monoalkyl substituted β-keto esters by such a treatment. The hydrolysis of these dialkyl β-keto esters necessitates the use of alkali at 250°. The ratio of the products formed in the cleavage of unsymmetrical 1,3-diketones varied greatly with variation in the environment during cleavage.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF NORTHWESTERN UNIVERSITY]

# THE USE OF KETENE IN THE PREPARATION OF SIMPLE AND MIXED ACID ANHYDRIDES

BY CHARLES D. HURD AND MALCOLM F. DULL

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Mixed acid anhydrides, R—CO—O—CO—$CH_3$, are generally made[1] either by refluxing the acid, RCOOH, with acetic anhydride or by the interaction[2] of any acyl chloride and sodium acetate or by reaction of the acid with acetyl chloride and pyridine. A purification procedure is essential in all of these cases. Such anhydrides as acetic propionic anhydride or acetic isovaleric anhydride are sufficiently stable to be distilled under diminished pressure, but the tendency of mixed anhydrides to disproportionate into the two symmetrical anhydrides often makes the isolation of the mixed anhydride difficult or impossible.

Ketene is an acetylating agent but it has never been considered for use in preparing mixed acetic anhydrides. Ketenes which have been added to acids to convert them into mixed anhydrides are diphenylketene and carbon suboxide.[3] Van Alphen's is the only account[4] of the reaction of ketene itself with acids. He used phenolic acids and observed acetylation of the phenolic group. No mention was made of the production of mixed anhydrides.

In the present work it has been found that ketene readily attaches itself to aliphatic or aromatic acids giving rise to mixed acetic anhydrides

$$RCOOH + CH_2{=}C{=}O \longrightarrow RCO{-}O{-}COCH_3$$

Since nothing else is formed, the purification procedure is greatly simplified. Thus, using ketene, acetic acid was quantitatively changed into acetic anhydride, *n*-butyric acid into acetic butyric anhydride, benzoic acid into acetic benzoic anhydride and furoic acid into acetic furoic anhydride.

Distillation of acetic benzoic anhydride or of acetic furoic anhydride, both of which were oils, gave rise to benzoic anhydride and furoic anhydride,

[1] Autenrieth, *Ber.*, **20**, 3187 (1887); **34**, 168 (1901); Béhal, *Ann. chim. phys.*, [7] **19**, 274 (1900); **20**, 418 (1900); Autenrieth and Thomae, *Ber.*, **57**, 423 (1924).

[2] Verkade, *Rec. trav. chim.*, **35**, 299 (1915); Kilpatrick and Kilpatrick, THIS JOURNAL, **52**, 1418 (1930).

[3] Staudinger, *Ann.*, **356**, 79 (1907); Diels and Lalin, *Ber.*, **41**, 3426 (1908).

[4] Van Alphen, *Rec. trav. chim.*, **44**, 838 (1928).

both solids, in excellent yields. Disproportionation was evident also with acetic butyric anhydride. Thus, this use of ketene serves to produce not only mixed acetic anhydrides, but also symmetrical acid anhydrides by pyrolysis of the mixed anhydrides. The reaction should be a perfectly general one for acids which possess no interfering groups such as hydroxyl or amino.

With aniline, acetic benzoic anhydride is converted into benzoic acid and acetanilide

$$C_6H_5CO{-}O{-}COCH_3 + C_6H_5NH_2 \longrightarrow C_6H_5COOH + C_6H_5NHCOCH_3$$

and not into acetic acid and benzanilide. This agrees with Béhal's finding that ammonia reacted with the mixed anhydride to give benzoic acid and acetamide almost exclusively. If the mixed anhydride was left for twenty-four hours before adding the aniline, both of the anilides and both acids were formed indicating the gradual transformation of the mixed anhydride into benzoic anhydride and acetic anhydride.

Acetic furoic anhydride behaved analogously in its reaction with aniline. The only anilide formed was acetanilide. In the case of acetic butyric anhydride, both anilides were produced but the yield of butyranilide exceeded that of acetanilide.

This behavior of aniline toward the mixed acetic anhydrides is predictable on the basis of the generally recognized greater electron attraction of aryl radicals than alkyl and the slightly greater attraction of methyl than *n*-propyl inasmuch as the molecule of the mixed anhydride is entirely symmetrical except for the terminal groups. The electronic configuration for benzoic acetic anhydride which expresses these factors is

$$C_6H_5{:}\ \underset{O}{C}{:}\ \ddot{\underset{\cdot\cdot}{O}}{:}\ \underset{O}{C}{:}\ CH_3$$

That the absorption of ketene by acids is not limited to organic acids was demonstrated by a few preliminary experiments with sulfuric and phosphoric acids. Ketene was quantitatively absorbed, presumably with the formation of acetylsulfuric acid and acetylphosphoric acid. The utility of the method with other inorganic acids, for example, in the synthesis of acetyl nitrate, is also evident.

## Experimental Part

Ketene was prepared from acetone[5] by pyrolysis. Instead of distilling the acetone into the reaction tube it was dropped in directly from a separatory funnel. In this way, such a rapid flow of acetone was maintained that the extent of decomposition at 700° was limited to 5–6%. Thus, from 108 g. of acetone 102 g. was recovered in an experiment lasting thirty minutes. The other 6 g. gave rise to a 72% yield of ketene since 10 g. of acetanilide was produced from it (*via* aniline + ketene).

**Acetic Acid[6] and Ketene.**—Slightly more than the theoretical quantity of ketene

[5] Hurd, "Organic Syntheses," John Wiley and Sons, New York, 1921, Vol. IV, p. 40.

[6] Compare Hurd and Martin, THIS JOURNAL, **51**, 3614 (1929).

was bubbled into acetic acid. From 20 cc. of this which was distilled, 17 cc. was collected between 136–138°. Thus, the conversion of acetic acid into acetic anhydride is nearly quantitative.

*n*-**Butyric Acid and Ketene.**—Two grams of butyric acid (b. p. 161–163°) was treated with the calculated quantity of ketene. Any admixed acetone was evaporated off *in vacuo* and the residual acetic butyric anhydride was analyzed. Whitford's method of analysis[7], which was developed for acetic anhydride, was found to apply with the mixed acetic anhydride. In it, the anhydride reacts with dry oxalic acid and pyridine to liberate carbon monoxide and carbon dioxide which are collected.

*Anal.* Subs., 0.2166, 0.2112; calcd. cc. of gas for $CH_3COOCOC_3H_7$, 72.9, 72.7; found, cc., 72.0, 72.1; per cent. of $C_6H_{10}O_3$, 98.7, 99.1.

The acetic butyric anhydride was found to boil[8] at 147–160°, above which the boiling point rose abruptly to that of butyric anhydride itself. At 18 mm. the mixed anhydride boiled at 70–85°. With aniline it reacted vigorously, yielding butyranilide and a smaller quantity of acetanilide. The butyranilide crystallized first and was removed but the acetanilide crystallized almost immediately thereafter. After recrystallization from water the former melted at 89–90° and the latter at 110–112°.

Inasmuch as there was no sharp boiling fraction for the mixed anhydride in the above experiment, it was repeated on a larger scale. Twenty grams of redistilled *n*-butyric acid (b. p. 161–162°) was treated with ketene until addition of anhydrous sodium carbonate failed to result in an evolution of carbon dioxide. The crude product was allowed to stand over anhydrous sodium carbonate for two hours, after which the excess solvent (anhydrous ether and some acetone which had carried over) was removed by evacuating for half an hour with a water pump. A portion, treated with aniline, resulted in the formation of both acetanilide and butyranilide, the latter predominating.

The crude material (30 g.) was then fractionated at 7 mm. pressure. The first fraction of 15.5 g. was collected at 41–60°, the second of 10.5 g. at 60–66°, and the third of about 3 g. at 66–67°. The third fraction was butyric anhydride, for it yielded only butyranilide on treatment with aniline. The first fraction produced acetanilide and butyranilide with acetanilide in excess. The fraction was evidently a mixture of acetic anhydride and acetic butyric anhydride. Redistillation of this fraction failed to produce a constant boiling fraction. It distilled at 41–62°.

The second fraction (10.5 g.) gave rise to both butyranilide and acetanilide with the latter in considerably smaller amounts. On redistillation, it came over almost entirely at 63–64.5°. A fraction was thus obtained weighing 9.5 g. which, with aniline, again yielded both butyranilide and acetanilide. Much of both anilides was lost in the steps of purification but it was certain that more butyranilide was obtained than acetanilide.

**Benzoic Acid.**—(a) Ketene was passed through a tower which contained powdered benzoic acid. Some ketene escaped but some reacted as witnessed by a heat of reaction and by a gradual liquefaction of the solid acid into the liquid benzoic acetic anhydride. Accumulation of this mixed anhydride was slow by this method. Furthermore, the heat of reaction seemed to cause a partial disproportionation into benzoic anhydride.

(b) Using ether as a solvent, the reaction was more rapid and the temperature was kept under control. Ketene was passed into a solution of twenty grams of benzoic acid in 100 cc. of ether. To follow the reaction a stirring rod was dipped occasionally into the solution and withdrawn. Evaporation of the solvent left a solid at the start

[7] Whitford, THIS JOURNAL, **47**, 2939 (1925).

[8] Autenrieth, *Ber.*, **34**, 177 (1901), gave 155–175° as the b. p.

but only an oil at the conclusion of the reaction. After evaporation of the ether, 31–32 g. of benzoic acetic anhydride remained which is a quantitative yield.

### Identification of Benzoic Acetic Anhydride

(a) **Analysis,** using dry oxalic acid and pyridine.

*Anal.* Subs. 0.2131, 0.2213; calcd. cc. of gas for $CH_3COOCOC_6H_5$, 58.2, 60.4; found, cc., 57.5, 59.3; per cent. of $C_9H_8O_3$, 98.8, 98.2.

(b) **Disproportionation to Benzoic Anhydride.**—The 31.5 g. of oil was distilled at 18 mm., giving 13 g. of acetic anhydride (collected below 210°) and 18.5 g. of benzoic anhydride which boiled at 210–210.5°. The latter solidified and melted at 41.5°. The 18.5 g. represents a 96% yield of benzoic anhydride.

In another run, two 25-g. portions of benzoic acid (each in 125 cc. of ether at room temperature) were connected in series to a stream of ketene. (The two were interchanged when the first portion was nearly converted.) In this run the acetone was dropped in the furnace at a rate of 4.5 cc. per minute. The time for the entire 50 g. to be changed to the mixed anhydride was 135 minutes. Distillation of the mixed anhydride gave 42 g. of benzoic anhydride (m. p. 42°) or a 93% yield.

(c) **Reaction with Aniline.**—To 10 g. of benzoic acetic anhydride (similar preparation from another experiment), 5.5 g. of aniline was added. Much heat was evolved and on cooling the mass solidified. By extraction with diluted sodium carbonate and subsequent acidification 6.5 g. of benzoic acid was obtained as compared with a theoretical yield of 7.4 g. The residue of acetanilide was dissolved in boiling water, whereupon 6.8 g. (calcd. is 8.2 g.) precipitated after filtering and cooling. About 0.3 g. of benzanilide, m. p. 163°, resisted solution in the water.

If the 10 g. of mixed anhydride was left for twenty-four hours before mixing it with aniline, there was considerable disproportionation as evidenced by the formation of 3.3 g. of benzoic acid, 4.1 g. of acetanilide and 4.2 g. of benzanilide.

**Furoic Acid.**—Ketene was passed into a solution of 25 g. of furoic acid in 150 cc. of ordinary ether. The details of this reaction were similar to those given with benzoic acid in ether solution. This run was completed in seventy-five minutes. On evaporation of the solvents, an oil remained which was furoic acetic anhydride. The yield was quantitative.

*Anal.* Subs. 0.1987, 0.2016: calcd. cc. of gas for $CH_3COOCOC_4H_3O$, 57.8, 58.6; found, cc., 56.7, 57.1. Per cent. of $C_7H_6O_4$, 98.1, 97.4.

**Reaction with Aniline.**—The mixed anhydride reacted vigorously with aniline. The exclusive products of the reaction were acetanilide (m. p. 113–114°) and furoic acid (m. p. 129–131°) which were separated and purified by crystallization from water.

**Vacuum Distillation of Furoic Acetic Anhydride.**—The mixed anhydride from 10 g. of furoic acid was distilled at 5 mm. Eleven grams of an almost odorless distillate was collected at 109–110°, and 2.7 g. at 150–152°. The latter quickly solidified (m. p. 71°) and was identified as furoic anhydride.[9] The eleven grams of liquid distillate was largely unchanged furoic acetic anhydride. Considerable disproportionation of the mixed anhydride occurred when the distillation was performed at 22 mm., the furoic anhydride distilling at 196–197°. Using atmospheric pressure for the distillation, there was complete and rapid pyrolysis to the symmetrical anhydrides.

## Summary

Mixed acetic anhydrides, RCO—O—$COCH_3$, may be prepared very smoothly by interaction of ketene with acids. The mixed anhydrides

[9] Baum, *Ber.*, **34**, 2505 (1901).

were analyzed, using dry oxalic acid and pyridine. The reaction with aniline was investigated. The disproportionation induced by heat was found to be a convenient method for synthesizing symmetrical acid anhydrides.

EVANSTON, ILLINOIS

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[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF THE COLLEGE OF LIBERAL ARTS OF NORTHWESTERN UNIVERSITY AND OF THE SCHOOL OF CHEMISTRY AND PHYSICS OF THE PENNSYLVANIA STATE COLLEGE]

# NEOPENTYL ALCOHOL AND ITS REARRANGEMENT PRODUCTS[1]

BY FRANK C. WHITMORE AND HENRY S. ROTHROCK[2]

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The literature on neopentyl alcohol (*tert.*-butylcarbinol) and the related halides[3] is unsatisfactorily incomplete, especially in view of the fact that these substances represent the simplest case in which removal of the alcoholic hydroxyl results in complete or nearly complete rearrangement of the carbon skeleton.[4]

The present study fills some of the gaps in our knowledge of this interesting group of substances. Neopentyl alcohol is stable to heat. Seven weeks at 230–240° gives no change. Heating to similar temperatures with iodine, anhydrous potassium carbonate or traces of hydrogen chloride gives little or no change. It dissolves in cold concentrated sulfuric acid with the formation of an acid ester from which the original alcohol can be recovered.

The preparation of halides from neopentyl alcohol is extraordinarily difficult. Its reactivity is much less than that of *n*-butyl alcohol. Dry hydrogen bromide very slowly forms an oxonium salt with neopentyl alcohol. This is stable at 40° but is slowly converted at 65° to a mixture of amyl bromides containing approximately 72% tertiary amyl bromide, 8% of a secondary bromide, probably secondary isoamyl bromide and 20% of one or more primary bromides. The composition of this mixture is not changed by heating at 105°.

The problem of the neopentyl halides and their rearrangements is being intensively studied in this Laboratory.

## Experimental

The neopentyl alcohol used in this research was prepared from *tert.*-butylmagnesium chloride and formaldehyde by R. W. Beattie, of the Intermediate Laboratory of the Public Health Institute of Chicago.

**Stability of Neopentyl Alcohol on Heating.**—The relatively high melting point of

[1] Submitted by Henry S. Rothrock in partial fulfilment of the requirements for the Ph.D. degree at the Pennsylvania State College.

[2] Du Pont Fellow, Northwestern University, 1928–1929.

[3] Tissier, *Ann. chim. phys.*, [6] **29**, 357 (1893); Samec, *Ann.*, **351**, 256 (1907); Richard, *Ann. chim. phys.*, [8] **21**, 323 (1910); Ingold, *J. Chem. Soc.*, **123**, 1706 (1923).

[4] See p. 3279.