(240%); (II) that the stretched tanned sheet is materially stronger in the direction of stretch than is the non-tanned sheet; (III) that in the non-tanned sheets there is no correlation between strength and direction of stretch, while in the tanned sheets this correlation is pronounced; (IV) that in the non-tanned sheets, stretching did not cause any observable increase in strength.

Since the strength of the stretched tanned sheet was several times greater than that of the non-stretched tanned sheet, it appeared advisable to investigate whether the tanning itself had been impeded by the stretching process. For this purpose, the softening points of the sheets were determined on circular samples of 25 mm. diameter, by the Ring and Ball method, in oil-bath.

The softening points of both of the non-tanned sheets were 60 ± 1°, while those of the stretched as well as the non-stretched tanned sheets exceeded 110°.

The elongation of the stretched sheets at the termination of the test was approximately 5%, and was thus insignificant in relation to the effects observed.

The condition of the gel sheet tanned without stretch was representative of similar gels tanned to a softening point exceeding 110°, regardless of the tanning agents employed, but the strength and elasticity of the stretched and tanned sheets far exceed anything the authors have ever seen in such gels having a softening point above 100° in their many years of experience with industrial protein gels of this general formulation. The high softening point conclusively proves that the tanning agent remained and was active in the tanned stretched sheets. Manifestly the continued stretch exerted a directional influence on the positioning of tanning bridges in relation to the protein molecules, so that the tanning bridges connecting the protein molecules were formed in positions not interfering with stretch and relaxation of the gel.

The condition of repeated stretching and relaxation is even present in the walls of the arteries of higher animals. The effect described above may be of considerable importance in delaying the aging of arteries, and may at least in part explain the slow progress of this aging in spite of the well-known presence of active tanning agents in the blood stream. The effect may also be a factor contributing to the beneficial effects of exercise, and to the atrophy of organs under conditions of continued absence of stretch.

Further work is in progress.

Summary

Rhythmical stretching and relaxation of a protein gel containing a tanning agent, caused a very great increase of tensile strength over a similarly tanned non-stretched gel, *in all directions in the gel.* The effect did not take place in the absence of the tanning agent. The softening point of the stretched gel rose as in normal tanning.

Analogies with conditions in human arteries are discussed.

CHICAGO, ILL. RECEIVED NOVEMBER 10, 1941

[CONTRIBUTION FROM THE RESEARCH LABORATORIES OF MERCK & CO., INC.]

N-Allylnormorphine

BY JOHN WEIJLARD AND A. E. ERICKSON

In a recent note McCawley, Hart and Marsh[1] described the preparation and properties of N-allylnormorphine, which appears to be the first N-substituted normorphine derivative to be reported. Our many efforts to repeat the preparation as outlined in this note have failed.

We have found that normorphine reacts readily with allyl bromide in the presence of chloroform at 110°. The properties of the product and of its hydrobromide are entirely different from those reported by McCawley, *et al.* That the N-allylnormorphine structure should be assigned to our product was proved by converting it into N-allylnorcodeine according to Rodionov's method.[2] A comparison of our N-allylnorcodeine with a sample synthesized from norcodeine by the procedure of von Braun[3] indicated that the two were identical.

The normorphine used in our investigation was prepared by the method of von Braun,[4] as well as

(1) McCawley, Hart and Marsh, THIS JOURNAL, **63**, 314 (1941).

(2) Rodionov, *Bull. soc. chim.*, **39**, 305 (1926).

(3) von Braun, *Ber.*, **49**, 977 (1916).

(4) von Braun, *ibid.*, **47**, 2312 (1914).

by the method of Speyer and Walther.[5] The normorphine prepared by the two methods was identical in every respect. The von Braun method gave a higher over-all yield than the Speyer and Walther method.

It is of interest to note that when normorphine is crystallized from methanol, it crystallizes with one-half mole of methanol which cannot be removed by drying *in vacuo* at 110°. By precipitating the base from an aqueous solution, we obtained a sample of anhydrous normorphine that analyzed correctly but melted several degrees higher than previously recorded in the literature.

Experimental

Normorphine.—The normorphine crystallized from methanol melted at 272–273°. *Anal.* Calcd. for $C_{16}H_{17}O_3N \cdot {}^1/_2CH_3OH$: C, 68.95; H, 6.67; N, 4.88. Found: C, 68.98; H, 6.48; N, 4.88.

0.2 gram of this normorphine was dissolved in 5 cc. of cold 1% sodium hydroxide solution, acidified with acetic acid and then made alkaline with ammonia. The crystals were collected on a filter, washed with ice water and dried *in vacuo;* m. p. 276–277°. *Anal.* Calcd. for $C_{16}H_{17}O_3N$: C, 70.82; H, 6.32; N, 5.17. Found: C, 70.64; H, 6.68; N, 5.14.

N-Allylnormorphine.—Thirty-five grams of normorphine (two mol. equivalents) and 7.95 g. of allyl bromide (one mol. equivalent) in 350 cc. of chloroform were heated in a sealed tube at 110° for three and one-half hours. The reaction mixture was filtered and the solid residue washed with chloroform. From this residue of normorphine hydrobromide 18 g. of normorphine was recovered by dissolving in water and precipitating the base with ammonia water at a *p*H of 8.

The chloroform solution was evaporated to dryness *in vacuo* and the residue triturated with 75 cc. of ether, cooled in an ice-bath two hours and filtered; yield 9.2 g. of crude N-allylnormorphine. The crude product was extracted for fifteen hours in a Soxhlet extractor with anhydrous ether. The ether extract was concentrated in absence of air to incipient crystallization and cooled in the ice box overnight. The white crystals were collected, washed with some ether and dried *in vacuo;* yield 5.6 g. of N-allylnormorphine; m. p. 208–209° (McCawley, *et al.*,[1] give 92–93°). *Anal.* Calcd. for $C_{19}H_{21}O_3N$: C, 73.26; H, 6.80; N, 4.50. Found: C, 73.19; H, 7.18; N, 4.54.

The base is soluble in dilute alkali and gives a positive ferric chloride test indicating a free phenolic group. It is soluble in chloroform, alcohol and acetone but sparingly soluble in ether or water.

N-Allylnormorphine Hydrobromide.—The free base was dissolved in ethanol and a slight excess of alcoholic hydrobromic acid was added; the hydrobromide crystallized out rapidly on scratching. The crystals were collected, washed with cold alcohol and dried *in vacuo;* m. p. 258–259° (McCawley, *et al.*[1], give 126°).

Conversion of N-Allylnormorphine to N-Allylnorcodeine.—Two grams of N-allylnormorphine was methylated according to Rodionov's method by treating the base with phenyltrimethylammonium hydrate in alcohol; yield 1.60 g. of crude material. The crude product was dissolved in 10 cc. of ether; on seeding with N-allylnorcodeine (made from codeine by the von Braun method[3]) crystallization occurred at once. It was chilled to −5°, filtered and washed with cold ether; yield 0.40 g.; m. p. 93°; mixed m. p. showed no depression.

An analytically pure sample was prepared by dissolving 0.37 g. in 0.75 cc. of ethyl acetate, chilling to −10°. The crystals were collected on a microfilter and washed with 3 drops of cold ethyl acetate; yield 0.10 g. first crop; m. p. 95°.

Anal. Calcd. for $C_{20}H_{23}O_3N$: C, 73.80; H, 7.13; N, 4.31. Found: C, 73.68; H, 7.20; N, 4.37.

Acknowledgment.—We are grateful to Dr. Max Tishler for helpful suggestions. We are also indebted to Messrs. D. F. Hayman, W. R. Reiss, H. S. Clark and R. N. Boos for microanalyses.

Summary

N-Allylnormorphine and its hydrobromide have been prepared and some of their properties described. The structure of N-allylnormorphine has been confirmed by methylation to N-allylnorcodeine.

RAHWAY, NEW JERSEY RECEIVED NOVEMBER 26, 1941

(5) Speyer and Walther, *Ber.*, **63**, 852 (1930).