hexanenitrile[4] with Adam's catalyst in the presence of acetic anhydride gave the desired compound in 58% yield as a red, viscous liquid, bp 173° (0.5 mm), n^{24}D 1.4679. *Anal.* ($C_8H_{16}N_2O_3$) C, H, N. Nef hydrolysis of this 4-nitro compound gave the previously unreported 4-ketohexanenitrile, bp 75–80° (0.5 mm), n^{20}D 1.4338. *Anal.* (C_6H_9NO) C, H, N.

(4) G. D. Buckley, T. J. Elliott, F. G. Hunt, and A. Lowe, *J. Org. Chem.*, **8**, 10 (1943).

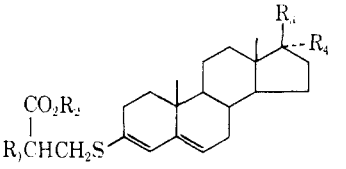
Cysteine Derivatives of Keto Steroids

ROBERT T. BLICKENSTAFF

Medical Research Laboratory, Division of Medicine, Veterans Administration Hospital, and Department of Biochemistry, Indiana University School of Medicine, Indianapolis, Indiana 46202

Received March 25, 1968

The condensation of L-cysteine derivatives with Δ^4-3-keto steroids in the presence of pyridinium chloride[1] has been found to give the corresponding diene thioethers.[2] When compared with testosterone in mice, **3** was devoid of androgenic, myotropic, and antiestrogenic activity.[3]



1, R_1 = $C_6H_5CH_2CONH$; R_2 = CH_3; R_3 = C_8H_{17}; R_4 = H
2, R_1 = $Cl^-H_3N^+$; R_2 = C_2H_5; R_3 = OH; R_4 = H
3, R_1 = $Cl^-H_3N^+$; R_2 = C_2H_5; R_3 = OH; R_4 = CH_3

Experimental Section[4]

Methyl S-(3,5-Cholestadien-3-yl)-N-phenylacetyl-L-cysteinate (1).—A solution of 500 mg (1.3 mmoles) of cholestenone in 25 ml of C_6H_6 was distilled until 5 ml had collected. A solution composed of 880 mg (5.2 mmoles) of methyl N-phenylacetyl-L-cysteinate,[5] 48 mg of pyridinium chloride, 6 ml of EtOH, and 4 ml of C_6H_6 was added. The solution was refluxed 3 hr, cooled, diluted with 30 ml of ether, and washed with two 25-ml portions of 1 *N* NaOH. After one H_2O wash the ethereal solution was dried (Na_2SO_4) and evaporated leaving 740 mg of semisolid. Precipitation from acetone–petroleum ether (bp 30–60°) gave 264 mg of **1**, mp 119–125°. Further work-up of the mother liquor gave another 100 mg of **1**, mp 100–119°, and 167 mg of recovered cholestenone. The analytical sample (*i*-Pr_2O) had mp 158–159°. *Anal.* ($C_{39}H_{57}NO_3S$) H, N, S.

Ethyl S-(17β-Hydroxy-3,5-androstadien-3-yl)-L-cysteinate Hydrochloride (2).—A similar condensation between testosterone and ethyl L-cysteinate hydrochloride gave **2** as an amorphous solid (acetone), mp 176–179°. *Anal.* ($C_{27}H_{38}ClNO_3S$) C, H, Cl, N, S.

Ethyl S-(17β-Hydroxy-17α-methyl-3,5-androstadien-3-yl)-L-cysteinate Hydrochloride (3).—Similarly, 17α-methyltestosterone and ethyl L-cysteinate hydrochloride gave **3**, needles (Me_2CO–C_6H_6), mp 171–172°. *Anal.* ($C_{25}H_{40}ClNO_3S$) C, H, Cl, N, S.

Acknowledgment.—This work was supported in part by U. S. Public Health Service Research Grant AM-04531.

(1) J. Roma, M. Romero, C. Djerassi, and G. Rosenkranz, *J. Am. Chem. Soc.*, **73**, 1528 (1951).

(2) Δ^4-3-Keto steroids are reported *not* to react with cysteine or ethyl cysteinate: S. Lieberman, *Experientia*, **2**, 411 (1945).

(3) We are indebted to Dr. R. Kraay, Eli Lilly and Co., for these assays.

(4) Ir spectra were obtained on an Infracord, uv spectra on a Beckman DU. Microanalyses are by Galbraith Laboratories, Knoxville, Tenn.

(5) Z. Foldi, *Acta Chim. Acad. Sci. Hung.*, **5**, 187 (1954); *Chem. Abstr.*, **50**, 9811 (1956).

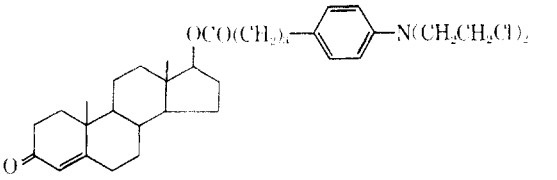
17β-(4′-{*p*-[Bis(β-chloroethyl)amino]phenyl}-butanoyloxy)-4-androsten-3-one

E. L. FOSTER AND R. T. BLICKENSTAFF

Medical Research Laboratory, Division of Medicine, Veterans Administration Hospital, and Department of Biochemistry, Indiana University School of Medicine, Indianapolis, Indiana 46202

Received March 25, 1968

The synthesis and antitumor evaluation of steroidal nitrogen mustards[1] prompted us to synthesize the chlorambucil ester of testosterone by treating chlorambucil chloride with the potassium salt of testosterone in refluxing benzene.



Experimental Section[2]

17β-(4′-{*p*-[Bis(β-chloroethyl)amino]phenyl}butanoyloxy)-4-androsten-3-one.[3]—Testosterone, 0.34 g (1.1 mmoles), was dissolved in dry C_6H_6, excess K was added, and the mixture was then refluxed overnight. After filtration of the unreacted K, the C_6H_6 solution of the potassium salt was added to residual chlorambucil chloride, which was prepared from 0.35 g (1.1 mmoles) of chlorambucil and 2 ml of $POCl_3$ in refluxing C_6H_6 with subsequent solvent removal. The esterification reaction mixture was refluxed 5 hr, then left at room temperature overnight. The solvent was evaporated to give 512 mg of crude product, which was chromatographed on 10 g of Al_2O_3. C_6H_6 eluted 60 mg of acid chloride, 43 mg of the ester (analytical sample), and 34 mg of impure ester, while C_6H_6–Et_2O (4:1) eluted 154 mg of additional ester. Rechromatography of the last two fractions (188 mg) plus 82 mg of similar product from another preparation on 8 g of Al_2O_3 gave 211 mg of ester eluted by C_6H_6–Et_2O (4:1). *Anal.* ($C_{33}H_{45}Cl_2NO_3$) C, H, N.

(1) (a) G. V. Rao and C. C. Price, *J. Org. Chem.*, **27**, 205 (1962); (b) S. H. Borstein and H. J. Ringold, *ibid.*, **26**, 3084 (1961); (c) W. J. Gensler and G. M. Sherman, *ibid.*, **23**, 1227 (1958); (d) A. M. Khaletskii, M. V. Vasil'eva, and E. M. Baldnova, *Sintetich. Produkty iz Kamfoli i Skipidara, Akad. Nauk Belorussk. SSR, Tsentr. Nauchn.-Issled. i Proektn. Inst. Lesokhim. Prom., Tr. Vses. Nauchn.-Tekhn. Soveshch., Gorki, 1963*, 227 (1964); *Chem. Abstr.*, **62**, 9194 (1965); (e) G. R. Yagasoar, H. I. Bolker, and A. F. McKay, *Can. J. Chem.*, **30**, 933 (1952); (f) R. E. Havranek and N. J. Doorenbos, *J. Am. Pharm. Assoc., Sci. Ed.*, **49**, 328 (1960); (g) T. Nogrady, K. M. Vagi, and V. W. Adamkiewicz, *Can. J. Chem.*, **40**, 2126 (1962); (h) L. N. Volovelskii and A. B. Simkina, *Zh. Obshch. Khim.*, **37**, 1571 (1967); (i) Nicolescu-Duvaz, A. Combanis, and E. Turmanceanu, *J. Med. Chem.*, **10**, 172 (1967); (j) C. R. Walk, T. C. Chou, and H. H. Liu, *ibid.*, **10**, 255 (1967).

(2) Ir spectra were obtained on an Infracord, uv spectra on a Beckman DU. Microanalyses are by Galbraith Laboratories, Knoxville, Tenn.

(3) This compound was submitted to the Cancer Chemotherapy National Service Center, Public Health Service, for an evaluation of its anticancer activity against acute lymphocytic leukemia.

2,2′-Hydrazobis(5-nitropyrimidines)

MOSHE AVRAMOFF

Department of Chemistry, The Weizmann Institute of Science, Rehovot, Israel

Received June 5, 1968

2-Amino-5-nitropyrimidine and its derivatives possess pronounced trichomonacidal activity.[1] We have shown that symmetrical 2,2′-hydrazobis(5-nitrothiazoles) also show a very strong antiprotozoal activity.[2] The combination of these two features

(1) R. M. Michaels and R. E. Strube, *J. Pharm. Pharmacol.*, **13**, 601 (1961); R. M. Michaels, *J. Protozool.*, **9**, 478 (1962).

(2) M. Avramoff, S. Adler, and A. Fonner, *J. Med. Chem.*, **10**, 1138 (1967).