

the paper is dried and sprayed with a freshly prepared solution of alkaline hydroxylamine (made by mixing equal volumes of *N* methanolic hydroxylamine hydrochloride and 1.1 *N* methanolic potassium hydroxide). After drying in air for about 10 minutes, the paper is sprayed (wetting of the paper should be avoided) with an aqueous solution containing 1–2% ferric chloride and 1% hydrochloric acid. A blue or mauve color is quickly formed in those areas containing the esters or lactones or ester lactones.

TABLE I

R_F VALUES OF CERTAIN LACTONES AND ESTERS

| Compound | R _F |
|---|----------------|
| (a) Using 1-butanol-ethanol-water ¹⁰ | |
| D-Xylono- γ -lactone | 0.41 |
| L-Rhamnono- γ -lactone | .50 |
| D-Glucono- γ -lactone | .32 |
| D-Galactono- γ -lactone | .35 |
| D-Mannono- γ -lactone | .25 |
| D-Glucoheptono- γ -lactone | .13 |
| D-Glucono- δ -lactone | .22 |
| Methyl β -D-glucofururonoside | .30 |
| Mannitol hexaacetate | .85 |
| Arabitol pentaacetate | .85 |
| (b) Using methyl ethyl ketone-water ¹¹ | |
| Mannosaccharo-1,4-3,6-dilactone | 0.60 |
| 3-Methyl-D-erythrono- γ -lactone | .73 |
| 2,3,5-Trimethyl-L-rhamnono- γ -lactone | 1.00 |
| 2,3,5-Trimethyl-D-galactono- γ -lactone | 0.90 |
| 3,4,6-Trimethyl-D-mannono- δ -lactone | .86 |
| 2,4-Dimethyl-D-galactosaccharo-3,6-lactone methyl ester | .91 |
| 2,3,4-Trimethyl-D-glucosaccharo-1,5-lactone methyl ester | .94 |
| 2,3,5-Trimethyl-D-glucosaccharo-1,4-lactone methyl ester | 1.00 |
| (c) Using methyl ethyl ketone-petroleum ether-water ¹¹ | |
| 2,3,5-Trimethyl-L-rhamnono- γ -lactone | 0.88 |
| 2,3,5-Trimethyl-D-galactono- γ -lactone | .58 |
| 2,3,5-Trimethyl-D-glucosaccharo-1,4-lactone methyl ester | .88 |
| 2,4-Dimethyl-D-galactosaccharo-3,6-lactone methyl ester | .59 |

This hydroxamic acid test can also be used for the detection of certain amides and methylamides of sugar acids and esters of amino acids.

Free acids are not directly detectable⁹ but by hanging the chromatograms for 10 to 15 minutes in a closed jar containing a dish of ethereal diazomethane, the acids are converted into methyl esters and the latter may then be detected as described above.

With this hydroxamic acid test it has been shown that butanol-ethanol-water can be employed for the separation of certain sugar lactones. This particular solvent is not convenient for the separation of the acetates of sugar alcohols since their *R_F* values are very similar. The test has shown that methylated lactones and methylated ester lactones may be separated like the methyl sugars with butanol-ethanol-water,¹⁰ with methyl ethyl

ketone¹¹ and with methyl ethyl ketone-petroleum ether (see Table I).

(11) L. Boggs, L. S. Cuendet, I. Ehrenthal, R. Koch and F. Smith, *Nature*, **166**, 520 (1950).

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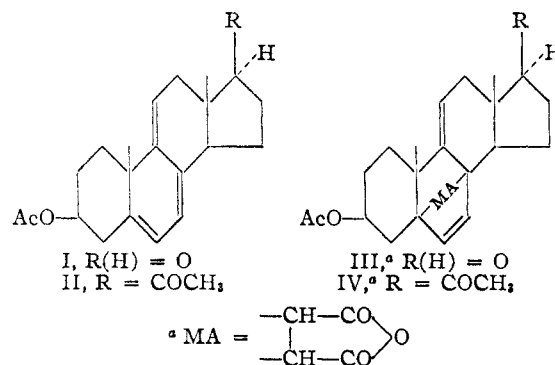
ST. PAUL, MINNESOTA

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$\Delta^{5,7}$ -Steroids. XI.¹ The Maleic Anhydride Adduct Products of $\Delta^{5,7,9(11)}$ -Steroidal Hormones

BY ROSE ANTONUCCI, SEYMOUR BERNSTEIN, DOMINIC J. GIANCOLA AND KARL J. SAX

In Paper VII² of this series the preparation of $\Delta^{5,7,9(11)}$ -androstatriene-3 β -ol-17-one acetate (I) and $\Delta^{5,7,9(11)}$ -pregnatriene-3 β -ol-20-one acetate (II) was described.



In this note, we wish to record the preparation of the maleic anhydride adduct products of these two trienes, and also to describe the pyrolysis of one of the adducts.³ Compounds I and II readily reacted with maleic anhydride in xylene⁴ at reflux temperature, and III and IV were obtained in good yield.

The maleic anhydride adduct (IV) of $\Delta^{5,7,9(11)}$ -pregnatriene-3 β -ol-20-one acetate was pyrolyzed in such a manner that the pyrolysis and evaporative distillation were carried out simultaneously (0.16 mm. pressure,⁵ 200–313°). These conditions led to co-distillation of a considerable amount of IV with the desired triene (II). Compound II was easily separated from IV by treatment of the distillate with ether; the adduct product was insoluble. The triene (II) so obtained was identical with an authentic sample of II.

Experimental

Maleic Anhydride Adduct (III) of $\Delta^{5,7,9(11)}$ -Androstatriene-3 β -ol-17-one Acetate.—A mixture of 1 g. of $\Delta^{5,7,9(11)}$ -androstatriene-3 β -ol-17-one acetate (I), 0.4 g. of maleic anhydride and 50 ml. of xylene was refluxed for 18 hours. The solvent and excess maleic anhydride were removed *in*

(1) Paper X, R. Antonucci, S. Bernstein, D. J. Giancola and K. J. Sax, *J. Org. Chem.*, in process of publication.

(2) R. Antonucci, S. Bernstein, D. J. Giancola and K. J. Sax, *ibid.*, **16**, 1159 (1951).

(3) The addition of maleic anhydride to a $\Delta^{5,7,9(11)}$ -triene (dehydroergosteryl acetate), and the pyrolysis of the resulting adduct have been described previously; see Windaus and Lüttringhaus, *Ber.*, **64**, 850 (1931), and Honigsmann, *Ann.*, **508**, 89 (1934).

(4) Benzene was not used in place of xylene in the reaction, but probably would be successful; see Bergmann and Stevens, *J. Org. Chem.*, **13**, 10 (1948).

(5) Subsequently, experience in this Laboratory with other similar compounds has shown that a pressure of 1–2 mm. would be preferable for this type of pyrolysis.

(9) Cf. G. Brante, *Nature*, **163**, 651 (1949).

(10) L. Hough, J. K. N. Jones and W. H. Wadman, *ibid.*, **163**, 448 (1948); *J. Chem. Soc.*, 2511 (1949).

vacuo. The residue was worked with ether, and filtered. This gave 1.1 g. of crude adduct product, m.p. 230° unsharp, dec., and with previous softening. Three recrystallizations from dilute acetic acid gave 0.57 g. of III, m.p. 244–246.5° dec., $n_{\text{max}}^{\text{abs. alc.}}$ none (possible maximum at 267 m μ , ϵ 500), $[\alpha]_D^{25} +124^\circ$, $[\alpha]_{\text{H}_2\text{O}}^{25} +190^\circ$ (19 mg. in 2 ml. of chloroform solution, 1-dm. semi-micro tube, gave $\alpha_D +1.18^\circ$, $\alpha_{\text{H}_2\text{O}} +1.80^\circ$), $\alpha_{\text{H}_2\text{O}}/\alpha_D$ 1.53, $[M]_D +326$.

*Anal.*⁷ Calcd. for $\text{C}_{25}\text{H}_{32}\text{O}_8$ (424.47): C, 70.74; H, 6.65. Found: C, 70.52; H, 6.83.

Maleic Anhydride Adduct (IV) of $\Delta^{5,7,9(11)}$ -Pregnatriene-3 β -ol-20-one Acetate.—A mixture of 3.0 g. of $\Delta^{5,7,9(11)}$ -pregnatriene-3 β -ol-20-one acetate (II), 1.2 g. of maleic anhydride and 150 ml. of xylene was refluxed for 19.5 hours. The product was worked up as above, wt. 3 g., m.p. 263–264°, dec. above m.p. Recrystallization from acetic acid gave 2.53 g. of IV, m.p. 264–265° dec. above m.p. From the mother liquors there was obtained an additional 100 mg. of IV, m.p. 263° dec. above m.p.; $[\alpha]_D^{25} +117^\circ$, $[\alpha]_{\text{H}_2\text{O}}^{25} +151^\circ$ (22.1 mg. in 2 ml. of chloroform solution, 1-dm. semi-micro tube, gave $\alpha_D +1.29^\circ$, $\alpha_{\text{H}_2\text{O}} +1.67^\circ$), $\alpha_{\text{H}_2\text{O}}/\alpha_D$ 1.29, $[M]_D +529$.

Anal. Calcd. for $\text{C}_{27}\text{H}_{32}\text{O}_8$ (452.53): C, 71.66; H, 7.13. Found: C, 71.48; H, 7.10.

Pyrolysis of the Maleic Anhydride Adduct (IV) of $\Delta^{5,7,9(11)}$ -Pregnatriene-3 β -ol-20-one Acetate.—Compound IV (0.5 g.) was pyrolyzed and evaporatively distilled in the following manner. A pressure of 0.18 mm. was maintained. The material was heated for about 5 hours from room temperature to 313°. The solid sublimate which appeared at 220°, became considerable at 250°. The sublimate was slurried with ether, and the insoluble starting material (IV) was removed by filtration; wt. 0.20 g., m.p. 261–264° dec. The ether filtrate was washed with water, dried, and concentrated. The solution was allowed to stand at room temperature overnight. During this time a very small amount of material was deposited as a film on the walls of the flask. It was separated by decantation. The ether decantate was concentrated with simultaneous addition of methanol until all of the ether was removed. Addition of water gave 60 mg. of impure II. Recrystallization from dilute methanol gave pure II, wt. 20 mg., m.p. 143–144°, $n_{\text{max}}^{\text{abs. alc.}}$ 312, 324 and 339 m μ , ϵ 10800, 12200, 7600, respectively.

(6) All melting points are uncorrected and were determined with uncalibrated Anschütz thermometers.

(7) We are indebted to Messrs. Louis M. Brancone, Samuel M. Modes and Edward B. Ruffing, Jr., for the microanalytical data.

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The Reaction of Benzylmagnesium Chloride and Dibenzylmagnesium with Pyridine

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In 1932 Bergmann and Rosenthal¹ reported that dibenzylmagnesium reacts with pyridine to form 2-benzylpyridine. In 1946 Veer and Goldschmidt² disputed this work and claimed that 4-benzylpyridine is formed exclusively and not the 2-isomer. The picrates of both of these isomers have about the same melting point (140–142°), and hence care must be exercised in identifying them.

Since the reaction of quinoline with dibenzylmagnesium is reported to yield largely the 2-isomer,^{1,3} it seemed likely that pyridine should give at least a mixture of the 2- and 4-benzyl isomers and

not exclusively one or the other as claimed by the previous workers.^{1,2} This was actually found to be the case although the 4-isomer was formed in larger amounts. The addition of dioxane to the Grignard solution did not seem to alter the ratio of the isomers; however, its presence did greatly increase the over-all yield of the benzylpyridines. This is in keeping with the observations made on quinoline.³

The 2- and 4-benzylpyridines were separated by carefully fractionating them through an efficient column. Mixed melting points of the picrates of these isomers and those obtained from authentic 2- and 4-benzylpyridine prepared by the method of Crook and McElvain⁴ completed the identification.

Experimental

Authentic 2- and 4-Benzylpyridine.—The method used for preparing these compounds was essentially that described by Crook and McElvain.⁴ The reaction product was fractionated through a Todd column with a vacuum jacketed 5-mm. wire spiral. Approximately 25.5 g. of the 2-isomer was collected boiling 275–278°₅₅ at 753 mm., $n_{\text{max}}^{20,55}$ 1.5792₅₅; d_{20}^{25} 1.055₅₅ and 5.1 g. of the 4-isomer boiling 284–287°₅₅ at 753 mm., $n_{\text{max}}^{20,55}$ 1.5810; d_{20}^{25} 1.062₅₅.

A picrate of the 2-benzylpyridine prepared in the usual manner melted at 141–142° (lit. 141.5–142°²). A picrate of the 4-isomer melted at 140.5–141° (lit. 141–142°²). A mixed melting point was depressed to 115–118°.

Reaction of Benzylmagnesium Chloride with Pyridine.—In a one-liter three-neck flask fitted with a reflux condenser, stirrer and dropping funnel was placed 24.3 g. (1.0 g. atom) of magnesium turnings and 65 ml. of anhydrous ether. To this was added dropwise and with stirring a solution of 126 g. (1.0 mole) of benzyl chloride in 185 ml. of anhydrous ether. When all the benzyl chloride solution had been added, stirring was continued for 30 minutes. Then 54 g. (0.67 mole) of freshly distilled anhydrous pyridine was added dropwise. A vigorous reaction set in. When all the pyridine had been added, the mixture was refluxed on a steam-cone for 24 hours with constant stirring. After the mixture had cooled it was immersed in an ice-bath, and an ice-cold 20% ammonium chloride solution was added dropwise to decompose the Grignard complex. The aqueous hydrolyzate was extracted with ether and the ether extracts were in turn treated with 5% sulfuric acid. This acid extract was neutralized with 5% potassium hydroxide and this solution was extracted with ether. These final ether extracts were dried over Drierite, and then the solvent was removed. The residual liquid was distilled through a Claisen head, and the fraction boiling over 100° (15 mm.) was collected. This was then distilled through a Todd column with a vacuum jacketed 5-mm. wire spiral. Approximately 2 g. of the 2-isomer boiling 274–277° at 759 mm. was obtained, n_{max}^{20} 1.5790 and 6 g. of the 4-isomer boiling 277–279° at 759 mm., n_{max}^{20} 1.5810. The over-all yield of benzylpyridines was about 8% of which about 20% was estimated to be the 2-isomer and 80% the 4-isomer. The identity of these isomers was established by mixed melting points with authentic samples of the picrates.

Reaction of Dibenzylmagnesium with Pyridine.—The benzylmagnesium chloride was prepared exactly as described before. Then 150 ml. of freshly purified⁵ dioxane was added to the Grignard reagent and the mixture was stirred for 30 minutes. To this suspension was added dropwise 64 g. (0.8 mole) of anhydrous pyridine after which the mixture was refluxed on a steam-cone for 24 hours with constant stirring. The reaction was worked up as described before and the fractionation again was made through the Todd column. Approximately 9 g. of the 2-isomer and 33 g. of the 4-isomer were obtained with identical physical constants as those shown above. This represents a total yield

(1) E. Bergmann and W. Rosenthal, *J. prakt. Chem.*, [2] **135**, 267 (1932).

(2) W. L. C. Veer and St. Goldschmidt, *Rec. trav. chim.*, **65**, 793 (1946).

(3) H. Gilman and G. C. Gainer, *THIS JOURNAL*, **71**, 2327 (1949).

(4) K. E. Crook and S. M. McElvain, *ibid.*, **52**, 4007 (1930).

(5a) See P. C. Teague, *ibid.*, **69**, 714 (1947); also E. H. Huntress and H. C. Walter, *ibid.*, **70**, 3704 (1948).

(5b) A. Tschitschibabin, *J. Russ. Phys. Chem. Soc.*, **33**, 255 (1901).

(6) L. F. Fieser, "Experiments in Organic Chemistry," D. C. Heath and Co., New York, N. Y., 1941, p. 369.