

Recrystallization of this material from chloroform-petroleum ether gave 0.05 g. of light-colored plates, m. p. 157–160°; the mixed melting point of these crystals with an authentic specimen of phenylacetamide was 158–160° cor. In order to prove that the product did not arise from impurities in the starting ketone, some of the isobutyl phenyl ketone was converted into the oxime in 98% yield, m. p. 72–73°; the oxime was reconverted into the ketone by hydrolysis with 6 *N* sulfuric acid. A repetition of the Willgerodt experiment with the recovered ketone gave the same results.

B. In Aqueous Dioxane Solution.³¹—A mixture of 2.4 g. of isobutyl phenyl ketone, 6.4 g. of sulfur, 12 ml. of ammonium sulfide solution (12 *M* in ammonia and 7.5 *M* in hydrogen sulfide by analysis³²) and 6 ml. of dioxane was heated in a sealed glass tube for four hours at 190°. The mixture was evaporated to dryness, extracted with 10 ml. of hot water, and the extracts concentrated to small volume; upon cooling, 0.035 g. of brown plates separated, m. p. 100–105°. Recrystallization from water, then from ether and petroleum ether, gave a small amount of α -methyl- γ -phenylbutyramide, m. p. 118–120°. The residue from the original reaction mixture, consisting mostly of unreacted sulfur, was washed with 20 ml. of hot alcohol; 0.29 g. of oil separated from the alcohol upon cooling. The alcohol solution was separated from the oil and evaporated to dryness, leaving 0.39 g. of semisolid. The mass was spread on a porous plate, leaving 0.03 g. of nearly colorless solid; recrystallization of the latter from ether-petroleum ether gave 0.01 g. of practically colorless plates,

m. p. 121–121.5° cor. A mixture of the final product with an authentic specimen of α -methyl- γ -phenylbutyramide, m. p. 121–122°, cor.; melted at 121–121.5°, cor.³²

Summary

Acetylenes and olefins were found to give carbonamides under conditions of the Willgerodt reaction. Under conditions of the Kindler reaction acetylenes and olefins were found to produce thioamides.

Several carbonyl compounds were investigated in the Willgerodt reaction. Isobutyl phenyl ketone, a typical branched chain compound, gave a small amount of α -methyl- γ -phenylbutyramide with one reagent, but formed phenylacetamide with another reagent.

Preliminary studies were made on the course of the Willgerodt and Kindler reactions.

(32) The sample of α -methyl- γ -phenylbutyramide for comparison was prepared by Mr. Collis H. Davis from the corresponding acid. This acid, which was liquid at room temperature, was synthesized by the hydrolysis and decarboxylation of ethyl ethyl- β -phenethylmalonate.¹¹ The acid was also converted into the anilide, m. p. 142–143° cor. (reported m. p. 140°¹³).

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The Willgerodt Reaction. IV. Acetylenes, Olefins, and Tertiary Carbinols^{1,2}

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In an extension of the previous studies of the Willgerodt reaction with acetylenes and olefins,¹ 1-heptyne and 1-heptene were both found to yield heptanamide. Undecylenic acid gave a mixture of amides containing some nonane-1,9-dicarbonamide; hydrolysis of the mixture yielded nonane-1,9-dicarboxylic acid, indicating that the primary reaction product of the Willgerodt reaction probably contained some of the ammonium salt of the monoamide as well as the diamide.

2-Vinylnaphthalene gave 2-naphthaleneacetamide. 2-Vinylpyridine produced 2-pyridineacetamide. The latter appears to be the first example of the use of a vinyl derivative of a heterocyclic nucleus in the Willgerodt type of amide synthesis; however, the conversion of 3-acetylpyridine to the isomeric 3-pyridineacetamide has been reported.⁴

The effect of branching of the chain in olefins was studied with 1,1-diphenylethylene, 2-phenylpropene, and 1,1-dineopentylethylene. Di-

phenylacetamide was the only product isolated from 1,1-diphenylethylene. Under a variety of reaction conditions 2-phenylpropene produced mixtures of α -phenylpropionamide and phenylacetamide. Total yields of as high as 56% of carbonamide were obtained. Although no satisfactory quantitative separation for the two homologous amides was found, it was possible to isolate each of the products in pure form.⁵ 1,1-Dineopentylethylene was cleaved with the elimination of one neopentyl group: the only identifiable product was a small amount of neopentylacetamide.

Dimethylphenylcarbinol and methylphenylcarbinol reacted to form the same products as 2-phenylpropene and 1,1-diphenylethylene, respectively. The yields were lower with the tertiary carbinols than with the corresponding olefins. It seems reasonable to assume that de-

(1) For the previous paper of this series, see Carmack and DeTar, *THIS JOURNAL*, **68**, 2029 (1946).

(2) From the Ph.D. Dissertation of Dexter B. Pattison, University of Pennsylvania, Philadelphia, Pennsylvania, 1946.

(3) Present address: J. E. Rhoads and Sons, Wilmington, Delaware.

(4) (a) Hartmann and Bosshard, *Helv. Chim. Acta*, **24**, 28E (1941);

(b) British Patent, 558,774; *British C. A.*, BII, 102 (1944).

(5) King and McMillan, *THIS JOURNAL*, **68**, 632 (1946), have recently reported the isolation of a 3% yield of α -phenylpropionamide in the Willgerodt reaction of 2-phenylpropene with ammonium polysulfide reagent. These authors apparently did not observe the side reaction involving the elimination of a methyl group and formation of phenylacetamide. Willgerodt and Merk, *J. prakt. Chem.*, [2] **80**, 192 (1909), and Arnold, Schultz, and Klug, *THIS JOURNAL*, **66**, 1606 (1944), have noted cleavages of aryl alkyl ketones to form derivatives of aryl carboxylic acids, and we have previously noted (ref. 1) the formation of phenylacetamide from phenyl isobutyl ketone.

hydration of the tertiary carbinols was the primary step in the formation of the carbonamides.⁶

The best reagent for the completely aliphatic acetylene, 1-heptyne, was the same as that used with the aliphatic ketones⁷—a solution in water-pyridine of ammonium polysulfide corresponding approximately to the composition $(\text{NH}_4)_2\text{S}_{5-8}$. The olefins, on the other hand, did not give particularly good yields of carbonamides with this reagent. Better results were obtained from olefins by the use of concentrated aqueous ammonia, sulfur, and pyridine (or dioxane).⁸

The highest yields were obtained from some of the olefins by a new variation of the reagent involving the use of ammonium thiosulfate⁹ in conjunction with the water-pyridine solution of ammonium polysulfide. In other words, the addition of ammonium thiosulfate to the reaction mixture more than offsets the disadvantage of using a high initial sulfide concentration. Sodium thiosulfate and ammonium sulfite produced a similar effect, but ammonium chloride and ammonium hydrogen phosphate did not significantly affect the yield of product from 2-phenylpropene.

Experimental

Procedures for the Willgerodt Reactions.—In general the procedures previously described^{4,7,8} were followed except for the variations in the composition of the starting reagent. Quantities of starting compound were in the range of 1.30 to 12.6 g. Temperatures were selected on the basis of preliminary runs so that the reactions were complete within a period of four to six hours. For compounds with unbranched chains temperatures in the range of 145 to 160° were usually satisfactory, but with the 1,1-disubstituted ethylenes and tertiary carbinols temperatures of 190 to 230° were required. All reactions were carried out in sealed glass tubes. Ammonium sulfide was eliminated from the resulting reaction mixtures by evaporation to dryness or by distillation to dryness under reduced pressure, after which the organic reaction products could be separated from the sulfur by extraction with appropriate solvents and recrystallization. Important variations in the composition of the reagent are summarized as follows. **Reagent I.** For each one-tenth mole of starting compound approximately 25 ml. of stock ammonium sulfide solution analyzing 7 M in sulfide and 12 M in ammonia,⁸ 0.5 to 1 gram-atomic weight of sulfur, and 12–25 ml. of pyridine (or dioxane where noted) were taken. **Reagent II.** In place of the 25 ml. of ammonium sulfide solution, 25 ml. of 15 M ammonium hydroxide was substituted, with about the same proportions of sulfur and organic solvent. **Reagent III** was the same as Reagent I except for the addition of approximately 0.1 mole

of crystalline ammonium thiosulfate for each one-tenth mole of starting compound. The crystalline ammonium thiosulfate was purchased from the Fairmount Chemical Company, New York, N. Y.

***n*-Heptanamide from 1-Heptyne.**—1-Heptyne¹⁰ (3.36 g.) when heated with Reagent I for four hours at 145° gave 35% of *n*-heptanamide, m. p. 97° cor., identified by melting point and mixed melting point with an authentic sample.

***n*-Heptanamide from 1-Heptene.**—1-Heptene¹¹ (1.96 g.) when heated with Reagent III for four hours at 155° gave 15% of *n*-heptanamide. When ammonium sulfite was used in place of ammonium thiosulfate in another run, a 13% yield of *n*-heptanamide resulted.

Nonane-1,9-dicarboxylic Acid from Undecylenic Acid.—Purified undecylenic acid¹² (3.68 g.) with Reagent III for four hours at 160° yielded a crude product with a wide melting range. It was simplest to hydrolyze the crude reaction product directly in alkali, after which acidification gave nonane-1,9-dicarboxylic acid. Recrystallization of the acid from chloroform-ligroin (Norite) afforded 1.52 g. (35%) of pure product, m. p. 111–112.5° cor. (reported m. p. 111°¹³).

Anal. Calcd. for $\text{C}_{11}\text{H}_{20}\text{O}_4$: C, 61.08; H, 9.32. Found: C, 60.81, 60.87; H, 9.17, 9.18.

If the crude amide mixture first isolated from the Willgerodt reaction was recrystallized directly from methanol, 12% of colorless nonane-1,9-dicarbonamide was obtained, m. p. 175–176° cor. (reported m. p. 173°¹⁴). A lower reaction temperature averaging 150° resulted in a yield of 25% of nonane-1,9-dicarboxylic acid. In another run at 160° the omission of pyridine lowered the yield of the diacid to 13%.

2-Naphthaleneacetamide from 2-Vinylnaphthalene.—2-Vinylnaphthalene¹⁵ (1.30 g.) with Reagent II for four hours at 145° gave 24% of naphthaleneacetamide, which melted, after recrystallization from chloroform-ligroin, at 198–200° cor. (dec.) (reported m. p. 200°¹⁶). Hydrolysis with aqueous sodium hydroxide gave 2-naphthaleneacetic acid, m. p. 140–141° cor. (reported m. p. 141–142°¹⁷).

2-Pyridineacetamide from 2-Vinylpyridine.—Freshly redistilled 2-vinylpyridine¹⁸ (12.6 g.) was treated with Reagent III at 150° for four hours. The volatile materials were removed from the reaction mixture by distillation under reduced pressure below 60° (to avoid darkening). The amide was extracted from the residue with hot water and the aqueous extracts, after clarification with Norite, were freed of water by distillation under reduced pressure. The crude amide was purified by solution in chloroform, separation of a small amount of insoluble oil, and addition of ligroin to induce crystallization. Two crops (5.04 g., 31%) of practically pure amide were obtained. An analytical sample was prepared by further recrystallizations from chloroform-ligroin as pale tan, irregular needles, m. p. 120–121° cor.

Anal. Calcd. for $\text{C}_7\text{H}_8\text{N}_2\text{O}$: C, 61.75; H, 5.92. Found: C, 61.52, 61.40; H, 5.78, 6.24.

The 2-pyridineacetamide was hydrolyzed in hot aqueous sodium hydroxide to form 2-pyridineacetic acid, m. p. 101–102° cor. (gas evolved) (reported m. p. 98°¹⁹).

When 2-vinylpyridine was allowed to react with Re-

(6) King and McMillan (ref. 5) have described the conversion of several secondary carbinols to amides under conditions of the Willgerodt reaction.

(7) Cavalieri, Pattison and Carmack, *THIS JOURNAL*, **67**, 1783 (1945).

(8) DeTar and Carmack, *ibid.*, **68**, 2025 (1946), found that the omission of hydrogen sulfide from the reagent produced the highest yields of amide from acetophenone and some other aryl alkyl ketones. Hydrogen sulfide in the starting reagent apparently also affects the yields from olefins adversely.

(9) We were prompted to investigate the effect of thiosulfates in the Willgerodt reagent by reports in the literature that sulfur reacts with hot aqueous ammonia to form ammonium thiosulfate and ammonium sulfide. For an excellent review of the reactions of sulfur and ammonia, as well as the chemistry of the ammonium polysulfides, see "Gmelins Handbuch der anorganischen Chemie," Verlag Chemie, Berlin, 8th ed., No. 23, pp. 243ff, 304ff, 1936.

(10) 1-Heptyne was prepared by the procedure of Guest, *THIS JOURNAL*, **50**, 1744 (1928).

(11) Prepared by Grignard coupling; cf. Kistiakowsky, Ruhoff, Smith and Vaughan, *ibid.*, **58**, 140 (1936).

(12) Commercial undecylenic acid was purified by two distillations through a small column under reduced pressure; m. p. 23°.

(13) Chuit, *Helv. Chim. Acta*, **9**, 266 (1926).

(14) Barnicoat, *J. Chem. Soc.*, 2928 (1927).

(15) A gift from the Rayon Department, E. I. du Pont de Nemours & Co., Buffalo, New York; m. p. 55–57°.

(16) Willgerodt, *J. prakt. Chem.*, [2] **80**, 188 (1909).

(17) Fulton and Robinson, *J. Chem. Soc.*, 201 (1939).

(18) Purchased from the Reilly Tar and Chemical Corporation.

(19) Oparina, *Khim. Farm. Prom.*, No. 4, 12 (1934); *C. A.*, **29**, 1820 (1935); *Chem. Zentr.*, **106**, I, 2536 (1935).

agent II and a large excess of sulfur (10 gram-atomic weights of sulfur per mole of olefin), yields as high as 38% were obtained; substitution of dioxane in place of pyridine did not alter the yield.

Diphenylacetamide from 1,1-Diphenylethylene.—1,1-Diphenylethylene²⁰ (2.00 g.) with Reagent II for six hours at 230° gave 37% of slightly impure diphenylacetamide. One recrystallization from chloroform–ligroin gave colorless needles, m. p. 167.5–169° cor. (reported m. p. 167.5–168.5²¹). The amide was converted into diphenylacetic acid, m. p. 146–147° cor. (reported m. p. 144–145²²). Both the amide and the acid were compared directly with authentic synthetic specimens. When the reaction of 1,1-diphenylethylene was carried out at 210° the yield of diphenylacetamide fell to 24%.

α -Phenylpropionamide and Phenylacetamide from 2-Phenylpropene.—2-Phenylpropene²³ (2.36 g.) with Reagent II for four hours at 190° yielded 0.51 g. of yellow plates, m. p. 98–100°, and 1.14 g. of crystals, m. p. 87–90°. Sublimation of the 0.51-g. fraction under reduced pressure and repeated recrystallizations from chloroform–petroleum ether yielded an amide melting at 158.5–160° cor. which gave no depression when mixed with phenylacetamide, m. p. 159–160° cor. Recrystallization of the 1.14-g. fraction from benzene yielded colorless plates of α -phenylpropionamide, m. p. 94–95° cor., not depressed by admixture with an authentic specimen, m. p. 95–96° (reported m. p. 91–92²⁴). The α -phenylpropionamide was hydrolyzed and the free acid converted into α -phenylpropionanilide, m. p. 131–132° cor., not depressed by admixture with an authentic specimen, m. p. 133–133.5° cor.²⁵ Since the separation of the two homologous amides by fractional crystallization was far from quantitative, it was not feasible to determine the relative yields of the two products. The total yield of amide was 55% calculated as phenylpropionamide, or 61% calculated as phenylacetamide.²⁶

When the reaction of 2-phenylpropene was carried out with Reagent III at the same time and temperature used in the above experiment, practically the same total yield of crude amide was isolated. The effect of varying the amount of ammonium thiosulfate was studied in a series of runs. The optimum amount of ammonium thiosulfate was found to be one mole equivalent per mole of starting compound. As the proportion of the salt was decreased the total weight of amide also decreased, the limiting yield when no ammonium thiosulfate was used (Reagent I) being about three-eighths the maximum yield obtained with a full mole equivalent of ammonium thiosulfate. Use of larger quantities up to four mole equivalents of ammonium thiosulfate did not appear to change the total

weight of amide significantly. Sodium thiosulfate improved the yield of amide, but addition of ammonium chloride or diammonium hydrogen phosphate to Reagent I gave no better results than Reagent I alone.

The results obtained with commercial 2-phenylpropene were duplicated in several check runs with a specimen of the olefin prepared by the dehydration of dimethylphenylcarbinol.

Neopentylacetamide from 1,1-Dineopentylethylene.—1,1-Dineopentylethylene²⁷ (3.36 g.) was treated with Reagent II for five hours at 210°. A crude weight of 0.21 g. of amide, m. p. 97–105° cor., was isolated. Recrystallization from chloroform–ligroin gave 0.14 g., m. p. 120–122° cor., and subsequent recrystallization from water gave a small amount of colorless needles melting constant at 140–141° cor., not depressed by admixture with an authentic specimen of neopentylacetamide (γ,γ -dimethylvaleramide; reported m. p. 141.0–141.5° cor.⁷). Since dineopentylacetamide, a possible product of this reaction, is reported^{27b} to form colorless needles melting at 139–140°, the identity of the product was confirmed by analysis.

Anal. Calcd. for neopentylacetamide, C₇H₁₅NO: C, 65.07; H, 11.70. Calcd. for dineopentylacetamide, C₁₂H₂₅NO: C, 72.30; H, 12.64. Found: C, 65.00; H, 11.61.

The Willgerodt Reaction with Dimethylphenylcarbinol.—Dimethylphenylcarbinol (2.72 g.) was treated with Reagent II for four hours at 190°. The crude product consisted of 1.14 g. of a mixture of α -phenylpropionamide and phenylacetamide, which corresponds to a total yield of 38% calculated on the minimum basis as phenylpropionamide. Each of the two amides was isolated in pure form by fractional crystallization.

The Willgerodt Reaction with Methylphenylcarbinol.—Methylphenylcarbinol²⁰ (3.96 g.) was treated with Reagent II for five hours at 210°, giving 14% of diphenylacetamide, m. p. 167–168° cor. The identity was proved by mixed melting point determination.

Summary

The behavior of a completely aliphatic acetylene, several further examples of olefins, and two tertiary carbinols under conditions of the Willgerodt reaction have been studied. All of the starting compounds produced carbonamides; the products usually had the same carbon skeleton as the starting compound, although side reactions involving the loss of alkyl groups and formation of amides with fewer carbon atoms were observed with several 1,1-disubstituted ethylenes.

Thiosulfates and ammonium sulfite were found to improve the yields of carbonamides when used in conjunction with the ammonium polysulfide reagent.

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(27) (a) The dineopentylethylene was a gift from Mr. Mark Snyder of the United Gas Improvement Company, Philadelphia, Pennsylvania. Mr. Snyder reported that the material had been specially purified by low temperature crystallization from acetone and had the following physical properties: b. p. 176.7° (760 mm.); m. p. –23.6°; n_D^{20} 1.4270; d_4^{20} 0.7540. (b) Cf. also Bartlett, Fraser and Underwood, *THIS JOURNAL*, **63**, 495 (1941).

(20) Prepared by Mr. Louis Cutler following the directions of Allen and Converse, "Organic Syntheses," Coll. Vol. I, 2nd ed., John Wiley and Sons, New York, N. Y., 1941, p. 226.

(21) Hellerman, Cohn and Hoen, *THIS JOURNAL*, **50**, 1725 (1928).

(22) Marvel, Hager and Caudle, "Organic Syntheses," Coll. Vol. I, 2nd ed., John Wiley and Sons, New York, N. Y., 1941, p. 224.

(23) We are indebted to the Dow Chemical Company for a generous gift of 2-phenylpropene; it was redistilled before use; b. p. 161–162°.

(24) Jannsen, *Ann.*, **250**, 136 (1888).

(25) α -Phenylpropionic acid for comparison was prepared by the reduction of phenyllactic acid with red phosphorus and hydriodic acid (ref. 24); the phenyllactic acid was prepared according to McKenzie and Wood, *J. Chem. Soc.*, **115**, 833 (1919).

(26) We hope to be able to report at a later time on the effect of experimental conditions on the relative yields of the two products.