packed with stainless steel helices[8] gave the pure carbamates as colorless to pale yellow liquids. Although there was considerable variation in yields, 60% appeared to be about average.

N,N'-Bis(4-fluoro-3-trifluoromethylphenyl)urea.—This compound was obtained as a by-product from the preparation of the carbamate of 5-amino-2-fluorobenzotrifluoride. It was recovered as an insoluble material from the petroleum ether extraction. Recrystallization from ethanol gave the pure compound, m.p. 223–224°.

Anal. Calcd. for $C_{15}H_8F_8N_2O$: C, 46.89; H, 2.10; N, 7.29. Found: C, 46.66; H, 2.28; N, 7.45.

5-Amino-2-fluorobenzotrifluoride.—To a stirred mixture of 2200 g. (39.4 g.-atoms) of iron filings and 5 l. of 0.78 *N* ammonium chloride solution at reflux temperature was added 2060 g. (9.85 moles) of 5-nitro-2-fluorobenzotrifluoride[9] in a period of 45 min. The amine was steam distilled from the reaction mixture, separated from the water layer, dried over anhydrous magnesium sulfate, and flash distilled, yielding 1512 g. (86%). Fractional distillation gave pure product, b.p. 207–207.5° (microcapillary), $n^{25}D$ 1.4641.

Anal. Calcd. for $C_7H_5F_4N$: C, 46.94; H, 2.81; N, 7.82. Found: C, 46.82; H, 2.95; N, 7.91.

The acetyl derivative was prepared in the usual manner. Vacuum sublimation gave a white solid, m.p. 60–61°.

Anal. Calcd. for $C_9H_7F_4NO$: N, 6.33. Found: N, 6.39.

3-Nitro-2,5-difluorobenzotrifluoride.[10]—To a stirred mixture of 88.6 ml. (2 moles) of fuming nitric acid (sp. gr. 1.49–1.5) and 350 ml. of fuming sulfuric acid (30% SO_3), 183 g. (1 mole) of 2,5-difluorobenzotrifluoride[11] was added dropwise and the exothermic reaction was controlled at 55–60°. After addition, stirring was continued for 1 hr. and the reaction mixture then was allowed to cool to room temperature. Upon pouring slowly over crushed ice, the crude product separated as a heavy oil. Sodium carbonate was added and the mixture was steam distilled, yielding 152 g. 67%). Vacuum fractional distillation gave pure material, b.p. 89° (20 mm.).

Anal. Calcd. for $C_7H_2F_5NO_2$: C, 37.02; H, 0.89; N, 6.17. Found: C, 37.29; H, 0.85; N, 6.28.

Evidence in support of the 3-position for the nitro group is based on the reduction of 3-nitro-2,5-difluorobenzotrifluoride to the amine and a subsequent Schiemann conversion to 2,3,5-trifluorobenzotrifluoride, b.p. 105°. The structure of the latter was verified by nuclear magnetic resonance study. Further evidence is supplied by a nitration study of 2-acetylamino-5-fluorobenzotrifluoride.[12]

3-Amino-2,5-difluorobenzotrifluoride.[10]—An iron reduction of 3-nitro-2,5-difluorobenzotrifluoride by the procedure previously described readily gave the corresponding amine. The crude amine was collected by steam distillation, yielding 97%. Vacuum distillation gave pure material as a heavy, colorless liquid, b.p. 58° (9.6 mm.)

Anal. Calcd. for $C_7H_4F_5N$: C, 42.65; H, 2.04; N, 7.11. Found: C, 42.72; H, 2.21; N, 7.21.

The acetyl derivative was prepared in the usual manner. Recrystallization from petroleum ether (b.p. 90–120°) gave white needles, m.p. 104.5–105.5°.

Anal. Calcd. for $C_9H_6F_5NO$: C, 45.20; H, 2.53; N, 5.86. Found: C, 45.33; H, 2.43; N, 5.82.

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(8) Heli-Pak No. 3008, Podbielniak Co., Chicago 17, Ill.

(9) G. C. Finger and C. W. Kruse, *J. Am. Chem. Soc.*, **78**, 6034 (1956).

(10) The assistance of H. G. Schneider in this preparation is acknowledged.

(11) G. C. Finger and F. H. Reed, *J. Am. Chem. Soc.*, **66**, 1972 (1944).

(12) G. C. Finger and M. Knell, *Trans. Illinois State Acad. Sci.*, **38**, 71 (1945).

Testosterone 17-Heptanoate 3-Benziloylhydrazone

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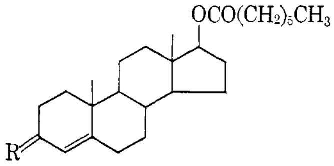
By converting testosterone 17-heptanoate (I) to its 3-benziloylhydrazone (II) it was observed that the androgenic effects of I could be substantially prolonged.[1] In combination with estradiol 3-monobenzoate and estradiol 3,17-diheptanoate, II was found to be useful for the supression of lactation[2,3] as well as for treatment of the menopausal syndrome.[4,5]



I, R = O
II, R = $NNHCOCOH(C_6H_5)_2$

Experimental

Testosterone 17-Heptanoate 3-Benziloylhydrazone (II).—To a solution of I (10 g.) in benzene (50 ml.) was added glacial acetic acid (0.5 ml.) and benziloylhydrazide (6.1 g.). The mixture was heated under reflux for 2 hr. The solvent was removed by distillation under reduced pressure, and the residue was taken up in ether (50 ml.). The ether solution was washed successively with water, 5% sodium bicarbonate solution, and water. After drying the organic phase over anhydrous sodium sulfate, isopropyl ether (75 ml.) was added, and the solution was chilled. The solid was separated by filtration and purified by recrystallization from ether–isopropyl ether (2:3) to yield 12.1 g. of II, m.p. 114–115°, $[\alpha]^{25}D$ +156° (*c* 1, ethanol), $\lambda_{\max}^{\mathrm{EtOH}}$ 282 mμ (ϵ 34,000).

Anal. Calcd. for $C_{40}H_{52}N_2O_4$: C, 76.88; H, 8.38; N, 4.48. Found: C, 77.08; H, 8.24, N, 4.55.

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(1) C. H. Gleason and J. M. Parker, *Endocrinology*, **65**, 508 (1959).

(2) M. J. A. Kelly and T. Primrose, *Can. Med. Assoc. J.*, **83**, 1240 (1960).

(3) S. M. Dodek, *Clin. Obstet. Gynecol.*, **3**, 1099 (1960).

(4) R. B. Greenblatt, W. E. Barfield, and E. C. Jungck, *Can. Med. Assoc. J.*, **86**, 113 (1962).

(5) M. Bertrand, *Union Med. Canada*, **91**, 291 (1962).

Amides from Nitriles and Alcohols by the Ritter Reaction

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A series of compounds of the type R'CONHR has been synthesized for screening as possible antispasmodics, anticonvulsants, and hypnotics. The amides which have been prepared appear in Tables I–III.

Table I

Amides, $RCONHCH_2C_6H_5$

R	% yield	M.p., °C.
CH_3	72.5	60–61[a]
CH_3CH_2	45	46–47[b]
$CH_2{=}CH$	50	67.6–68.2[c]
$C_6H_5CH_2$	27	119–121[d]
C_6H_5	55	103.2–104.2[e]

[a] J. Shakosch, *Ber.*, **5,** 697 (1872). [b] C. A. Buehler and C. A. Mackenzie, *J. Am. Chem. Soc.*, **59,** 421 (1937). [c] G. Kránzlein and M. Corell, German Patent 752,481 (Nov. 10, 1952); *Chem. Abstr.*, **50,** 10132 (1956). [d] R. Delaby, P. Raynaud, and F. Lilly, *Bull. Soc. Chim. France*, 2067 (1961). [e] E. Beckman, *Ber.*, **23,** 3334 (1890).

Experimental

Two typical experiments are described.

N-Benzhydrylacetamide.—Acetonitrile (0.2 mole, 8.2 g.) and concentrated sulfuric acid (0.1 mole, 10.1 g.) were placed in a 250-ml. flask. To the rapidly stirred mixture, benzhydrol (0.1 mole, 18.4 g.), dissolved in 50 ml. of anhydrous di-*n*-butyl