determined, and according to the test, this means any dry mixture containing less than 20% hog bile salts. The precipitate, because of its nature, cannot be washed well. This latter defect, however, is relative, and can be taken care of by the use of the solubility curve shown as Fig. 1.

It is true the curve may vary with different lots of hog and beef bile salts, but even then the deviation is not unreasonable, as shown in the final column of Table I, when the standard curve is used.

CONCLUSION

1. An identification test is proposed for hog bile. This test, together with increasing availability and pharmaceutical use of hog bile, suggests the advisability of including hog bile extract in either the U. S. Pharmacopeia or the National Formulary. The monograph on the official product might well include: Description; Solubility; Acidity; Insoluble Substances; Qualitative Color Test—Purple Color; Assay; Quantitative Precipitation from Mixture if Not Pure; Packaging and Storage; Dosage (same as ox bile extract).

2. The proposed assay method is not for a specific bile acid in hog bile, as for hyodesoxycholic acid, but the test provides for the identity of a pure hog bile salt by a qualitative color test. Where the color test indicates the possible presence of bile salts other than those of hog bile, the precipitation method described above indicates the amount of hog bile salt, and the amount of beef and/or sheep bile present.

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Alkamine Esters and Amides of Cumic Acid*

By M. B. MOORE

A series of previously unreported esters and amides of cumic acid is presented, with appropriate physical data. None was found to surpass the β-diethylaminoethyl ester in value as a local anesthetic.

THE PUBLICATION of a paper by Bryan and Foote (1) on esters of cumic acid has prompted this report of a number of similar esters synthesized in these laboratories for testing as local anesthetics. Since the esters of this series show no advantage as local anesthetics over the diethylaminoethyl ester, their publication may prevent needless repetition of work. Included are two amides which were prepared and tested at the same time. Pertinent data are summarized in Table I.

Except for those reported by Bryan and Foote (1), the only alkamine esters of cumic acid found in the literature were included in the series by Reasenberg and Goldberg (2) in which the alkamine residue contained a secondary amine, and by McElvain and Carney (3) in which the amine was the 2-methyl-1-piperidine radical. In neither case did the cumic acid esters appear to be as effective therapeutically as those derived from some other acids.

The syntheses were carried out by a conventional method, in which the acid chloride and amino alcohol or diamine were allowed to react in dry benzene. The salts of the amides proved to be very difficult to purify, and when the results of the pharmacologic testing of these two became known, no further members were synthesized.

The pharmacologic tests were carried out by Dr. R. K. Richards and his staff. Compounds

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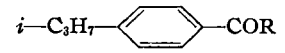
TABLE I.—ESTERS AND AMIDES OF CUMIC ACID



No.	R	Yield, %	B. P.	Mm.	Hydrochloride[c] M. P.	Hydrochloride[c] Formula	Analysis, % N Calcd.	Analysis, % N Found
1	$OCH_2CH_2N(C_2H_5)_2$[a]	40	...	...	118–121	$C_{16}H_{25}NO_2 \cdot HCl$	4.67	4.71
2	$OCH_2CH_2N(n\text{-}C_4H_9)_2$	50	...	...	105–106	$C_{20}H_{33}NO_2 \cdot HCl$	3.94	3.78
3	$O(CH_2)_3N(n\text{-}C_4H_9)_2$	62	...	...	130–131	$C_{21}H_{35}NO_2 \cdot HCl$	3.79	3.62
4	$OCH_2C(CH_3)_2CH_2N(CH_3)_2$	57.5	...	...	140–142	$C_{17}H_{27}NO_2 \cdot HCl$	4.46	4.35
5	$OCH_2C(CH_3)_2CH_2N(CH_3)_2O(CH_2)_2$	70	...	...	142–144	$C_{19}H_{29}NO_2 \cdot HCl$	3.94	3.90
6	$OCH_2CH_2NH-C(CH_3)(CH_2-O-CH_2-O-CH_3)_2$	32.5	205–207	4	...	$C_{17}H_{25}NO_4$	4.57	4.55
7	$NHCH_2CH_2N(C_2H_5)_2$[b]	63	...	...	136–137	$C_{16}H_{28}N_2O \cdot HCl$	9.38	8.84
						$C_{16}H_{28}N_2O \cdot HCl \cdot H_2O$	8.78	
8	$NHCH(CH_3)(CH_2)_3N(C_2H_5)_2$	30	200–218	5	158–159	$C_{19}H_{32}N_2O$	9.20	9.11

[a] Reported by Bryan and Foote (1) to have m. p. 131–132° (corr.).
[b] Sample recrystallized successively from methyl propyl ketone, benzene, di-isopropyl ketone, and soaked in alcohol.
[c] Melting points are uncorrected.

1 and 7 were approximately equal to procaine in anesthetic effect in wheals, but were irritating. The other compounds listed were in no case less irritating and usually were much more so. All except compounds 6 and 8 were reported to have local anesthetic effect.

EXPERIMENTAL[1]

γ-Di-*n*-butylaminopropyl Cumate.—γ-Di-*n*-butylaminopropanol, 9.5 Gm. (0.05 mole), in 30 cc. of dry benzene was added gradually through a dropping funnel to a stirred and refluxing solution of 9.2 Gm. (0.05 mole) cumoyl chloride in 50 cc. of dry benzene. After an hour of refluxing, no precipitation occurred. The solution was filtered and the filter washed with a little benzene; crystallization began and the filtrate became a crystal mush. The crystals were removed by filtration and dried at 100°; yield, 13 Gm. (70%). The product was recrystallized from ethyl acetate and again from benzene, m. p. 130–131°.

N-δ-Diethylamino-α-methylbutyl Cumoylamide.—Cumoyl chloride, 9.2 Gm. (0.05 mole), was dissolved in 50 cc. of dry benzene. To the stirred solution 10 Gm. (about 0.05 mole) of Novoldiamine (δ-diethylamino-α-methylbutylamine) was added dropwise to prevent too rapid heating; the product was then refluxed for three hours to assure completion of the reaction. The solvent was removed on the steam bath, the residue was taken up in water with a little excess hydrochloric acid, the aqueous solution was shaken out with ether to remove nonbasic impurities and was filtered with the aid of a little charcoal. The clear aqueous solution was made strongly alkaline; the base was shaken out in ether finally distilled after removal of the ether, b. p. 200–218° (5 mm.); yield, 5 Gm. (30%).

[1] The cumoyl chloride and compound 1 were first prepared in these laboratories by Dr. E. E. Moore. All analyses were performed by Mr. E. F. Shelberg, Chief Microanalyst, and his staff.

SUMMARY

Some new alkamine esters and amides of cumic acid have been synthesized, and their hydrochlorides have been studied as local anesthetics. The variety of different groups used has shown no member with outstanding activity devoid of irritating effects.

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