pentachloride, added in small portions with cooling and shaking of the mixture. After thirty minutes the slight excess of phosphorus pentachloride was removed by filtration. The clear filtrate was added dropwise to a vigorously stirred solution of 17.2 g. (0.1 mole) of sulfanilamide in 75 ml. of pyridine. A gummy precipitate was obtained. The reaction mixture was diluted with 200 ml. of water, the ether distilled off, and concentrated sodium hydroxide solution added to dissolve the gummy material. This alkaline solution was concentrated *in vacuo* to remove pyridine. The sirupy residue, diluted with water, was adjusted to *p*H 8 with 6 *N* hydrochloric acid while being stirred vigorously. The product that precipitated weighed 9.2 g.; m. p. 135–150°. Recrystallization from dilute ethanol gave 6.6 g. of N^4-(2,3,4,6-diisopropylidene-2-keto-L-gulonyl)-sulfanilamide (15.5%); m. p. 172–173°; $[\alpha]^{25}\mathrm{D}$ +16.8° (*c*, 1.90; acetone).

Anal. Calcd. for $C_{18}H_{24}O_8N_2S$: C, 50.5; H, 5.6; N, 6.5. Found: C, 50.8; H, 5.8; N, 6.5.

N^4-(2-Keto-L-gulonyl)-sulfanilamide.—A suspension of 10 g. of N^4-(2,3,4,6-diisopropylidene-2-keto-L-gulonyl)-sulfanilamide in a mixture of 200 ml. of water and 1 ml. of concentrated hydrochloric acid was heated on the steam-bath for thirty minutes. On cooling the resulting solution, 5 g. of a crystalline product deposited (61%); m. p. 199°. Two recrystallizations from water gave colorless prisms of N^4-(2-keto-L-gulonyl)-sulfanilamide; m. p. 210–211° (dec.). A water solution of this substance reduced hot Fehling solution.

Anal. Calcd. for $C_{12}H_{16}O_8N_2S$: C, 41.4; H, 4.6; N, 8.0. Found: C, 41.7; H, 4.8; N, 8.1.

1-(4-Sulfamylphenyl)-pyrrole.—One mole (172 g.) of sulfanilamide was dissolved in a boiling mixture of 1250 ml. of water and 100 ml. of acetic acid and treated with 1 mole (248 g.) of potassium acid D-glucosaccharate. The solution was heated on a steam-bath for sixteen hours and cooled to room temperature. The solid material which separated was recrystallized from 5% sodium hydroxide solution. The yield of 1-(4-sulfamylphenyl)-pyrrole was 55 g. (25%); m. p. 246–247°. Another recrystallization raised the melting point to 247–248°. Several grams more were obtained on concentrating the mother liquor.

Anal. Calcd. for $C_{10}H_{10}N_2O_2S$: C, 54.0; H, 4.5; N, 12.6; S, 14.4. Found: C, 54.1; H, 4.5; N, 12.7; S, 14.4.

Acknowledgment.—The author is indebted to Dr. F. F. Blicke of the University of Michigan for the sample of 1-phenylpyrrole,[3] to Charles Pfizer and Company, Inc., for furnishing a supply of diisopropylidene-2-keto-L-gulonic acid, and to Dr. L. B. Lockwood of the Fermentation Division of this Laboratory for the sample of calcium 2-keto-D-gluconate. He is also grateful to Dr. R. D. Coghill of the Abbott Laboratories for the antibacterial tests. The microanalyses were performed by Mr. C. H. Van Etten and the absorption spectra work by Miss Ruth Johnston of this Laboratory.

Summary

1. N^4-Acyl-sulfanilamides have been synthesized by the reaction of sulfanilamide with D-glucono-δ-lactone and the acid chlorides of diisopropylidene-2-keto-D-gluconic and diisopropylidene-2-keto-L-gulonic acids. Acid hydrolysis of the latter two compounds produced N^4-(2-keto-D-gluconyl)-sulfanilamide and N^4-(2-keto-L-gulonyl)-sulfanilamide, respectively. None of these products have significant bacteriostatic properties.

2. An attempt to prepare N^4-D-glucosaccharic acid substituted sulfanilamide by the condensation of potassium acid D-glucosaccharate with sulfanilamide yielded 1-(4-sulfamylphenyl)-pyrrole.

PEORIA, ILLINOIS RECEIVED MARCH 12, 1947

[CONTRIBUTION FROM THE THOMPSON LABORATORY OF THE PHILLIPS EXETER ACADEMY]

Diaryl Acetylenic Ketones

BY CHARLES L. BICKEL

A recent paper from this Laboratory reported the preparation of *o*-chlorophenylbenzoylacetylene from α-bromo-*o*-chlorobenzalacetophenone by the action of potassium hydroxide in a mixture of acetone and water.[1] One other acetylenic ketone has been prepared from a compound with the same carbon skeletal structure, Fuson[2] reporting the isolation of mesitylbenzoylacetylene from the products obtained by treating the enol methyl ethers of 2,4,6-trimethylbenzoylacetonitrile with phenylmagnesium bromide. The immediate precursor of this acetylenic ketone is, however, not yet identified.

The general methods of preparing acetylenic ketones involve either the condensation of a metal acetylide with an acid halide,[3,4,5,6]

$$\mathrm{R{-}C{\equiv}C{-}Na + ClCOR' \longrightarrow R{-}C{\equiv}C{-}COR'}$$

or the condensation of the acid chloride of a propiolic acid with an aryl group by the Friedel–Crafts reaction[7]

$$\mathrm{R{-}C{\equiv}C{-}COCl + H{-}R' \longrightarrow R{-}C{\equiv}C{-}COR'}$$

In general, α-bromo ethylenic ketones can be prepared more easily than the substances from which acetylenic ketones have previously been obtained. The present paper describes the preparation of four acetylenic ketones from the corresponding α-bromo ketones and thus indicates that this method of preparation may be of general application. Further work on this problem is in progress and will be reported at a later date.

The α-bromo derivatives of benzalacetophenone, *p*-methoxybenzalacetophenone, benzal-*p*-methoxyacetophenone and benzal-*p*-bromoacetophenone give the corresponding acetylenic

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(1) Bickel, THIS JOURNAL, **69**, 73 (1947).

(2) Fuson, Ullyot and Hickson, *ibid.*, **61**, 410 (1939).

(3) Nef, *Ann.*, **308**, 276 (1899).

(4) Manchot, *ibid.*, **387**, 285 (1912).

(5) Barat, *J. Indian Chem. Soc.*, **7**, 851 (1930).

(6) Fuson and Meek, *J. Org. Chem.*, **10**, 551 (1945).

(7) Watson, *J. Chem. Soc.*, **85**, 1319 (1904).

ketones when treated with potassium hydroxide in a mixture of acetone and water

$$R\text{—}CH\text{=}CBr\text{—}COR' \longrightarrow R\text{—}C\equiv C\text{—}COR'$$

There is a marked difference in the five reactions studied to date. The highest yield, about 90%, of acetylenic ketone is realized with *o*-chlorophenylbenzoylacetylene. However, this substance is most easily crystallized from the oil which invariably accompanies the desired product and the apparent difference in yield may therefore not be significant. α-Bromo-*p*-methoxybenzalacetophenone loses hydrogen bromide with the most difficulty and the product is therefore subjected to a more prolonged attack by the basic solution, resulting in cleavage and consequent loss of the acetylenic ketone.

The conditions under which the acetylenic ketones are formed from the bromo compounds can be more sharply defined than was possible in the previous paper.[1] The formation of viscous, oily by-products is reduced by adding the aqueous solution of the base dropwise to the boiling acetone solution of the bromo compound. As might be expected, the removal of hydrogen bromide from the bromo compounds is hastened by an increase in the *p*H of the aqueous solution; unfortunately, the decomposition of the acetylenic ketones is also accelerated by this same increase in basicity. There is no measurable tendency for the α-bromo ketones to lose hydrogen bromide in the presence of potassium acetate; in fact, α-bromo ketones are prepared from α,β-dibromo ketones by this reagent. Under comparable conditions, potassium hydroxide effects a rapid conversion of the bromo ketone to the acetylenic ketone, sodium carbonate acts much more slowly, and sodium bicarbonate acts very slowly indeed.

Attempts to replace acetone as the solvent were unsuccessful, the α-bromo ketone being recovered when carbon tetrachloride, chloroform and ether were used. The α-bromo ketone was also unaffected when an ether solution was heated with silver oxide for several hours.

Experimental

Preparation of the α-Bromo Ketones.—α-Bromobenzalacetophenone, α-bromobenzal-*p*-bromoacetophenone and α-bromobenzal-*p*-methoxyacetophenone were prepared by the action of methyl alcoholic potassium acetate on the corresponding dibromides. These substances have been adequately described elsewhere, the last two by Weygand.[8]

α-Bromo-*p*-methoxybenzalacetophenone was prepared by the method of Pond and Schoffstall.[9] In view of the meager experimental details presented by these authors, particularly with respect to yields, the method of preparation is briefly outlined below. A solution of 81 g. of bromine in 50 cc. of chloroform was added to a stirred solution of 119 g. (0.5 mole) of *p*-methoxybenzalacetophenone in 300 cc. of chloroform, separation of the dibromide starting just as the last of the bromine solution was added. One hundred and ninety grams of dibromide melting at 140° was obtained, a yield of 95%. Fifty grams of the dibromide, heated for one hour on the steam-bath with 150 cc. of methanol, gave 36 g. of α-bromo-β-methoxy-*p*-methoxybenzylacetophenone melting at 102°, a yield of 82%. Thirty grams of the 102° compound, heated at 170–180° for one hour, gave 25.5 g. of α-bromo-*p*-methoxybenzalacetophenone melting at 94°, a yield of 93%. It is, however, much simpler to go from the dibromide to the α-bromo unsaturated ketone in one operation. Thus, a suspension of 50 g. of the dibromide in 125 cc. of methanol was heated on the steam-bath until the methanol evaporated, the temperature then being raised to 170–180° until gas evolution ceased. The residue gave 30 g. of the α-bromo compound.

Preparation of the Acetylenic Ketones.—The following method was used to prepare each of the acetylenic ketones. About 5 g. of the α-bromo compound was refluxed with about 25 cc. of acetone (free of methanol) and 25 cc. of water while a solution of an equivalent quantity of potassium hydroxide in about 20 cc. of water was added dropwise to the boiling mixture, the addition requiring about thirty minutes. Refluxing was then continued for twenty minutes, followed by cooling of the mixture, dilution with water, acidification with dilute hydrochloric acid, extraction with ether and isolation of the acetylenic ketone from the ether solution.

α-Bromo-*o*-chlorobenzalacetophenone gave a 90% yield of *o*-chlorophenylbenzoylacetylene by the above procedure. The per cent. yield of acetylenic ketone was the same when 25 g. of starting material was used.

Benzoylphenylacetylene was identified by converting it into dibenzoylmethane, either by the action of concentrated sulfuric acid[1] or by the action of methyl alcoholic potassium hydroxide, followed by acidification.[1] The yield of benzoylphenylacetylene was increased from about 40% to nearly 55% by using 40 g. of α-bromobenzalacetophenone.

A 50% yield of anisoylphenylacetylene, melting at 99° and first prepared by Watson,[7] was realized. The acetylenic ketone was converted into anisoylbenzoylmethane by the methods outlined above.

When the above method of preparation was applied to α-bromo-*p*-methoxybenzalacetophenone, approximately one-half of the starting material was recovered. A part of the product was cleaved by the alkali, recovered benzoic acid accounting for about one-half of the converted material. The yield of *p*-methoxyphenylbenzoylacetylene, melting at 81° and first prepared by Manchot,[4] was not more than 30% based on the α-bromo compound which reacted. The acetylenic ketone gave anisoylbenzoylmethane when treated with methyl alcoholic potassium hydroxide, followed by acidification.

α-Bromobenzal-*p*-bromoacetophenone gave a 40% yield of phenyl-*p*-bromobenzoylacetylene. Phenyl-*p*-bromobenzoylacetylene is soluble in ether and sparingly soluble in petroleum ether. It crystallizes in pale yellow flat needles and melts at 110°.

Anal. Calcd. for $C_{15}H_9OBr$: C, 63.2; H, 3.19. Found: C, 63.3; H, 3.21.

Phenyl-*p*-bromobenzoylacetylene gave *p*-bromodibenzoylmethane when treated with concentrated sulfuric acid (method of Nef). β-Ethoxybenzal-*p*-bromoacetophenone,[10] melting at 114°, was obtained by the action of ethyl alcoholic potassium hydroxide on the acetylenic ketone and the β-ethoxyl compound was then converted into *p*-bromodibenzoylmethane by acid hydrolysis.

Experiments with α-Bromo-*o*-chlorobenzalacetophenone

A. Sodium Carbonate.—A mixture of a solution of 5 g. of α-bromo-*o*-chlorobenzalacetophenone in 30 cc. of acetone and a solution of 1.65 g. of sodium carbonate in 30 cc. of water was refluxed for two hours. Approximately 75% of the starting material was recovered, the remaining 25% being converted into the acetylenic ketone.

B. Sodium Bicarbonate.—Substitution of 2 g. of sodium bicarbonate for the sodium carbonate used in

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[8] Weygand, *Ann.*, **459**, 99–122 (1927).

[9] Pond and Schoffstall, THIS JOURNAL, **22**, 658–685 (1900).

[10] Kohler and Addinall, *ibid.*, **52**, 3734 (1930).

method A resulted in less than 10% conversion to the acetylenic ketone, about 90% of the starting material being recovered.

C. **Silver Oxide.**—A solution of 5 g. of the α-bromo compound in 50 cc. of anhydrous ether was refluxed with 5 g. of silver oxide for five hours. The starting material was recovered.

D. **Other Solvents than Acetone.**—When a solution of α-bromo-*o*-chlorobenzalacetophenone in carbon tetrachloride, chloroform, or alcohol-free ether was refluxed for three hours with an equivalent quantity of potassium hydroxide in water solution, the starting material was recovered.

Summary

The preparation of acetylenic ketones from α-bromobenzalacetophenones has been extended to include benzoylphenylacetylene, anisoylphenylacetylene, *p*-methoxyphenylbenzoylacetylene and phenyl-*p*-bromobenzoylacetylene.

EXETER, NEW HAMPSHIRE RECEIVED MAY 7, 1947

[CONTRIBUTION NO. 218 FROM THE CHEMICAL DEPARTMENT, EXPERIMENTAL STATION, E. I. DU PONT DE NEMOURS & COMPANY]

Synthesis of Tetrahydro-5-substituted-2(1)-*s*-Triazones

BY WM. JAMES BURKE[1]

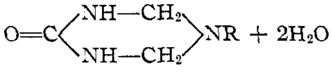
Considerable attention has been given to the reaction of secondary amines with methylol compounds resulting from the condensation of formaldehyde with urea,[2] thiourea,[3] amides[4] and other compounds having hydrogen attached directly to nitrogen. The resulting formation of substituted aminomethyl derivatives is illustrated with dimethylolurea in the equation

$$2R_2NH + HOCH_2NHCONHCH_2OH \longrightarrow (R_2NCH_2NH)_2CO + 2H_2O$$

Feldman and Wagner[5] have recently described the formation of heterocyclic derivatives by condensations involving formaldehyde and compounds containing both amino and amido groups. In a related type of reaction, acetaldehyde and ammonia have been found to react with thiourea[6] and urea[6b] to form the corresponding tetrahydro-4,6-dimethyl-2(1)-*s*-triazones, while use of an isocyanate[6c] in place of urea yields a tetrahydro-1,4,6-trisubstituted-2(1)-*s*-triazone.

The object of the present work was to study the reaction of dimethylolurea with primary amines. As a result, it was found that a series of new urea derivatives, the tetrahydro-5-substituted-2(1)-*s*-triazones, can be conveniently prepared as indicated in the following reaction.[7] The structure

$$RNH_2 + HOCH_2NHCONHCH_2OH \longrightarrow$$



assigned to these products is analogous to that given the related compounds prepared from secondary amines and dimethylolurea,[2] which is a symmetrical derivative of urea. The reaction was also found to be applicable to substituted primary amines, such as 2-aminoethanol and 2-dimethylaminoethylamine. Identical products were formed when dimethylolurea was replaced with urea and formaldehyde in a molar ratio of 1:2, respectively.

In a study of the scope of the reaction, thiourea, formaldehyde, and primary aliphatic amines were also found to react readily in a 1:2:1 molar ratio with the formation of crystalline condensates and elimination of two moles of water. Similar results were obtained when 1,3-diphenylthiourea was used in place of thiourea and also when formaldehyde was replaced with acetaldehyde. A tetrahydro-5-alkyl-2-thio-2(1)-*s*-triazone structure is proposed for these products in view of the fact that urea and thiourea have been reported[5] to behave in an analogous fashion in the reaction with acetaldehyde and ammonia.

The reaction occurred readily in an aqueous system except in syntheses involving such water-insoluble reactants as 1,3-diphenylthiourea or dodecylamine. In such instances it was found desirable to employ a water-miscible, inert solvent such as dioxane, which permitted the reaction to occur in a single phase. Although thiourea reacted readily with formaldehyde and primary amines in all instances at room temperature to give a high yield of condensation product, it was found advantageous with urea to heat the reaction mixture at 70–100°.

Experimental

Tetrahydro-5-(2-hydroxyethyl)-2(1)-*s*-triazone.—2-Aminoethanol (122 g., 2 moles) was added with cooling to 240 g. of dimethylolurea (2 moles) in 340 cc. of water. The resulting solution was heated under reflux at 90–100° for two hours and kept at room temperature overnight. The reaction mixture was concentrated under reduced pressure and the resulting 166 g. of crude product recrystallized from 95% ethanol, m. p. 158°, yield 57%.

Anal. Calcd. for $C_5H_{11}N_3O_2$: C, 41.37; H, 7.64; N, 28.95. Found: C, 41.44; H, 7.62; N, 28.76.

Comparable yields of the same product were obtained

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(1) Present address: Department of Chemistry, University of Utah, Salt Lake City, Utah.

(2) (a) Einhorn and Spröngerts, *Ann.*, **361**, 139 (1908); (b) Weaver, Simons and Baldwin, THIS JOURNAL, **66**, 222 (1944); (c) Burke, British Patent 559,771 (1944).

(3) Bögemann and Zaucher, German Patent 575,114 (1933).

(4) (a) Einhorn, Bischkopff and Szelinski, *Ann.*, **343**, 223 (1905); (b) Einhorn and Feibelmann, *ibid.*, **361**, 140 (1908).

(5) Feldman and Wagner, *J. Org. Chem.*, **7**, 31 (1942).

(6) (a) Nencki, *Ber.*, **7**, 158 (1874); (b) Steindorff and Pacquin, U. S. Patent 2,016,521 (1935); (c) Dixon, *J. Chem. Soc.*, **61**, 509 (1892).

(7) Burke, U. S. Patent 2,304,624 (1942).