NOTES

Nicotinic Acid. Miscellaneous Esters[1]

By C. O. Badgett and C. F. Woodward

Several esters of nicotinic acid have been reported recently.[2,3] Some new miscellaneous esters have been prepared in this Laboratory, and, since the work has been terminated, we are reporting these compounds and the two additional methods used in their preparation.

The first method used was the direct reaction of the alcohol with nicotinyl chloride hydrochloride. The second method involves the reaction of nicotinic anhydride[4] with the alcohol. The following examples will serve to illustrate the methods.

Method A. Glycol Dinicotinate

Into a round-bottomed, three-necked flask equipped with air-tight stirrer, dropping funnel, and condenser equipped with a calcium chloride drying tube was placed 61.5 g. (0.5 mole) of nicotinic acid. Stirring was started, and 178 g. (1.5 moles) of redistilled thionyl chloride was added dropwise at a fairly rapid rate. After addition was complete, the reaction mixture was refluxed for two hours. The condenser was then set for distillation, and the excess thionyl chloride was distilled off while the reaction mixture was stirred to prevent formation of a hard cake. Approximately 300 cc. of anhydrous benzene was added. The nicotinyl chloride hydrochloride was filtered off, washed twice with 100-cc. portions of anhydrous benzene and sucked almost dry on a Buchner funnel.

The nicotinyl chloride hydrochloride was immediately transferred to a 600-cc. beaker, and 9 g. (0.145 mole) of ethylene glycol was added with stirring. The reaction was exothermic. After evolution of hydrogen chloride had ceased, the mixture was heated to about 100° on a hot-plate with continuous stirring for fifteen minutes. The reaction mixture was then dissolved cautiously in water and made strongly alkaline with concentrated ammonium hydroxide, and the crystalline glycol dinicotinate was filtered off. The product was washed with three 100-cc. portions of dilute ammonium hydroxide and dried. The yield was 36 g. or 91.2% of theoretical. The glycol dinicotinate thus prepared had a m. p. of 127.0–128.0°. Recrystallization from 400 cc. of 40% alcohol following Norit treatment gave 32 g. of product of the same melting point. Three recrystallizations did not raise the melting point.

Method B. Trinicotinin

Into a 200-cc. round-bottomed, three-necked flask equipped with a stirrer and reflux condenser equipped with a drying tube, was placed 20.5 g. (0.09 mole) of nicotinic anhydride, 12 cc. of anhydrous pyridine and 1.84 g. (0.02 mole) of redistilled, anhydrous glycerol. The mixture was heated on the steam-bath for four hours with continuous stirring. The reaction mixture was poured into 100 cc. of water and made strongly alkaline with sodium carbonate solution, and the oil layer was extracted with three 40-cc. portions of chloroform. The chloroform extract was washed with three 25-cc. portions of water and dried over anhydrous sodium sulfate. The chloroform and pyridine were removed by evaporation, leaving an oil which crystallized when scratched with a stirring rod and cooled in an ice-bath. The yield of trinicotinin was the theoretical. The melting point was 87.7–88.8°. The melting point was not raised by repeated recrystallization from acetone-petroleum ether.

Isopropylidene glycerol[5,6] and α-monomyristin[7] were prepared in accordance with the literature methods and used in the preparation of the mixed glycerides. Table I gives the analytical data and physical constants of the new esters.

Table I

Properties of Nicotinic Acid Esters

Compound[a]	Formula	M. p., °C.	Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found	Nitrogen Calcd.	Nitrogen Found	Milliequiv. alkali per g. of ester Calcd.	Milliequiv. alkali per g. of ester Found
Nicotinate										
Phenyl	$C_{12}H_9NO_2$	74.2–75.0	72.35	72.69	4.55	4.70	7.03	6.87	5.02	5.01
Cyclohexyl	$C_{12}H_{15}NO_2$	[b]	70.22	70.29	7.37	7.34	6.82	6.79	4.87	4.84
Isopropylidene glycerol[c]	$C_{12}H_{15}NO_4$	41.4–41.9[d]	60.75	60.27	6.37	6.33	5.91	5.85	4.21	4.18
Glycol di-[e]	$C_{14}H_{12}N_2O_4$	126.7–127.1	61.76	62.30	4.44	4.94	10.29	10.29	7.34	7.35
α-Naphthyl	$C_{16}H_{11}NO_2$	70.0–70.6	77.09	77.45	4.41	4.68	5.63	5.62	4.01	4.02
Pentaerythritol tetra-	$C_{29}H_{24}N_4O_8$	162–163	62.58	62.30	4.35	4.49	10.07	9.61	7.20	7.20
Inositol hexa-	$C_{42}H_{30}N_6O_{12}$	254.3–254.9	62.22	62.16	3.73	4.12	10.37	9.97	7.40	7.36
Trinicotinin[f]	$C_{21}H_{17}N_3O_6$	87.6–87.8	61.91	61.42	4.21	4.34	10.31	10.28	7.36	7.39
α-Monomyristin dinicotinin[c]	$C_{29}H_{40}N_2O_6$	58.6–59.2	67.94	68.07	7.87	8.04	5.47	5.42	5.85	5.85

[a] These substances were all made by Method A unless otherwise indicated. [b] B. p. 144.5° at 4.1 mm.; n^{25}_D 1.5177; d^{25}_4 1.0941. [c] Used Method B. [d] B. p. 143–144° at 1.2 mm. [e] Yield, Method A, 91.2%; yield, Method B, 93.6%. [f] Used Methods A and B.

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[1] Article not copyrighted.

[2] Badgett, Provost, Ogg and Woodward, This Journal, **67**, 1135 (1945).

[3] Huber, Boehme and Laskowksi, *ibid.*, **68**, 187 (1946).

[4] Badgett, *ibid.*, **69**, 2231 (1947).

(5) Irvine, McDonald and Soutar, *J. Chem. Soc.*, **107**, 337 (1915).

(6) Newman and Renoll, This Journal, **67**, 1621 (1945).

(7) Averill, Roche and King, *ibid.*, **51**, 866 (1929).

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The Iodination of ω-Cyanoacetophenone

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During the course of work with 2-(cyanoacetyl)-coumarone, the material, when treated with iodine and aqueous sodium hydroxide, gave a yellow precipitate having an odor and melting point like that of iodoform. The material was not iodoform as shown by a mixed melting point.

This reaction has been studied using ω-cyanoacetophenone and found to produce the hitherto unreported triiodoacetonitrile along with benzoic acid. Triiodoacetonitrile is an unstable material, decomposing on standing to give iodine, cyanogen iodide, and an unidentified oil. Heating triiodoacetonitrile with aqueous sodium hydroxide produces carbon tetraiodide, ammonia, sodium carbonate, and an unidentified isocyanide.

Experimental

Preparation of Triiodoacetonitrile.—To a solution of 1.0 g. (0.0069 mole) of ω-cyanoacetophenone[1] in 30 ml. of 10% sodium hydroxide diluted to 100 ml. was added 5.3 g. (0.021 mole) of iodine and 10.0 g. of potassium iodide in 75 ml. of water. The yellow precipitate was sucked off, washed with water, and dried at 3° for fourteen hours. The product, 2.3 g. (80% yield) melted at 120–122° dec., and, when mixed with iodoform, melted at 110°. It was soluble in common organic solvents with liberation of iodine.

Anal. Calcd. for C_2I_3N: C, 5.7; H, 0.0; N, 3.3; I, 90.9. Found: C, 5.5; H, 0.06; N, 3.2; I, 90.4. Calcd. for diiodoacetonitrile, C_2HI_2N: C, 8.2; H, 0.34; N, 4.8; I, 86.7.

The product, stable when wet, was unstable dry but could be dried under carbon dioxide or nitrogen. Washing the wet product with aqueous potassium iodide also increased its stability during drying. Triiodoacetonitrile, dried by any of the above methods, decomposed on standing to give iodine, a brown oil, and white needles of cyanogen iodide, which sublimed from the decomposition mixture—m. p. 132–133°; recorded,[2] 146.0°.

Anal. Calcd. for ICN: C, 7.8; H, 0.0; N, 9.2; I, 83.0. Found: C, 8.1; H, 0.2; N, 9.3; I, 80.0.

With quinoline in ether, the cyanogen iodide gave a complex melting at 102–103°; recorded, 104°.[3]

The filtrate from the triiodoacetonitrile preparation gave 1.134 g. crude and 0.461 g. pure (or 55%) benzoic acid which did not depress the melting point of an authentic sample.

Triiodoacetonitrile and Sodium Hydroxide.—One gram of triiodoacetonitrile in 25 ml. of 5% aqueous sodium hydroxide was heated at 60° for one hour with stirring. The reddish-orange solid was sucked off and steam-distilled to remove unchanged triiodoacetonitrile. The red solid remaining was sublimed at 130–140° under 1–2 mm. pressure, giving crystals of carbon tetraiodide.

Anal. Calcd. for CI_4: C, 2.3; H, 0.0; N, 0.0; I, 97.7. Found: C, 2.6; H, 0.05; N, less than 0.1; I, 97.1.

The filtrate above gave a positive test for ammonia, carbonate ion, and an isocyanide by odor and by acid hydrolysis to formic acid.

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(1) Prepared by the method of Arndt and Loewe, *Ber.*, **71**, 1630 (1938).

(2) Cook and Robinson, *J. Chem. Soc.*, 1002 (1935).

(3) Mumm and Bruhn, *Ber.*, **68**, 176–183 (1935).

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Purification of Thianaphthene

BY CORWIN HANSCH

In the preparation of thianaphthene by the reduction of 3-thianaphthenol[1,2] with zinc and acetic acid, thianaphthene is obtained which does not have a sharp melting point and apparently contains small amounts of 2,3-dihydrothianaphthene. Refluxing thianaphthene thus prepared with 10% by weight of sulfur for four hours, then isolating the product by steam distillation from a dilute sodium hydroxide solution, gives thianaphthene melting sharply at 32°.

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(1) Friedländer, *Ber.*, **41**, 231 (1908).

(2) Hansch and Lindwall, *J. Org. Chem.*, **10** 381 (1945).

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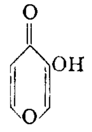
A Synthesis of Maltol

BY M. A. SPIELMAN AND MORRIS FREIFELDER

Maltol (III) has been isolated from pine needles,[1] larch bark,[2] the destructive distillates of various organic materials[3] and the alkaline hydrolysis products of streptomycin.[4] However, no synthesis has been reported.

We have condensed pyromeconic acid (I) with piperidine and formaldehyde to give the Mannich base (II). There was no evidence of a second condensation such as takes place with kojic acid, a similar 3-hydroxy-4-pyrone.[5] Hydrogenation of the base over a palladium catalyst gave maltol (III) in poor yield. Meconic and pyromeconic acids have been made artificially,[6] and the total synthesis of maltol is therefore complete.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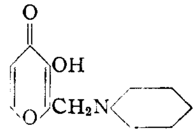
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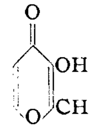
III

Experimental[7]

3-Hydroxy-2-piperidinomethyl-4-pyrone.—To 3.5 g. of pyromeconic acid in 20 ml. of alcohol was added 2.8 ml. of piperidine and 1.4 ml. of 40% aqueous formaldehyde. There was a mild heat of reaction after which the mixture was heated for five minutes on the steam-bath. It was cooled, acidified with ethereal hydrogen chloride, diluted with two volumes of ether and left in the cold for several hours. The precipitate was recrystallized from 1:5 alcohol–acetone. The yield of pure hydrochloride, m. p. 193–195° with foaming, was 2.8 g. and 0.5 g. of less pure product, m. p. 189–190°, was recovered from the mother liquors.

Anal. Calcd. for $C_{11}H_{16}ClNO_3$: N, 5.70. Found: N, 5.73.

The free base was prepared with the aid of silver carbonate. It is very soluble in the usual organic solvents except petroleum ether. After two crystallizations from benzene–petroleum ether, it melted at 125–126°.

Anal. Calcd. for $C_{11}H_{15}NO_3$: N, 6.69. Found: N, 6.61.

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(1) Feuerstein, *Ber.*, **34**, 1804 (1901).

(2) Peratoner and Tamburello, *ibid.*, **36**, 3407 (1903).

(3) Brand, *ibid.*, **27**, 806 (1894); Kiliani and Bazlen, *ibid.*, **27**, 3115 (1894); Erdmann and Schaefer, *ibid.*, **43**, 2398 (1910); Reichstein and Beitter, *ibid.*, **63**, 824 (1930); Goos and Reiter, *Ind. Eng. Chem.*, **38**, 132 (1946).

(4) Schenck and Spielman, THIS JOURNAL, **67**, 2276 (1945).

(5) Woods, *ibid.*, **68**, 2744 (1946).

(6) Peratoner, *C. A.*, **6**, 994 (1912); Thoms and Pietrulla, *Ber. pharm. ges.*, **31**, 4 (1921); Wibaut and Kleipool, *Rec. trav. chim.*, **66**, 24 (1947).

(7) Microanalyses by E. F. Shelberg.