With sodium methoxide in ether it gives rise to methyl hydrocinnamate, as shown by hydrolysis to the acid. If α-chloro-α-phenylacetone is refluxed for nine to ten hours in a solution of sodium methoxide in anhydrous methanol, there is obtained a mixture of methyl hydrocinnamate and the dimethyl acetal (IV) of α-hydroxy-α-phenylacetone.

$$\underset{\mathrm{(VIII)}}{\mathrm{C_6H_5CHClCOCH_3}} \longrightarrow \mathrm{C_6H_5CH_2CH_2COOCH_3} +$$



$$\mathrm{C_6H_5{-}CH(OH){-}C(OCH_3)_2{-}CH_3}$$

(IV)

Despite careful attempts to exclude moisture, up to 10% of hydrocinnamic acid usually occurs. If an equivalent or more of water is introduced into the methanol solution in which the chloroketone is rearranged, forming a solution of sodium hydroxide in methanol, a 45% yield of hydrocinnamic acid is obtained directly.

The hydroxyacetal (IV) is hydrolyzed by acidic 2,4-dinitrophenylhydrazine reagent and forms the dinitrophenylosazone of methylphenylglyoxal, identified by comparison with an authentic sample.[5] On treatment with semicarbazide hydrochloride, it forms the disemicarbazone of methylphenylglyoxal.[5]

Benzyl chloromethyl ketone, isomeric with α-chloro-α-phenylacetone, reacts much faster with

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[1a] Richard, *Compt. rend.*, **200**, 1944 (1935).

[2] Aston and Greenburg, THIS JOURNAL, **62**, 2590 (1940); Aston, Clarke, Burgess and Greenburg, *ibid.*, **64**, 300 (1942).

[3] Richard, *Compt. rend.*, **197**, 1432 (1933).

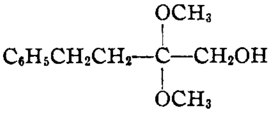
[4] Bergmann and Miekeley, *Ber.*, **64**, 802 (1931).

[5] v. Auwers and Ludewig, *Ann.*, **526**, 137 (1936); v. Auwers, *Ber.*, **50**, 1612 (1917).

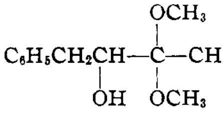
sodium methoxide in methanol, forming methyl hydrocinnamate in 80% yield after forty-five minutes of refluxing. In this instance no other product was isolable.

The two isomeric benzylchloroacetones (IX and X), in contrast, give only small yields of acids or esters upon treatment with sodium hydroxide in methanol. Chloromethyl β-phenylethyl ketone (X) yielded 8% of γ-phenylbutyric acid, identified by means of its S-benzylthiuronium salt. Its isomer, α-benzyl-α-chloroacetone (IX), afforded a small amount of an acidic oily material which was neither the expected γ-phenylbutyric acid nor α-methylhydrocinnamic acid. This material was probably a mixture and was not identified. Thus we were unable to confirm Richard's statement that this ketone produces γ-phenylbutyric acid.

The principal products from these chloroketones are the hydroxyacetals (V) and (VI). The former reacts with acidic phenylhydrazine reagent to form the phenylhydrazone of hydroxymethyl β-phenylethyl ketone, and the latter in a similar manner gives the phenylosazone of benzylmethylglyoxal. The hydroxyacetal (V) apparently is mixed with some of the corresponding hydroxyketone (VII), as indicated by analyses.


$C_6H_5CH_2CH_2-C(OCH_3)_2-CH_2OH$

V

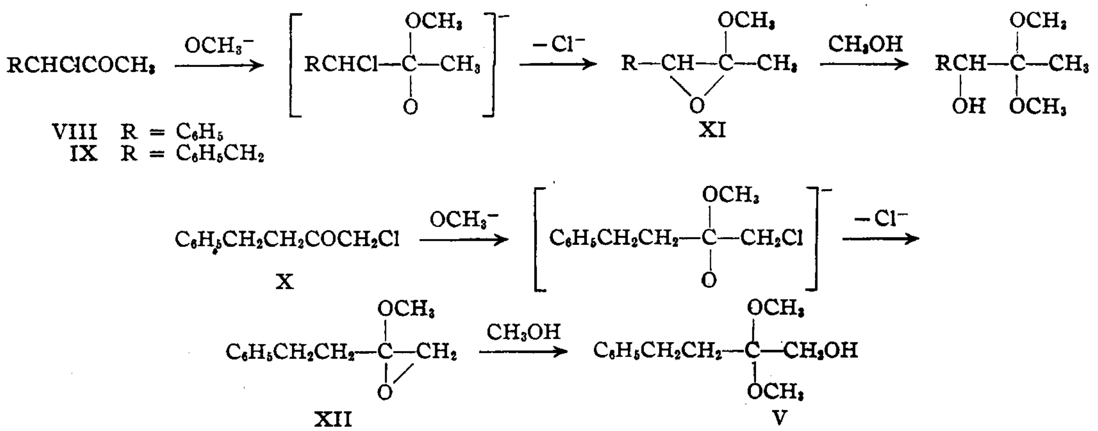

$C_6H_5CH_2CH(OH)-C(OCH_3)_2-CH_3$

VI

$C_6H_5CH_2CH_2COCH_2OH$

VII

Unfortunately, we did not study the reactions of α-chloro-α,α-diphenylacetone since we were unable to synthesize this ketone in useful yields.



The formation of hydroxyacetals from halogenated ketones has been reasonably explained by means of ethylene oxide intermediates.[4,6] The oxide ring is ruptured by reaction with a molecule of alcohol, forming the hydroxyacetal.

The same type of intermediate has been postulated by Aston[2] also to form esters by rearrangement. It is to be noted that the Aston group obtained esters only in ether solution, and that introduction of an alcohol gave rise to corresponding amounts of hydroxyacetals. When methanol was used as solvent, they did not detect any ester. In our experiments on the phenylchloroacetones, the course of the reaction was found to be relatively indifferent to solvent.

The ethylene oxide intermediate satisfactorily explains the acids formed from the chloromethyl ketones, as does the ketene mechanism of Richard.[3] Without modification it does not successfully deal with the isomeric α-chloroketones since it predicts increased branching of the carbon chains. Transformation of the epoxide (XI) into (XII) appears to be a necessary modification of this scheme.

The reaction forming acids or esters may very likely take another course. Since both phenylchloroacetones form the same acid or ester, a common intermediate for both isomers is indicated. The relative ease of formation of this intermediate would govern the amount of acid or ester produced in relation to hydroxyacetal. Such an intermediate might be $[RCH_2COCH_2]^+$ (XV), of transitory existence. Rearrangement of this ion to $[RCH_2CH_2CO]^+$ (XVII), by the migration of the RCH_2 group, gives an ion which can react with hydroxyl or alkoxyl ions to form an acid or ester. The resonance forms (XIV) and (XVI) provide the common intermediate for both ketones.

Recently, examples of the rearrangement of a chloromethyl ketone to esters have been reported by Eastham, Fisher, Kulka and Hibbert.[7a] Chloromethyl 3,4-dimethoxybenzyl ketone, on treatment with ethanolic alkali, forms a compound, $C_{13}H_{18}O_4$, of b. p. 104° (0.04 mm.), and with methanolic alkali, a compound, $C_{12}H_{16}O_4$, of m. p. 40–41°. The products are assigned, un-

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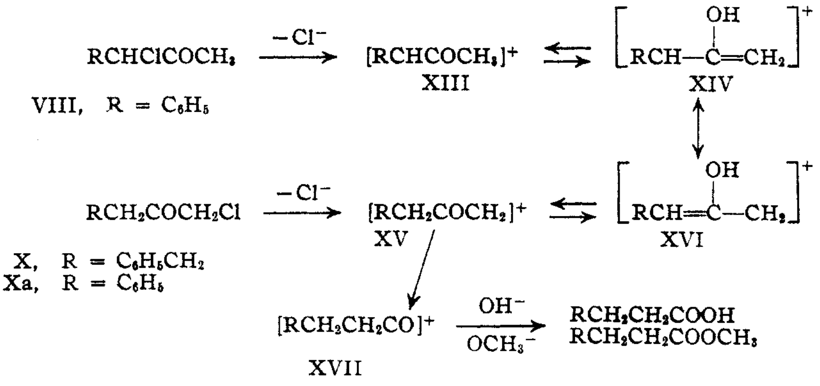
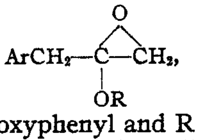
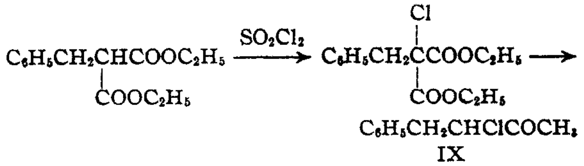
(6) Ward, *J. Chem. Soc.*, 1544 (1929).

(7) (a) Eastham, Fisher, Kulka and Hibbert, THIS JOURNAL, 66, 26 (1944); (b) Child and Pyman, *J. Chem. Soc.*, 2010 (1929); (c) Lewis, Ramage and Robinson, *ibid.*, 1412 (1935).



doubtedly on the basis of Aston's work,[2] the structures  $\mathrm{ArCH_2{-}\underset{OR}{\overset{O}{C}}{-}CH_2}$, where Ar represents 3,4-dimethoxyphenyl and R ethyl or methyl. It is significant that these "carbonyl-free ethers" give no carbonyl derivatives upon treatment with semicarbazide or acidified 2,4-dinitrophenylhydrazine, contrary to expectation. In view of the results of the present publication, it must be concluded that these compounds are esters of the structures $ArCH_2CH_2COOR$. Both esters have been described previously. Child and Pyman[7b] give a b. p. of 193° (20 mm.) for the ethyl ester and a m. p. of 38–39° for the methyl ester. Lewis, Ramage and Robinson[7c] report a m. p. of 37° for the latter.

α-Chloro-α-phenylacetone was prepared without difficulty by the chlorination of phenylacetone with sulfuryl chloride.[8] The chlorination of benzylacetone with this reagent, however, gave reaction products which could not be distilled without decomposition. The use of gaseous chlorine produced mixtures. The synthesis of α-benzyl-α-chloroacetone was finally accomplished by treating ethyl benzylacetoacetate in the cold with sulfuryl chloride and carrying out a ketonic cleavage in acetic acid containing some sulfuric acid.



$$\mathrm{C_6H_5CH_2\underset{COOC_2H_5}{CH}COOC_2H_5 \xrightarrow{SO_2Cl_2} C_6H_5CH_2\overset{Cl}{\underset{COOC_2H_5}{C}}COOC_2H_5 \longrightarrow C_6H_5CH_2CHClCOCH_3}$$

IX

This method affords satisfactory yields of the pure chloroketone and leaves no doubt of the structure of the product.

The synthesis of the chloromethyl ketones was accomplished by means of the reaction of diazomethane with acid chlorides. In common with other workers,[9] we could not repeat the results of Clibbens and Nierenstein,[10] but did obtain satisfactory yields when the acid chloride was added to an ethereal solution of two equivalents of diazomethane, and the resulting diazoketone treated with gaseous hydrogen chloride. The products thus obtained are strikingly different from those described by Clibbens and Nierenstein. Benzyl chloromethyl ketone, as prepared in this Laboratory, is a nearly colorless liquid, b. p. 127° (17 mm.). Clibbens and Nierenstein describe a crystalline product of m. p. 73° and b. p. 160° (17 mm.). Their chloromethyl β-phenylethyl ketone was reported to melt at 84–85°, while ours melts at 39–40°. Henze and Holder,[11] who prepared the latter ketone by the chromic acid oxidation of the corresponding carbinol, report m. p. 40–41°.

In the preparation of solid derivatives of the chlorophenylacetones, carbonyl reagents were of little value. These ketones, however, condense readily with sodium benzenesulfinate in alcoholic solution, forming crystalline phenylsulfonyl ketones of definite melting points. The benzylchloroacetones react smoothly with 2,4-dinitrophenylhydrazine to form dinitrophenylhydrazones.

Experimental[12]

Phenylacetone.—Technical phenylacetone (Commercial Solvents Corp.) was purified through the sodium bisulfite adduct; b. p. 105–106° (23 mm.); $n^{20}D$ 1.5173. It forms a **2,4-dinitrophenylhydrazone,** fine yellow needles from a mixture of equal volumes of ethanol and chloroform, m. p. 155.5–156.5°.

Anal. Calcd. for $C_{15}H_{14}N_4O_4$: C, 57.32; H, 4.49. Found: C, 57.51; H, 4.68.

α-Chloro-α-phenylacetone (VIII).[8]—A solution of 50 g. (0.37 mole) of phenylacetone in 50 cc. of carbon tetrachloride is heated to 45° and 55 g. (0.41 mole) of sulfuryl chloride added with stirring in an hour and a quarter. The solution is kept warm for an additional quarter hour, then washed twice with water and dried over calcium chloride. The solvent is evaporated under reduced pressure on the steam-bath, and the lachrymatory product distilled at 115–118° (16 mm.); yield, 53 g. (84%); $n^{20}D$ 1.5373; d^{23}_{23} 1.161.

α-(Phenylsulfonyl)-α-phenylacetone.—α-Chloro-α-phenylacetone (VIII) (3.0 g., 0.018 mole) is added to a solution of 3.0 g. (0.018 mole) of sodium benzenesulfinate in 20 cc. of boiling 95% ethanol. After refluxing for one hour, the product is precipitated with water and filtered; yield, 4.3 g. (88%); m. p. 120.5–122.5°. After recrystallization from dilute ethanol, the derivative melts at 122–123°.

Anal. Calcd. for $C_{15}H_{14}OS_3$: C, 65.67; H, 5.14. Found: C, 65.67; H, 5.08.

Benzyl Chloromethyl Ketone.—A solution of 0.10 mole of diazomethane in about 250 cc. of anhydrous ether is prepared from 20 cc. of nitrosomethylurethan and a solution of 12 g. of potassium hydroxide in 50 cc. of *n*-propyl alcohol, the nitrosomethylurethan and ether being added in

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[8] Richard, *Compt. rend.*, **199**, 71 (1934).

[9] Bradley and Schwarzenbach, *J. Chem. Soc.*, 2904 (1928).

[10] Clibbens and Nierenstein, *ibid.*, **107**, 1491 (1915).

[11] Henze and Holder, THIS JOURNAL, **63**, 1943 (1941).

[12] Analyses by Robert Bauman. Melting points are corrected.

portions until all the diazomethane has been distilled. To this is added, dropwise with stirring, 6.6 cc. (7.7 g., 0.05 mole) of phenylacetyl chloride. After standing for two hours, the solution is cooled in ice, and dry hydrogen chloride introduced until the passage of the gas no longer produces effervescence. It is then washed with water and sodium bicarbonate solution, dried, evaporated, and distilled. The product is a pale yellow oil, b. p. 133–135° (19 mm.); yield, 7.0 g. (83%); $n^{20}\text{D}$ 1.5379; $d^{22}{}_{22}$ 1.162.

Anal. Calcd. for C_9H_9ClO: C, 64.10; H, 5.38. Found: C, 63.73; H, 5.14.

Benzyl Phenylsulfonylmethyl Ketone.—When treated with an alcoholic solution of an equivalent of sodium benzenesulfinate, benzyl chloromethyl ketone readily forms a phenylsulfone melting at 89.5–90.5° after recrystallization from dilute alcohol.

Anal. Calcd. for $C_{15}H_{14}O_3S$: C, 65.67; H, 5.14. Found: C, 65.75; H, 5.17.

Chloromethyl β-Phenylethyl Ketone (X).—The procedure for benzyl chloromethyl ketone is used, the phenylacetyl chloride being replaced by an equivalent quantity (7.4 cc.) of hydrocinnamoy lchloride. On the evaporation of the ether solution, the product is obtained as an orange solid melting at 38–39.5°. After drying by crushing and several hours evacuation at 2 mm., it weighs 7.6 g. (85% yield). It crystallizes from alcohol as white needles melting at 39–40°. The 2,4-dinitrophenylhydrazone[11] recrystallized from chloroform–petroleum ether melts at 145–146°.

Ethyl α-Benzyl-α-chloroacetoacetate.—Over a period of one hour 82 g. (0.61 mole) of sulfuryl chloride is added with stirring to 120 g. (0.54 mole) of ice-cold ethyl benzylacetoacetate ($n^{20}\text{D}$ 1.5010). Then the ice is removed and the material heated on the steam-bath for thirty minutes. After dilution with 100 cc. of ether, the solution is washed with water, dried over calcium chloride, evaporated, and distilled. The yield of product, b. p. 121–125° (1 mm.), is 95 g. (69%); $n^{20}\text{D}$ 1.5089; $d^{22.5}{}_{22.5}$ 1.164.

Anal. Calcd. for $C_{13}H_{15}ClO_3$: C, 61.30; H, 5.93. Found: C, 61.13; H, 5.90.

α-Benzyl-α-chloroacetone (IX).—A solution of 20 g. of α-benzyl-α-chloroacetoacetic ester, 50 cc. of glacial acetic acid, 4 cc. of water, and 2.5 cc. of concentrated sulfuric acid is refluxed in a ground-jointed apparatus for twenty-one hours. It is then diluted freely with water and extracted twice with ether. After the ether solution has been washed five or six times with water, it is freed of the remaining acetic acid by a single wash with dilute sodium bicarbonate solution, dried over calcium chloride, evaporated, and distilled. The yield of product boiling at 97–99° (4 mm.) is 12.1 g. (84%); $n^{20}\text{D}$ 1.5268; $d^{22}{}_{22}$ 1.126.

Anal. Calcd. for $C_{10}H_{11}ClO$: C, 65.75; H, 6.07. Found: C, 65.53; H, 6.22.

α-Benzyl-α-chloroacetone 2,4-dinitrophenylhydrazone crystallizes as stubby orange rods from a mixture of chloroform and petroleum ether; m. p. 138.5–139.5°. The admixture of the 2,4-dinitrophenylhydrazone (m. p. 145–146°) of the isomeric chloromethyl β-phenylethyl ketone caused a melting point depression of 11°.

Anal. Calcd. for $C_{16}H_{15}ClN_4O_4$: C, 52.97; H, 4.17. Found: C, 52.93; H, 4.34.

α-Chloro-α-phenylacetone (VIII) and Sodium Methoxide.—To a stirred, refluxing solution of sodium methoxide prepared by dissolving 2.6 g. (0.11 mole) of sodium in 60 cc. of absolute methanol, there is added dropwise over a period of twenty minutes 15 g. (0.089 mole) of α-chloro-α-phenylacetone in 10 cc. of absolute methanol. Stirring and refluxing are continued for ten hours to complete the reaction. Then the bulk of the methanol (50–60 cc.) is removed by distillation and the residue taken up in ether and water. The ether layer is dried, evaporated, and distilled. There is obtained 8.7 g. (60% yield) of methyl hydrocinnamate, b. p. 118–120° (21 mm.). Acidification of the aqueous layer may precipitate as much as 1.5 g. (9% yield) of hydrocinnamic acid, m. p. 45–48°.

Hydrolysis of the methyl hydrocinnamate with dilute sodium hydroxide yields hydrocinnamic acid, m. p. 49–51°, forming a *p*-bromophenacyl ester, m. p. 104–106°. The melting points of the acid and ester with authentic samples are not depressed.

Dimethyl Acetal of α-Hydroxy-α-phenylacetone.—A higher boiling fraction, b. p. 120–128° (21 mm.), solidified on standing; weight, 2.4 g. (14% yield). After recrystallization from petroleum ether it had m. p. 63–65°.

Anal. Calcd. for $C_{11}H_{16}O_3$: C, 67.32; H, 8.22. Found: C, 67.84; H, 8.23.

After standing an hour with 2,4-dinitrophenylhydrazine reagent,[13] the acetal deposits the 2,4-dinitrophenylosazone of methylphenylglyoxal,[5] m. p. 258°, and showing no depression in m. p. on admixture with an authentic sample.

When refluxed for three hours with two equivalents of semicarbazide hydrochloride and sodium acetate in dilute alcohol, the acetal forms the disemicarbazone of methylphenylglyoxal,[5] m. p. 228–229°.

α-Chloro-α-phenylacetone (VIII) and Sodium Hydroxide.—If to the sodium methoxide solution there is added 2.5 cc. (0.14 mole) of water before introduction of the α-chloro-α-phenylacetone, there is obtained a 48% yield of hydrocinnamic acid, m. p. 50–53°, upon acidification of the aqueous layer. The hydroxyacetal in 20% yield is found in the ether layer.

Benzyl Chloromethyl Ketone and Sodium Methoxide.—The reaction is carried out in a manner similar to that for α-chloro-α-phenylacetone, with the exception that refluxing and stirring are continued for only forty-five minutes after the ketone (3.0 g., 0.018 mole in 10 cc. of methanol) is added to a solution of 0.5 g. sodium (0.022) mole in 25 cc. of methanol. The yield of methyl hydrocinnamate is 2.4 g. (80%); b. p. 109–110° (13 mm.); $n^{20}\text{D}$ 1.5031. The refractive index of a carefully purified sample of this ester prepared from the pure acid is $n^{20}\text{D}$ 1.5030. Hydrolysis of the ester obtained from the ketone gives hydrocinnamic acid, m. p. and mixed m. p. 49.5–50.5°.

Chloromethyl β-Phenylethyl Ketone (X) and Sodium Hydroxide.—Two grams (0.011 mole) of the ketone in 10 cc. of methanol is treated in the same way with a solution of 0.30 g. (0.013 mole) of sodium in 20 cc. of methanol and 0.3 cc. (0.017 mole) of water, refluxing and stirring being continued for two hours after introduction of the ketone. Acidification and ether extraction of the aqueous layer produced 0.15 g. (8% yield) of an oil which could not be induced to crystallize. When purified by distillation under reduced pressure in a sublimation apparatus, it gave a neutral equivalent of 167. It was identified as γ-phenylbutyric acid (neut. equiv. 164) by means of its S-benzylthiuronium salt, m. p. 141–141.5°. The m. p. of this salt with an authentic specimen was not depressed.

From the ether layer there was obtained 1.2 g. of material boiling at 112–116° (2 mm.). This product is probably a mixture of hydroxymethyl β-phenylethyl ketone and its dimethylacetal. Analytical values on different fractions bear out this conclusion.

Anal. Found: C, 70.43; H, 7.97, and C, 69.50; H, 8.23. Calcd. for 55% $C_{12}H_{18}O_3$ and 45% $C_{10}H_{12}O_2$: C, 70.62; H, 8.06. Calcd. for 75 and 25%, respectively: C, 69.70; H, 8.32.

Eight-tenths gram of this product is refluxed for ten minutes in 10 cc. of ethanol containing a drop of dilute hydrochloric acid and the solution refluxed for ten minutes with 1 cc. of freshly distilled phenylhydrazine. On cooling and dilution with about 1 cc. of water, the **phenylhydrazone of hydroxymethyl β-phenylethyl ketone** crystallizes from the solution, m. p. 113–114° (0.65 g.). It is recrystallized as pale yellow, narrow plates from a mixture of 5 cc. of ethanol and 4 cc. of water; m. p. 114.5–115.5° (0.43 g.).

Anal. Calcd. for $C_{16}H_{18}N_2O$: C, 75.56; H, 7.13. Found: C, 75.52; H, 7.03.

α-Benzyl-α-chloroacetone and Sodium Hydroxide.—This reaction is carried out in a similar way with equal

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[13] Shriner and Fuson, "The Systematic Identification of Organic Compounds," John Wiley and Sons, Inc., New York, N. Y., 1940, p. 65.

quantities of reagents, the refluxing and stirring being continued for five hours. There is obtained from the aqueous layer 0.10 g. of an acidic oil which could not be crystallized. It forms an S-benzylthiuronium salt of m. p. 134° after recrystallization from alcohol.

From the ether-soluble material is obtained 1.4 g. (54% yield) of the **dimethyl acetal of α-benzyl-α-hydroxyacetone,** b. p. 119–121° (6 mm.); $n^{20}\text{D}$ 1.5080; $d^{24.5}{}_{24.5}$ 1.067; mol. ref.: calcd., 58.8; found, 58.6.

Anal. Calcd. for $C_{12}H_{18}O_3$: C, 68.55; H, 8.63. Found: C, 68.53; H, 8.68.

This hydroxyacetal gives no precipitate after twenty minutes in the cold with 2,4-dinitrophenylhydrazine reagent,[13] but reacts readily on warming. Hydrolysis in alcohol containing a small amount of hydrochloric acid followed by treatment with freshly distilled phenylhydrazine gives the phenylosazone of benzylmethylglyoxal,[14] m. p. 169.5–171° after recrystallization from dilute alcohol.

Anal. Calcd. for $C_{22}H_{22}N_4$: C, 77.16; H, 6.48. Found: C, 77.31; H, 6.47.

On standing for six weeks, an ether solution of the hydroxyacetal deposited a white solid which recrystallizes from methanol as short, glistening needles, m. p. 180–182.5°. This is apparently a lactolide analogous to the one obtained by Bergmann and Miekeley.[4]

Anal. Calcd. for $C_{22}H_{28}O_4$: C, 74.13; H, 7.92. Found: C, 74.05; H, 8.01.

S-Benzythiuronium γ-Phenylbutyrate.—The general method of Donleavy[15] was followed in preparing the salts used for identification. This example illustrates the procedure. One gram (0.0061 mole) of γ-phenylbutyric acid is dissolved in 3 cc. of 50% ethanol, neutralized with 10% potassium hydroxide solution, and made weakly acidic with a drop of dilute hydrochloric acid. To this warmed solution is added 1.60 g. (0.0078 mole) of S-benzylthiuronium chloride dissolved in 10 cc. of hot alcohol. The salt begins to separate within a few seconds. On cooling and filtering there is obtained 1.77 g. (88% yield) of the S-benzylthiuronium salt, m. p. 140–141°. Recrystallization from alcohol raises the m. p. to 141–141.5°.

Anal. Calcd. for $C_{18}H_{22}N_2O_2S$: C, 65.42; H, 6.72. Found: C, 65.64; H, 6.93.

S-Benzylthiuronium α-Methylhydrocinnamate.—Prepared as above, it melts at 144–144.5°.

Anal. Calcd. for $C_{18}H_{22}N_2O_2S$: C, 65.42; H, 6.72. Found: C, 65.51; H, 6.99.

Summary

1. On treatment with sodium methoxide in methanol, benzyl chloromethyl ketone gives an 80% yield of methyl hydrocinnamate; α-chloro-α-phenylacetone gives a mixture of the same ester, the free acid, and the dimethyl acetal of α-hydroxy-α-phenylacetone.

2. Under similar conditions chloromethyl β-phenylethyl ketone gives hydroxymethyl β-phenylethyl ketone, its dimethyl acetal, and a small quantity of γ-phenylbutyric acid; α-benzyl-α-chloroacetone gives the dimethyl acetal of α-benzyl-α-hydroxyacetone.

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[14] Müller and v. Pechmann, *Ber.*, **22**, 2132 (1889), report the m. p. of this compound as 172–173°.

[15] Donleavy, THIS JOURNAL, **58**, 1004 (1936).

[CONTRIBUTION FROM THE CANCER CLINIC AND LABORATORY, DEPARTMENT OF PREVENTIVE MEDICINE AND PUBLIC HEALTH OF THE UNIVERSITY OF TEXAS MEDICAL BRANCH AND THE M. D. ANDERSON HOSPITAL FOR CANCER RESEARCH]

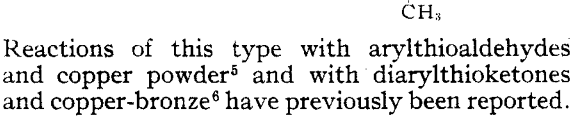
Thiocarbonyls. I. Condensation of Thioacetophenone with Activated Nickel

BY J. K. CLINE,[1] E. CAMPAIGNE[2] AND J. W. SPIES[3]

In a search for simpler methods of synthesizing stilbene derivatives to test for possible carcinogenic action, it was thought that the reaction of Raney nickel with the readily available arylthioaldehydes and alkylarylthioketones might furnish a quick and convenient mode of preparation. To avoid complicating side reactions, the production of the simpler stilbenes was used initially as a model for further experimentation.

Recently Mozingo, Wolf, Harris and Folkers[4] postulated two courses by which Raney nickel might react with an organic sulfur compound to split out sulfur. In one case a Wurtz-type reaction might occur, in which the two organic radicals combined, and in the second case the hydrogen present in the nickel might replace the sulfur. These investigators found that, using organic sulfides, disulfides, sulfoxides, and sulfones, the reaction with Raney nickel took the second course, in which the carbon–sulfur bond was replaced by a carbon–hydrogen bond.

An instance in which the alternate path of the reaction was followed, has been found. The thiocarbonyl group in thioacetophenone was found to react with Raney nickel in a Wurtz-type reaction to form a carbon–carbon double bond.



$$2C_6H_5\text{—}\overset{\overset{\displaystyle S}{\|}}{C}\text{—}CH_3 + 2Ni \longrightarrow C_6H_5\text{—}\overset{\overset{\displaystyle CH_3}{|}}{C}\text{=}\underset{\underset{\displaystyle CH_3}{|}}{C}\text{—}C_6H_6 + 2NiS$$

Reactions of this type with arylthioaldehydes and copper powder[5] and with diarylthioketones and copper-bronze[6] have previously been reported. Copper powder was found to be ineffective as a condensing agent for alkylarylthioketones. The investigation of this type of condensation is being extended to other alkylarylthioketones.

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[4] Mozingo, Wolf, Harris and Folkers, THIS JOURNAL, **65**, 1013 (1943).

[5] Richtzentrain and Van Hofe, *Ber.*, **72**, 1890 (1939); Wood, Bacon, Meibohm, Throckmorton, and Turner, THIS JOURNAL, **63**, 1334 (1941).

[6] Schonberg, Schutz and Nickel, *Ber.*, **61B**, 1375 (1928).