dry nitrogen. This treatment gave 596 mg. of a clear, neutral oil which was chromatographed in benzene on 18 g. of Fisher reagent grade silicic acid previously wetted with *n*-pentane. Elution (employing 50-ml. eluates throughout) was initiated with benzene, followed by benzene–ether mixtures in which the increment of ether added each time the solvent was changed amounted to 2.5. Benzene–ether (95.0–5.0 and 92.5–97.5) eluates furnished 422 mg. (62%) of crystalline 11-deoxycorticosterone (III) which melted at 138–142°. One recrystallization from ether gave pure III, m.p. 141.5–142.5° cor., $[\alpha]^{25}D$ +184 ± 6° (*c* 0.20, $CHCl_3$), λ_{max}^{alc} 240 mμ (4.3).

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2-Guanidino-4(5)-*p*-chlorophenylimidazoles

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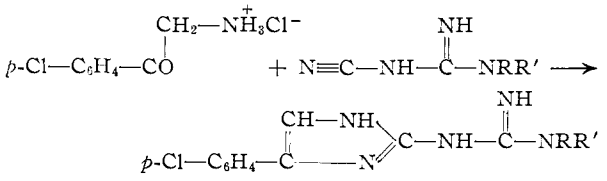
In continuation of a program of synthesis of heterocyclic guanidines,[1,2] imidazole analogs have been prepared as indicated



Although successful condensations were effected with derivatives of dicyandiamide, we were unable to obtain satisfactory condensations from *p*-chlorophenacylamine hydrochloride with cyanamide, dicyandiamide or sodium dicyanamide.

In addition, *p*-chlorophenacylamine hydrochloride was converted into 2-mercapto-4(5)-*p*-chlorophenylimidazole by the procedure of Wohl and Marckwald.[3] However, a marked improvement in yields was obtained in this reaction by using glacial acetic acid in place of aqueous ethanol as the reaction medium. Oxidation of the mercapto compound to 4(5)-*p*-chlorophenylimidazole was effected in rather poor yield with nitric acid.

Experimental

***p*-Chlorophenacylamine hydrochloride** has been prepared[4] by reduction of isonitroso-*p*-chloroacetophenone. For the present work it was prepared conveniently by the procedure of Long and Troutman[5] and melted with decomposition at 290°.[4]

N-Cyano-N′-*p*-hydroxyphenylguanidine was prepared from *p*-aminophenol and sodium dicyanamide according to published procedure.[6] After crystallization from butyl alcohol and from butyl cellosolve, it melted at 269–270°.

Anal. Calcd. for $C_8H_8N_4O$: C, 54.6; H, 4.6; N, 31.8. Found: C, 54.2; H, 4.4; N, 31.7.

2-Guanidino-4(5)-*p*-chlorophenylimidazoles all were prepared by a reasonably standardized procedure in which *p*-chlorophenacylamine hydrochloride and the appropriate cyanoguanidine[6] were mixed in equimolar (usually 0.01 mole) amounts in a test-tube and placed in an oil-bath at 180°. The mixture fused and evolved steam after which it was maintained at 150–200° for about 30 minutes and allowed to cool. The resulting brown glassy material was extracted with acetone which removed tarry matter. The residual hydrochlorides[7] of the desired products were dissolved in hot water and the free bases liberated with ammonium hydroxide, filtered and crystallized to constant melting point. The yields of purified material, which were in all cases about 30%, cannot be considered particularly significant because of losses encountered in finding suitable solvents for crystallization.

The compounds so prepared (Table I) are readily soluble in dilute hydrochloric acid and the resulting solutions can be boiled extensively without decomposition.

2-Mercapto-4(5)-*p*-chlorophenylimidazole.—Five grams (0.035 mole) of *p*-chlorophenacylamine hydrochloride and 3.9 g. (0.035 mole) of potassium thiocyanate were refluxed in 100 ml. of glacial acetic acid for 10 minutes. Addition of water and thorough chilling resulted in the separation of 5 g. (97% yield) of material melting at 285–291° dec. A sample was recrystallized from absolute ethanol to a melting point of 293–295° dec.

Anal. Calcd. for $C_9H_7ClN_2S$: N, 13.2; S, 15.2. Found: N, 13.1; S, 15.2.

4(5)-*p*-Chlorophenylimidazole.—To 100 ml. of boiling 10% nitric acid was added 3 g. of powdered 2-mercapto-(45)-*p*-chlorophenylimidazole over a period of 5 minutes. Heating was continued for 10 minutes and the solution was filtered while hot. Upon cooling, the filtrate deposited a small amount of material melting at 179–180°.[8] Neutralization of the filtrate produced a material melting at 140–143°. The substance was crystallized from hot water giving a white product, m.p. 145–147°. During several preparations, the yields of purified material varied from 10–30%.

Anal. Calcd. for $C_9H_7ClN_2$: C, 60.5; H, 4.0; N, 15.7. Found: C, 60.7; H, 4.0; N, 15.7.

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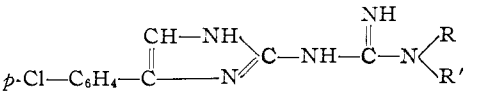
TABLE I



R	R′	M.p., °C.	Cryst. solvent	Formula	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Nitrogen, % Calcd.	Nitrogen, % Found
H–	$-CH(CH_3)_2$	163–165	Benzene	$C_{13}H_{16}ClN_5$	56.2	56.0	5.9	6.1	25.1	25.0
C_2H_5–	$-C_2H_5$	102.5–104.5	Benzene–pet. eth.	$C_{14}H_{18}ClN_5$	57.6	57.5	6.2	6.1	24.0	24.0
H–	$-CH_3$	214–216	50% Alcohol	$C_{11}H_{12}ClN_5$	52.9	53.2	4.9	5.1	28.1	27.9
CH_3–	$-CH_3$	186–188	50% Alcohol	$C_{12}H_{14}ClN_5$	54.7	54.7	5.4	5.1	26.6	26.6
H–	$-C_4H_9(n)$	187.5–189.5	80% Alcohol	$C_{14}H_{18}ClN_5$	57.6	57.5	6.2	6.1	24.0	24.0
H	$-C_6H_5$	171–173	95% Alcohol	$C_{16}H_{14}ClN_5$	61.6	61.5	4.5	4.5	22.5	22.4
H–	$-C_6H_4$–OH(*p*)	222–224	80% Alcohol	$C_{16}H_{14}ClN_5O$	58.6	58.7	4.3	4.4	21.4	21.3

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(3) A. Wohl and W. Marckwald, *Ber.*, **22**, 568, 1353 (1889).
(4) R. P. Edkins and W. H. Linnell, *Quart. J. Pharm. Pharmacol.*, **9**, 75 (1936).
(5) L. Long and H. Troutman, THIS JOURNAL, **71**, 2473 (1949)
(6) T. S. Kenny and A. G. Murray, British Patent 599,722.
(7) The crude salts were obtained in yields of 46–79%. They were not characterized by analysis due to their hygroscopic nature.
(8) This material had approximately the nitrogen content (17.4%) to be expected from the *nitrate* of *p*-chlorophenylimidazole (17.7%). Upon treatment with sodium carbonate, the latter was formed.