[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE JOHNS HOPKINS UNIVERSITY]

A Group of Isomeric Esters[1]

BY JOHN R. RUHOFF[2] AND E. EMMET REID

The preparation and investigation of the group of esters having the formula RCOOR′, where R and R′ are normal saturated aliphatic residues, containing fifteen carbon atoms together, were undertaken in connection with other work on the general problem of the relation of structure to physical properties. The present paper describes the synthesis and the determination of the more common physical constants of these compounds. Further physical and chemical studies are being carried on in this Laboratory.

Although certain of these esters have been prepared before, it was felt desirable, in order to make significant comparisons of physical properties, to have samples of comparable purity. All of the fifteen isomers have been made in quantities sufficient (usually 1 mole, 256 g.) to permit of a

TABLE I

PROPERTIES OF THE ISOMERIC ESTERS

C atoms in		B. p., °C. at 30 mm.	M. p., °C.	n_D^{20}	d_4^0	d_4^{25}	Coeff. of exp. × 10^4	M_D^{20} (calcd. 77.62)
Alkyl group	Acid							
1	15	199.0	15.46[h]	1.4390	Solid[l]	0.8618	8.91	77.86
2	14	195.0[a]	11.94[i]	1.4362	Solid[m]	.8573	8.96	77.83
3	13	194.0	− 5.74	1.4357	0.8748	.8555	8.90	77.92
4	12	194.0[b]	− 6.84	1.4354	.8747	.8555	8.91	77.88
5	11	193.0	−21.17	1.4356	.8752	.8560	8.86	77.86
6	10	193.0	−17.67	1.4351	.8743	.8553	8.79	77.85
7	9	192.5[d]	−15.54	1.4350	.8745	.8553	8.87	77.84
8	8	192.5[e]	−18.08[f]	1.4352	.8745	.8554[g]	8.87	77.85
9	7	193.0	−11.14	1.4352	.8745	.8552	8.91	77.87
10	6	193.0	−19.29	1.4353	.8743	.8552	8.82	77.88
11	5	193.5	−23.14	1.4358	.8752	.8560	8.87	77.89
12	4	194.5[c]	−22.64	1.4353	.8754	.8562	8.91	77.80
13	3	195.0	− 0.42	1.4363	.8767	.8574	8.94	77.84
14	2	197.0[k]	14.00[j]	1.4373	Solid[n]	.8581	8.97	77.93
15	1	201.5	13.69	1.4399	Solid[o]	.8618	8.93	78.00

[a] B. p. atm. 295°, Reimer and Will, *Ber.*, **18**, 2016 (1885). [b] B. p. 18 mm. 180°, König and Otten, *Ann.*, **473**, 249 (1929). [c] B. p. 19 mm. 177–178°, König and Otten, *ibid.* [d] B. p. 75 mm. 210°, König and Otten, *ibid.* [e] B. p. atm. 305.9°, Gartenmeister, *Ann.*, **233**, 289 (1886). [f] M. p. −9 to −12°, Gartenmeister, *ibid.* [g] d_0^0 0.8755, Gartenmeister, *ibid.* [h] M. p. 10°, Eckert and Halla, *Monatsh.*, **34**, 1821 (1913). M. p. 18.5°, Le Sueur, *J. Chem. Soc.*, **87**, 1898 (1905). [i] M. p. 10.5–11.5°, Nördlinger, *Ber.*, **18**, 2623 (1885). M. p. 11.93°, Meyer and Reid, Ref. 4. [j] M. p. 14.01°, Meyer and Reid, *ibid.* M. p. 11°, Garner and Rushbrooke, *J. Chem. Soc.*, 1351 (1927). M. p. 12–13°, Krafft, *Ber.*, **16**, 1720 (1883). [k] B. p. 15 mm. 175.5–176.5°, Krafft, *ibid.* [l] d_4^{35} 0.8541. [m] d_4^{35} 0.8497. [n] d_4^{35} 0.8503. [o] d_4^{35} 0.8541.

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(1) From a part of the Ph.D. dissertation of John R. Ruhoff, June, 1932.

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high degree of purification and to allow the determination of a wide range of physical and chemical properties.

Emphasis was placed primarily on the preparation of compounds of the highest purity consistent with the attendant experimental difficulties, rather than on high yields. Yields are therefore not reported, but in almost all reactions they were 70% or more. All distillations were carried out in precision stills.[3] Each intermediate was fractionated; except in a few instances, the portion used for synthesis boiled with a range of 0.4° or less.

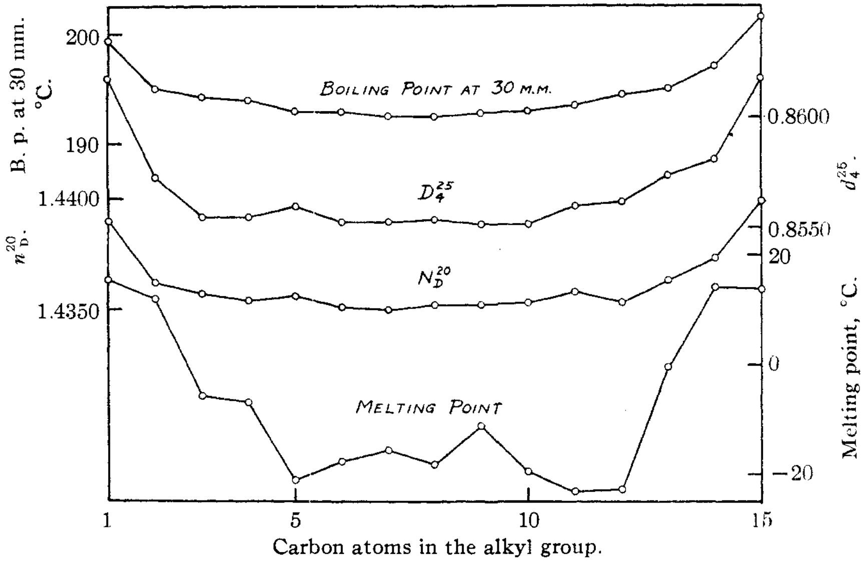

Fig. 1.

The results of the physical measurements are given in Table I and summarized in Fig. 1. When the data are plotted against the number of carbon atoms in the alcohol, the curves obtained for the boiling points, refractive indexes, and densities are very similar. Distinct alternation of the refractive indexes and densities occurs near the ends of the curves; the values for the middle five esters are practically identical. It is noteworthy that high values are found for the 5-11 and 11-5 compounds. The boiling points are remarkably close together; the extreme range is 9° and all except three of the compounds boil within 2.5° of each other. The melting points, on the other hand, cover a range of almost 40°; for the most part they show alternation.

Experimental

(A) **Alcohols.**—Amyl alcohol was prepared by the Grignard reaction from butyl bromide and formaldehyde. Hexyl, nonyl, undecyl, tridecyl, tetradecyl, and penta-

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[3] Peters and Baker, *Ind. Eng. Chem.*, **18**, 69 (1926).

decyl alcohols were prepared by the reduction of an ester of the corresponding acid with sodium in butyl alcohol.[4] Octyl, decyl and dodecyl alcohols were obtained by the fractionation of "Lorol," purchased from Germany. Heptyl alcohol was prepared by the reduction of heptaldehyde with iron filings in acetic acid,[5] with a small amount of nickel chloride as a catalyst. Baker 40-mesh degreased cast iron fillings were used. In over fifty reductions made in this Laboratory, the reaction has never failed to occur when nickel chloride was added.

(B) **Acids.**—Valeric, tridecylic and pentadecylic acids were prepared from the proper bromides and potassium cyanide.[6] Caproic and pelargonic acids were prepared by the malonic ester synthesis from butyl and heptyl bromides, respectively. Anhydrous butyl alcohol was used as a solvent. Caprylic, capric, lauric and myristic acids were obtained by the fractionation of the ethyl esters made from coconut oil acids. Undecylic acid was obtained by the hydrogenation of ethyl undecylenate at 220°, using a high speed stirrer[7] and 4% of nickel formate as a catalyst. Heptoic acid was prepared by the oxidation of heptaldehyde with potassium permanganate and 20% sulfuric acid at 20°.

(C) **Esters.**—**Methyl pentadecylate, ethyl myristate and propyl tridecylate** were prepared by heating together 1 mol of the acid, 4 mols of alcohol containing 3–5% of anhydrous hydrochloric acid, and 30 g. of anhydrous calcium chloride.

Butyl Laurate.—To 1 mol of lauric acid was added 3 mols of anhydrous butyl alcohol, containing 20 g. of anhydrous hydrochloric acid. After the solution had been refluxed a short time two layers formed. The lower (water) layer was removed, and the butyl alcohol distilled off slowly.

Amyl Undecylate, Hexyl Caprate, Heptyl Pelargonate, Octyl Caprylate, Nonyl Heptoate, Decyl Caproate and Undecyl Valerate.—One mol of alcohol, 1 mol plus 10 g. of acid, and 15 g. of anhydrous hydrochloric acid were warmed together until two layers were formed. The lower layer was removed, and the residue was gradually heated to 180° during the course of two hours while a slow stream of carbon dioxide was passed through it.

Dodecyl Butyrate and Tridecyl Propionate.—One mol of alcohol, 1.5 mols of acid (3 mols in the case of the propionic acid), and 25 g. of anhydrous hydrochloric acid were distilled together slowly until the boiling point rose to that of the acid.

Tetradecyl acetate was prepared from the alcohol, acetic anhydride and sodium acetate by the usual well-known procedure.

Pentadecyl Formate.—One hundred and eighty grams of pentadecyl alcohol, 460 g. of 90% formic acid and 400 cc. of carbon tetrachloride were heated in a continuous esterification apparatus for twenty-four hours; at the end of that time the reaction was 85% complete. The pentadecyl formate and the residual pentadecyl alcohol were separated and refluxed for six hours with 460 g. of anhydrous formic acid.[8] The ester layer was separated and distilled slowly with 600 cc. of carbon tetrachloride and 230 g. of anhydrous formic acid until the boiling point rose to 100°.

Purification of Esters.—The esters, with the exception of pentadecyl formate, were washed twice with warm water, then with warm 1 to 50 ammonia water, twice with warm water again, dried with calcium chloride, filtered, and distilled at 30 mm.

Freezing Points.—The freezing points were determined with a copper–constantan thermocouple in an apparatus designed by R. H. Smith, and similar to that described by Andrews, Kohman and Johnston.[9]

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(4) Meyer and Reid, THIS JOURNAL, **55**, 1574 (1933).

(5) Clarke and Dreger, "Organic Syntheses," Vol. VI, p. 52.

(6) Adams and Marvel, THIS JOURNAL, **42**, 312 (1920).

(7) Milligan and Reid, *Ind. Eng. Chem.*, **15**, 1048 (1923).

(8) Garner, Saxton and Parker, *Am. Chem. J.*, **46**, 236 (1911).

(9) Andrews, Kohman and Johnston, *J. Phys. Chem.*, **29**, 914 (1925).

TABLE II

ANALYTICAL DATA ON NEW COMPOUNDS

Compound	%C	%H	Saponification value	Compound	%C	%H	Saponification value
Calcd.	74.93	12.59	256.3	Calcd.	74.93	12.59	256.3
3–13	74.81	12.66	259.3	10–6	74.85	12.43	258.1
5–11	74.94	12.46	256.7	11–5	74.92	12.69	258.2
6–10	74.88	12.59	256.3	13–3	74.94	12.51	258.8
9–7	74.91	12.61	258.0	15–1	75.10	12.65	259.5

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Summary

Fifteen isomeric esters have been prepared and their more common physical constants have been determined.

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The Structure of Cuscohygrine. Synthesis of Ethyl Homohygrinate

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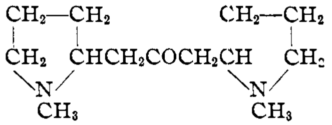
Two structures have been proposed for cuscohygrine, one of the alkaloids associated with cocaine occurring in "cusco" leaves, a variety of South American coca. The structure (I) was suggested by Liebermann and Cybulski,[1] who were the first to isolate and study the alkaloid. Hess and his associates[2] have suggested the isomeric formula (II). Both structures are in agreement with the fact that cuscohygrine gives the typical reactions for a ketone group[2a] and that oxidation with chromic acid yields hygrinic acid (III) whose structure had been established by Willstätter.[3] Although Formula I is the only one which is consistent with the formation of *n*-undecane and *n*-undecanol-6 by an exhaustive methylation and degradation[4] of dihydrocuscohygrine, the structure represented by II has been



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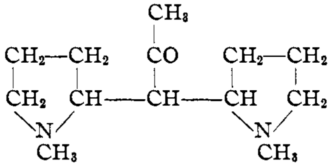

II

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(1) Liebermann and Cybulski, *Ber.*, **28**, 578 (1895).

(2) (a) Hess and co-workers, *ibid.*, **53**, 781 (1920); (b) **54**, 2310 (1921); (*c*) **48**, 1986 (1915).

(3) Willstätter, *ibid.*, **33**, 1160 (1900).

(4) Hess and Bappert, *Ann.*, **441**, 137 (1925).