with two 50-ml. portions of benzene. The solvents were combined, and evaporated to one-half volume on the steam-bath. On cooling a precipitate formed which was recrystallized from alcohol. Yield was 12.5%; m.p. 151.5°.

Anal.[9] Calcd. for $C_{20}H_{22}N_2O_2$: C, 74.48; H, 6.90. Found: C, 74.30; H, 6.82.

p-Dimethylaminophenyl-6-ethoxyquinaldylcarbinol.—The above procedure was followed. The mixture was refluxed for two hours prior to the hydrolysis until the precipitate turned yellow. Yield was 24.9%; m.p. 153.6°.

Anal.[9] Calcd. for $C_{21}H_{24}N_2O_2$: C, 74.94; H, 7.21. Found: C, 74.69; H, 7.33.

Styryls.—The carbinols were dehydrated to the respective styryl derivatives by boiling in 2 *M* hydrochloric acid for one hour; the carbinol dehydrated *ca.* 99%, the 6-methoxy *ca.* 75% and the 6-ethoxy *ca.* 50%. Mixed melting points showed no depression with the corresponding styryl compounds synthesized by procedures in the literature.[10,11]

Acknowledgment.—We should like to thank Dr. H. S. Mosher for helpful comments in the preparation of this manuscript.

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DEPARTMENT OF PHARMACOLOGY AND THERAPEUTICS
STANFORD UNIVERSITY SCHOOL OF MEDICINE
SAN FRANCISCO 15, CALIFORNIA

A Stable Chloroform Adduct of 11-Epi-17α-hydroxycorticosterone

BY HELMUTH CORDS

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In view of the recent interest in Δ^4-pregnene-11α,17α,21-triol-3,20-dione,[1-7] the 11-epimer of the most important adrenal secretory product 17α-hydroxycorticosterone, we wish to describe a stable adduct of this substance with chloroform. The adduct is formed readily when the steroid is crystallized from chloroform, in which it is very difficultly soluble. It forms colorless platelets, m.p. 206–209°, $[\alpha]^{23}D$ +88 ± 2° (0.5% in ethanol) (calculated for an adduct containing one mole of chloroform: +87.8°).[8] The substance was analyzed after drying *in vacuo* (1 mm.) at 100° for two hours. *Anal.* Calcd. for $C_{21}H_{30}O_5 \cdot CHCl_3$: C, 54.83; H, 6.49; Cl, 22.08. Found: C, 54.92; H, 6.59; Cl, 21.99.

The infrared spectrum of the chloroform adduct, sampled as nujol mull, differs from that of the free 11-epi-17α-hydroxycorticosterone in that it contains a deep band at 13.28 μ, characteristic for chloroform. Moreover, the C_{21}–carbonyl band shifted from 5.83 μ for the free steroid to 5.88 μ for the adduct.

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(8) The specific rotation of the free steroid is +117° (0.5% in ethanol).

Its low solubility in chloroform, its well formed crystal shape and its stability to heat and vacuum render the chloroform adduct very suitable for purification of 11-epi-17α-hydroxycorticosterone. Microbiological synthesis of Δ^4-pregnene-11α,17α,21-triol-3,20-dione[1] generally yields slightly colored material. Recrystallization of this material from chloroform produces an almost colorless chloroform adduct (well formed platelets). The steroid can be readily freed of chloroform by crystallization from the lower alcohols, acetone or ethyl acetate.

Δ^4-Pregnene-11α,17α,21-triol-3,20-dione 11,21-diacetate[2-6,9,10] forms a similar complex with chloroform, whereas the corresponding 21-monoacetate, which was obtained in crystalline form from acetic acid–water, crystallizes from chloroform without solvate formation.

Another adduct has been observed with 5,16-pregnadiene-3β-ol-20-one and chloroform. One mole of chloroform is attached here to two moles of the steroid. This adduct, colorless platelets, is obtained by crystallization of the steroid from chloroform, and is stable to a vacuum of 1 mm., yet labile to heat. The melting point is unchanged from that of the free compound. The optical rotation, $[\alpha]^{23}D$ 20 ± 2° (0.5% in ethanol) differs, as expected, 19% from that of the free steroid. *Anal.* Calcd. for $C_{21}H_{30}O_2 \cdot {}^1/_2CHCl_3$: C, 69.02; H, 8.22; Cl, 14.22. Found: C, 69.27; H, 8.34; Cl, 14.21.

The adduct shows the strong band at 13.32 μ, characteristic for chloroform, and three additional bands at 10.54, 11.78 and 11.99 μ. The C_{20}-carbonyl shifted from 6.05 to 6.02 μ in the adduct, and four minor bands of the free steroid (8.62, 10.45, 12.41 and 12.52 μ) appeared at slightly lower wave lengths. The band at 9.86 μ is missing in the complex.

$\Delta^{5,16}$-Pregnadiene-3β-ol-20-one acetate does not form a similar adduct.

I am indebted to Dr. N. Coy for the spectrometric measurements and to Mr. J. Alicino for the microanalytical determinations.

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THE SQUIBB INSTITUTE FOR MEDICAL RESEARCH
E. R. SQUIBB AND SONS
DIVISION OF MATHIESON CHEMICAL CORPORATION
NEW BRUNSWICK, NEW JERSEY

Phenyl Esters

BY ALFRED R. BADER AND ANTHONY D. KONTOWICZ

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The preparations of phenyl esters have hitherto been rather tedious as they have involved the use of acid chlorides, acid anhydrides or $POCl_3$, or in the case of phenyl esters of reactive acids such as acrylic[1] or methacrylic acid,[2] somewhat circuitous synthetic routes. Phenyl esters even of reactive acids have recently been prepared with trifluoro-

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TABLE I

PHENYL ESTERS

Acid	Formula	M.p., °C.	Solvent of cryst.	Analyses, % Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found
Benzoic	$C_{13}H_{10}O_2$	70–71					
Diglycolic	$C_{16}H_{14}O_5$	73–75	Heptane–toluene	67.12	67.45	4.93	4.91
Levulinic	$C_{11}H_{12}O_3$	32	Methanol–water	68.73	68.92	6.30	6.46
Maleic[a]	$C_{16}H_{12}O_4$	71–72	Heptane–toluene	71.63	72.01	4.51	4.72
Methacrylic[b]	$C_9H_{10}O_2$	17					
Phthalic[a,c]	$C_{20}H_{14}O_4$	73–74	Toluene–acetone				
Salicylic	$C_{13}H_{10}O_3$	42–43	Methanol				
Stearic[d]	$C_{24}H_{40}O_2$	51–52	Toluene				

[a] The anhydride was used as the starting material. [b] This agreed in b.p. and n_D with the lit. values,[2] and crystallized easily in the ice-box. [c] E. Huntress and S. P. Mulliken, "Identification of Pure Organic Compounds," John Wiley and Sons, Inc., New York, N. Y., 1941, p. 291. [d] *Ibid.*, p. 287.

acetic anhydride[3] which is not, however, readily accessible.

Phenyl esters of most carboxylic acids can be prepared easily and in good yields simply by heating the free acids with phenol in the presence of polyphosphoric acid on the steam-bath. In all cases tried the phenyl esters were easily separated from unreacted starting materials through their insolubility in dilute aqueous alkali. All solid phenyl esters crystallized beautifully, and we are tempted to suggest them as derivatives for the characterization of acids.

Experimental

Table I lists the esters prepared.

In a representative experiment, 50 g. of salicylic acid, 150 g. of phenol and 100 g. of polyphosphoric acid (Victor Chemical Co.) were stirred and heated on the steam-bath for 24 hours. The cooled mixture was diluted with water, extracted with toluene; and the toluene solution was extracted with aqueous sodium bicarbonate solution from which 14 g. of unreacted salicylic acid was recovered on acidification. The toluene solution was washed, stripped *in vacuo* and the residue distilled to yield unreacted phenol and 53 g. (95% based on unrecovered salicylic acid) of phenyl salicylate, b.p. 108–110° at 0.4 mm., which crystallized in the receiver. There was no flask residue. One crystallization from methanol yielded 49 g. of pure product melting at 42–43°.

Substantial quantities of polyphosphoric acid are desirable. In the preparation of diphenyl phthalate, phenolphthalein also was formed, and during the separations of phenyl levulinate and phenyl methacrylate, the aqueous alkali extracted products other than only starting materials. The yields (based on unrecovered organic acid) of phenyl levulinate and phenyl methacrylate were 35 and 55%, respectively, and in the other preparations yields ranged from 85 to 98%.

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THE RESEARCH LABORATORIES
THE PAINT DIVISION
THE PITTSBURGH PLATE GLASS COMPANY
MILWAUKEE, WISCONSIN

Preparation of 1-Methyl-4-phenyl-4-(aminomethyl)- and 1-Methyl-4-phenyl-4-(methylaminomethyl)-piperidine

BY F. F. BLICKE AND EU-PHANG TSAO

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When 1-methyl-4-phenyl-4-cyanopiperidine was heated with sodium and ethanol, Bergel, *et al.*,[1] obtained 1-methyl-4-phenylpiperidine. Provinciala[2] stated that sodium and ethanol, at 0°, reduced the 4-cyano to the corresponding 4-aminomethyl derivative which was claimed to be an active analgesic; a hydrochloride was obtained which melted at 190–192°. Kwartler and Lucas[3] prepared the 4-aminomethyl compound in 66.7% yield by hydrogenation of the 4-cyano derivative, in the presence of Raney nickel and ammonia, under 500 pounds pressure. According to them,[3a] the compound has negative analgesic activity; their dihydrochloride melted at 287–288°.

We found also that when 1-methyl-4-phenyl-4-cyanopiperidine was heated with sodium and ethanol, the cyano radical was replaced by hydrogen. The hydrochloride of the 1-methyl-4-phenylpiperidine obtained melted at 191–193°.[4] However, reduction with lithium aluminum hydride yielded the 4-aminomethyl compound in 83% yield; the dihydrochloride melted at 291–292°.

Formylation of the 4-aminomethyl derivative with chloral[5] produced the N-formyl derivative which was reduced with lithium aluminum hydride to the 4-methylaminomethyl compound.

Tested for analgesic activity in the Parke, Davis and Company laboratories under the direction of Dr. C. V. Winder, both the 4-aminomethyl and the 4-methylaminomethyl compound were found to be inactive as analgesics at the aspirin dose level.

Experimental

1-Methyl-4-phenyl-4-(aminomethyl)-piperidine.—1-Methyl-4-phenyl-4-cyanopiperidine (20.0 g.), dissolved in 50 cc. of ether, was reduced by adding the solution to 3.0 g. of lithium aluminum hydride, dissolved in 150 cc. of ether, in the usual manner. After the addition of 6 cc. of water, the mixture was filtered. From the filtrate there was obtained 16.6 g. (83%) of the desired product; b.p. 109–112° (1 mm.).[6]

The dihydrochloride precipitated when an ethereal solution of the base was treated with hydrogen chloride; m.p. 291–292° (dec.) after recrystallization from methanol.[7]

Anal. Calcd. for $C_{13}H_{22}N_2Cl_2$: N, 10.11; Cl, 25.63. Found: N, 10.37; Cl, 25.70.

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(4) O. Eisleb (*Ber.*, **74**, 1433 (1941)), who decarboxylated 1-methyl-4-phenylpiperidine-4-carboxylic acid, stated that the hydrochloride melted at 196–197°.

(5) F. F. Blicke and C. J. Lu, THIS JOURNAL, **74**, 3933 (1952).

(6) Ref. 3, b.p. 170–172° (12.5 mm.).

(7) Ref. 3, m.p. 287–288°.