[CONTRIBUTION FROM THE CLIMAX MOLYBDENUM CO. OF MICHIGAN RESEARCH LABORATORY][1]

Reactions of Molybdenum Pentachloride with Monocarboxylic Acids

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The reaction of molybdenum pentachloride with monocarboxylic acids in carbon tetrachloride results in the formation of crystalline molybdenum trichloride dicarboxylates. Molybdenum trichloride dibenzoate, $MoCl_3(C_6H_5COO)_2$, is thermally stable at relatively elevated temperatures (*ca.* 200°), whereas the analogous aliphatic acid carboxylates decompose at considerably lower temperatures (*ca.* 80°). These compounds undergo Friedel–Crafts condensation reactions with aromatics to form ketones.

Introduction

The synthesis of simple molybdenum carboxylates has not been previously reported. This is probably the result of the unavailability of an intermediate soluble in organic solvents which possesses specific reactivity for protolytic compounds. The molybdate anion in aqueous solution will also normally undergo condensation polymerization under acidic conditions unless prevented by chelate stabilization, *e.g.*, with oxalate ion. Therefore, the recent commercial availability of pure molybdenum pentachloride as a chemical intermediate was utilized. This compound was found to possess the desired properties of organic solubility and specific reactivity.

Only in the case of titanium and zirconium tetrachlorides have the reactions of simple monocarboxylic acids with transition metal chlorides been systematically studied. Pande and Mehrotra[2] demonstrated that the reactions of acetic acid and acetic anhydride with titanium tetrachloride resulted in facile and specific reaction to give the diacetate. Further reaction was slow and accompanied by polymerization to yield a mixture of basic acetates

$$TiCl_4 + 2(CH_3CO)_2O \xrightarrow{\text{fast}} TiCl_2(CH_3COO)_2 + 2CH_3COCl$$

$$TiCl_2(CH_3COO)_2 + (CH_3CO)_2O \xrightarrow{\text{slow}} TiCl(CH_3COO)_3 + CH_3COCl$$

$$TiCl(CH_3COO)_3 + TiCl_2(CH_3COO)_2 \longrightarrow [TiCl(CH_3COO)_2]_2O + CH_3COCl$$

Zirconium tetrachloride is reported[3] to react with acetic acid to yield the tetra-acetate which thermally decomposes to yield basic diacetate and acetic anhydride.

The synthesis of these carboxylates in benzene is apparently not accompanied by Friedel–Crafts condensation when carboxylic acid is present in excess of one equivalent. This side reaction was not reported by Pande and Mehrotra. A systematic study has been made of the effectiveness of titanium tetrachloride as a Friedel–Crafts catalyst for the acylation of aromatics.[4] Using carboxylic acids as the acylating reagents, it was found, as in the case of aluminum trichloride, that two to three equivalents of titanium tetrachloride was required to obtain maximum yields. This is explained by the intermediate formation of the acid chloride coordination complex

$$RCOOH + TiCl_4 \longrightarrow TiCl_3(RCOO) + HCl$$

$$TiCl_3(RCOO) + TiCl_4 \longrightarrow TiCl_2 + TiCl_3RCOCl$$

It was observed, however, that only with acid anhydrides was there appreciable formation of the acid chlorides.

Molybdenum pentachloride reacts easily with monocarboxylic acids or acid anhydrides in carbon tetrachloride to give molybdenum trichloride dicarboxylates, $MoCl_3(RCOO)_2$ (R = phenyl or alkyl). These are hydrolytically unstable, green crystalline solids. The benzoate was isolated in almost quantitative yield because of its relative insolubility, whereas the yield of the acetate (34%) and the stearate (17%) were significantly lower because of their greater solubility in carbon tetrachloride. When the synthesis of molybdenum trichloride distearate was carried out at room temperature, a small amount of dark-green, crystalline solid, insoluble in carbon tetrachloride, believed to be a complex of molybdenum pentachloride and stearic acid, was also formed. When the synthesis was repeated at 50°, however, a similar amount of molybdenum tetrachloride was formed. It is believed that the C_{17}-alkyl chain of stearic acid reacts independently to reduce molybdenum pentachloride. Previous studies by Senderoff and Labrie[5] have demonstrated that *n*-hexadecane (cetane) reduces molybdenum pentachloride to the tetrachloride. The benzoate is thermally stable up to its melting point, 210–220°. The acetate and the stearate, however, melt much lower, at approximately 80°. While the acetate rapidly decomposes at the melting point to evolve hydrogen chloride, the stearate can be heated to 100° before this decomposition becomes appreciable. All of these compounds are soluble, with reaction, in polar, oxygenated organic solvents such as acetone, alcohol and ethyl acetate. Reaction with alcohols yields the corresponding ester. The solvolysis of molybdenum trichloride dibenzoate in refluxing ethyl acetate solution resulted in the formation of benzoic anhydride and no ethyl benzoate.

Extended refluxing of a benzene solution of five moles benzoic acid with molybdenum pentachloride yields a stable, insoluble, polymeric complex whose analysis corresponds to $Mo_2ClO_2(C_6H_5COO)_3$. The same product was obtained by the extended reflux in benzene of a reaction mixture of three moles benzoic acid and molybdenum trichloride dibenzoate. Attempts

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[1] Presented in part at the 135th Meeting of the American Chemical Society, Boston, Mass.

[2] K. C. Pande and R. C. Mehrotra, *J. prakt. Chem.*, **5**, 101 (1957).

[3] R. N. Kapoor, K. C. Pande and R. C. Mehrotra, *J. Indian Chem. Soc.*, **35**, 157 (1958).

[4] N. M. Cullinane, S. J. Chard and D. M. Leyshon, *J. Chem. Soc.*, 376 (1952).

[5] S. Senderoff and R. J. Labrie, *J. Electrochem. Soc.*, **102**, 77 (1955).

TABLE I

REACTIONS OF MOLYBDENUM PENTACHLORIDE WITH EXCESS BENZOIC ACID IN BENZENE[a]

Mole ratio $MoCl_5$: C_6H_5-COOH	$MoCl_5$, mole	C_6H_5-COOH, mole	Reflux time, days	M.p., °C. dec.	Formula	Carbon, %		Hydrogen, %		Chlorine, %		Molybdenum, %	
						Calcd.	Found	Calcd.	Found	Calcd.	Found	Calcd.	Found
1:3	0.16	0.49	5.0	220–221	$MoCl_{2.4}O_{0.3}(C_6H_5COO)_{1.9}$	38.3	38.15	2.34	2.32	20.8	20.40	23.2	23.14
1:4	.14	.56	1.69	218–219	$MoCl_{2.4}O_{0.4}(C_6H_5COO)_{1.9}$	38.09	38.21	2.39	2.37	20.14	20.53	22.71	22.74
1:5	.17	.85	5.0	[b]	$Mo_2ClO_2(C_6H_5COO)_3$	40.5	39.49	2.41	2.40	5.7	5.40	30.8	29.73

[a] Volume of benzene, 500 ml. [b] Thermally decomposes above 300° without melting.

were made to synthesize basic molybdenum chloride benzoates intermediate between $MoCl_3(C_6H_5COO)_2$ and $Mo_2ClO_2(C_6H_5COO)_3$ (see Table I). Extended refluxing of a benzene solution of three moles benzoic acid with molybdenum pentachloride yielded a product whose elemental analysis corresponded to the formula $MoCl_{2.4}O_{0.3}(C_6H_5COO)_{1.9}$. Essentially the same product was obtained by a shorter reflux period using four moles of benzoic acid. These results serve to emphasize the facile nature of the reaction of molybdenum pentachloride with two moles of benzoic acid to yield $MoCl_3(C_6H_5COO)_2$. Reaction with additional benzoic acid in benzene is slow and yields basic molybdenum oxychloride benzoates by an unknown mechanism. No benzoic anhydride or benzophenone was isolated from the reaction mixtures.

The specific reactivity of two chlorines bonded to molybdenum toward benzoic acid can be interpreted from the crystal structure of molybdenum pentachloride, as determined recently by Sands and Zalkin.[6] This structure consists of a dimeric molecule (Mo_2Cl_{10}) with the chlorine atoms forming two distorted octahedra which have a common edge. The molybdenum atoms occupy the centers of the octahedra and are joined by two chlorine bridge bonds. The apical Mo–Cl bonds are bent toward each other to form an angle of about 84° with a line connecting the two molybdenum atoms of the Mo_2Cl_6 plane.

It is proposed that molybdenum pentachloride preserves its dimeric state in carbon tetrachloride and that the four apical chlorines are preferentially reactive toward the monocarboxylic acids. For example, in the formation of molybdenum trichloride dibenzoate, only the apical chlorines are believed to react, whereas the basal chlorines are unreactive. Support for this proposal is found in the structures of niobium pentachloride[7] whose structure is isomorphic with molybdenum pentachloride, and niobium oxytrichloride. The molecular structure of the latter[8] consists of planar Nb_2Cl_6 groups, as found in niobium pentachloride, in which the apical chlorines have been replaced by oxygen. By analogy, the apical chlorines of molybdenum pentachloride are those which form the Mo–O bonds of the molybdenum trichloride dicarboxylates.

The attempted synthesis of molybdenum tetrachloride benzoate, $MoCl_4(C_6H_5COO)$, by refluxing a carbon tetrachloride reaction mixture of equimolar quantities of molybdenum pentachloride and benzoic acid resulted in an impure product by a dehydrochlorinative decomposition.

The molybdenum chloride carboxylates undergo Friedel–Crafts condensation with benzene to yield the corresponding ketone. An attempted synthesis of molybdenum tetrachloride benzoate, $MoCl_4(C_6H_5COO)$, by the reaction of equimolar quantities of benzoic acid and molybdenum pentachloride in benzene resulted in formation of a benzophenone complex $MoOCl_3[(C_6H_5)_2CO]$. The corresponding reaction with toluene gave a very specific benzoylation with a 70% yield of 4-methylbenzophenone. This result corresponds very favorably with the non-specificity of the aluminum trichloride reaction which gave a 40% yield of the 4-methyl- and a 20% yield of the 2-methylbenzophenone.[9] The reaction of acetic acid with an equimolecular weight of molybdenum pentachloride in refluxing benzene resulted in a 29% yield of acetophenone. This lower yield can be explained by the low temperature dehydrochlorinative decomposition of the molybdenum chloride acetate intermediate. A Friedel–Crafts type reaction sequence is postulated

$$C_6H_5COOH + MoCl_5 \longrightarrow MoCl_4(C_6H_5COO) + HCl$$

$$MoCl_4(C_6H_5COO) + C_6H_6 \longrightarrow MoOCl_3[(C_6H_5)_2CO] + HCl$$

It is suggested that the high covalent coördination power of molybdenum pentachloride and its ready formation of stable molybdenum oxychlorides help explain its unique activity for acylation using carboxylic acids, and may also explain the intramolecular condensation of molybdenum trichloride dibenzoate in ethyl acetate to form benzoic anhydride

$$MoCl_3(C_6H_5COO)_2 \longrightarrow MoOCl_3 + (C_6H_5CO)_2O$$

Experimental

All experiments were performed under a dry nitrogen atmosphere. All material transferals were conducted in a dry-box.

Materials.—The molybdenum pentachloride was Climax Molybdenum Co. pure grade, 99^+ % pure. Carbon tetrachloride, the reaction solvent, was Merck reagent, refluxed and distilled over phosphorus pentoxide. Benzene and toluene, Baker reagents, were refluxed and distilled over calcium hydride. Acetic anhydride, Merck reagent, was purified by fractional distillation. The benzoic acid and the glacial acetic acid, 99.8% pure, were Merck and Baker reagents, respectively. The stearic acid was Armour and Co. "Neo-

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(6) D. E. Sands and A. Zalkin, UCRL-1951, "The Crystal Structure of $MoCl_5$," report of work performed at the University of California under the auspieces of the U. S. Atomic Energy Commission.

(7) A. Zalkin and D. E. Sands, *Acta Cryst.*, **11**, 615 (1958).

(8) D. E. Sands, A. Zalkin and R. E. Elson, *ibid.*, **12**, 21 (1959).

(9) J. F. Morris and A. J. Klemka, THIS JOURNAL, **62**, 1432 (1940).

Fat-18," 93% stearic acid, 5% palmitic acid and 2% oleic acid.

Molybdenum Trichloride Dibenzoate.—To 33.7 g. (0.28 chloride was added 37.5 g. (0.14 mole) of molybdenum pentachloride over a 10-minute period. A green solid was immediately formed with no noticeable evolution of heat. The reaction mixture was then refluxed for 16 hours with non-cessation of hydrogen chloride evolution. After cooling to room temperature, a fine, crystalline solid was separated by vacuum filtration through fritted glass. The solid was vacuum (oil-pump) dried overnight at room temperature to obtain 57.2 g. of light-green solid (93.3 % yield), m.p. 210–220° dec. Upon exposure to the atmosphere, the solid turned brown with evolution of hydrogen chloride, and the pungent odor of benzoyl chloride became apparent. No benzoyl chloride, however, was isolated from the reaction mixture filtrate by fractional distillation.

The solid product was found to be greater than 2% soluble in acetone and ethanol to give dark-brown solutions. Refluxing a methanol solution for three hours gave a 77% yield of methyl benzoate. Although the compound is insoluble in water because of hydrolysis to benzoic acid, it is soluble in an ethanol–water solvent pair. It is appreciably soluble in ethyl acetate, tetrahydrofuran and 1,2-dimethoxyethane to give dark-green solutions. Refluxing an ethyl acetate solution for 2.5 hours gave a 44% yield of benzoic anhydride and no ethyl benzoate. It is only slightly soluble in diethyl ether, and it is completely insoluble in carbon disulfide, carbon tetrachloride and petroleum ether. Although it is insoluble in benzene at room temperature, it yields less than one mole equivalent of benzophenone after refluxing.

Anal. Calcd. for $C_{14}H_{10}Cl_3MoO_4$: C, 37.82; H, 2.27; Cl, 24.0; Mo, 21.6. Found: C, 37.08, 36.98; H, 2.31, 2.30; Cl, 23.29, 23.20, 24.27, 24.27; Mo, 20.73, 20.77, 21.00, 20.62.

Attempted Synthesis of Molybdenum Tetrachloride Benzoate.—To 17.3 g. (0.14 mole) of benzoic acid stirred with 250 ml. of carbon tetrachloride was added 38.7 g. (0.14 mole) of molybdenum pentachloride. The reaction mixture was refluxed for 17 hours with noncessation of HCl evolution. After cooling to room temperature, a gray-green, apparently inhomogenous solid, was separated by vacuum filtration through fritted glass. After the product was washed on the filter with 200 ml. of carbon tetrachloride, it was vacuum (oil-pump) dried overnight at room temperature to yield 38.7 g. The solid product was analyzed: C, 19.43, 19.31, 19.16, 19.17; H, 1.21, 1.19, 1.18, 1.17; Cl, 38.9, 37.4, 39.6, 37.1; Mo, 30.74, 30.72. This corresponds to an empirical composition of $C_5H_4Cl_{3.4}MoO_2$, which demonstrates that the product is the result of partial dehydrochlorination decomposition. It was found to decompose rapidly above 100° with the formation of a black melt and evolution of hydrogen chloride.

Molybdenum Oxytrichloride Benzophenone.—To 21.9 g. (0.18 mole) of benzoic acid dissolved in 500 ml. of benzene there was added 48.75 g. (0.18 mole) of molybdenum pentachloride over an 8-minute period. The reaction mixture was refluxed for five days without cessation of hydrogen chloride evolution. The reaction mixture was concentrated by distillation of 350 ml. of benzene. Since hydrogen chloride was still evolved, the reaction mixture was refluxed overnight, but hydrogen chloride was still evolved. After cooling to room temperature, it was cooled by brief refrigeration. A fine, crystalline, light-green solid was separated by filtration and washed with benzene. The product was found to have appreciable benzene solubility. After vacuum drying, 50.6 g. (70%) was obtained. This product was immediately hydrolyzed by water.

Anal. Calcd. for $C_{13}H_{10}Cl_3MoO_2$: C, 38.98; H, 2.52; Cl, 26.6; Mo, 24.0. Found: C, 38.07, 38.02, 38.19; H, 2.55, 2.47, 2.53; Cl, 26.92. 26.91, 26.94; Mo, 23.80, 24.35, 23.86, 24.10.

After treatment with water, benzophenone was isolated, b.p. 108–109° (0.7 mm.); 2,4-dinitrophenylhydrazone, m.p. 238–239° (literature m.p. 239°); oxime, m.p. 141–142° (literature m.p. 141°).

Benzoylation of Toluene Using Molybdenum Pentachloride.—To a solution of 22.7 g. (0.19 mole) of benzoic acid in 500 ml. of toluene was added 50.8 g. (0.19 mole) of molybdenum pentachloride over an 8-minute period. This resulted in a slightly exothermic reaction to give a brown solution and considerable evolution of hydrogen chloride. The reaction mixture was refluxed for 17 hours during which a fine, crystalline solid formed. It was stirred into 500 ml. of 10% hydrochloric acid. Because of the gelatinous nature of the brown, inorganic hydrolysis product, it was difficult to separate by filtration. Saturating the aqueous acid layer with ammonium chloride increased the filtration rate. The aqueous layer was separated and extracted with ether. The combined ether extract and toluene solution was washed with water, treated with Drierite, and distilled to strip off the organic solvents. The pot residue was dissolved in ether, and this solution was extracted with 10% aqueous sodium hydroxide. From this alkali extract, after acidification, 0.3 g. of benzoic acid was obtained. The non-alkali extracted organic product was fractionally distilled through a Vigreux column yielding only one fraction, b.p. 103–105° (0.225 mm.), m.p. 55–57°. The yield was 26 g. (70%). This was identified as 4-methylbenzophenone, m.p. 55–57°, by its 2,4-dinitrophenylhydrazone, m.p. 200–201° (literature m.p. 200°).

Molybdenum Trichloride Diacetate.—To 56.2 g. (0.55 mole) of acetic anhydride stirred with 250 ml. of carbon tetrachloride was quickly added 30.2 g. (0.11 mole) of molybdenum pentachloride. There was immediate formation of light-green crystals. The reaction mixture was stirred at room temperature for 22 hours. The green, crystalline solid was separated by filtration and oil-pump vacuum dried for two hours at room temperature and for 0.5 hour at 35° on a water-bath. The yield of molybdenum trichloride diacetate was 12.0 g. (34%), m.p. 80–85°, decomposition with hydrogen chloride evolution. This compound is very readily hydrolyzed by atmospheric moisture to a brown liquid. The product is very soluble in polar, oxygenated solvents such as water, acetone and butyl acetate. It reacts with alcohols to give acetic acid esters.

Anal. Calcd. for $C_4H_6Cl_3MoO_4$: C, 14.99; H, 1.89; Cl, 32.2; Mo, 29.9. Found: C, 14.95, 15.03, 15.08, 14.99; H, 1.90, 1.91, 1.90; Cl, 32.02, 32.07, 32.05, 32.05; Mo, 30.29, 30.55, 30.17, 30.05.

The reaction mixture filtrate was fractionally distilled to give 17.6 g. (0.22 mole) of acetyl chloride, b.p. 52–55°. Intermittent refluxing and distillation over nearly 5 hours caused the slow separation of an additional 11.6 g. (0.15 mole) of acetyl chloride.

Acylation of Benzene Using Molybdenum Pentachloride.—To a solution of 10.9 g. (0.18 mole) of glacial acetic acid in 500 ml. of benzene there was quickly added 49.6 g. (0.18 mole) of molybdenum pentachloride. After refluxing for two hours, the reaction mixture was worked up as described above for the benzoylation of toluene. The fractional distillation gave a liquid, b.p. 84–87° (16 mm). The yield was 6.4 g. (29%). This was identified as acetophenone by its 2,4-dinitrophenylhydrazone, m.p. 246–247° (literature m.p. 250°). The pot residue was a solid resin, 6.63 g.

Molybdenum Trichloride Distearate.—A solution of 50.0 g. (0.18 mole) of stearic acid in 500 ml. of carbon tetrachloride was obtained by warming. After cooling the solution to room temperature, 24.1 g. (0.09 mole) of molybdenum pentachloride was quickly added. The reaction mixture was stirred for 26 hours at room temperature. By vacuum filtration, there was separated approximately 5 g. of a heavy, dark-green, crystalline solid. This solid was hydrolyzed by water and was dissolved in ethanol to give ethyl stearate. This is believed to be the initially formed stearic acid addition product of molybdenum pentachloride. The reaction mixture filtrate was vacuum concentrated on a water-bath at 40° to approximately half the original volume. A green, gelatinous solid was separated. Since this solid could not be filtered, it was found necessary to use centrifugation. This caused separation of a top layer of light-green solid, which was washed with carbon tetrachloride and separated again by centrifuging. The solid was dried by oil-pump vacuum drying on a water-bath at 45–50°. The yield was 11.4 g. (17%), m.p. 78–80°. The product is soluble in ethanol and acetone at room temperature. The compound is insoluble in petroleum ether at room temperature but dissolves upon heating. It is hydrolyzed by water to give a quantitative yield of stearic acid. Refluxing an ethanol solution for 5 hours gave a 93% yield of ethyl benzoate.

Anal. Calcd. for $C_{36}H_{70}Cl_3MoO_4$: C, 56.21; H, 9.17; Cl, 13.83; Mo, 12.47. Found: C, 56.71, 56.48, 56.44; H, 9.29, 9.24, 9.24; Cl, 12.77, 12.72, 12.74, 12.79, 12.68, 12.60; Mo, 12.55, 12.51, 12.48, 12.48.

The above-described synthesis was repeated using the reaction of 40.42 g. (0.15 mole) of molybdenum pentachloride with 84.2 g. (0.30 mole) of stearic acid in 500 ml. of carbon tetrachloride. Instead of using room temperature for the initial reaction, the reaction mixture was heated at 50° for 16 hours. It was then filtered to separate 3.12 g. of black, crystalline solid. This solid was found to have the X-ray diffraction pattern reported for molybdenum tetrachloride.[10]

Anal. Calcd. for Cl_4Mo: Cl, 59.65; Mo, 40.35. Found: Cl, 60.06, 60.06; Mo, 38.52, 38.46, 38.76.

The reaction mixture filtrate was treated by various procedures to determine the most efficient purification method. One portion of the filtrate was vacuum evaporated to give a dark, gray-green solid, m.p. 67–72°.

Anal. Calcd. for $C_{36}H_{70}Cl_3MoO_4$: Cl, 13.83; Mo, 12.47. Found: Cl, 12.65, 12.63; Mo, 11.33, 11.30.

This solid dissolved in petroleum ether upon slight heating, and no precipitation occurred upon cooling. Addition of an excess of petroleum ether to a carbon tetrachloride solution of the product did not cause precipitation.

Partial vacuum evaporation of another portion of the reaction mixture filtrate caused precipitation of a green, gelatinous solid which slowly separated to form an indistinct top layer. This was crudely separated by decantation, washed with carbon tetrachloride, and separated as before. A portion of the separated layer was vacuum evaporated to dryness to give a light, gray-green solid, m.p. 73–75°.

Anal. Calcd. for $C_{36}H_{70}Cl_3MoO_4$: Cl, 13.83; Mo, 12.47. Found: Cl, 12.97, 13.01; Mo, 11.83, 11.79.

The remainder of the decanted solid was filtered and washed on the filter with carbon tetrachloride. After vacuum drying, a very light-green solid, m.p. 78–80°, was obtained. It evolved hydrogen chloride slightly when heated above 100°. The infrared spectrum of this solid was identical with that of the solid, m.p. 78–80°, separated by centrifugation, as described above.

Anal. Calcd. for $C_{36}H_{70}Cl_3MoO_4$: Cl, 13.83; Mo, 12.47. Found: Cl, 12.97, 12.90, 13.04; Mo, 12.47, 12.41.

Reactions of Molybdenum Pentachloride with Excess Benzoic Acid in Benzene.—These reactions were conducted using the procedure described above for the synthesis of molybdenum trichloride dibenzoate. The results are summarized in Table I.

The products of the 3- and 4- mole reactions were very similar. They were both sensitive to atmospheric moisture and several minutes exposure to water was required for noticeable hydrolysis to give benzoic acid. No appreciable benzoyl chloride could be detected in the reaction mixture filtrates by vacuum distillation or by treatment with concentrated ammonium hydroxide to give benzamide.

The 5-mole reaction was found to give a light-green, crystalline solid which possessed considerable hydrolytic stability. The same product, as confirmed by elemental, infrared and m-ray diffraction analyses, was obtained by the extended (five days) reflux of a benzene reaction mixture of molybdenum trichloride dibenzoate with three moles of benzoic acid. This product was washed with water and methanol without reaction. It is completely non-hygroscopic and resists attack by nitric and hydrochloric acids. It is completely soluble in concentrated sulfuric acid to release benzoic acid. Refluxing for several hours with 10% aqueous sodium hydroxide is required for saponification. The product is completely insoluble in common organic solvents with the exception of chloroform and pyridine, in which it reacts to replace benzoate.

Only trace benzoyl chloride and no benzoic anhydride or benzophenone could be detected in these reaction mixtures.

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The infrared spectra were determined by the Anderson Physical Laboratory, Champaign, Ill. Some of the elemental microanalyses were performed by the Huffman Microanalytical Laboratories, Wheatridge, Colo.

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[10] Private communication from Dwight E. Couch, National Bureau of Standards, to Robert E. Herfert, Climax Molybdenum Co., July 21, 1958.

[CONTRIBUTION FROM DEPARTMENTS OF BIOCHEMISTRY AND OF OBSTETRICS AND GYNECOLOGY, COLLEGE OF PHYSICIANS AND SURGEONS, COLUMBIA UNIVERSITY]

The Cleavage of Androsterone β-D-glucopyranosiduronic Acid in Organic Media

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A kinetic study of the acid hydrolysis of androsterone β-D-glucopyranosiduronic acid under various conditions has revealed that rapid cleavage of this conjugate can be effected at low temperatures and low acid concentrations. At temperatures of 26–50°, this model conjugate was cleaved in good yield when dissolved in certain organic media containing between 0.01–0.1 *N* perchloric acid and less than 0.1–0.5% of water. Under these conditions other acids such as sulfuric acid and *p*-toluenesulfonic acid were ineffective.

In an effort to develop a general chemical procedure for the cleavage of urinary glucopyranosiduronides (glucuronosides) of at least certain classes of steroids, this study of the acid-catalyzed cleavage of androsterone glucuronoside was undertaken. Although other conjugates are present, most of the steroid hormone metabolites are excreted into the urine as glucuronosides. Because no mild chemical methods are known for the hydrolysis of these compounds,[3] the usual procedure involves the use of strong acid (1–10 *N*) and elevated temperatures. Even then, it is sometimes difficult to obtain complete hydrolysis. Furthermore, these drastic conditions simultaneously result in side reactions which alter many of the steroid aglycones. The use of the enzyme, β-glucuronidase, for the cleavage of these conjugates is considered the most satisfactory method available at present since it preserves the chemical integrity of the aglycones. Because of the possible occurrence of enzyme competitors and inhibitors in urine, which could lead to grossly erroneous results,

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[3] R. S. Teague, *Adv. Carbohydrate Chem.*, **9**, 199 (1954).