isomer had a density of only 0.051 at this point for the same concentration).

Beer's law was found to be constant in the range of 50–75% *cis* compound. This was determined by making five known mixtures in this range and calculating their concentrations from the observed optical densities. The concentrations of the unknowns in this concentration range were obtained by direct calculations from their observed optical densities according to the procedure utilized by Zimmerman.[10] The analytical method proved accurate to within 3% when tested with mixtures of known composition.

For concentrations above 80% *cis* isomer there were large deviations from Beer's law. This was determined by making three knowns in this range and calculating their concentrations from the observed optical densities. Determinations in this range were performed according to the method described by Burwell and Shields.[11] The unknowns analyzed according to this method were adjudged accurate to within 3% of the actual value.

Some Additional Effects of Acid Concentration. 1. The Mercuration of Allyl Ether in the Presence of Excess Strong Acid.—To 95.6 g. (0.30 mole) of reagent mercuric acetate dissolved in 250 ml. of water containing 108 g. of concentrated nitric acid was added 16.5 g. (0.17 mole) of freshly distilled allyl ether. The mixture was shaken until all of the allyl ether was absorbed and sufficient water was added to make 500 ml. of solution. The solution was then allowed to stand for 48 hours at 25°, after which it was worked up as the preceding experiments. There was obtained 43.5 g. (0.118 mole) of material from which there was isolated 6.1 g. of *trans*-2,5-bis-(iodomethyl)-*p*-dioxane by recrystallization from carbon disulfide and methanol. The remainder of the material consisted of almost pure I.

2. The Preparation of *cis*-2,5-Bis-(iodomethyl)-*p*-dioxane (III).—In 300 ml. of water containing 171.0 g. (0.50 mole) of mercuric nitrate there was added slowly 30.5 g. (0.52 mole) of allyl alcohol and the mixture was vigorously stirred. After three hours the reaction was terminated and the precipitate which had formed was collected by filtration. There was thus obtained 61.5 g. of solid which was assumed to be *trans*-2,5-bis-(nitratomercurimethyl)-*p*-dioxane. The filtrate from the mercuration reaction was added to 1.5 liters of 1 *M* sodium hydroxide solution and considerable amounts of free mercury were formed. Upon addition of aqueous potassium iodide a precipitate was formed which after treatment with iodine as described in section A-3 yielded 9.8 g. (0.027 mole) of material which after recrystallization from methanol yielded 0.86 g. (0.0023 mole) of *trans*-2,5-bis-(iodomethyl)-*p*-dioxane and 1.0 g. (0.0027 mole) of III, m.p. 96–97° for a 0.93% yield of III. This latter substance did not depress the m.p. of authentic III in a mixed m.p. determination.

(10) H. E. Zimmerman, THIS JOURNAL, **78**, 1172 (1956).

(11) R. L. Burwell and A. D. Shields, *ibid.*, **77**, 2766 (1955).

Evaporation of the filtrates from recrystallization yielded 7.5 g. of material which because of its infrared spectrogram in potassium bromide was presumed to contain *cis*- and *trans*-2,5-bis-(iodomethyl)-*p*-dioxane as well as some I or II.

Since both isomers of 2,6-bis-(iodomethyl)-*p*-dioxane absorbed strongly at 10.6 μ in the infrared, the presence of this peak indicated the presence of I or II or both. Since *cis*-2,5-bis-(iodomethyl)-*p*-dioxane possessed characteristic absorptions at 10.85 and 11.5 μ in the infrared whereas the *trans* isomer absorbed strongly at 11.1 μ, the presence of these absorbancies indicated the presence of *cis*- and *trans*-2,5-bis-(iodomethyl)-*p*-dioxane.

3. The Mercuration of Allyl Alcohol. The Isolation, after Workup, of *cis*-2,6-Bis-(iodomethyl)-*p*-dioxane (I).—To a solution containing 70 ml. of concd. nitric acid and 45 ml. of water there was added 108.3 g. (0.50 mole) of mercuric oxide. When solution was complete, 200 ml. of water was added and the solution was cooled to 0°. To this cooled solution was added 30.5 g. (0.52 mole) of allyl alcohol with vigorous stirring. This mixture stood for 6 hours and the precipitate which had formed was removed by filtration. The filtrate from the mercuration reaction was made basic by the addition of 4 *N* sodium hydroxide, and with addition of aqueous potassium iodide a precipitate formed which upon treatment with iodine yielded 3.3 g. (0.0089 mole) of I for a 1.8% yield. After recrystallization from methanol the compound melted at 91–92°, and when the compound was mixed with authentic *cis*-2,5-bis-(iodomethyl)-*p*-dioxane, the mixture melted at 73–77°. The infrared spectrogram of this compound in carbon disulfide was identical to that of authentic I. In a mixed melting point determination with authentic I the mixture melted at 91–92°.

4. The Reaction of Mercuric Acetate with Allyl Alcohol.—To 300 ml. of water containing 25 ml. of glacial acetic acid there was added 159.4 g. (0.50 mole) of mercuric acetate. Sufficient water was added to make 500 ml. of solution and then 30.5 g. (0.52 mole) of allyl alcohol was slowly added. The mixture was allowed to stand at 25° for 6 hours during which time no precipitate formed. Then the reaction mixture was poured into a liter of 1.5 *M* aqueous sodium hydroxide solution where a small amount of a yellow precipitate was formed. Aqueous potassium iodide was added and a gummy, gray precipitate was formed which was filtered, treated with iodine, and the product isolated in the manner described in section A-3. There was obtained 1.0 g. of material, m.p. 85–130°, which by virtue of its infrared spectrogram in potassium bromide was adjudged to contain only *cis*- and *trans*-2,5-bis-(iodomethyl)-*p*-dioxane.

The absence of an absorption at 10.6 μ indicated the absence of I and II in the product, whereas the presence of absorptions at 10.85, 11.5 and 11.1 μ indicated the presence of both *cis*- and *trans*-2,5-bis-(iodomethyl)-*p*-dioxane.

EVANSTON, ILL.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY]

The Synthesis of Substituted Penicillins and Simpler Structural Analogs. XII. 6-Benzylsulfonamidopenicillanic Acid

BY JOHN C. SHEEHAN AND DALE R. HOFF[1]

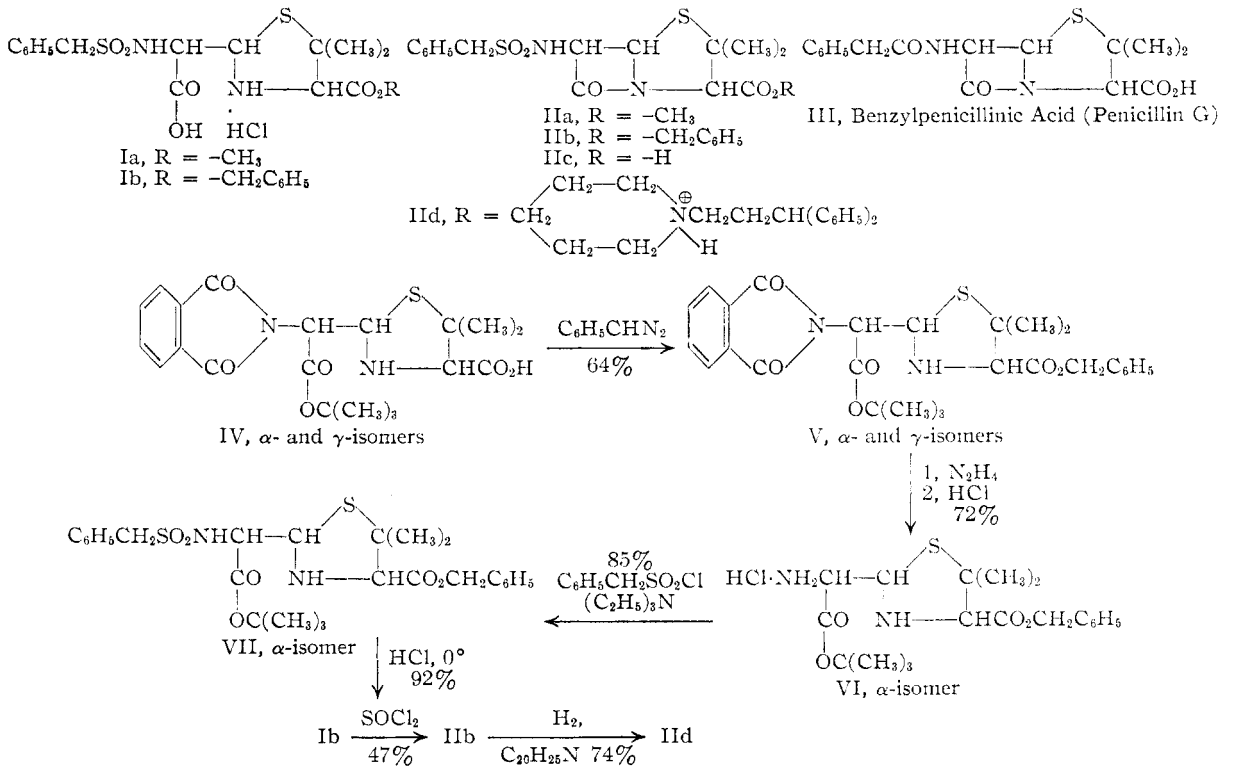
RECEIVED JULY 13, 1956

An acid-stable, biologically active "sulfonyl analog" of benzylpenicillinic acid (penicillin G) has been synthesized as a crystalline tertiary amine salt. This analog, a racemate, differs from the natural antibiotic structurally only in the replacement of the carbonyl group of the side-chain amide with a sulfonyl function, and the configuration corresponds to that of the natural penicillins. A promising intermediate for the synthesis of penicillin analogs and penicillanic acids, *t*-butyl 4-carbobenzyloxy-5,5-dimethyl-α-amino-2-thiazolidineacetate hydrochloride (VI), was prepared. Acylation of VI with benzylsulfonyl chloride, followed by acid cleavage of the *t*-butyl ester and cyclization, yielded benzyl 6-benzylsulfonamidopenicillanate (IIb), which afforded the free penicillanic acid (IIc) upon catalytic hydrogenolysis.

Recently, the synthesis has been reported[2] of the methyl ester of the "sulfonyl analog" of benzylpenicillin (penicillin G) in which the phenylacetamido side chain was replaced with the benzylsulfonamido group. Cyclization of isomeric benzylsulfonamidopenicilloates (Ia) produced the corresponding isomeric 6-benzylsulfonamidopenicil-

(1) National Science Foundation Predoctoral Fellow, 1953–1954 and 1954–1955.

(2) J. C. Sheehan and P. A. Cruickshank, THIS JOURNAL, **78**, 3683 (1956).



lanates[3] IIa, one of which was shown to correspond in configuration to the natural penicillins.

This sulfonyl analog displays remarkable resistance to mineral acid, as is attested by its formation in the presence of hydrogen chloride and thionyl chloride, a potentially useful feature which would be expected since the typical acid-catalyzed rearrangement to a penillic acid[4] is structurally precluded.

Preliminary biological testing revealed the presence of significant antibiotic activity in the methyl ester IIa. However, in order to apply routine penicillin assay procedures it was necessary first to hydrolyze the methyl ester to the free acid, best accomplished through pre-treatment with an esterase contained in guinea pig serum. Insolubility of the methyl ester in aqueous solutions handicapped the ester hydrolysis and rendered the assay procedure less reliable. This communication describes the preparation of the essential intermediates for the penicillanate synthesis, carried through as the benzyl esters instead of the methyl esters, hence potentially convertible to free acids by catalytic hydrogenolysis. The key intermediate VI presents possibilities for synthesis of a variety of penicillanates differing in the acyl substituent on the side-chain amino group, and with the penicillamine carboxyl function protected as the benzyl ester. Moreover, the accessibility of free penicillanic acids should make possible resolution into the optically active forms.

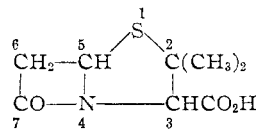
As an example of the utility of this procedure, the preparation and cyclization of the benzylsulfonylpenicilloate was repeated in the benzyl ester series and converted to the free acid IIc which was isolated as a stable, crystalline salt IId for testing.

Synthesis of the amino ester VI and the penicillanate IIb were completely analogous to the procedures previously reported.[2,5]

The two isomers of the "phthaloylpenicilloate IV," arbitrarily designated α and γ, were obtained by the condensation of *t*-butyl phthalimidomalonaldehydate with penicillamine as described by Sheehan and Cruickshank.[5] Treatment of the acids with phenyldiazomethane afforded the isomeric benzyl esters V in 64% over-all yield. The two isomers were obtained in a ratio of approximately 2:9, the γ-isomer predominating. Conversion of the γ-isomer to the α-isomer was brought about in refluxing triethylamine. An equilibrium was established and, upon cooling, the α-isomer crystallized out of the reaction mixture directly in 43% conversion. In one run the unchanged γ-isomer in the mother liquors was recycled twice to give a total yield of 68% of pure α-isomer. The α-isomer has been shown to correspond in configuration to the natural penicilloates.[5]

Removal of the phthaloyl group was accomplished by the action of hydrazine at room temperature, affording the isomeric amino esters VI. Treatment of the α-isomer with benzylsulfonyl chloride in the presence of triethylamine produced the sulfonamide VII. Anhydrous hydrogen chlo-

(3) The term "penicillanic acid" has been suggested for the ring system, J. C. Sheehan, K. R. Henery-Logan and D. A. Johnson, THIS JOURNAL, **75**, 3292 (1953).



(4) H. T. Clarke, J. R. Johnson and R. Robinson, editors, "The Chemistry of Penicillin," Princeton University Press, Princeton, N. J., 1949, p. 62.

(5) J. C. Sheehan and P. A. Cruickshank, THIS JOURNAL, **78**, 3677 (1956).

ride in benzene at ice-bath temperature liberated the α-carboxyl function in Ib.

The cyclization procedure of Sheehan and Cruickshank[6] was modified somewhat. The quantity of thionyl chloride employed as a cyclizing reagent was reduced; a 1% solution of 10 molar equivalents proved optimum when employed under mild conditions. The lactam crystallized directly without preliminary purification except for a bicarbonate wash, but a purer product was obtained in 47% yield after chromatography over alumina.

Hydrogenolysis of the benzyl ester IIb was carried out at room temperature in 5% acetic acid in dioxane; hydrogen uptake was complete in six minutes. The free acid IIc was not isolated in crystalline form, but the stable, crystalline amine salt IId was prepared readily in methylene chloride and crystallized from benzene. The tertiary amine employed, N-(3,3-diphenylpropyl)-piperidine (Bristol Laboratories "Aspasan"), yielded a salt which possessed an appreciable solubility in benzene but was nearly insoluble in ether and water. Compounds IIb, IIc and IId exhibited strong absorption bands at 5.62 μ, characteristic of the fused β-lactam-thiazolidine carbonyl function.

The activity of the "Aspasan" salt, as determined by standard penicillin assay techniques[7] against *D. pneumoniae* was found to be 10.9 units/mg. The calculated activity of the free acid, 18.6 units/mg., compares favorably with that of cephalosporin C (8–10 units/mg. against *S. aureus*),[8] a natural antibiotic considered to be one of the penicillins, but is much lower in activity/mg. than benzylpenicillin. Since the synthetic analog is a racemate, it is probable that most, if not all, of the observed activity is due to the isomer derived from D-penicillamine.[9]

Experimental

All melting points are corrected. We are indebted to Dr. S. M. Nagy and his associates for the microanalyses.

***t*-Butyl 4-Carboxy-5,5-dimethyl-α-phthalimido-2-thiazolidineacetate (IV).**—This product was prepared essentially by the method of Sheehan and Cruickshank.[6] The γ-isomer separated directly from the reaction mixture and processing of the filtrate gave a second crop which was chiefly α-isomer containing a small amount of γ.

***t*-Butyl 4-Carbobenzoxy-5,5-dimethyl-α-phthalimido-2-thiazolidineacetate (V). γ-Isomer.**—The first crop obtained from the condensation described above (25.14 g., 0.060 mole) was suspended in 200 ml. of purified dioxane and stirred at room temperature while an ethereal solution of phenyldiazomethane[10] was added in 5-ml. portions (concn. approx. 0.58 mmole/ml.). About 20 minutes was required to decolorize each portion of reagent. After the acid had completely dissolved and the pink color of the reagent had persisted for 30 minutes, a few drops of formic acid were added to decompose the excess diazo compound. The reaction mixture was diluted with 400 ml. of ethyl ether, washed with two 50-ml. portions of 5% sodium bicarbonate solution and dried over magnesium sulfate. Concentration at aspirator pressure (40–50°) gave a viscous yellow oil which deposited colorless needles after solution in 20 ml. of ether, 19.91 g., m.p. 124–127° (65%). A sample recrystallized from absolute ethanol (colorless prisms) had m.p. 126.8–127.9°.

Anal. Calcd. for $C_{27}H_{30}N_2O_6S$: C, 63.51; H, 5.92; N, 5.49. Found: C, 63.56; H, 6.18; N, 5.26.

α-Isomer.—The crude α-acid prepared above was treated with phenyldiazomethane in the same manner. The acid was almost completely soluble in 100 ml. of dioxane and reacted rapidly with the reagent until the reaction was nearly complete. The product was worked up following the procedure for the γ-isomer and crystallized from ethyl ether after addition of petroleum ether. Recrystallization of the crude product, m.p. 125–145°, from absolute ethanol gave 4.95 g., as large prisms, m.p. 165.2–166.7°.

Anal. Calcd. for $C_{27}H_{30}N_2O_6S$: C, 63.51; H, 5.92; N, 5.49. Found: C, 63.58; H, 5.81; N, 5.45.

The mother liquors yielded a second crop, 2.63 g., m.p. 126–127°, identical to the lower-melting isomer. Total yield of both purified isomers was 7.58 g., 62%.

Isomerization of the γ-Isomer to the α-Isomer.—A solution of 5.42 g. of the γ-diester in 50 ml. of purified triethylamine was refluxed under nitrogen for 15 hours. After cooling in a refrigerator overnight, the crystalline α-isomer (2.69 g.) was collected by filtration. Additional γ-diester (1.84 g.) was added to the triethylamine filtrate and refluxing was continued for 20 hours and cooled as before to give an additional 2.60 g. of α-isomer. The mother liquors were heated for another 15 hours to afford a third crop of product (0.90 g.). The combined product was recrystallized from absolute ethanol to yield 4.97 g. (68%), m.p. 166–167°.

***t*-Butyl 4-Carbobenzyloxy-5,5-dimethyl-α-amino-2-thiazolidineacetate Hydrochloride (VI), α-Isomer.**—Hydrazine hydrate (0.930 g., 18.57 mmoles) was added to a solution of 7.62 g. (14.93 mmoles) of V in 100 ml. of purified dioxane, the mixture was stored at room temperature for 21 hours, and then lyophilized. To a solution of the lyophilization residue in 60 ml. of glacial acetic acid was added 1.57 ml. of concentrated hydrochloric acid. After 20 minutes at room temperature, the mixture was lyophilized, and the residue was extracted with two 20-ml. portions of cold methanol. Addition of absolute ethyl ether to the combined methanol extracts gave the amino ester hydrochloride VI as fine needles, yield 4.46 g. (72%), m.p. 160.1–160.5° dec.

Anal. Calcd. for $C_{19}H_{29}N_2O_4SCl$: C, 54.73; H, 7.01; N, 6.71. Found: C, 54.89; H, 7.25; N, 6.71.

***t*-Butyl 4-Carbobenzoxy-5,5-dimethyl-α-(α-toluenesulfonamido)-2-thiazolidineacetic (VII).**—A solution of 3.43 g. of the "aminopenicilloate" VI (8.24 mmoles) and 0.84 g. (8.28 mmoles) of triethylamine in 100 ml. of purified methylene chloride at 5° was stirred rapidly during the simultaneous addition of α-toluenesulfonyl chloride (1.59 g., 8.34 mmoles) in 25 ml. of methylene chloride and an additional 0.84 g. of triethylamine in 25 ml. of methylene chloride. Addition required 55 minutes and the reaction mixture was stored in a refrigerator for 20 hours. After removal of 0.38 g. of unreacted VI, the solvent was removed (aspirator, room temperature) and the residue was recrystallized from benzene–petroleum ether, yielding 3.32 g. (85%) of VII, m.p. 116–120°. A sample recrystallized from benzene-petroleum ether had m.p. 120.3–122.7°.

Anal. Calcd. for $C_{26}H_{34}N_2O_6S_2$: C, 58.40; H, 6.41; N, 5.24. Found: C, 58.50; H, 6.49; N, 5.33.

4-Carbobenzoxy-5,5-dimethyl-α-(α-toluenesulfonamido)-2-thiazolidineacetic Acid Hydrochloride (Ib).—A solution of 1.24 g. (2.32 mmoles) of the diester VII in 8 ml. of dry benzene was saturated with anhydrous hydrogen chloride at 0°. After several hours at 0°, the crystalline product was collected by filtration as 1.10 g. (92%) of colorless needles, m.p. 124.6–127.5° dec.

Anal. Calcd. for $C_{22}H_{27}N_2O_6S_2Cl$: C, 51.30; H, 5.28; N, 5.44. Found: C, 51.93, 52.12; H, 5.32, 5.58; N, 5.65.

Benzyl 6-(α-Toluenesulfonamido)-penicillanate (IIb).—A suspension of 1.10 g. (2.13 mmoles) of Ib in 200 ml. of purified methylene chloride to which 1.0 ml. of thionyl chloride had been added, was stirred vigorously for one hour, during which time a rapid stream of nitrogen was passed through the mixture. An additional 0.5 ml. of thionyl chloride was

(6) J. C. Sheehan and P. A. Cruickshank, THIS JOURNAL, **78**, 3680 (1956).

(7) We are indebted to Merck and Company, Inc., Rahway, New Jersey, for these measurements, reported to us by Dr. Karl Pfister.

(8) G. G. F. Newton and E. P. Abraham, *Nature*, **175**, 548 (1955).

(9) It is interesting to note that an unsuccessful attempt was made to produce "benzylsulfonyl penicillin" biosynthetically by the use of N-benzylsulfonyl-DL-valine as a precursor [O. K. Behrens *et al.*, *J. Biol. Chem.*, **175**, 782 (1948)]. In view of the relatively low antibiotic activity associated with this penicillin, it is possible that the substance was formed but escaped detection by the differential assay employed.

(10) H. Staudinger, *Ber.*, **49**, 1897 (1916).

added and the mixture was warmed to gentle reflux. The suspended solid dissolved completely at the end of 20 minutes and the solution was diluted with 100 ml. of dry benzene. The solvent was removed (aspirator, room temperature) and the residue was flushed with benzene. A solution of the residue in 10 ml. of benzene was washed with 5 ml. of 5% sodium bicarbonate solution followed by 5 ml. of water, and then was lyophilized. The light yellow residue from the lyophilization was dissolved in 5 ml. of benzene and chromatographed over 12 g. of Brockman activity III ethyl acetate neutralized alumina, with benzene as the eluent. Residue from the first 50 ml. of eluate was crystallized from benzene–petroleum ether to afford 0.46 g. (47%) of needles, m.p. 123–7°. A sample recrystallized from acetone–petroleum ether had m.p. 128.1–129.8°.

Anal. Calcd. for $C_{22}H_{24}N_2O_5S_2$: C, 57.37; H, 5.25; N, 6.08. Found: C, 57.56; H, 5.46; N, 6.02.

6-(α-Toluenesulfonamido)-penicillanic Acid (IId).—A suspension of 140 mg. of 30% palladium on charcoal in a solution of 0.25 ml. of glacial acetic acid in 5 ml. of purified dioxane was prereduced at room temperature and atmospheric pressure. Benzyl ester IIb (45.7 mg.) was added and hydrogenation was continued. The theoretical quantity of hydrogen had been absorbed at the end of six minutes, but the reduction was continued for one hour. Catalyst was removed by filtration and the filtrate was lyophilized. The residue was taken up in 5 ml. of methylene chloride, N-(3,3-diphenylpropyl)-piperidine (Bristol Laboratories "Aspasan") (29.4 mg., 0.105 mmole) was added and the methylene chloride was removed by evaporation under reduced pressure. Lyophilization of the residue from benzene yielded the salt as a colorless amorphous solid which crystallized immediately upon solution in 0.5 ml. of benzene. A second crop was obtained by the addition of ethyl ether. The total yield was 48.4 mg., 74%, m.p. 112–115° dec.

Anal. Calcd. for $C_{35}H_{43}N_3O_5S_2$: C, 64.68; H, 6.67; N, 6.47. Found: C, 64.73; H, 6.98; N, 6.31.

CAMBRIDGE, MASSACHUSETTS

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY]

Cyclic Polyolefins. XLI. Reaction of Acetyl Bromide and Propionyl Chloride with Cycloöctatetraene

BY ARTHUR C. COPE, THEODOR A. LISS[1] AND DOUGLAS S. SMITH[2]

RECEIVED AUGUST 3, 1956

Acetyl bromide and propionyl chloride react with cycloöctatetraene in the presence of aluminum chloride in nitrobenzene solution to form *o*-methylcinnamaldehyde and *o*-ethylcinnamaldehyde, respectively, in low yield.

This paper describes the results of initial attempts to prepare acyl derivatives of cycloöctatetraene, now available by other routes,[3,4] by the Friedel–Crafts acylation of cycloöctatetraene. It appeared possible that cycloöctatetraene would react with acid halides in the manner characteristic of many olefins,[5] forming adducts that could be converted to acyl cycloöctatetraenes by dehydrohalogenation. The reaction was investigated under various conditions with acetyl chloride, acetyl bromide, benzoyl chloride and acetic anhydride as acylating agents, employing zinc chloride, acetylsulfoacetic acid,[6] stannic chloride and aluminum chloride as catalysts. Only with aluminum chloride in dilute nitrobenzene solution at 0–5° was any isolable product obtained, and then only in low yield. The reaction was accompanied by extensive polymerization, presumably caused by the strong Lewis acid catalyst. The product was isolated by steam distillation, followed by repeated distillation.

It was evident that the light-yellow liquid product obtained from the reaction of cycloöctatetraene with acetyl bromide was not an acetyl derivative, for it was readily oxidized by air to an acid, m.p. 176–176.5° (I). The acid I was characterized by oxidation to *o*-toluic acid and by quantitative reduction with the absorption of 98% of one molar equivalent of hydrogen forming β-*o*-tolylpropionic acid (II), which was oxidized to *o*-phthalic acid, isolated as the anhydride. Literature values for the melting point of *o*-methylcinnamic acid are 169°[7] and 174–175°.[8] That compound I was indeed *o*-methylcinnamic acid was shown by comparison with an authentic sample prepared from *o*-tolualdehyde and malonic acid. None of the reported preparations of I has been identified as the *cis* or *trans* isomer. The ultraviolet spectrum of the authentic acid I prepared as described above has a maximum at 274 mμ (log ε 4.18). The ultraviolet spectra of *cis*- and *trans*-cinnamic acid have maxima at 264 mμ (log ε 3.98) and 273 mμ (log ε 4.32), respectively.[9] Accordingly, the acid I probably is the *trans* isomer.

The above results indicated that the original Friedel–Crafts product is *o*-methylcinnamaldehyde (III). An authentic sample of III was prepared by condensation of *o*-tolualdehyde with acetaldehyde in the presence of sodium hydroxide. The identity of the two samples of III was established by their ultraviolet maxima at 283 mμ, comparison of their infrared spectra, and mixed melting points of the semicarbazones, which showed no depression.

In order to obtain information concerning the source of the methyl group in III, cycloöctatetraene was treated with propionyl chloride under the conditions used with acetyl bromide. The product proved to be *o*-ethylcinnamaldehyde (IV), which was purified by extraction with Girard reagent T and regeneration. An authentic sample of the aldehyde IV was synthesized by condensation of *o*-ethylbenzaldehyde with acetaldehyde. Both samples had ultraviolet maxima at 291 mμ and infrared spectra that were identical within experimental error, and contained bands at 2809 and 2747 cm.$^{-1}$

(1) National Science Foundation Fellow, 1952–1955.

(2) Atomic Energy Commission Fellow, 1951–1952.

(3) A. C. Cope and D. J. Marshall, THIS JOURNAL, **75**, 3208 (1953).

(4) A. C. Cope and R. M. Pike, *ibid.*, **75**, 3220 (1953).

(5) C. A. Thomas, "Anhydrous Aluminum Chloride in Organic Chemistry," Reinhold Publishing Corp., New York, N. Y., 1941, p. 752 ff.

(6) T. F. Doumani and J. F. Cuneo, U. S. Patent 2,411,823; *C. A.*, **41**, 375 (1953).

(7) J. F. J. Dippy and J. E. Page, *J. Chem. Soc.*, 357 (1938).

(8) K. v. Auwers, *Ann.*, **413**, 265 (1917).

(9) A. E. Gillam and E. S. Stern, "Electronic Absorption Spectroscopy," Edward Arnold, Ltd., London, 1954, p. 233.