mit their associated crystal structures to be classified as typical double-chain-length structures. It is shown in this paper that most of these abnormal values can be interpreted as due to triple-chain-length structures analogous to that of the mixed unsaturated C_{18} triglyceride, 2-oleyldistearin. This triple structure presumably arises from a sorting of chains—sorting of short from long chains in the case of mixed saturated triglycerides, in manner similar to the sorting of unsaturated from saturated chains for 2-oleyldistearin.

These considerations lead to the proposal of a new type of molecular configuration in triglyceride crystals, a "chair" type of arrangement for certain unsymmetrical compounds in contrast to the generally accepted "tuning fork" arrangement.

Long spacings corresponding to quadruple-chain length structure have also been noted.

IVORYDALE, OHIO RECEIVED[11] AUGUST 13, 1947

(11) Original manuscript received March 6, 1947.

[CONTRIBUTION FROM THE DIVISION OF MEDICINAL CHEMISTRY, THE SQUIBB INSTITUTE FOR MEDICAL RESEARCH]

The Skraup Reaction with Acrolein and its Derivatives[1]

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A recent report[2] from these laboratories has described the synthesis of 6-methoxy-8-nitroquinoline in 42.3% yield, by a modified Skraup reaction. Some additional studies on the utilization of this reaction in the preparation of quinoline derivatives have now been completed. The results are summarized in Table I. Method A refers to the reaction conditions previously reported[2] while Method B is a new modification of the Skraup reaction employing acrolein and 85% phosphoric acid with arsenic acid as the oxidizing agent at 100°.

In the preparation of 6-methoxy-8-nitroquinoline by Method B a 60% yield is obtained at 100°, however, at 25°, the yield is 25% and at 65°, 54%; The use of 100% phosphoric acid has only a very slight advantage over 85% acid (65% yield as compared to 60%) but a marked decrease in yields occur with 75% acid (35%) and 50% acid (24%).

Acrolein diethyl acetal, β-ethoxypropionaldehyde and β-ethoxypropionaldehyde diethyl acetal, each of which is capable of yielding acrolein under the modified Skraup conditions, were substituted for acrolein in the reaction with 3-nitro-4-aminoanisole and 2-amino-5-nitroanisole; each gave slightly lower yields of the substituted quinoline.

TABLE I

SKRAUP REACTION WITH ACROLEIN AND ITS DERIVATIVES

Amine	Quinoline derivative Yield, % Method A	Method B	M. p., °C. Found
Aniline[a]	Trace	3[b]	199–200
o-Nitroaniline	32	26	87–88
p-Nitroaniline	28	32	147–148
p-Anisidine	13	...	27
p-Bromoaniline	5[b]	5[b]	209
2-Amino-4-nitroanisole	5	59	148–149
2-Amino-5-nitroanisole[c]	30	67	147–148[g]
4-Amino-5-nitroveratrole	36	51	125–126
3-Nitro-4-aminoanisole[d,e,f]	42	60	157–158

[a] Ardashev, *J. Gen. Chem.* (*U. S. S. R.*), **16**, 47 (1946), recently has reported the synthesis of quinoline in poor yield from aniline and acrolein in the presence of sulfuric and hydrochloric acids. [b] Isolated as the picrate. [c] β-Ethoxypropionaldehyde by Method B gave 60% yield. [d] The acetylated amine with acrolein by Method A gave 43% yield. [e] The amine with various acrolein derivatives by Method A gave: with β-ethoxypropionaldehyde, 39%; with β-ethoxypropionaldehyde diethyl acetal, 34%; with acrolein diethyl acetal, 21%. [f] The amine with α-methylacrolein gave the corresponding methyl quinoline in 19% yield by Method A; in 59% yield by Method B, m. p. 173–174°. *Anal.* Calcd. for $C_{11}H_{10}O_3N_2$: C, 60.55; H, 4.59; N, 12.84. Found: C, 60.87; H, 4.64; N, 12.96, 12.76. [g] *Anal.* Calcd. for $C_{10}H_8O_3N_2$: N, 13.72. Found: N, 13.52.

Acknowledgment.—The authors are indebted to Mr. W. A. Lott for his interest and encouragement. The microanalyses were carried out by Mr. J. F. Alicino.

Experimental

All temperatures are uncorrected.

Method B.—Skraup Reactions with Phosphoric Acid.—A mixture of 33.6 g. (0.2 mole) of 3-nitro-4-aminoanisole and 56.8 g. (0.4 mole) of arsenic acid in 200 ml. of 85% phosphoric acid was placed in a 1-liter, 3-necked flask fitted with a thermometer, dropping funnel, reflux condenser and mercury-sealed stirrer. The reaction mixture was warmed to 100° and 19 ml. (0.3 mole) of acrolein added dropwise with vigorous stirring. The rate of addition was regulated so as to maintain the temperature at 100 ± 2°. After all the acrolein had been added (twenty-five minutes), the reaction mixture was stirred for an additional thirty minutes during which time the temperature was maintained at 100° by warming with an oil-bath. The solution was poured into 800 ml. of water, treated with Hyflo and decolorizing carbon and filtered. The filtrate was made alkaline with aqueous ammonia and the precipitated product filtered. The dried solid was refluxed with 600 ml. of ethyl acetate and decolorizing carbon, filtered, and concentrated until crystallization started. The product weighed 25 g. (60% yield), m. p. 157–158°.

Summary

A modified Skraup reaction with acrolein and α-methylacrolein has been carried out with substituted anilines. The reaction has been extended to include compounds capable of yielding acrolein, *in situ*.

NEW BRUNSWICK, N. J. RECEIVED APRIL 28, 1947

(1) Presented before the Division of Organic Chemistry of the American Chemical Society, Atlantic City, N. J., April 15, 1947.

(2) Yale, THIS JOURNAL, **69**, 1230 (1947).