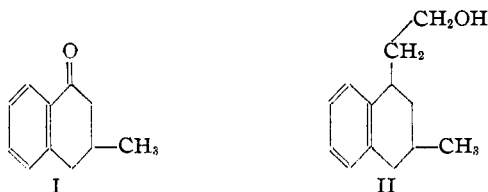


NOTES

The Preparation of 3-Methyl-1-tetralone and β -[1-(3-Methyl-1,2,3,4-tetrahydronaphthyl)]-ethyl Alcohol

BY W. E. BACHMANN AND W. S. STRUVE

In the course of an investigation β -[1-(3-methyl-1,2,3,4-tetrahydronaphthyl)]-ethyl alcohol (II) was required. The starting material for the preparation was γ -phenyl- β -methylbutyric acid, which was prepared from 1-allylbenzene according to the procedure of Carter.¹ Cyclization of the acid through its acid chloride by means of aluminum chloride gave 3-methyl-1-tetralone (I), whose structure was established by its conversion to β -methyl-naphthalene by Clemmensen reduction and subsequent dehydrogenation of the product. By means of the Reformatsky reaction with methyl bromoacetate and subsequent dehydro-



tion of the resulting hydroxy ester, the ketone was converted into what is probably the methyl ester of 1-(3-methyl-3,4-dihydronaphthyl)-acetic acid, although the position of the double bond was not established. Reduction of the ester by means of sodium and alcohol yielded the desired alcohol (II). The alcohol reacted with phosphorus tribromide to give the corresponding bromide.

Experimental

3-Methyl-1-tetralone.—A mixture of 25.5 g. of γ -phenyl- β -methylbutyric acid, 20 cc. of thionyl chloride, and 5 drops of pyridine was allowed to stand at room temperature for a half hour. The thionyl chloride was evaporated under reduced pressure, 150 cc. of carbon disulfide was added and the solution was cooled in an ice-salt mixture. Twenty-two grams of aluminum chloride was added in portions and the mixture was refluxed for ten minutes. After hydrolysis of the complex with ice and hydrochloric acid, the organic layer was separated, the carbon disulfide was evaporated, and the residue was dissolved in benzene. The benzene solution was washed with dilute ammonium hydroxide and with water and the benzene was evaporated. The 3-methyltetralone distilled under reduced pressure as

a colorless liquid at 94–96° at 0.3 mm.; weight, 16.7 g. (73%).

Anal. Calcd. for $C_{11}H_{12}O$: C, 82.5; H, 7.5. Found: C, 82.4; H, 7.4.

The **oxime** crystallizes from dilute alcohol as colorless needles; m. p. 122.5–123.5°.

Anal. Calcd. for $C_{11}H_{12}NO$: N, 8.0. Found: N, 7.8.

A mixture of 5 g. of the above ketone, 25 g. of amalgamated zinc, 50 cc. of concentrated hydrochloric acid, 25 cc. of water, and 2.5 cc. of acetic acid was refluxed for twenty-four hours, an additional 50 cc. of concentrated hydrochloric acid being added in portions over this time. The oil was extracted with ether, the ether extract was dried with anhydrous sodium sulfate, and the residue obtained by evaporation of the ether was distilled at 12 mm. pressure. The colorless distillate was heated for four hours at 200–220° with 2.3 g. of powdered sulfur. A small amount of copper bronze was then added and the heating was continued for ten minutes more. The mixture was extracted with ether, the filtered ether solution, after having been dried with anhydrous sodium sulfate, was evaporated, and the residue was distilled at 10 mm., giving 2.0 g. of colorless distillate which solidified on cooling to room temperature; m. p. 29–30.5°. After being purified through the picrate, the hydrocarbon melted at 34–35°. The mixed melting point with authentic β -methyl-naphthalene gave no depression. The picrate melted at 115–116.5° and the mixed melting point with authentic β -methyl-naphthalene picrate gave no depression.

Methyl 1-(3-Methyl-3,4-dihydronaphthyl)-acetate.—A mixture of 20 g. of 3-methyl-1-tetralone, 14.4 cc. of methyl bromoacetate, 48 g. of zinc, 480 cc. of dry ether, 480 cc. of dry benzene, and a small amount of iodine was refluxed for four hours, additional zinc and iodine being added at the end of each hour and an additional 14.4 cc. of methyl bromoacetate being added at the end of the second hour. The complex was decomposed with ice and hydrochloric acid, the organic layer was washed with ammonium hydroxide and then with water, and the benzene and ether were evaporated. The hydroxy ester was dehydrated by heating with 100 cc. of anhydrous formic acid on a steam-bath for fifteen minutes; water was added and the ester was extracted several times with benzene. The benzene extract was washed with dilute sodium carbonate solution and then with water, the benzene was evaporated, and the residue was distilled under reduced pressure, the yellowish liquid distilling at 130–133° at 0.4 mm. being collected; weight, 23 g. (85%).

Anal. Calcd. for $C_{14}H_{16}O_2$: C, 77.8; H, 7.4. Found: C, 77.8; H, 7.6.

β -[1-(3-Methyl-1,2,3,4-tetrahydronaphthyl)]-ethyl Alcohol.—To a boiling solution of 25 g. of the above ester in 125 cc. of absolute methanol was added 21.3 g. of sodium metal over a period of fifteen minutes. After the vigorous reaction had subsided, another 50 cc. of methanol was added. When all of the sodium had reacted, 100 cc.

(1) Carter, *J. Biol. Chem.*, **108**, 622 (1935).

of water was added and the mixture was refluxed for three hours. The mixture was cooled, acidified with dilute sulfuric acid, and extracted several times with benzene. The benzene extracts were extracted with 2 *N* sodium carbonate solution and with water, the benzene was evaporated, and the residue was distilled under reduced pressure, the colorless viscous liquid distilling at 134–137° at 0.4 mm. being collected; weight, 12.4 g. (57%).

Anal. Calcd. for C₁₃H₁₈O: C, 82.1; H, 9.5. Found: C, 81.8; H, 9.4.

The acid obtained by acidification of the alkaline washings was esterified with methanolic hydrochloric acid, purified by distillation (7 g., b. p. 128–133° at 0.4 mm.), and this recovered ester could be used in subsequent reductions.

β - [1 - (3 - Methyl - 1,2,3,4 - tetrahydronaphthyl)]-ethyl Bromide.—A mixture of 5.0 g. of the above alcohol and 2 cc. of phosphorus tribromide was heated on a steam-bath for two hours. The mixture was taken up in benzene and washed with 2 *N* sodium carbonate solution and then with water. The residue obtained by evaporation of the benzene was distilled, the colorless liquid distilling at 137–140° at 0.4 mm. being collected; weight, 5.2 g. (75%).

Anal. Calcd. for C₁₃H₁₇Br: Br, 31.6. Found: Br, 31.8.

CHEMISTRY LABORATORY
UNIVERSITY OF MICHIGAN
ANN ARBOR, MICHIGAN

RECEIVED APRIL 6, 1940

The Preparation of Pentaacetyl-*d*-gluconyl Chloride

BY CHARLES E. BRAUN, S. H. NICHOLS, JR., J. L. COHEN
AND THEIS E. AITKEN

In the course of work being carried out in these laboratories a method has been developed for the preparation of pentaacetyl-*d*-gluconyl chloride in quantity. This new procedure, based upon that of Major and Cook,¹ involves much less manipulation and gives consistently good results. The details are presented here for those interested.

Anhydrous pentaacetylgluconic acid² (25 g. or 0.062 mole) was dissolved in 185 cc. of anhydrous ethyl ether and an excess of phosphorus pentachloride (15 g. or 0.072 mole) was added without cooling. The reactants were allowed to stand at room temperature from four to twelve hours (usually overnight). The excess phosphorus pentachloride was then filtered off on a sintered glass funnel, and the ethereal filtrate concentrated to about one-half of its volume *in vacuo* at room temperature. The concentrated solution was kept at zero degrees or below³ for fifteen to twenty-four hours. The mother liquor was then decanted, *care being taken not to break up or disturb the crystals which had formed on the bottom of the flask.* The crystalline mass was next broken up, mechanically removed and filtered on

a sintered glass funnel. After thorough washing with petroleum ether (Eastman Kodak Company, practical, b. p. 35–55°), the crystalline acid chloride was preserved *in vacuo* over calcium chloride and potassium hydroxide at room temperature.

The decanted mother liquor, after being concentrated *in vacuo* at room temperature to one-half of its volume, was allowed to stand at zero degrees or below for another twenty-four hours. The second crop of crystals thus obtained was treated as described above. The concentrated mother liquor which contained all of the phosphorus oxychloride was usually discarded. By this procedure pentaacetyl-*d*-gluconyl chloride was produced as large colorless crystals; m. p. 68–71°; [α]²⁰_D +1.71° (alcohol-free chloroform, *c*, 4.38).

Anal. Calcd. for C₁₆H₂₁O₁₁Cl: Cl, 8.35. Found: Cl, 8.20.

The yields obtained in five typical preparations were 83%, 86%, 92%, 88% and 93%, or an average yield of 88.4%.

DEPARTMENT OF CHEMISTRY
THE UNIVERSITY OF VERMONT
BURLINGTON, VERMONT

RECEIVED MARCH 25, 1940

Additional Observations on the Vitamin K Activity of Quinones

BY ERHARD FERNHOLZ, H. B. MACPHILLAMY AND S. ANSBACHER

Several months ago we reported that phlorone (2,5-dimethyl-1,4-benzoquinone) has vitamin K activity,¹ an observation recently confirmed by H. J. Almquist.² In this connection it seemed of interest to investigate whether 2-methyl-5,6,7,8-tetrahydro-1,4-naphthoquinone possesses the great potency of the parent substance. The hydrogenated quinone, first synthesized by Chuang and Han,³ was prepared by catalytic hydrogenation of 2-methyl-1,4-naphthoquinone. It was found to be active at 1 mg., a degree of activity which should be considered practically negligible, since it is common to a great number of quinones.

We have also studied the analogous hydrogenation product of vitamin K₁ (β , γ ,5,6,7,8-hexahydrovitamin K₁). It showed no vitamin K activity, not even in a dose of 2 mg. In contrast to this, Fieser, Tishler, and Sampson⁴ reported it to have slight activity, although the dosage is not indicated.

We wish to point out that we have prepared and assayed the naphthotocopherol and its quin-

(1) Major and Cook, *THIS JOURNAL*, **58**, 2477 (1936).

(2) Major and Cook, *ibid.*, **58**, 2475 (1936).

(3) At higher temperatures the yields are decreased appreciably due to the increase in solubility of the acid chloride in the anhydrous ether.

(1) Ansbacher and Fernholz, *J. Biol. Chem.*, **131**, 399 (1939).

(2) 52nd Annual Meeting, Am. Physiol. Soc., New Orleans, May 16 (1940).

(3) Chuang and Han, *Ber.*, **68**, 876 (1935).

(4) Fieser, Tishler and Sampson, *THIS JOURNAL*, **62**, 996 (1940).

oid oxidation product recently mentioned by Fieser, *et al.*⁴ The latter authors gave no biological data for the oxidation product and stated that the tocopherol was active at 0.3 mg. We found that 1 mg. of the tocopherol was totally inactive, but the oxidation product was fully active at that dose.⁵

Experimental

2-Methyl-5,6,7,8-tetrahydro-1,4-naphthoquinone.—A solution of 1.72 g. of 2-methyl-1,4-naphthoquinone in glacial acetic acid was completely hydrogenated using platinum oxide catalyst. The reaction mixture was decanted from the catalyst, diluted with water and extracted with ether. The ethereal solution was washed, dried and the solvent evaporated. The quinone was obtained by steam distilling a suspension of the crude hydroquinone in a ferric chloride solution. The distillate was extracted with ether, the extract dried and the solvent evaporated. The residue after recrystallization from light petroleum ether yielded 1.6 g. (94%) of quinone melting at 58–59°.

Anal. Calcd. for $C_{11}H_{12}O_2$: C, 74.97; H, 6.87. Found: C, 74.95; H, 6.71.

β , γ -5,6,7,8-Hexahydro Vitamin K₁.—One gram of the synthetic vitamin was hydrogenated as described above. The hydroquinone was oxidized with silver oxide in dry ether. The yield was 0.95 g. (95%) of yellow oil giving with alcoholic alkali a pink color which darkened to brown on standing.

Anal. Calcd. for $C_{31}H_{46}O_2$: C, 81.52; H, 11.47. Found: C, 81.17; H, 11.60.

Naphthotocopherol.—A mixture of 3.5 g. of 2-methyl-1,4-naphthoquinone, 5 g. of phytol, 5 g. of anhydrous zinc chloride and 50 cc. of xylene⁶ was refluxed for twenty-four hours. The solvent was removed *in vacuo* and the residue taken up in ether. The ethereal solution was washed repeatedly with 2% potassium hydroxide solution containing hydrosulfite and finally with dilute hydrochloric acid and water. After drying and removal of the solvent, the remaining brown oil was taken up in petroleum ether (b. p. 40–60°), and extracted with Claisen alkali. The small amount of yellow oil obtained on working up the soluble portion gave the typical Dam-Karrer reaction for vitamin K₁.

The petroleum ether portion was washed, dried and the solvent evaporated. The residue was purified by chromatographic adsorption on activated alumina in petroleum ether solution. The yield was about 1.0 g. (13% based on phytol), of reddish-brown oil which strongly reduced an alcoholic silver nitrate solution in the cold.

Anal. Calcd. for $C_{31}H_{46}O_2$: C, 82.24, H, 10.70. Found: C, 82.48; H, 10.72.

Oxidation of Naphthotocopherol.—Two hundred milligrams of the above tocopherol was oxidized with ferric

chloride in alcoholic solution. The reaction mixture was diluted with water, extracted with ether, and the ethereal solution washed, dried and concentrated. The residue was purified by chromatographing in petroleum ether solution on activated calcium sulfate. About 100 mg. (48%) of dark orange oil was obtained.

Anal. Calcd. for $C_{31}H_{46}O_3$: C, 79.43; H, 10.30. Found: C, 79.42; H, 10.03.

THE SQUIBB INSTITUTE FOR MEDICAL RESEARCH
DIVISION OF ORGANIC CHEMISTRY
NEW BRUNSWICK, N. J.

RECEIVED APRIL 22, 1940

Collidine Treatment of 2-Bromocholestanone

BY ROBERT P. JACOBSEN

In the course of preparation of certain steroids for photochemical study, the author has had occasion to employ the collidine method of Butenandt, *et al.*,¹ for the splitting of hydrogen bromide from 2-bromocholestanone to form 1-cholestenone. On refluxing a collidine solution of the bromo compound for two hours, these workers obtained the α,β -unsaturated ketone (m. p. 95°, $[\alpha]_D + 64.5^\circ$) in 77% yield. Butenandt and Wolff² had earlier reported the preparation of 1-cholestenone (m. p. 111–112°, $[\alpha]_D - 32.1^\circ$; oxime, m. p. 146–147°), in poor yield by the potassium acetate-acetic acid treatment of 2-bromocholestanone. This latter compound the German workers now call "hetero- Δ^1 -cholestenone" and state that the "normal Δ^1 -ketone" is the substance melting at 95°.

In the experience of the author, the collidine reaction appears to follow a less straightforward course than that indicated by Butenandt and his collaborators. 2-Bromocholestanone (m. p. 169°) was refluxed in collidine³ for two, four, or six hours without effecting the complete fission of hydrogen bromide. After twelve hours of boiling, a non-homogeneous, crystalline, halogen-free product (m. p. 89–92° to a sludge which cleared at about 100°) was obtained in 74% yield. By repeated crystallization from methanol this gave a very small amount of material, m. p. 126–127.5° (nearly pure cholestanone), which showed no selective absorption⁴ in the ultraviolet region between 2200 and 2600 Å. No pure 1-cholestenone could be obtained from the intermediate fractions by crystallization, although some sam-

(1) Butenandt, Mamoli, Dannenberg, Masch and Paland, *Ber.*, **72**, 1617 (1939).

(2) Butenandt and Wolff, *ibid.*, **68**, 2091 (1935).

(3) Obtained from the Research Department of the Barrett Company, 90% of the material boiling in the range 170.7–171.9°.

(4) Ultraviolet absorption measurements by Dr. P. A. Cole and Mr. C. Z. Nawrocki of this Laboratory.

(5) Reported by the senior author in a lecture at Columbia University on December 4, 1939.

(6) Jacob, Sutcliffe and Todd, *J. Chem. Soc.*, 331 (1940), report an unsuccessful attempt to effect this condensation in boiling decalin. In our experience the tocopherol is destroyed at that temperature.

ples⁵ which melted at 93–96° showed an ultraviolet absorption maximum at 2275 Å. ($\log \epsilon$ 4.07, cyclohexane). By brominating the combined intermediate fractions (0.5 g.) in cold acetic acid (5 cc.) there was obtained 0.20 g. of impure 1-cholestenone dibromide (effervesces at 85°). On allowing the filtrate to stand for a few minutes, hydrogen bromide was evolved and there separated 0.095 g. of needles, m. p. 152–156°. The dibromide liberated iodine on warming in an alcoholic sodium iodide solution but the needles did not. The latter on crystallization from methyl acetate melted at 169° and mixed with 2-bromocholestanone showed no depression. The crude dibromide was debrominated with sodium iodide or zinc dust in alcohol, or potassium iodide in 80% acetone, to give the corresponding unsaturated ketone, m. p. 102–104°. By repeating the purification through the dibromide, pure 1-cholestenone, crystallizing as a hydrate from 98% methanol or aqueous acetone, m. p. 107–108° ($[\alpha]^{24D} +65^\circ$).

These observations indicate that the collidine treatment of 2-bromocholestanone, under the conditions specified, gives principally a mixture of 1-cholestenone and cholestanone. The formation of the latter compound is not surprising in view of

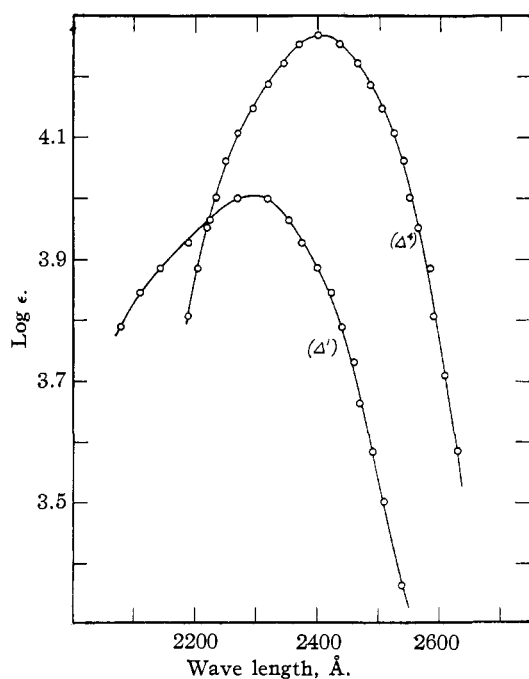


Fig. 1.

(5) These properties correspond closely to those of the product (m. p. 95°) of Butenandt, *et al.*, who reported a maximum at 230 m μ ($\log \epsilon$ 4.03).

the work of Schwenk and Whitman,⁶ who obtained cholestanone as the principal product of the treatment of 2-bromocholestanone with dimethylaniline.

The ultraviolet absorption in alcohol of 1-cholestenone hydrate (calculated on the anhydrous basis) in the region of the maximum is compared with that of the Δ^4 -isomer in Fig. 1.

The preparation of 1-cholestenone will be detailed later in connection with a report of photo-dehydrogenation studies now in progress.

(6) Schwenk and Whitman, *THIS JOURNAL*, **59**, 949 (1937).

WASHINGTON BIOPHYSICAL INSTITUTE

BETHESDA, MARYLAND

RECEIVED APRIL 27, 1940

The Behavior of Certain Substituted Allenes toward the Meinel Color Test¹

BY F. B. LAFORGE AND FRED ACREE, JR.

A method for the detection of conjugated double bonds has been proposed by Meinel^{1a} based upon the treatment of the compound to be tested with one molecular equivalent of bromine in methanol solution. The isolated reaction product is then treated with a suspension of silver thiocyanate containing ammonium ferric sulfate. The formation of a red color of variable intensity depending upon the compound is indicative of the presence of a conjugated system of double bonds.

Conant and Jackson² have reported the formation of dibromo compounds along with the methyl hypobromite addition products when bromine in methanol solution is allowed to react on an unsaturated compound. Thus, while Meinel indicated that the methyl hypobromite addition product is responsible for the reaction with silver thiocyanate, there also is the possibility that the dibromo addition product might be the influencing factor in the reaction.

Meinel subjected a number of compounds to the test but did not include any that possessed a cumulated system of double bonds.

In studying the reaction of halogens³ on compounds of this class it was of interest to determine whether or not they would also respond to the color test.

It was found that 1-phenyl-1,2-butadiene, 2,3-pentadiene, 1-cyclohexyl-2,3-pentadiene, and pyrethrene gave a positive reaction. When com-

(1) Not subject to copyright.

(1a) K. Meinel, *Ber.*, **70B**, 429 (1937).

(2) J. B. Conant and E. L. Jackson, *THIS JOURNAL*, **46**, 1727 (1924).

(3) Fred Acree, Jr., and F. B. LaForge, *J. Org. Chem.*, (in press).

pared with myrcene, 1-pentene and styrene dibromide, the approximate speed and the intensity of the color formation were greatest in the case of the 1-phenyl-1,2-butadiene and decreased in the order named with the other compounds.

Since compounds possessing a cumulated system of double bonds respond to the Meinel tests, the method is not specific for the conjugated system.

BUREAU OF ENTOMOLOGY AND PLANT QUARANTINE
U. S. DEPARTMENT OF AGRICULTURE
WASHINGTON, D. C. RECEIVED APRIL 10, 1940

Preparation of Phenylacetone

BY J. PHILIP MASON AND LEWIS I. TERRY

Phenylacetone has been prepared by several methods.¹ We have obtained it in a 32% yield from benzene, chloroacetone and anhydrous aluminum chloride.

Experimental

Forty-one grams (0.31 mole) of anhydrous aluminum chloride and 100 ml. of anhydrous benzene (free from thiophene) were put in a 500-ml. three-necked flask which was equipped with a mercury-sealed stirrer, a reflux water condenser and a small addition funnel. The top of the condenser was connected to a sulfuric acid trap and this trap was connected to a gas absorption bottle. The mixture was stirred, heated to refluxing on a steam-bath and 13.9 g. (0.15 mole) of chloroacetone was allowed to drop in slowly during a period of thirty minutes. After refluxing for five hours, the mixture was practically black. After cooling to room temperature, the reaction mixture was decomposed by adding water slowly through the addition funnel, stirring during the addition. When no more hydrogen chloride was evolved, 20 ml. of water and 20 ml. of concentrated hydrochloric acid were added. The benzene layer was separated and the aqueous layer extracted with four 25-ml. portions of benzene. All of the benzene solutions were combined and filtered. The benzene was distilled and the remaining viscous oil was distilled under reduced pressure. Nine grams of liquid boiling below 123° (20–22 mm.) was obtained. Approximately 10 g. of high-boiling liquid was left in the distilling flask.

Phenylacetone was recovered from the distillate by making the sodium bisulfite addition product, filtering, decomposing the addition product with sodium carbonate solution and steam distilling as long as any oil distilled. The distillate was extracted with ether, the ether solution dried over anhydrous magnesium sulfate and the ether distilled on a steam-bath. The phenylacetone was distilled under reduced pressure, b. p. 108–114° at 20–22 mm.; yield, 6.5 g. or 32%. The semicarbazone melted at 188°.²

Several variations of this procedure were tried in an effort to increase the yield. The yield was decreased by

(a) decreasing the time of refluxing to one or two hours after the addition of the chloroacetone, (b) lowering the temperature of the reaction and allowing a longer time for its completion, (c) adding the aluminum chloride in small portions over a period of two hours to a boiling mixture of benzene and chloroacetone, and then refluxing for two hours. No change in the yield occurred when (a) the ratio of chloroacetone and aluminum chloride to benzene was increased, or (b) the ratio of aluminum chloride was increased from two equivalents to 2.5 equivalents.

CHEMISTRY LABORATORY
BOSTON UNIVERSITY
BOSTON, MASSACHUSETTS RECEIVED MARCH 14, 1940

Vapor Pressures of Trimethylphosphine, Trimethylarsine and Trimethylstibine

BY E. J. ROSENBAUM AND C. ROGER SANDBERG

We prepared pure samples of the methyl derivatives of phosphorus, arsenic and antimony for an investigation of their Raman spectra. Because of the paucity of data on the physical constants of these compounds we have measured their vapor pressures. Phosphorus methyl and antimony methyl were prepared from methylmagnesium iodide and the corresponding trichloride.¹ The crude phosphorus methyl was purified by precipitation with silver iodide,² washing thoroughly and heating gently in a vacuum to regenerate the phosphorus methyl. Arsenic methyl was prepared by a modification of the method of Renshaw and Holm.³ A small amount of arsenic trichloride was condensed on zinc methyl cooled by a carbon dioxide-acetone bath, which was slowly removed until the reaction was complete. Then the bath was replaced and more arsenic trichloride was condensed. This procedure was repeated until all of the reagents were used up. The resulting double salt was decomposed with sodium hydroxide solution, forming arsenic methyl.

In all cases the products were dried over phosphorus pentoxide and fractionated many times, the final fractionation being in a vacuum. The vapor pressures of head and tail fractions agreed to within 1 part in 500. The Raman spectra of these compounds showed no lines which could not be attributed to the compounds themselves. This, of course, is not a very sensitive criterion of purity.

The vapor pressures were measured in the range –25 to +25° with a mercury manometer and a cathetometer. The temperatures were measured

(1) Herbst and Manske, "Organic Syntheses," Vol. XVI, 1936, p. 47. Additional references on p. 50.

(2) Pickard and Kenyon, *J. Chem. Soc.*, **105**, 1124 (1914).

(1) Hibbert, *Ber.*, **39**, 160 (1908).

(2) Mann, Wells and Purdie, *J. Chem. Soc.*, 1828 (1937).

(3) Renshaw and Holm, *THIS JOURNAL*, **42**, 1468 (1920).

with a type K potentiometer and a copper-constantan thermocouple calibrated against a thermometer which had been calibrated by the Bureau of Standards. The molecular weights were determined by the vapor density method.

The measured vapor pressures could all be represented by an equation of the conventional form: $\log p = A/T + B$. The values of the constants, the average deviation of the observed from the calculated vapor pressures and the values of certain derived quantities and of the molecular weights are given in the table.

Compd.	P(CH ₃) ₃	As(CH ₃) ₃	Sb(CH ₃) ₃
A	-1518	-1456	-1697
B	7.7627	7.3936	7.7068
Av. dev., %	1	1.5	<1
B. p., °C.	37.8 ^a	49.5 ^b	78.5 ^c
ΔH_{vap} , cal.	6943	6660	7760
Trouton's constant, cal./T	22.3	20.6	22.1
Mol. wt.	Obsd.	75.5	119.0
	Calcd.	76.10	120.03

^a Previous recorded value, 40–42° (Cahours and Hofmann, *Ann.*, 104, 29 (1857)). ^b Previous recorded values, 51.9° (Renshaw and Holm, *THIS JOURNAL*, 42, 1468 (1920)); 51–53° (Dyke and Jones, *J. Chem. Soc.*, 2426 (1930)); 68–73° (G. Natta, *Chem. Zentr.*, 98, I, 416 (1927)); 74° (Paneth and Loleit, *J. Chem. Soc.*, 366 (1935)). ^c Previous recorded values, 82° (Paneth and Loleit, *ibid.*, 366 (1935)); 80.6° (Landolt, *J. prakt. Chem.*, 84, 329 (1861)).

DEPARTMENT OF CHEMISTRY
UNIVERSITY OF CHICAGO
CHICAGO, ILL.

RECEIVED MARCH 18, 1940

Hydrogen Fluoride as a Condensing Agent. XI. The Reaction of Alcohols and Ethers with Benzene¹

BY J. H. SIMONS AND S. ARCHER

Hydrogen fluoride has been found² to be an effective catalyst for alkylations in which aliphatic alcohols and ethers are used. We have now made additional studies of this reaction using primary, secondary, and tertiary alcohols and their ethers. Good yields were obtained with secondary and tertiary compounds at room temperature; but with primary compounds except benzyl alcohol and ether, 100° was necessary to obtain appreciable yields. *n*-Butyl alcohol and *n*-butyl ether both gave *s*-butylbenzene in about 20% yield. Benzyl alcohol and benzyl ether

(1) For the previous paper see Simons, Archer and Randall, *THIS JOURNAL*, 62, 485 (1940).

(2) (a) Calcott, Tinker and Weigmayr, *ibid.*, 61, 1010 (1939); (b) Simons, Archer and Passino, *ibid.*, 60, 2956 (1938).

both gave a 65–70% yield of diphenylmethane at room temperature. From the reaction of isopropyl alcohol with benzene in a mole ratio of about one to seven, four compounds were isolated: isopropylbenzene, 1,4-diisopropylbenzene, 1,2,4-triisopropylbenzene, and 1,2,4,5-tetraisopropylbenzene, in yields of 22.4, 14, 26, and 28%, respectively. The ether gave the same products in yields of 26, 24, 25, and 8%. *t*-Butyl alcohol and *t*-amyl alcohol reacted with benzene, when the mole ratios were about one to seven, to give about 40% monoalkylated and 50% dialkylated products.

Several items of interest are noted from the above experimental results. Alcohols react more readily, *i. e.*, give a good yield at lower temperature, than the corresponding chlorides. For example, secondary chlorides reacted very slowly to give low yields in a twenty-four hour reaction time at room temperature, whereas secondary alcohols or ethers gave high yields at the same temperature. Although the mechanism of the reaction is unknown, one fact is obvious and may be a contributing factor when it is known. When the chlorides are used, hydrogen chloride is evolved; and for reactions at atmospheric pressure its thermodynamic activity in the reaction mixture must equal that for the gas at one atmosphere. When alcohols or ethers are used, water is a product of the reaction; and it remains in solution in the hydrogen fluoride. Its activity in this solution is very much lower than liquid water at the same temperature. For certain mechanisms this difference would contribute to the driving force of the reaction.

The other point of interest lies in the fact that when aluminum chloride is used as the condensing agent, the chlorides react more readily than the alcohols. Reasoning from this and also from the fact that chlorides can be made from the alcohols by treatment with aluminum chloride, the formation of the chloride may be postulated as the first step in the reaction. As the ease of reaction is in the opposite order when hydrogen fluoride is used, the reaction in this case may proceed through a different mechanism.

The ease of reaction of benzyl alcohol is a strong argument against the hypothesis that an olefin is an intermediate in the reaction. Such a mechanism has been postulated by McKenna and Sowa³ for reactions between alcohols and benzene

(3) McKenna and Sowa, *ibid.*, 59, 470 (1937).

in which boron trifluoride was employed. The formation of mesitylene from toluene and methanol in the presence of aluminum chloride reported by Norris and Ingraham⁴ also supports this argument.

Calcott, Tinker, and Weinmayr^{2a} reporting condensation reactions catalyzed by hydrogen fluoride state, "Dibenzyl ether gave benzyl isocyclic compounds while benzyl alcohol polymerized to 1,2,3,4,5,6-hexaphenylcyclohexane." In our hands, both the alcohol and the ether reacted to give diphenylmethane when treated with benzene and hydrogen fluoride. At room temperature and at 100° alkylation rather than polymerization was the only reaction.

(4) Norris and Ingraham, *THIS JOURNAL*, **60**, 1421 (1938).

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Hydrogen Fluoride as a Condensing Agent. XII. Reactions of Methyl, Ethyl and Phenyl Compounds with Benzene and its Derivatives¹

BY J. H. SIMONS AND H. J. PASSINO

The use of hydrogen fluoride to promote alkylations has been shown in recent publications from this Laboratory. We are now reporting a study of its use in conjunction with a variety of reagents of potential value for methylation, ethylation, and phenylation. An alcohol, ester and halide were used in investigating each alkylation, and other reagents were used in some cases. Ethylation proceeded with a variety of substances, namely: ethyl alcohol, ethyl iodide, ethyl chlorocarbonate, ethyl acetate, and ethyl ether. Ethyl alcohol and benzene at 200° gave very high yields of ethyl- and diethylbenzenes, while the other reagents gave varying yields with benzene and toluene. Ethylene was tried at 0°, but although indications of the formation of ethylbenzene were observed no product was isolated; and the reaction was not attempted at higher temperatures. Methyl alcohol, methyl acetate, and methyl iodide failed, however, to react with benzene, toluene, or phenol to give methylated products at temperatures up to 200°. The reaction between phenol and methyl alcohol resulted in the formation of anisole, instead of alkylated phenol. Phenol, phenyl acetate, chlorobenzene, and diphenyl ether

(1) For the previous paper of this series see Simons and Archer, *THIS JOURNAL*, **62**, 1623 (1940).

all failed to give phenylated products, when treated with hydrogen fluoride and an aromatic compound at temperatures up to 200°. Acylation occurred when phenyl acetate was caused to react with benzene at 200° and some acetophenone and phenol were formed.

The formation of anisole led to the attempt at similar reactions. From a reaction between ethyl alcohol and phenol no phenetole was isolated although ethylation occurred, and phenol heated alone at 200° with hydrogen fluoride failed to give diphenyl ether. When diphenyl ether was heated alone with hydrogen fluoride at 210°, some splitting did occur as a small amount of phenol was isolated. The stability of the phenyl ethers is in marked contrast to the ease of reaction of the aliphatic ethers. Anisole has previously been made by the condensation of phenol and methyl alcohol using boron fluoride as the condensing agent.²

The failure of hydrogen fluoride to effect methylations is in contrast to the use of aluminum chloride for these reactions. Investigators³ have recently been able to methylate using methyl alcohol and aluminum chloride. Methylations by means of methyl chloride in the presence of aluminum chloride are well known.

Very little tar formation was experienced with reactions at 200° with the exception of a few experiments in which phenol was used as a reagent.

(2) Sowa, Hennion and Nieuwland, *ibid.*, **57**, 709 (1935).

(3) Norris and Ingraham, *ibid.*, **60**, 1421 (1938); Tsukervanik and Vikhrova, *J. Gen. Chem. (U. S. S. R.)*, **7**, 632-636 (1937).

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Saponins and Sapogenins. XV. The Interrelationship of Echinocystic Acid and Oleanolic Acid

BY DAVID TODD, G. H. HARRIS AND C. R. NOLLER

Previous work¹ has indicated that echinocystic acid is closely related to other triterpenoid sapogenins but no derived products identical with those from other triterpenoids have been obtained in which the carbon skeleton remained intact. It has now been found that Clemmensen reduction of norechinocystenone or norechinocystendione gives a hydrocarbon which is identical

(1) Bergsteinsson and Noller, *THIS JOURNAL*, **56**, 1403 (1934); Noller, *ibid.*, **56**, 1582 (1934); White and Noller, *ibid.*, **61**, 983 (1939).

as determined by melting and mixed melting points, optical rotation and crystal form with oleanene III, obtained by Winterstein and Stein² from oleanolic acid. Inasmuch as the preparation of both hydrocarbons involves a Clemmensen reduction which Winterstein and Stein² have shown results in a molecular rearrangement in the case of oleanene III, and both hydrocarbons are decarboxylated derivatives, it is not possible to state that echinocystic acid and oleanolic acid have exactly the same skeletons but the possibility that such is the case is very likely.

Experimental

A solution of 0.132 g. of norechinocystenone in 250 cc. of 95% ethyl alcohol was added to 5 g. of amalgamated zinc. The mixture was boiled under a reflux condenser and a slow stream (2-3 bubbles per second) of dry hydrogen chloride was passed in for thirty-six hours. The solution was poured into an equal volume of water and evaporated to 50 cc. After dilution with water to 100 cc. the mixture was extracted with ether. The ether layer was washed with dilute hydrochloric acid, sodium hydroxide and water and dried over anhydrous sodium sulfate. After removal of the ether the residue was crystallized from methyl alcohol in which it is only slightly soluble, and then from acetone to a constant melting point of 224-225°; $[\alpha]^{25}_D +31.3 \pm 3^\circ$; $c = 1.408$ in toluene, $l = 0.5$ dm.

Anal. Calcd. for $C_{29}H_{48}$: C, 87.80; H, 12.20. Found: C, 87.79; H, 12.12.

The same product as determined by melting and mixed melting points was obtained on reducing norechinocystendione by the above procedure.

Oleanylene II and oleanene III were prepared from oleanolic acid³ according to the procedures of Winterstein and Stein.² The oleanene III was crystallized twice from glacial acetic acid and then from acetone until its melting point was 216.5-220.5°; $[\alpha]^{25}_D +30.7 \pm 3^\circ$; $c = 2.082$ in toluene, $l = 0.5$ dm.

A mixture with an equal part of the hydrocarbon obtained from norechinocystenone, m. p. 218-221.5°⁴, melted at 216.5-221°. The melting points of the mixture and of the two pure products were taken simultaneously in the same bath. Slow evaporation of solutions of the hydrocarbons from both sources gave well formed hexagonal plates which were indistinguishable under a lens. The properties of oleanene III recorded by Winterstein and Stein² are m. p. 225-226°; $[\alpha]^{20}_D +30.1$, $c = 1.76$ in chloroform.

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(2) Winterstein and Stein, *Ann.*, **503**, 223 (1933).

(3) We are indebted to Dr. C. N. Anderson of Lever Brothers Company, Cambridge, Mass., for a supply of crude barium oleanolate derived from clove oil residues.

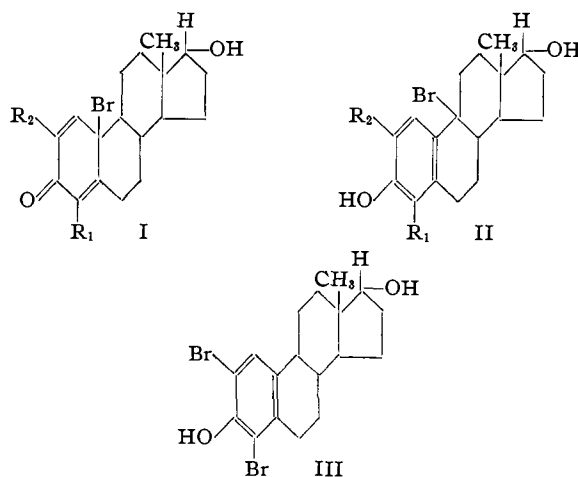
(4) The maximum melting point of 224-225° is obtained only with difficulty and large losses, so that the lower melting product was used for comparison purposes.

2,4-Dibromo- α -oestradiol

BY ROBERT BURNS WOODWARD

As evidenced by the investigations of Doisy,¹ Butenandt,² and Marrian,³ the phenolic sex hormones are extensively halogenated under the conditions obtaining in the determination of the iodine number with the Rosenmund-Kuhnmann reagent. The number of halogen atoms consumed by one mole of the hormone varied widely with the conditions. Although both Butenandt and Doisy isolated halogen-containing products, these were insufficiently characterized and until further investigation must be regarded as of equivocal nature. Only in the case of equilenin has a definitely pure halogen-substituted hormone been prepared, *viz.*, monobromoequilenin, prepared by Girard, *et al.*,⁴ likewise by the action of the Rosenmund-Kuhnmann reagent. On the other hand, Marrian and Haslewood³ found that the methyl ethers of the hormones consumed approximately one mole of halogen quite smoothly in the iodine number determinations, and this result was confirmed by the isolation of monobromoestrone methyl ether and monobromoestriol methyl ether.

In the course of a related investigation, we have found that α -oestradiol is converted smoothly and almost quantitatively into a dibromoestradiol on standing overnight in alcohol solution with the theoretical quantity of N-bromoacetamide. Since no halogen was removed on treatment with alcoholic silver nitrate or potassium hydroxide, the product was not 2-(or 4)-10-dibromo- $\Delta^{1,4}$ -oestra-



(1) Thayer, Levin and Doisy, *J. Biol. Chem.*, **91**, 791 (1931).

(2) Butenandt, Störmer and Westphal, *Z. physiol. Chem.*, **208**, 149 (1932).

(3) Marrian and Haslewood, *J. Soc. Chem. Ind.*, **51**, 277T (1932).

(4) Girard, Sandulesco, Fridenson and Rutgers, *Compt. rend.*, **195**, 981 (1932).

dienon-3-ol-17 (I, R_1 or $R_2 = H$ or Br), nor the corresponding pseudo-bromide, 2-(or 4)-9-dibromo- α -oestradiol (II, R_1 or $R_2 = H$ or Br). Consequently our product has the only alternative structure, 2,4-dibromo- α -oestradiol (III).

It is highly probable that the introduction of bromine by bromoacetamide will be of service in the case of other phenolic compounds which defy clean-cut halogenation by the more usual methods.

Experimental

One-half gram of α -oestradiol and 0.54 g. of recrystallized N-bromoacetamide were dissolved in 40 cc. absolute alcohol and the reaction mixture was allowed to stand at room temperature for about eighteen hours. By this time the originally faintly yellow solution had become almost colorless. The alcohol solution was evaporated on the hot plate to about one-third of its volume and allowed to cool, when the brominated product was precipitated by the addition of water. On crystallization from alcohol-water, 0.54 g. of 2,4-dibromo- α -oestradiol was obtained as beautiful colorless rosetts of needles, melting at 215.5–216.5° (cor.) to an emerald-green liquid, with gas evolution. From the filtrate another 0.2 g. of the product was obtained by dilution with water and recrystallization.

*Anal.*⁵ Calcd. for $C_{18}H_{22}O_2Br_2$: C, 50.20; H, 5.14. Found: C, 50.10; H, 5.13.

No turbidity developed when an alcoholic silver nitrate solution of the substance was allowed to stand for twenty hours, and the material was recovered unchanged after solution for an hour in alcoholic potassium hydroxide.

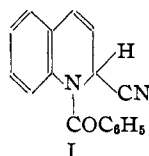
(5) Analysis by D. M. Bowen.

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The Formation of Reissert's Compounds in Non-aqueous Media

BY ROBERT BURNS WOODWARD

By shaking quinoline with benzoyl chloride and an aqueous solution of potassium cyanide, Reissert¹ prepared 1-benzoyl-1,2-dihydroquinaldonitrile (I).



This compound was remarkable in that it split on hydrolysis into benzaldehyde and quinaldonic acid. The availability of a considerable number of substances differing from Reissert's original

(1) Reissert, *Ber.*, **38**, 1610 (1905).

compound only in the nature of the acyl group would afford the possibility of a new general method for the reduction of carboxylic acids to aldehydes. However, the ready hydrolysis of many aliphatic acid chlorides vitiates Reissert's original method.

In an attempt to surmount this difficulty, we have investigated the formation of Reissert's compound in non-aqueous media. Dieckmann and Kämmerer² observed the formation of the substance in unstated amount while investigating the action of quinoline and other tertiary bases in accelerating the formation of benzoyl cyanide from benzoyl chloride and hydrogen cyanide in ether solution. We found that the formation of acyl cyanide was largely preponderant when benzoyl chloride was used and exclusive in the case of acetyl chloride, either on conducting the reaction in ether or other inert solvents, or on using quinoline as its own solvent. No reaction was observed when acetonitrile, benzonitrile, ether, dioxane, acetone or chloroform was substituted for water in the original procedure of Reissert.

On the other hand, quinoline and potassium cyanide reacted smoothly with either benzoyl or cinnamoyl chloride³ in liquid sulfur dioxide to give the corresponding aroyl dihydroquinaldonitrile in excellent yield. The use of acetyl chloride, however, led to the formation of intractable dark mixtures from which no pure product could be isolated.

The striking difference in this case between liquid sulfur dioxide and the organic solvents is in consonance with the probable ionic character of the reaction.

Experimental

1-Benzoyl-1,2-dihydroquinaldonitrile.—Ten grams of benzoyl chloride, 10 g. of quinoline (freshly distilled *in vacuo*) and 7 g. of potassium cyanide were placed in a pressure bottle. After approximately 35 cc. of liquid sulfur dioxide had been added, the bottle was sealed and allowed to stand with occasional shaking for twenty-four hours. The sulfur dioxide was then allowed to evaporate, and the residue washed successively with water, dilute hydrochloric acid and ether. On crystallization from alcohol of the white powder so obtained, 16 g. of 1-benzoyl-1,2-dihydroquinaldonitrile separated as glistening needles, m. p. 154–155°, of a very faint greenish tinge which was lost on two further crystallizations.

(2) Dieckmann and Kämmerer, *ibid.*, **40**, 3737, Note 2 (1907).

(3) Cf. Sugawara and Tsuda, *J. Pharm. Soc. Japan*, **56**, 557 (1936); *C. A.*, **32**, 5836 (1938). The original is here incorrectly reported as appearing on p. 103.

