ide it was found that the substance suffered loss of alcohol to give benzoylcyanamide.

The needed N-benzoyl-O-ethylisourea was prepared by modifications of the methods of Wheeler and Johnson.[1] In the preparation of ethyl benzoylthioncarbamate the reaction with alcohol must be conducted below 25° to avoid mercaptan formation. Temperatures above 70° in the removal of the solvent also lowered the yield. The highest yield of N-benzoyl-O-ethylisourea was obtained when exactly two moles of ammonia were used for each mole of thion ester.

Experimental

Ethyl Benzoylthioncarbamate.—To a stirred mixture of 52.4 g. (0.54 mole) of dry powdered potassium thiocyanate and 38 cc. of toluene was added 70.3 g. (0.50 mole) of benzoyl chloride. The temperature was increased to gentle reflux which was maintained for 24 hours. The mixture was cooled to 15–17° and 35 cc. (0.59 mole) of absolute alcohol was added. After standing 24 hours at this temperature 90.4 g. (80%) of product was obtained by filtration and removal of the solvent under diminished pressure. It crystallized from absolute alcohol in long needles, m.p. 73–74° (lit.[1] 73–74°).

N-Benzoyl-O-ethylisourea.—Five grams (0.024 mole) of ethyl benzoylthioncarbamate was dissolved in 50 cc. of absolute alcohol containing 0.82 g. (0.048 mole) of anhydrous ammonia. Evolution of hydrogen sulfide began at once. After three days at room temperature the alcohol was distilled at atmospheric pressure. The residue then was treated with 50 cc. of water to which had been added 1 cc. of 1% potassium hydroxide solution. The filtered dry product weighed 4.11 g. (89.5%). Long colorless needles were obtained by crystallization from petroleum ether; m.p. 74–75° (lit.[1] 74–75°). Mixed with the starting material the melting point dropped to 45° (lit.[1] 45°).

Benzoylcyanamide.—To a stirred solution of sodium ethoxide prepared from 14 g. (0.60 mole) of sodium and 220 cc. of absolute alcohol was added at room temperature 38.4 g. (0.20 mole) of N-benzoyl-O-ethylisourea. The mixture was warmed slowly to 60° and kept at this temperature for 8 hours. After standing at room temperature the sodium salt of benzoylcyanamide was filtered, dissolved in ice-cold water and converted to benzoylcyanamide by an excess of hydrochloric acid, yield 25.53 g. (87.5%). It was recrystallized by adding petroleum ether to a saturated solution in ether; m.p. 141–142°. It was identical with a sample of the known compound prepared from calcium cyanide (m.p. 141–142°).

Anal. Calcd. for $C_8H_6ON_2$: N, 19.22. Found: N, 19.05.

(1) H. L. Wheeler and T. B. Johnson, *Am. Chem. J.*, **24**, 189 (1900).

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7-*t*-Butyl-2,4-quinazolinedione

BY GLENN S. SKINNER AND HOWARD C. ZELL

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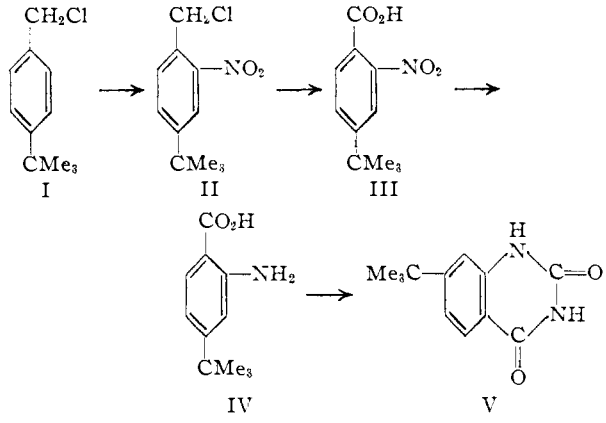
The monochloromethylation of *t*-butylbenzene gives a product which is almost entirely the *para* isomer.[1] This result appeared to afford a suitable synthetic route to 7-*t*-butyl-2,4-quinazolinedione (VI) according to the scheme shown.



The desired product was obtained but in poor over-all yield. The product containing II is evidently a mixture of isomers, since from the oxidation product there were isolated III and the known 4-*t*-butyl-3-nitrobenzoic acid. This oxidation was the most difficult step and succeeded only after preheating II with potassium hydroxide solution followed by long oxidation with permanganate.

The nitro acid III was reduced smoothly. The amino acid IV was insoluble in dilute hydrochloric acid and was unsuited for conversion to V through the ureide. The amino acid thereupon was fused with urea to yield V since 2,4-quinazolinedione had been made in a similar manner from anthranilic acid.[2]

7-*t*-Butyl-2,4-quinazolinedione[3] showed no hypnotic activity. The acute intraperitoneal toxicity LD-50 in mice is 421 ± 38.4 mg./kg. The compound is inactive against influenza virus PR8 *in ovo*. It is inactive against *Staphylococcus aureus, Pseudomonas aeruginosa, Escherichia coli, Brucella abortus, Proteus vulgaris, Hemophilus pertussis, Microsporum audouini, Trichophyton mentagrophytes, Aspergillus niger, Candida albicans* and *Blastomyces dermatitidis*. It does inhibit *Mycobacterium tuberculosis in vitro* if more than 400 micromolar in dimethylformamide.

Experimental

3-*t*-Butyl-6-chloromethylnitrobenzene (II).—The procedure for the nitration[4] of *t*-butylbenzene was used. From 400 g. (2.195 moles) of I, 195 g. (2.195 moles) of nitric acid (d. 1.42) and 237 cc. of sulfuric acid (d. 1.84) there was obtained 316 g. of reddish oil, b.p. 133–140° (1.25 mm.), $n^{25}D$ 1.5433. The analytical sample had b.p. 117–119° (0.5 mm.), $n^{25}D$ 1.5431, d^{25}_4 1.1644.

Anal. Calcd. for $C_{11}H_{14}O_2NCl$: N, 6.15; Cl, 15.57; M_D 61.34. Found: N, 5.94; Cl, 15.84; M_D 61.64.

4-*t*-Butyl-2-nitrobenzoic Acid (III).—A mixture of the above product II (25 g., 0.11 mole), 62.5 cc. of 10% potassium hydroxide solution and 125 cc. of water was stirred and refluxed for one hour. More of the potassium hydroxide solution (75 cc.) and 24.2 g. (0.153 mole) of potassium permanganate were added dropwise during 40 minutes while the mixture was stirred and refluxed. The stirring and refluxing were continued for 13 hours. Refluxing 20 to 37 hours did not affect the yield and the product became dark in color. The excess of permanganate was destroyed with methanol. The hot mixture was filtered through Super-cel and the cake was washed three times with boiling water. The cold alkaline filtrate was extracted with benzene. The water layer was concentrated to about 200 cc. by distillation under diminished pressure. The ice-cold concentrate was acidified with hydrochloric acid to give an oily product which solidified after collection in ether and removal of the ether under diminished pressure. To the hot filtered solution in benzene was added hexane to incipient cloudiness. On standing large crystals formed. The product III had m.p.

(1) G. S. Skinner, J. A. Gladner and R. F. Heitmiller, THIS JOURNAL, **73**, 2330 (1951).

(2) M. T. Bogert and G. Scatchard, *ibid.*, **41**, 2052 (1919).

(3) Pharmacological tests by Sharp and Dohme, West Point, Penna.

(4) D. Craig, THIS JOURNAL, **57**, 195 (1935).

138–143° after three recrystallizations from a mixture of benzene and hexane; yield 6.6 g. (27%).

Anal. Calcd. for $C_{11}H_{13}O_4N$: N, 6.27; neut. equiv., 223. Found: N, 6.19; neut. equiv., 213.

The brown oil from the mother liquors solidified on standing. This by reworking with benzene and ligroin gave 4-*t*-butyl-3-nitrobenzoic acid, m.p. 163–164°, neut. equiv. 218 (calcd. 223), whose m.p. was undepressed on admixture of an authentic sample.[5]

2-Amino-4-*t*-butylbenzoic Acid (IV).—A mixture of the above nitro acid III (8 g.), 0.4 g. of platinum oxide catalyst and 150 cc. of absolute alcohol was shaken in an atmosphere of hydrogen until the theoretical amount had been absorbed (45 min.). Two crystallizations of the product from a mixture of alcohol and water gave 4.9 g. (71%) of IV, m.p. 167–168°.

Anal. Calcd. for $C_{11}H_{15}O_2N$: N, 7.25. Found: N, 7.11.

7-*t*-Butyl-2,4-quinazolinedione.—One gram (0.00518 mole) of IV was ground in a mortar with 1.24 g. (0.0207 mole) of urea. The mixture was fused at 140–150° for 3 hours. The cooled mass was dissolved in hot glacial acetic acid. The solution after refrigeration overnight had deposited a crystalline product which was filtered and recrystallized from glacial acetic acid; yield 0.25 g. (22%), m.p. 270–271°. The use of smaller amounts of urea decreased the yield.

Anal. Calcd. for $C_{12}H_{14}O_2N_2$: N, 12.84. Found: N, 12.80.

(5) C. C. Price and D. C. Lincoln, THIS JOURNAL, **72**, 2807 (1950).

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Isolation of the Sterols of the White Potato[1,2]

BY JOSEPH J. SCHWARTZ AND MONROE E. WALL

RECEIVED MAY 26, 1955

The sterols of the white potato (*Solanum tuberosum* L.) were investigated at this Laboratory as part of a comprehensive study of potato constituents. Although the steroidal alkaloid solanidine[3] and an unidentified steroidal glycoside[4] have been isolated from potatoes, and Lindemann[5] has reported 3.5% sterols in fat extracted from industrial potato starch, a study of the literature indicated that no information was available on the nature of the free sterols.

A large batch of dried, unpeeled Maine Katahdin potatoes (1950 crop) was extracted with boiling isopropyl alcohol. The unsaponifiable fraction was obtained in the usual manner. Digitonin precipitation yielded an amount of sterols equal to 0.002% of the weight of potatoes on a moisture-free basis. This is close to the value 0.003% calculated from the data of Lindemann.[5] Pyridine cleavage of the digitonides gave 6.7 g. of crude sterol fraction. Conversion to the dinitrobenzoate followed by chromatography on alumina and Florisil[6] removed non-steroidal impurities but accomplished no significant separation of the sterols themselves. Fractional crystallization of the dinitrobenzoates followed by chromatography on silica gel gave two fractions differing about 6° in melting point, of which the higher-melting, less soluble fraction was the minor constituent. Both fractions were hydrolyzed. The major, more soluble, fraction after numerous crystallizations gave β-sitosterol. The sterol was characterized by the melting points and rotations of the free sterol, acetate, benzoate and dinitrobenzoate, which agreed well with literature values. In addition, the infrared spectrum was essentially identical to that given by Dobriner, Katzenellenbogen and Jones.[7]

The minor, less soluble fraction, was identified as stigmasterol. The melting points and rotations of the free sterol and the benzoate were in close agreement with literature values. Further, the infrared spectrum was identical to that of authentic stigmasterol.

Experimental[8]

Isolation of Crude Sterols.—Dried potatoes (276 kg.) containing 8.8% moisture were extracted in 5 batches with a total of 178 gal. of boiling 99% isopropyl alcohol. The residue from the alcohol was saponified with boiling 10% KOH–methanol solution. The mixture was treated in the usual manner, and 46.0 g. of unsaponifiable matter was obtained.

The sterols were isolated by a modification of method F of Sperry.[9] The unsaponifiables, dissolved in 1060 ml. of boiling absolute ethanol, were treated with 21.1 g. of digitonin (Merck) in 716 ml. of 80% ethanol. The mixture was boiled for one minute, 265 ml. of water was added, and the mixture was brought to a boil again. After standing overnight the digitonides were filtered off and washed. They were then treated with pyridine according to the method of Schoenheimer and Dam[10] to obtain the free sterols.

Preparation and Purification of Dinitrobenzoates.—The sterols (6.7 g.) were heated two hours on a steam-bath with an equal weight of 3,5-dinitrobenzoyl chloride and 35 ml. of pyridine. The mixture was treated with 1 ml. of water to decompose excess reagent and cooled. Extraction with ether in the usual manner yielded 9.5 g. of solids.

After chromatography on alumina and Florisil, with little improvement in melting point, the dinitrobenzoates were fractionally crystallized from ethyl acetate, and each fraction was chromatographed on a 1:1 mixture of silica gel–Hyflo Supercel.[6] Finally all the fractions were combined into two main fractions A and B. Fraction A, m.p. 204–215°, was less soluble than the lower melting fraction B, m.p. 202–207°.

Saponification and Purification of Sterols.—Fractions A and B were saponified with 5% KOH in methanol, extracted with ether in the usual manner, and crystallized from 95% ethanol. Each fraction was then digested with two small portions of warm light petroleum ether,[11] which removed waxy, non-steroidal impurities. The insoluble residues (A and B) were crystallized six times from 90% ethanol. Fraction B yielded β-sitosterol, 0.67 g., plates, m.p. 138–138.5°, $[\alpha]_D$ −35° (lit.[12] gives m.p. 136–137°, $[\alpha]_D$ −36.6°).

Anal. Calcd. for $C_{29}H_{50}O$: C, 83.99; H, 12.15. Found: C, 84.14; H, 12.36.

β-Sitosteryl Acetate.—The product was prepared from β-sitosterol in the usual manner by heating with acetic anhydride–pyridine for 1 hour at 90°; plates from methanol, m.p. 127–129°, $[\alpha]_D$ −45°. (Lit.[12] gives m.p. 125–126°, $[\alpha]_D$ −41.0°.)

Anal. Calcd. for $C_{31}H_{52}O_2$: C, 81.52; H, 11.48. Found: C, 80.93; H, 11.47.

β-Sitosteryl Benzoate: rectangular plates from acetone,

(1) Article not copyrighted.

(2) This is paper XXIX in a series on steroids and steroidal sapogenins. Paper XXVIII, M. E. Wall, H. E. Kenney and E. S. Rothman, THIS JOURNAL, **77**, Nov. 5 (1955).

(3) G. R. Clemo, *et al.*, *J. Chem. Soc.*, 1299 (1936).

(4) W. Völksen, *Arch. Pharm.*, **283**, 203 (1950).

(5) E. Lindemann, *Die Stärke*, **3**, 141 (1951).

(6) The mention of commercial products does not imply that they are endorsed or recommended by the Department of Agriculture over others of a similar nature not mentioned.

(7) K. Dobriner, *et al.*, "Infrared Absorption Spectra of Steroids, an Atlas," Interscience Publishers, Inc., New York, N. Y., 1953, chart 58.

(8) Melting points were obtained with a Kofler hot-stage. Optical rotations were taken in chloroform at 25°.

(9) W. M. Sperry, *J. Biol. Chem.*, **118**, 377 (1937).

(10) R. Schoenheimer and H. Dam, *Z. physiol. Chem.*, **215**, 59 (1933).

(11) G. Soliman and W. Saleh, *J. Chem. Soc.*, 1506 (1954).

(12) E. S. Wallis and P. N. Chakravorty, *J. Org. Chem.*, **2**, 335 (1937).