Anal. Calcd. for $C_{18}H_{36}O_2$: neut. equiv., 284. Found: neut. equiv., 283.

The acid was identified as stearic acid by mixed m.p. with an authentic specimen, and by preparation of the *p*-phenylphenacyl ester, m.p. and mixed m.p. with an authentic sample 97°.

Oxidation of Scabrin.—To a stirred suspension of 1.8 g. of scabrin in 120 ml. of water, maintained at 60°, 11.6 g. of finely powdered potassium permanganate (equivalent to 10 moles of oxygen) was added in small portions. When the reaction mixture had become colorless, the manganese dioxide was filtered and washed thoroughly with warm water. The combined aqueous filtrates were concentrated down to 35 ml. and made acid to congo red with sulfuric acid. The solution was steam distilled to remove completely the volatile acids and then extracted with ether in a continuous extractor. The ether solution was freed of solvent, and the partly crystalline residue was subjected to sublimation in a micro sublimator. Five hundred and seventy mg. of colorless solid was obtained, which sublimed at 100–110° (15 mm.) and melted at 185–186° (dec.). It rapidly reduced an aqueous solution of potassium permanganate.

Anal. Calcd. for $C_2H_2O_4$: neut. equiv., 45. Found: neut. equiv., 45.

The substance was identified as anhydrous oxalic acid by a mixture melting point determination with an authentic specimen (m.p. 186–187° dec.) and by preparation of the di-*p*-phenylphenacyl ester, m.p. and mixed m.p. with authentic material 165.5° (dec.).

The yield of oxalic acid was 58% (1.16 moles).

The sublimation residue, after recrystallization from ethyl acetate, yielded 561 mg. of colorless crystals, m.p. 187–188°.

Anal. Calcd. for $C_4H_6O_4$: neut. equiv., 59. Found: neut. equiv., 58.

The substance was identified as succinic acid by a mixture melting point determination, m.p. 187.5–188.0°, and by preparation of the di-*p*-phenylphenacyl ester, m.p. 208°. An additional 220 mg. of succinic acid (total yield 61%, 1.22 moles) was obtained from the ethyl acetate mother liquors, together with a tarry residue which could not be made to crystallize, and which was obviously polymerized material.

The solution of steam-volatile acids obtained above was neutralized with sodium hydroxide solution, concentrated to a small volume on the steam-bath, and acidified to congo red with sulfuric acid. The solution was rapidly steam distilled until all material acid to congo red had distilled over. The distillate was neutralized with 0.1 *N* NaOH solution (47.50 ml. was required), the neutral solution was evaporated to dryness, and the *p*-phenylphenacyl ester was prepared. It melted at 82° and a mixed melting point determination with authentic *p*-phenylphenacyl butyrate, m.p. 82°, showed no depression. The yield of butyric acid, therefore, amounted to approximately 87%.

The distillated above was neutralized with sodium hydroxide solution, concentrated on the steam-bath to 15 ml., acidified to congo red with sulfuric acid, and extracted with ether in a continuous extractor. The ether solution was dried and freed of solvent. The crystalline residue sublimed completely at 90–95° (15 mm.). One recrystallization from Skellysolve B gave 0.55 g. (69%) of colorless feathery needles, m.p. 107°, containing nitrogen.

Anal. Calcd. for $C_6H_{11}NO_3$: N, 9.66; neut. equiv., 145. Found: N, 9.74; neut. equiv., 145.

The substance was identified as N-isobutyloxamic acid by a mixture melting point determination with a synthetic sample, m.p. 107°.

Summary

A pungent isobutylamide of an unsaturated C_{18} acid has been isolated from the roots of *Heliopsis scabra* Dunal. The substance, for which the name "scabrin" is proposed, is appreciably more toxic than the pyrethrins to house flies.

Hydrogenation of the amide gave N-isobutylstearamide, and on oxidation it yielded butyric, oxalic, succinic and N-isobutyloxamic acids.

On the basis of these degradations and of its ultraviolet absorption spectrum, scabrin was shown to be the N-isobutylamide of either 2,4,8,10,14-, 2,4,8,12,14-, 2,6,8,10,14- or 2,6,10,12,14-octadecapentaenoic acid, or a mixture of these isomers.

Also isolated from the roots were two crystalline compounds, and a fluorescent oil which is also considerably toxic to house flies. These compounds will be investigated further.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF WAYNE UNIVERSITY]

α-Halogenation of Secondary Nitriles[1,2]

BY CALVIN L. STEVENS AND T. H. COFFIELD

Recently the reaction of isobutyronitrile with phosphorus pentachloride and phosphorus pentabromide to give α-chloro- and α-bromoisobutyronitrile[3] in good yield was reported. The purpose of this paper is to extend the scope of this reaction for secondary aliphatic nitriles.

Phosphorus pentachloride has been used by Von Braun, *et al.*,[4] to α-chlorinate aliphatic secondary iminochlorides in good yield at the temperature of refluxing benzene. At about 200°, phosphorus pentachloride is reported[5] to chlorinate α-methylbutyryl chloride in unspecified yield. α-Chloroisobutyronitrile has been obtained by the direct chlorination of isobutyronitrile in sunlight.[6] The action of bromine on aliphatic nitriles has been reported[7] to give 85–95% of bromonitriles from which the α-bromonitriles could not be isolated in pure form.

In this work, four aliphatic secondary nitriles (IX): α-methylbutyronitrile, α-ethylbutyronitrile, α-ethylcapronitrile and cyclohexanecarbonitrile were chlorinated and brominated with the phosphorus pentahalides under mild conditions in the absence of solvents to give the α-halonitriles (X) in 70–95% yield (see Table I, compounds I to VIII).

$$\underset{\text{IX}}{R_1R_2CHCN} + PX_5 \longrightarrow \underset{\text{X}}{R_1R_2CXCN} + HX + PX_3$$

Evidence that the halogen entered the α-position was obtained by acid hydrolysis of the bromo- and chlorocyclohexanecarbonitrile and the bromo- and chloro-α-ethylbutyronitrile to give 70–95% of known amides (see Table II). Hydrolysis of the halonitriles with unsymmetrical alkyl groups gave amides that melted at or below room temperature.

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(2) Presented before the Organic Division of the American Chemical Society in Atlantic City in Sept., 1949.

(3) Stevens, THIS JOURNAL, **70**, 165 (1948).

(4) Von Braun, Jostes and Münch, *Ann.*, **453**, 127 (1927).

(5) *Ibid.*, **453**, 146 (1927).

(6) Loder, U. S. Patent, 2,175,810, Oct. 10, 1939.

(7) Merckx and Bruylants, *Bull. soc. chim. Belg.*, **43**, 200 (1934).

TABLE I

α-HALONITRILES

Nitrile	Yield, %	B. p., °C.	Mm.	n^{25}D	d^{25}_4	Nitrogen, % Calcd.	Nitrogen, % Found	Halogen, % Calcd.	Halogen, % Found
$C_2H_5C(CH_3)Cl—CN$ (I)[a]	95	135–136		1.4158	0.9782	11.92	12.03	30.16	30.47
$C_2H_5C(CH_3)Br—CN$ (II)[b]	70	66–67	27	1.4512	1.3227	8.62	8.67	49.32	49.24
$(C_2H_5)_2CCl—CN$ (III)	85	157–158		1.4254	0.9763	10.89	10.68	26.94	26.68
$(C_2H_5)_2CBr—CN$ (IV)[c]	78	85–86	32	1.4583	1.2967	7.96	7.94	45.39	45.38
$C_4H_9C(C_2H_5)Cl—CN$ (V)	76	98–100	30	1.4340	0.9432	8.77	8.54	22.20	21.80
$C_4H_9(C_2H_5)Br—CN$ (VI)	92	112–113	29	1.4600	1.1760	6.86	6.97	39.15	39.02
$CH_2(CH_2)_4CClCN$ (VII)	86	84–86	21	1.4655	1.0668	9.76	9.71	24.69	24.49
$CH_2(CH_2)_4CBr—CN$ (VIII)	70	114–117	36	1.4996	1.3891	7.45	7.58	42.79	42.76

[a] Naster and Gavriloff, *Bull. soc. chim. Belg.*, **42**, 519 (1933). [b] Bockmühl and Schwarz, German Patent 412,820; *Chem. Centr.*, 96, II, 92 (1925). [c] Hoering and Baum, German Patent 186,739; *C. A.*, **2**, 354 (1908).

α-Chloro-α-ethylbutyramide and α-chloro-α-methylbutyramide were shown by independent synthesis to be identical with the amides obtained by hydrolysis of the halonitriles (X).

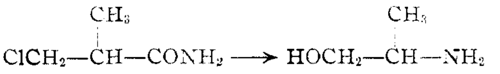
Further evidence for the structure of the α-halonitriles was obtained by a Hofmann degradation of each of the α-haloamides (XI) to the corresponding dialkyl ketone (XII) generally in 40–70% yield.

$$\underset{\text{XI}}{R_1R_2CXCONH_2} + NaOBr \longrightarrow \underset{\text{XII}}{R_1COR_2}$$

β-Chloroisobutyramide and β-chloropropionamide were subjected to the same Hofmann degradation to determine whether a β-haloamide would also give a ketone or aldehyde by reactions XIII → XV; however, no carbonyl compound was produced. With β-chloroisobutyramide (XVI) a 49% yield of 2-amino-1-propanol (XVII) was formed.

$$\underset{\text{XIII}}{R_1CHCl—CHR—CONH_2} + NaOBr + NaOH \longrightarrow$$

$$\underset{\text{XIV}}{R_1CH{=\!=}CR—CONH_2} \longrightarrow \underset{\text{XV}}{R_1CH_2—CO—R}$$



$$\underset{\text{XVI}}{ClCH_2—\overset{\displaystyle CH_3}{\overset{|}{C}H}—CONH_2} \longrightarrow \underset{\text{XVII}}{HOCH_2—\overset{\displaystyle CH_3}{\overset{|}{C}H}—NH_2}$$

XVI XVII

The purity of the α-halonitriles (X) prepared by the halogenation reaction was proven by comparison with the product obtained by the dehydration of an authentic α-haloamide with phosphorus pentoxide. The nitriles from these two reactions were identical in all respects.

Previously, ethyl methyl ketone cyanohydrin was reported to react with phosphorus pentachloride to give α-chloro-α-methylbutyronitrile,[8] but the chloronitrile was not identical with the compound prepared above. Also, hydrolysis of the chloronitrile made from the cyanohydrin gave only an oily amide. Since acetone cyanohydrin gave only β-chloroisobutyronitrile when treated with phosphorus pentachloride under the same conditions,[3] the chloronitrile made from ethyl methyl ketone cyanohydrin also undoubtedly contained a large percentage of β-chloronitrile.

The reaction of phosphorus pentahalides with primary nitriles is a more complicated reaction and will be discussed later.

Experimental

Starting Nitriles.—α-Methylbutyronitrile,[9] b.p. 123–125°; n^{25}D 1.3885, was prepared from α-methylbutyric acid *via* the acid chloride,[10] b.p. 114–115°, and the amide,[10] m.p. 112–113°, in 58% over-all yield.[11]

α-Ethylbutyronitrile,[12] b.p. 142–143°, n^{25}D 1.4001, was prepared similarly in 76% over-all yield from the acid *via* the acid chloride,[13] b.p. 137–139° and the amide,[14] m.p. 112–113°.

α-Ethylcaproamide,[15] m.p. 103°, was prepared in 60% yield from the acid *via* the acid chloride,[13] b.p. 94–96° (31 mm.).

Dehydration of the amide using phosphorus pentoxide gave 88% of α-ethylcapronitrile,[16] b.p. 99–100° (26 mm.); n^{25}D 1.4145. This nitrile contained 11.39% nitrogen (calcd. 11.19%).

Cyclohexanecarboxamide,[17] m.p. 183–185°, was prepared in 70% yield from the acid,[18] b.p. 108–109° (5 mm.), *via* the acid chloride,[19] b.p. 184–187°, or in 60% yield by hydrogenating benzamide at 1100 lb. pressure and a temperature of 100° using Raney nickel catalyst.[20] Dehydration of the amide using phosphorus pentoxide gave cyclohexanecarbonitrile,[21] b.p. 187–188°, n^{25}D 1.4500, in 80% yield.

α-Chlorination of Secondary Nitriles.—In a 100-ml. round-bottomed flask equipped with a reflux condenser and a calcium chloride drying tube, 0.3 mole of the secondary nitrile and an equivalent amount of phosphorus pentachloride were mixed and heated to reflux. After about 5 hours, when the evolution of hydrogen chloride ceased, the mixture was fractionated through a 15 × 1.5 cm. column, packed with glass helices and equipped with a variable take-off total reflux head. The lower boiling fraction consisted of phosphorus trichloride, b.p. 74–76°, in 70–90% yield. After a small intermediate fraction, the pure α-chloronitriles were isolated in 70–90% yield (see Table I).

α-Bromination of Secondary Nitriles.—Phosphorus pentabromide was made by adding one equivalent of bromine to one equivalent of cooled phosphorus tribromide. One equivalent of the secondary nitrile was added to the pentabromide and the reaction mixture heated gently at 60° for about 5 hours, during which time the reaction mixture was protected against moisture. After the hydrogen bromide ceased to be evolved, the reaction mixture was cooled and added with stirring to twice its volume of cracked ice. The organic layer was then taken up in ether, washed successively with sodium carbonate solution and water, dried over magnesium sulfate and fractionated under reduced pressure

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(8) Servais, *Rec. trav. chim.*, **20**, 56 (1901).

(9) Kenyon, Phillips and Pittman, *J. Chem. Soc.*, 1072 (1935).

(10) Newbold and Spring, *ibid.*, 373 (1947).

(11) *Cf.* Kent and McElvain, *Org. Syntheses*, **25**, 58, 61 (1945).

(12) Bowden, THIS JOURNAL, **60**, 131 (1938).

(13) Whitmore, *et al.*, *ibid.*, **63**, 643 (1941).

(14) Hommelen, *Bull. soc. chim. Belg.*, **42**, 243 (1933).

(15) Blicke and Centolella, THIS JOURNAL, **60**, 2924 (1938).

(16) Levene and Kuna, *J. Biol. Chem.*, **140**, 259 (1941).

(17) Aschan, *Ann.*, **271**, 264 (1892).

(18) *Cf.* Gilman and Kirby, "Organic Syntheses," Coll. Vol. 1, John Wiley and Sons, Inc., New York, N. Y., p. 364, 1941.

(19) Wieland, Schapiro and Metzger, *Ann.*, **513**, 103 (1934).

(20) Pavlic and Adkins, THIS JOURNAL, **68**, 1471 (1946).

(21) Grignard, Bellet and Courtot, *Ann. chim.*, [9] **12**, 368 (1919).

TABLE II

AMIDES FROM α-HALONITRILES

Amide	Yield, %	Physical constants	Nitrogen, % Calcd.	Nitrogen, % Found
$C_2H_5C(CH_3)Cl{-}CONH_2$[a]	80	M. p. 36–37°	10.57	10.30
$C_2H_5C(CH_3)Br{-}CONH_2$	85	M. p. 46.5–48°	7.78	7.78
$(C_2H_5)_2CCl{-}CONH_2$	80	M. p. 56–58° (lit.[b] 56–58°)	9.36	9.14
$(C_2H_5)_2CBr{-}CONH_2$	70	M. p. 63–64° (lit.[c] 67°)	7.21	6.98
$\underbracket{CH_2(CH_2)_4C}Br{-}CONH_2$	95	M. p. 115–116° (lit.[d] 117–118°)	8.67	8.69
$\underbracket{CH_2(CH_2)_4C}Cl{-}CONH_2$	73	M. p. 134–136° (lit.[e] 136°)	6.80	7.04
$C_4H_9C(C_2H_5)Cl{-}CONH_2$	75	B. p. 121–123° (5 mm.); $n^{25}D$ 1.4667; d^{25}_4 1.0264	7.89	7.78
$C_4H_9C(C_2H_5)Br{-}CONH_2$	75	B. p. 128–131° (5 mm.); $n^{25}D$ 1.4926; d^{25}_4 1.2724	6.34	6.56

[a] *Anal.* Calcd. for $C_5H_{10}ClNO$: Cl, 26.15. Found: Cl, 25.94. [b] Ref. 23. [c] Fuchs, *Z. angew. Chem.*, **17**, 1508 (1904). [d] Price and Schwarcz, THIS JOURNAL, **62**, 2895 (1940). [e] Fourneau, Montagne and Puyal, *Anales soc. espan. fis. quim.*, [2] 19, 192 (1921); *C. A.*, **16**, 240 (1922).

through the 15 × 1.5 cm. column described above. From 0.2 mole of nitrile, the yield of α-bromonitrile was 70–90% (see Table I).

Amide Derivatives of the Halonitriles.—Derivatives of the nitriles were obtained by hydrolysis to the corresponding amides with sulfuric acid[22] (see Table II). One gram of the nitrile was heated with 2.0 g. of sulfuric acid and poured into cracked ice. The solid amide was filtered and recrystallized from petroleum ether. The unsymmetrically dialkylated α-haloamides melted at about room temperature or below.

α-Chloro-α-ethylbutyramide and Nitrile.—A mixture of 78 g. (0.59 mole) of α-ethylbutyryl chloride and 240 g. (1.8 moles) of sulfuryl chloride were heated with 0.25 g. of iodine for 36 hours. The mixture was then distilled under reduced pressure and fractionated through a four-plate column to give 60 g. (62%) of α-chloro-α-ethylbutyryl chloride,[23] b.p. 84–86° (27 mm.).

The α-chloroacid chloride (20 g., 0.15 mole) was added to 300 ml. of concentrated ammonia at 0° and the resulting amide filtered, dried and recrystallized from petroleum ether, yield 93%, m.p. 57–59°. The melting point of the mixture of this amide with the amide from α-chloro-α-ethylbutyronitrile (III) was not depressed, m.p. 56–58°.

A mixture of 17 g. (0.11 mole) of the purified amide and 18 g. (0.14 mole) of phosphorus pentoxide were heated to 170° at 20 mm. pressure; under these conditions the nitrile distilled as it was formed. Fractionation of the nitrile gave 11 g. (75%) of α-chloro-α-ethylbutyronitrile, identical in all physical properties with III.

α-Chloro-α-methylbutyramide.—This α-chloroamide was prepared in the same manner as the α-chloro-α-ethylbutyramide above. From 31.5 g. (0.26 mole) of α-methylbutyryl chloride and 101 g. (0.75 mole) of sulfuryl chloride, 24.6 g. (56%) of α-chloro-α-methylbutyryl chloride was obtained, b.p. 59–62° (37 mm.). The α-chloroacid chloride (5 g., 0.03 mole) was added to concentrated ammonia and the amide filtered and recrystallized from petroleum ether, yield 95%, m.p. 36–37°. A melting point of the mixture of this amide with the amide from the α-chloronitrile (I) was not depressed, m.p. 35–37°.

Hofmann Degradation of α-Halodialkylacetamides.—A solution of sodium hypobromite was prepared by the addition of 0.6 ml. (0.12 mole) of bromine to a solution of 2.4 g. (0.06 mole) of sodium hydroxide in 20 ml. of water at 0°. The amide (0.01 mole) was dissolved in the sodium hypobromite solution, after which the solution was heated to 70° for 20 minutes. The resulting dialkyl ketone was isolated by steam distillation of the basic reaction mixture. The water soluble ketones were separated from the distillate by salting the product from solution with potassium carbonate. The crude ketones, which were isolated generally in 40–70% yield, were identified by solid derivatives (see Table III).

TABLE III

HOFMANN DEGRADATION OF α-HALOAMIDES

Amide from α-halonitrile	Product, ketone	Yield, %	Derivatives,[a] m. p., °C.
I	Ethyl methyl	10	SC, 136-137; NPH, 128-130
II	Ethyl methyl	53	SC, 135-137, NPH, 130-131
III	Diethyl	47	DNPH, 155-156; NPH 141-143
IV	Diethyl	43	DNPH, 156-157; NPH 141-142
V	*n*-Butyl ethyl	40	SC,[b] 101-102
VI	*n*-Butyl ethyl	70	SC, 99-100
VII	Cyclohexanone	42	DNPH, 159-160; NPH, 144-145
VIII	Cyclohexanone	41	DNPH, 159-161; NPH, 147

[a] SC (semicarbazone); NPH (*p*-nitrophenylhydrazone); DNPH (2,4-dinitrophenylhydrazone). Except as indicated all are common derivatives, *cf.* ref. 22, p. 240. [b] Pickard and Kenyon, *J. Chem. Soc.*, 1936 (1913).

The Hofmann degradation of β-chloropropionamide,[24] m.p. 101–103°, and β-chloroisobutyramide,[8] m.p. 102–104°, under the same reaction conditions gave no carbonyl compounds. From 3.6 g. (0.03 mole) of β-chloroisobutyramide, 1.1 g. (49%) of 2-amino-1-propanol was obtained as a viscous oil and characterized by the preparation of two known derivatives, the phenylthiourea, m.p. 141.5–142°, and the chloroplatinate, m.p. 196–197°, in good yield.

Reaction of Ethyl Methyl Ketone Cyanohydrin with Phosphorus Pentachloride.—Ethyl methyl ketone cyanohydrin was prepared in 60% yield and 10 g. (0.1 mole) was treated with 20 g. (0.1 mole) of phosphorus pentachloride according to the procedure of Servais.[8] The product was isolated in 40% yield, b.p. 60–61° (32 mm.); $n^{25}D$ 1.4300; d^{25}_4 0.9265. The usual hydrolysis failed to give α-chloro-α-methylbutyramide.

Summary

1. Four dialkylacetonitriles were α-halogenated at 60–100° with phosphorus pentachloride and phosphorus pentabromide to give 70–90% of the α-halonitriles.

2. The α-halonitriles were converted in good yield to the α-haloamides each of which gave a dialkyl ketone by the Hofmann degradation.

DETROIT 1, MICHIGAN RECEIVED JUNE 2, 1950

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[22] McElvain, "The Characterization of Organic Compounds," The Macmillan Co., New York, N. Y., 1945, p. 146.

[23] Altwegg and Pivot, U. S. Patent, 1,493,182, May 6, 1924.

[24] Price and Zomlefer, *J. Org. Chem.*, **14**, 210 (1949).