hours. The molten reaction mixture was poured into water, and the heavy oily layer was thoroughly digested with water and then dissolved in benzene. After drying over sodium sulfate the solvent was removed, leaving an uncrystallizable, colorless oil which was used directly for the next step.

To a solution of the crude dibenzyl chloroacetanilido-malonate in 20 ml. of benzene was added 1 g. of triethyl-amine. Crystalline triethylamine hydrochloride started to separate immediately. After allowing the reaction mixture to stand overnight, a 93% yield (0.68 g.) of tri-ethylamine hydrochloride was obtained. Removal of the solvent left a viscous, yellow oil, which solidified during storage. Recrystallization from cyclohexane afforded 1.6 g. of colorless, cubic crystals, m. p. 94–95°. The over-all yield of the crystalline β-lactam from dibenzyl anilino-malonate was 88.5%.

Anal. Calcd. for $C_{25}H_{21}O_5N$: C, 72.30; H, 5.06; N, 3.38. Found: C, 72.20; H, 5.31; N, 3.52.

1-Phenyl-4,4-dicarboxy-2-azetidinone (VII).—Hydro-genolysis of 3 g. of VI was carried out at room temperature in ethyl acetate solution, using 0.25 g. of palladium on charcoal (Darco) as a catalyst. The time required was 1.75 hours. After removal of the catalyst, the solvent was evaporated, yielding an oil (1.6 g., 96%) which solidified completely. On recrystallization from a mixture of ethyl acetate and ligroin, the melting point was 171–172° with decomposition and evolution of gas.

Anal. Calcd. for $C_{11}H_9O_5N$: C, 56.17; H, 3.86; N, 5.96. Found: C, 55.77; H, 4.17; N, 6.04.

1-Phenyl-4-carboxy-2-azetidinone (V)—(a) From 1-Phenyl-4-carbethoxy-2-azetidinone (IV).—To 0.4 g. of IV in 5 ml. alcohol was added 0.104 g. of potassium hy-droxide dissolved in 10 ml. of alcohol. After storing the solution overnight at room temperature, excess ether was added. A potassium salt was obtained as crystalline clus-ters (0.26 g., 61%). To a concentrated aqueous solution of this salt (0.15 g.) was added hydrochloric acid, the solu-tion was extracted with ether and the extract was dried over sodium sulfate. After removing the solvent, 0.120 g. (96%) of a solid, m. p. 119–122°, was obtained. By re-crystallization from ether–petroleum ether colorless needles, m. p. 123°, were obtained. On standing over-night in a drying oven, the m. p. rose to 148°. Another sample prepared in the same manner gave rhombic crys-tals, m. p. 148–148.5°. The melting point of a mixture of the two types of crystals melted at 148–148.5°.

Anal. Calcd. for $C_{10}H_9O_3N$: C, 62.82; H, 4.75; N, 7.33. Found: C, 63.05; H, 5.05; N, 7.18.

(b) From 1-Phenyl-4,4-dicarboxy-2-azetidinone (VII). —Decarboxylation of VII to V was achieved by heating on

an oil-bath (130°) 0.2 g. of VII with a drop of pyridine as a catalyst. The residue was taken up in ether and washed with a hydrochloric acid solution. After drying the ethereal solution over sodium sulfate, the solvent was re-moved, leaving 0.13 g. (80%) of a colorless solid, m. p. 139–144°. Recrystallization from ether–petroleum ether raised the m. p. to 147–148°. A mixture of this material with V obtained by procedure (a) melted undepressed at 147–148°.

1-(β-Naphthyl)-4,4-dicarbethoxy-2-azetidinone (VIII). —The procedure outlined for obtaining VI from dibenzyl anilinomalonate was used with 2 g. of ethyl β-naphthyl-malonate.⁶ The intermediate chloroacetylated compound was obtained as 2.35 g. of viscous oil. The corresponding β-lactam VIII was isolated as 2.15 g. (95%) of a crystal-line solid. Recrystallization from ligroin or cyclohexane gave a product melting at 75–76°.

Anal. Calcd. for $C_{19}H_{19}O_5N$: C, 66.85; H, 5.61; N, 4.10. Found: C, 66.87; H, 5.76; N, 4.15.

Infrared Absorption Spectra.—The infrared spectra shown in Fig. 1 were determined with a Baird Infrared Re-cording Spectrophotometer, Model B. Five per cent. solu-tions in carbon tetrachloride were used for curves A, B and C. A ten per cent. solution in methylene chloride was used for D and a five per cent. solution in tetrachloroethane for E.

Summary

A series of β-lactams has been synthesized by a new method involving the cyclization of chloro-acetamidomalonic esters by treatment with tri-ethylamine at room temperature. Uniformly high yields were obtained; no tendency to form compounds containing larger rings or those result-ing from linear polymerization was observed.

The stepwise saponification and decarboxyla-tion of 1-phenyl-4,4-dicarbethoxy-2-azetidinone lead successively to 1-phenyl-4-carboxy-4-carb-ethoxy-2-azetidinone, and 1-phenyl-4-carboxy-2-azetidinone. The structure of the latter was proved by an independent synthesis from 1-phenyl-4,4-dicarbobenzoxy-2-azetidinone by hy-drogenolysis and decarboxylation, thus demon-strating that the β-lactam ring survived the two selective alkaline hydrolyses.

Cambridge 39, Massachusetts

[Contribution from the Chemistry Laboratory of The Ohio State University]

A New Synthesis of α-Alkoxy Ketones[1]

By Melvin S. Newman and Philip F. Beal III

Attention has previously been called to the similarity between the Curtius rearrangement of acid azides and the Wolff rearrangement of α-diazoketones.[2] Since it had recently been shown that the Curtius rearrangement was acid catalyzed[3] we were led to study the acid catalyzed reactions of diazoketones.

(1) Presented in part at the American Chemical Society Meeting at Atlantic City, August, 1948. Taken in part from the Ph.D. thesis of P. F. B., Ohio State, 1949.

(2) B. Eistert, *Ber.*, **68**, 208 (1935).

(3) M. S. Newman and H. Gildenhorn, This Journal, **70**, 317 (1948).

Inasmuch as protonic acids were known to react with diazoketones to yield unrearranged ketones containing the proton and anion of the acid attached to the carbon which originally held the diazo group, a non-protonic acid was indicated. When an ether or benzene solution of diazoaceto-phenone was treated with boron fluoride etherate, nitrogen was evolved immediately at room tem-perature. The reaction product, however, was a dark colored tar. When methanol was the solvent, a good yield of α-methoxyacetophenone was ob-tained. This reaction proved to be quite general

even when t-butyl alcohol was used, although in the latter case the t-butyl ether formed was further converted to phenacyl alcohol in yields which depended on reaction conditions. Thus a new general method for the preparation of α-alkoxy-ketones is available.

$$C_6H_5COCHN_2 + ROH \xrightarrow{BF_3} C_6H_5COCH_2OR + N_2 \quad (1)$$
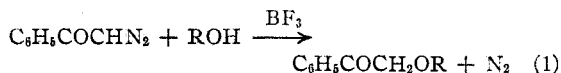
An effort was made to obtain a Wolff rearrangement by using a diazoketone containing a group with a migration aptitude greater than that of phenyl. Accordingly α-diazo-p-methoxyacetophenone was allowed to react with alcohols as above. Only unrearranged keto ethers were obtained.

An attempt to prepare β-tetralone by treatment of β-phenethyl diazomethyl ketone with ethereal sulfuric acid[4] was made, but di-(4-phenyl-2-ketobutyl) sulfate was obtained. This appears to be the first example of this class of compound.

$$2C_6H_5CH_2CH_2COCHN_2 + H_2SO_4 \longrightarrow (C_6H_5CH_2CH_2COCH_2)_2SO_4 + 2N_2 \quad (2)$$
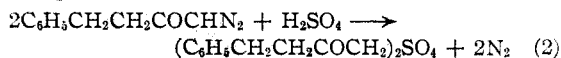
Experimental

The aromatic diazoketones were prepared by the improved method recently described.[5] The aliphatic diazoketones were prepared from the acid chlorides using an excess of diazomethane. All reactions involving diazoketones were carried out in a three-neck flask equipped with a sealed stirrer, dropping funnel, and reflux condenser connected to an azotometer. After the nitrogen evolved had been collected (over 95% of the theoretical was obtained in all successful experiments) the solvent was removed under reduced pressure and the residue taken up in ether–benzene. This extract was washed with bicarbonate solution, saturated sodium chloride solution, and was dried over sodium sulfate. After removal of the solvents, the residue was vacuum distilled. Frequently these distillates gave correct analytical figures for the compound expected, yet some did not. A derivative was made from each of the latter and compared with an authentic sample or with literature values. Most of the experiments were checked at least once.

Aluminum chloride and stannic chloride could be used in place of boron fluoride etherate but these experiments are not described since they were so similar. A solid phosphoric acid catalyst (obtained from the Harshaw Company) was also effective.

α-**Methoxyacetophenone.**—In a typical experiment gas evolution started immediately on adding about 0.3 g. of boron trifluoride etherate to a solution of 7.5 g. of diazoacetophenone in 150 ml. of methanol at 25°. After thirty minutes the theoretical amount of nitrogen had been collected. There was obtained 6.1 g. (79%) of α-methoxyacetophenone, b. p. 124–126° at 19 mm. An authentic sample was prepared by reaction of phenylmagnesium bromide with methoxyacetonitrile.[6] Comparison was effected through the semicarbazone,[7] m. p. and mixed m. p. 128–129°.

α-**Ethoxyacetophenone.**—A solution of 5.0 g. of diazoacetophenone in 10 ml. of ethanol and 100 ml. of ether was treated with 0.2 g. of boron fluoride etherate. After 90

minutes at 25° 91% of nitrogen had been evolved. There was obtained 81% of α-ethoxyacetophenone,[8] b. p. 125–127° at 11 mm. The semicarbazone melted at 127–128°.[8]

α-**Isopropoxyacetophenone.**—A solution of 5.0 g. of diazoacetophenone in 150 ml. of isopropyl alcohol was treated with 0.5 g. of boron fluoride etherate. The reaction which was sluggish at 25° yielded the theoretical amount of nitrogen after 75 minutes at 55°. There was obtained 69% of α-isopropoxyacetophenone,[9] b. p. 87° at 2 mm. The 2,4-dinitrophenylhydrazone melted at 165.6–166.8°.

Anal. Calcd. for $C_{17}H_{18}O_5N_4$: C, 57.3; H, 5.1; N, 15.6. Found[10c]: C, 57.1; H, 4.9; N, 15.6.

α-t-**Butoxyacetophenone.**—A solution of 5.0 g. of diazoacetophenone in 50 ml. of t-butyl alcohol was heated to 70° and treated with 0.3 g. of boron fluoride etherate. After 45 minutes 95% of the theoretical nitrogen was evolved. After the usual work-up there was obtained 4.9 g. of a mixture of about 80% of α-t-butoxyacetophenone and 20% of phenacyl alcohol, as indicated by carbon and hydrogen analyses.

Anal. Calcd. for $C_8H_8O_2$: C, 70.6; H, 5.9. Calcd. for $C_{12}H_{16}O_2$: C, 75.0; H, 8.3. Calcd. for 80% $C_{12}H_{16}O_2$–20% $C_8H_8O_2$: C, 74.1; H, 7.8. Found[c]: C, 74.2; H, 7.8.

This mixture yielded the pure 2,4-dinitrophenylhydrazone of t-butoxyacetophenone, m. p. 185–187°, in good yield.

Anal. Calcd. for $C_{18}H_{20}O_5N_4$: C, 58.1; H, 5.4; N, 15.1. Found[c]: C, 58.0; H, 5.4; N, 15.1.

Phenacyl Alcohol.—When an experiment similar to the above was carried out with 2 g. of boron fluoride etherate, an 86% yield of crude but crystalline phenacyl alcohol was obtained. On recrystallization from petroleum ether, b. p. 65–69°, pure phenacyl alcohol, m. p. and mixed m. p. with an authentic sample,[11] 85–86° resulted. Phenacyl alcohol also was produced in good yield when a solution of the above-described crude mixture of t-butoxyacetophenone and phenacyl alcohol in ether was treated with boron fluoride etherate at room temperature. On standing a brown color developed and on working up, the product crystallized on isolation, m. p. 76–80°. Recrystallization yielded pure phenacyl alcohol.

α,4-**Dimethoxyacetophenone.**—A solution of 6.0 g. of α-diazo-p-methoxyacetophenone in 10 ml. of methanol and 100 ml. of ether was treated with 0.5 g. of boron fluoride etherate at 25°. After 70 min. the theoretical nitrogen was evolved and the product crystallized on removal of solvent. Recrystallization from low boiling petroleum ether yielded 4.2 g. (67%) of dimethoxyketone,[12] m. p. 39.2–40.2°. The semicarbazone[12] melted at 149–150°.

α-t-**Butoxy-p-methoxyacetophenone.**—When a solution of 3.0 g. of α-diazo-p-methoxyacetophenone in 50 ml. of t-butyl alcohol was treated with 0.3 g. of boron fluoride etherate at 65° for 40 min., the theoretical amount of nitrogen was evolved. The product, b. p. 147° at 5 mm., on crystallization from petroleum ether, b. p. 65–69°, yielded 2.1 g. (57%) of α-t-butoxy-p-methoxyacetophenone, m. p. 71.8–72.6°.

Anal. Calcd. for $C_{13}H_{18}O_3$: C, 70.2; H, 8.2. Found[k]: C, 70.6; H, 8.1.

The 2,4-dinitrophenylhydrazone melted at 202–204°.

Anal. Calcd. for $C_{19}H_{22}O_6N_4$: C, 56.7; H, 5.5; N, 13.9. Found[c]: C, 56.6; H, 5.4; N, 13.7.

α-**Methoxypropiophenone.**—A solution of 5.2 g. of α-diazopropiophenone[13] in 20 ml. of methanol was treated with 0.1 g. of boron fluoride etherate at 25°. In 30 min. the theoretical nitrogen was evolved. On distillation 3.3 g.

(4) Compare J. W. Cook and R. Schoental, *J. Chem. Soc.*, 288 (1945).

(5) M. S. Newman and P. F. Beal, THIS JOURNAL, **70**, 1566 (1949).

(6) R. B. Moffett and R. L. Shriner, *Org. Syntheses*, **21**, 79 (1941).

(7) C. F. H. Allen and J. A. Scarrow, *Can. J. Research*, **11**, 400 (1934).

(8) M. Sommelet, *Ann. chim.*, [8] **9**, 522 (1906).

(9) H. R. Henze, et al., THIS JOURNAL, **64**, 1222 (1942).

(10) Analyses marked[c] by H. S. Clark Microanalytical Laboratories,[k] by Mrs. E. Klotz O.S.U.

(11) W. L. Evans, *Am. Chem. J.*, **35**, 120 (1906).

(12) D. D. Pratt and R. Robinson, *J. Chem. Soc.*, 750 (1923).

(13) A. L. Wilds and A. L. Meader, *J. Org. Chem.*, **13**, 763 (1948).

(60%) of crude ketoether, b. p. 89–95° at 4 mm. resulted. This product was transformed in good yield into its 2,4-dinitrophenylhydrazone, m. p. 159.5–160.5°.

Anal. Calcd. for $C_{16}H_{18}O_5N_4$: C, 55.8; H, 4.7; N, 16.2. Found[c]: C, 55.9; H, 4.7; N, 16.3.

α-Methoxypinacolone.—When a solution of 4.9 g. of α-diazopinacolone in 40 ml. of methanol was treated with 0.3 g. of boron fluoride etherate at 25° the nitrogen (96%) was evolved in 20 min. Distillation yielded 3.0 g. (59%) of α-methoxypinacolone, b. p. 81–83° at 48 mm. A sample of the same ketone was prepared in 2% yield by treating *t*-butylmagnesium bromide with methoxyacetonitrile. Both samples yielded identical 2,4-dinitrophenylhydrazones, m. p. and mixed m. p. 188.0–189.2°.

Anal. Calcd. for $C_{13}H_{18}O_5N_4$: C, 50.3; H, 5.8; N, 18.1. Found[k]: C, 50.7; H, 5.8; N, 18.2.

Di-(4-phenyl-2-ketobutyl) Sulfate.—A solution of 5.0 g. of β-phenethyl diazomethyl ketone, obtained in 97% yield as a viscous yellow oil from the acid chloride, in 100 ml. of dry ether was treated dropwise with 2.6 g. of concentrated sulfuric acid. Gas evolution was vigorous, 650 cc. of nitrogen being liberated in five minutes. After washing this solution with sodium bicarbonate solution, the ether was dried over sodium sulfate. On removing the ether under reduced pressure the residue solidified almost completely as colorless needles. On several recrystallizations from benzene–petroleum ether (low boiling) without attempting to avoid losses there were obtained colorless needles of the neutral sulfate, m. p. 51–52°.

Anal. Calcd. for $C_{20}H_{22}O_6S$: C, 61.5; H, 5.7; S, 8.5. Found[c]: C, 61.3; H, 5.9; S, 8.5.

Summary

The decomposition of α-diazoketones is shown to be non-protonic acid catalyzed. In the absence of alcohols, only tar results from this treatment but in the presence of typical primary, secondary and tertiary alcohols, the corresponding alkoxy ketones are obtained.

In one case, a neutral sulfate was obtained by treating an α-diazoketone with ethereal sulfuric acid.

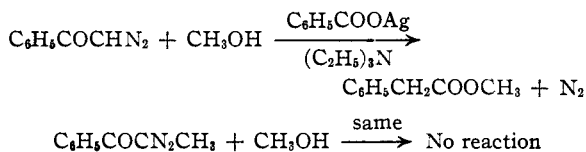# An Improved Wolff Rearrangement in Homogeneous Medium[1]

BY MELVIN S. NEWMAN AND PHILIP F. BEAL III

In our experience, the Wolff rearrangement of α-diazo ketones using methanol and silver oxide[2] has proved to be somewhat erratic. In different runs using the same diazo ketone large variations in yield were experienced for no apparent reason. Accordingly we undertook to develop a procedure whereby the rearrangement might take place in a homogeneous medium. In this paper we report a new procedure by which this rearrangement may be carried out in solution and under conditions milder than those which usually obtain.[2]

The new reagent consists of a solution of silver benzoate in triethylamine. When a few milliliters of this reagent are added to a solution of diazomethyl ketone in methanol at room temperature nitrogen evolution soon starts and the solution darkens owing to the precipitation of metallic silver. As nitrogen evolution slackens the addition of more silver reagent is made. Usually only a few additions are needed before the theoretical amount of nitrogen is evolved. To effect completion only a small proportion of silver is needed. The methyl ester of the acid to be expected is then isolated by suitable means from the reaction mixture in quite acceptable yields which are easily duplicated.

A number of experiments designed to elucidate the requirements for successful reaction were executed. When α-diazopropiophenone was treated under the same conditions which led to successful rearrangement of α-diazoacetophenone

(1) Taken from the Ph.D. thesis of P. F. B. Ohio State University, 1949.

(2) W. E. Bachman and W. S. Struve, "Organic Reactions," John Wiley and Sons, Inc., New York, N. Y., 1942, p. 52.

no reaction occurred, even after a silver precipitate and mirror were produced by addition of a small amount of formalin. These experiments

$$C_6H_5COCHN_2 + CH_3OH \xrightarrow[(C_2H_5)_3N]{C_6H_5COOAg}$$
$$C_6H_5CH_2COOCH_3 + N_2$$

$$C_6H_5COCN_2CH_3 + CH_3OH \xrightarrow{same} \text{No reaction}$$

indicate that the alpha hydrogen is necessary.

When a solution of hydroquinone was added to a reaction that was running smoothly gas evolution ceased abruptly. On further addition of the silver solution, in excess of the equivalent amount of hydroquinone remaining, the evolution of nitrogen started again. This stopping and starting could be repeated several times by making the necessary additions of hydroquinone and silver solutions. The hydroquinone probably stops the reaction by reducing the silver ion, or a necessary reaction intermediate.

The necessity for triethylamine (or a similar base) was demonstrated by the following experiment. A solution of silver trifluoroacetate in benzene was added to a solution of diazoacetophenone in methanol. No reaction occurred. However, when triethylamine was added, evolution of nitrogen commenced. Thus triethylamine is important not only because of its solvent action on silver benzoate but also because of its basic properties.

It thus appears that a base and catalytic amount of an oxidizing agent is required in this modification of the Wolff rearrangement. A