mixture treated with dilute hydrochloric acid and ether, the ether dried over sodium sulfate and distilled. The residue was heated on the steam bath 2 hr. with 1.0 ml. of α-naphthylisocyanate and an excess of reagent decomposed with 90% aqueous acetone. The mixture was concentrated to dryness, the residue boiled with petroleum ether (b.p. 60–80°) and the extract poured over 20 g. of silica gel. The column was washed with 500 ml. of 1:1 benzene-petroleum ether and the product eluted with benzene. Crystallization of the residue from petroleum ether yielded 0.8 g. *l*-ethylphenylcarbinyl-α-naphthylurethane (VII) as needles, m.p. 113–115°. Recrystallization from the same solvent raised the m.p. to 116–117°, $[\alpha]_D$ −31.5°.

A duplicate experiment using racemic base (3.7 g.) gave racemic ethylphenylcarbinyl-α-naphthylurethane, 1.1 g., needles from petroleum ether, m.p. 102–103° (lit.,[9] m.p. 102°).

Levo-ethylphenylcarbinol[4] was converted to the *l*-α-naphthylurethane, needles from petroleum ether, m.p. 115–116°, $[\alpha]_D$ −31.5°.

Anal. Calcd. for $C_{20}H_{19}NO_2$: C, 78.66; H, 6.27; N, 4.59. Found: C, 78.55; H, 6.24; N, 4.81.

Acknowledgment: We would like to thank C. G. VanArman and Miss Norma Bylenga for the pharmacological results. Discussions with R. M. Dodson on stereochemistry and with R. Pappo on the von Braun degradation were very helpful.

We are indebted to R. T. Dillon, H. W. Sause and their associates for analyses and rotations. Analytical samples were dried under high vacuum one hour at 118° unless otherwise stated. Rotations were determined at 25 ± 3° in methanol at a concentration of 1%.

G. D. Searle & Co.
Chicago 80, Illinois

(9) V. T. Bickel and H. E. French, *J. Am. Chem. Soc.*, **48**, 747 (1926).

Rearrangements During Phosphoryl Chloride–Pyridine Dehydrations

R. R. Sauers and J. M. Landesberg[1]

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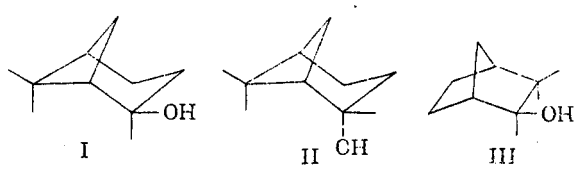
In an extension of some earlier work[2] on the effect of structure on the course of phosphoryl chloride–pyridine dehydration of tertiary alcohols we have examined the effect of these reagents on *cis*-methylnopinol (I), *trans*-methylnopionol (II),[3] and camphene hydrate (III).

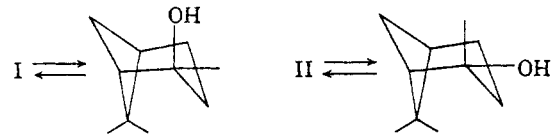


(1) Abstracted in part from the Bachelors thesis of J. M. L. (1960).

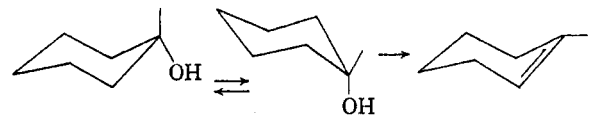
(2) R. R. Sauers, *J. Am. Chem. Soc.*, **81**, 4873 (1959).

(3)(a) W. D. Burrows and R. H. Eastman, *J. Am. Chem. Soc.*, **81**, 245 (1959); (b) W. Huckel and E. Gelchsheimer, *Ann.*, **625**, 12 (1959).

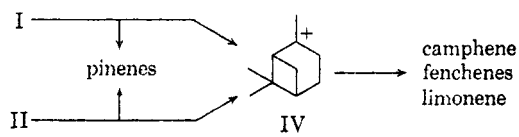
If alcohols I and II are considered in the indicated conformations, the *cis* alcohol would be expected to lead to β-pinene (exocyclic double bond) and the *trans* alcohol would be expected to lead to α-pinene (endocyclic double bond), owing to the equatorial and axial nature of the respective hydroxyl groups.[2] Ring inversion would reverse the axial-equatorial relationships and consequently the dehydration products. It should be noted that ring inversion relieves a 1,3-diaxial interaction and creates a 1,4-methyl-hydrogen interaction. Thus,



if these forms are rapidly equilibrating, both isomers would be expected to lead to α-pinene since 1-methylcyclohexanol gives only 1-methylcyclohexene[2]:



Experimentally, it was found that both alcohols gave mainly α-pinene.[4] Of even greater interest is the formation of considerable amounts of camphene, limonene, β-pinene and some of the fenchenes. The reaction product was too complex (*ca.* ten components) to be completely resolved by vapor phase chromatography and accurate data on the ratios of the components were therefore not attainable. The two mixtures were clearly different, however, ruling out the possibility of a common intermediate. It does not seem unreasonable to assume that part of the elimination proceeds *via* a common symmetrically solvated carbonium ion (IV) and the remainder through either an unsymmetrically solvated carbonium ion or by an E_2 mechanism. The carbonium ion IV could be



transformed into the indicated products by well known rearrangements.

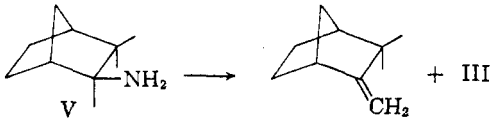
It is clear from these results that the use of this reaction for dehydration of alcohols of unknown structure should be accompanied by careful product determination and possible rearrangements considered.

Dehydration of camphene hydrate gave only camphene. In this system, elimination must be

(4) M. Vilkas, G. DuPont, and R. Dulou, *Compt. rend.*, **242**, 1329 (1950) reported that I was dehydrated to a 5:1 mixture of α:β-pinene. These authors did not examine this product by vapor phase chromatography.

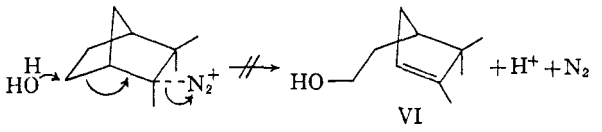
rapid compared to rearrangement and ring opening since no limonene was found in the product.

The method of preparation of the camphene hydrate used in this study is of some interest. 3-Amino-*d,l*-isocamphane[5] (V) was diazotized with nitrous acid to give a 40:60 mixture of camphene-camphene hydrate. Virtually no α-terpineol was found in the product in accord with expectations



based on Streitwieser's mechanism[6] for nitrous acid deamination. The "hot" ion theory[7] could also explain this result if it is assumed that the camphyl ion reacts faster than it rearranges to the bornyl ion. It becomes necessary then, to postulate two different bornyl carbonium ions (tetrahedral carbonium ions) since bornylamine but not isobornylamine gives α-terpineol on deamination.[8]

The possibility of another mode of decomposition of the amine V was also examined. Attack of solvent at C_5 with concurrent loss of nitrogen could be envisaged to lead to ring-opened products as follows:



No evidence for this type of decomposition could be found by careful examination of the vapor chromatogram of the deamination product.[9]

EXPERIMENTAL

cis-Methylnopinol (I).[3b] β-Pinene epoxide was prepared in 50% yield from 20 g. of β-pinene in 50 ml. of dry ether by addition to an ice-cold mixture of 30 g. of 40% peracetic acid, 3 g. of anhydrous sodium acetate, and 250 ml. of dry ether. After stirring for 2.5 hr. at 25° the mixture was quenched with 150 ml. of water and the aqueous phase extracted with ether. The extracts were washed with sodium carbonate solution, dried, and evaporated. Distillation of the residue at 20 mm. gave some β-pinene and 11.4 g. of β-pinene oxide, b.p. 89–96° [lit.,[3b] b.p. 83° (12 mm.)].

The epoxide was reduced with lithium aluminum hydride[3b] to give *cis*-methylnopinol, m.p. 77–79° $[\alpha]_D^{25}$ −24.0° after chromatography (lit., m.p. 78–79°, $[\alpha]_D^{20}$ −24.39°[10] and m.p. 77.5–78°, $[\alpha]_D^{20}$ −24.5°[4]).

trans-Methylnopinol (II) was prepared by the action of methylmagnesium iodide on nopinone[3b] and had m.p. 58–59°, $[\alpha]_D^{25}$ −4.30° (lit., m.p. 57–59°, $[\alpha]_D^{20}$ −4.35°[3b] and m.p. 58–59°, $[\alpha]_D^{18}$ −4.99°[11]).

Dehydrations of alcohols I and II. The *cis* alcohol I was dehydrated by treatment of 0.65 g. in 10 ml. of ice-cold pyridine with 2.5 ml. of phosphoryl chloride. After standing for 20 hr. at 0° the mixture was poured onto 50 ml. of an ice-water mixture and extracted with pentane. The extracts were washed with dilute hydrochloric acid, sodium carbonate solution, and water. Evaporation of the pentane gave 0.30 g. of product.

The *trans* alcohol II (1.5 g.) was dehydrated similarly in 15 ml. of pyridine with 3.75 ml. of phosphoryl chloride to give 1.05 g. of product.

The components of the mixtures were identified by analysis on three different vapor phase chromatographic columns: silver nitrate–triethylene glycol (5 ft., 60°), Carbowax 20M (5 ft., 113°) and silicone grease (10 ft., 113°). The standards used to identify the pinenes, camphene, and limonene were commercial samples. The fenchenes were prepared by repeated distillation of fenchol (obtained by reduction of fenchone with lithium aluminum hydride) over potassium bisulfate. The product was a mixture of at least six different fenchenes and it was therefore not possible to make definite correlations with the dehydration products from the nopinols. There was also considerable overlapping of the fenchene peaks with the other possible products making accurate quantitative results unobtainable. It was estimated that α-pinene made up only about one third of the total dehydration product mixtures. β-Pinene was present in very small amounts whereas camphene and limonene were present in substantial quantity in both mixtures. Four high boiling products were present in the product mixtures, one of which had the same retention time as bornyl chloride (silicone column only).

Diazotization of 3-amino-d,l-isocamphane (V). A slurry of 10 g. (0.065 mole) of amine V in a solution of 5 ml. of glacial acetic acid in 70 ml. of water was treated with a saturated aqueous solution of 4.5 g. (0.065 mole) of sodium nitrite. The mixture was heated for 5 hr. on a steam bath after which time it was made basic with sodium hydroxide and stirred overnight at 25°. Extraction with ether gave 7.5 g. of a mixture which contained 60% camphene hydrate and 40% camphene as determined by vapor phase chromatography on the Carbowax column at 152°. Only trace amounts of isoborneol and α-terpineol could be detected. No alcohol VI[9] could be detected. The camphene hydrate was identified by isolation of a small amount by chromatography on alumina (washed with ethyl acetate) and had m.p. 149–150° after sublimation (lit.,[12] m.p. 150–151°). A small amount of camphene was still present as shown by vapor phase chromatography.

A further identification was made by comparing the vapor chromatogram with that obtained from the product obtained by diazotization of a mixture of bornyl- and isobornylamines[3b] (obtained by reduction of camphor oxime with lithium aluminum hydride). The latter product contained camphene, camphene hydrate (major product), α-terpineol, and an unidentified peak.

Dehydration of camphene hydrate. A 2-g. sample of camphene hydrate (containing a small amount of camphene) was dissolved in 20 ml. of ice-cold pyridine and treated with 5 ml. of phosphoryl chloride. After standing overnight at

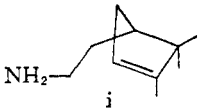
(5) G. A. Stein, M. Sletzinger, H. Arnold, D. Reichold, W. Gaines, and K. Pfister, *J. Am. Chem. Soc.*, **78**, 1514 (1956). We are deeply indebted to Dr. Stein for a sample of this material.

(6) A. Streitwieser, Jr., *J. Org. Chem.*, **22**, 861 (1957).

(7) D. Semenow, C. Shih, and W. G. Young, *J. Am. Chem. Soc.*, **80**, 5472 (1958) and references cited therein.

(8) W. Huckel and P. Rieckmann, *Ann.*, **625**, I (1959).

(9) The reverse reaction, *i.e.*, ring closure by diazotization of amine i, was also investigated but no definite conclusion could be reached due to the complexity of the product mixture (*ca.* ten components by vapor phase chromatography) (unpublished results of R. R. S.). The major product was alcohol VI.



(10) A. Lipp, *Ber.*, **56**, 2098 (1923).

(11) O. Wallach, *Ann.*, **356**, 227 (1907).

(12) O. Aschan, *Ber.*, **41**, 1092 (1908).

0° the mixture was poured onto ice and the product extracted into pentane. Pure camphene (1.0 g.) was obtained and identified by its infrared spectrum and by vapor phase chromatography on a 5-ft. silver nitrate column.

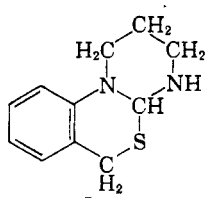
DEPARTMENT OF CHEMISTRY
RUTGERS, THE STATE UNIVERSITY
NEW BRUNSWICK, N. J.

Pyrimidobenzothiazine Derivatives. I

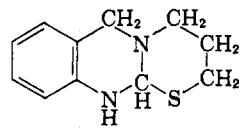
(MISS) N. GILL, N. K. RALHAN, H. S. SACHDEV, AND K. S. NARANG

Received April 18, 1960

Ring systems I and II appear to be quite interesting from the point of view of potential antibacterial activity. Moreover, neither is known in the literature:

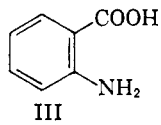


I

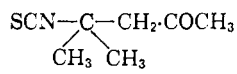


II

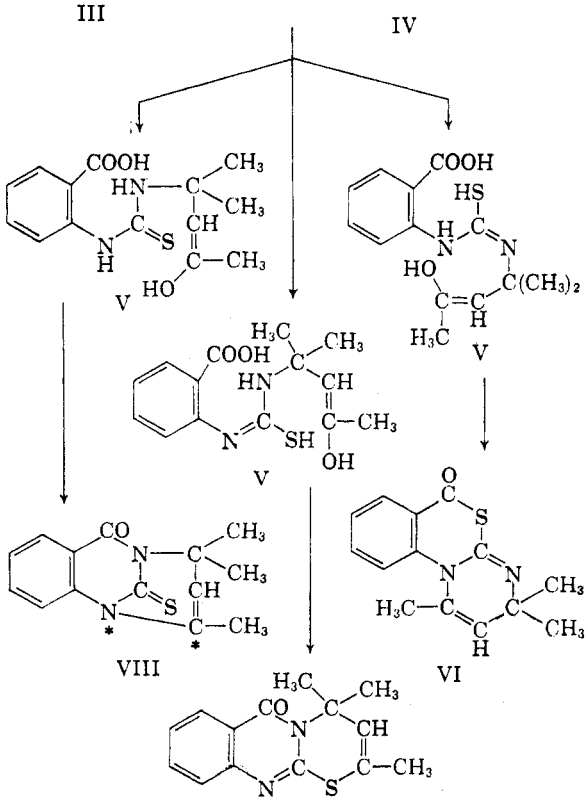
The present investigation records a study of the condensation between anthranilic acids (III) and



III



IV



V

V

V

VIII

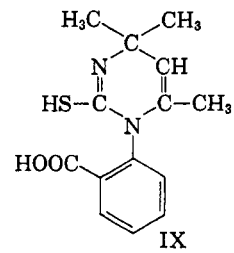
VI

VII

4-isothiocyano-4-methyl-2-pentanone (IV). The first step would lead to the formation of the intermediate (V) which could cyclize in three different ways giving rise to VI, VII, or VIII.

So far the condensation of IV with various anthranilic acids has given only one product in each case (Table I). The model of VIII shows that C and N (marked *) cannot approach near enough for cyclization.

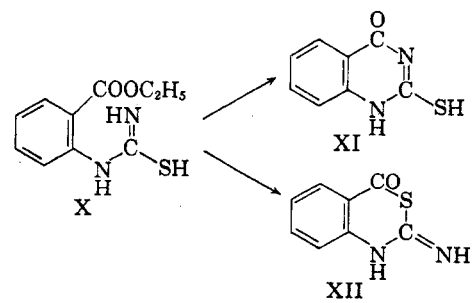
The structure (VI) appears to be the most probable for the products given in Table I. To gain further information on the structure a reaction between anthranilic acid and the isothiocyano ketone (IV) was carried out in sodium bicarbonate solution at 50°. The product obtained on acidification was an acid (m.p. 185–90°). The same acid was obtained by prolonged treatment (twelve hours) of the condensation product of III, R = H, and IV with sodium hydroxide at room temperature followed by acidification. This obviously would have the structure IX.



IX

Repeated crystallization of the acid (IX) gives back the ring closed compound. Ring opening with dilute alkali in the cold indicates that the product obtained by the condensation of anthranilic acid with IV probably has the assigned structure (VI).

2 - Carbethoxyphenylthiourea (X) on warming readily gives 2-thio-4-oxotetrahydroquinazoline (XI)[1] in good yields; the isomeric thiazine (XII) derivative has not so far been isolated. This also indicates that in the present case VII is probably formed.



X

XI

XII

The formation of VI in the present case indicates that the pyrimidine ring system is formed first giving rise to the intermediate IX and this is followed by the formation of the thiazine ring system. It is significant that the sodium salt of this inter-

(1) H. Rupe, *Ber.*, 30, 1098 (1897).