cipitate which formed on acidification of this material was dissolved in 50 cc. of 5% sodium bicarbonate solution, treated with charcoal and filtered. Acidification of this solution gave 2.1 g. (55%) of the acid. Recrystallization from hexane gave fine colorless needles, m.p. 78.5–79.0°.

Anal. Calcd. for $C_{12}H_{14}O_3$: C, 69.88; H, 6.84. Found: C, 70.08; H, 6.93.

2-Crotyloxy-3,5-dimethylbenzoic Acid (V).—This acid was prepared by essentially the above procedure from the sodium salt of 5.0 g. of methyl 3,5-dimethylsalicylate and 8.5 g. of crotyl bromide.[20] The product was obtained in 37% yield which melted at 103.5–104° after crystallization from hexane.

Anal. Calcd. for $C_{13}H_{16}O_3$: C, 70.88; H, 7.32. Found: C, 71.14; H, 7.58.

2-α-Methylallyl-4,6-dimethylphenol (VI).—2-Crotyloxy-3,5-dimethylbenzoic acid (2.6 g.) was heated for 30 minutes at 125° under nitrogen. The resulting light yellowish oil was combined with three small batches resulting from rate runs and dissolved in benzene. The solution was washed with 5% sodium bicarbonate solution to remove acidic material, and then extracted with a total of 60 cc. of Claisen alkali in three portions. The combined Claisen alkali extracts were acidified and extracted with a benzene-ether mixture. The organic layer was separated and dried. Evaporation of solvent and distillation under diminished pressure gave 2.1 g. of pale yellowish oil, which was redistilled to give a colorless oil, b.p. 126.5° (17.5 mm.).

Anal. Calcd. for $C_{12}H_{16}O$: C, 81.77; H, 9.15. Found: C, 81.56; H, 9.22.

The phenylurethan, recrystallized from ligroin, formed colorless needles, m.p. 100.0–100.5°.

Anal. Calcd. for $C_{19}H_{21}NO_2$: C, 77.25; H, 7.17. Found: C, 77.26; H, 7.05.

The α-naphthylurethan, prepared similarly, melted at 144.5–145.5°.

Anal. Calcd. for $C_{23}H_{23}NO_2$: C, 79.97; H, 6.71. Found: C, 80.02; H, 6.84.

Ozonization of VI.[11]—A solution of 0.2981 g. of 2-α-methylallyl-4,6-dimethylphenol (VI) in 15 cc. of dry carbon tetrachloride was ozonized for an hour, the exit gases being passed through two water absorption tubes. The tubes were then washed into 50 cc. of 1% aqueous methone solution at 100°. The mixture was cooled to 70°, and the crystalline methone derivative isolated; it weighed 0.1092 g. (22.6%) and melted at 187–188°, which is the reported[21] m.p. for the methone derivative of formaldehyde.

2-Allyl-4,6-dimethylphenol (IV) was formed by heating 2-allyloxy-3,5-dimethylbenzoic acid (III) under nitrogen at 140° for 30 minutes. The product boiled at 121–122° (22 mm.) and its phenylurethan melted at 108.5–109°; the reported[22] m.p. is 109°.

Determination of Rate of Rearrangement.—The apparatus used was a simple gasometer comprised of an inverted buret and a brine-filled leveling bulb. The buret was attached by glass and rubber tubing to a standard size test-tube in which the rearrangements were carried out. The tubes were immersed about one-quarter of their length in a wax-bath maintained at the desired temperature; temperature control within 0.5° was possible using an electric heating element connected with a Varitran. All rubber to glass joints in the system were sealed with varnish and the system tested for leaks under a slight negative pressure before each run. Approximately 0.2 g. of acid was used each time, which gave convenient amounts of carbon dioxide for measurement. Buret readings were recorded at suitable intervals as the rearrangements proceeded.

Readings taken at room temperature before and after completion of the reaction gave the total amount of carbon dioxide evolved. Since the same portion of the system was heated throughout the procedure, the initial room temperature volume could be corrected to reaction temperature by applying the difference between the final readings at reaction temperature and room temperature. The volume of gas evolved for any given reading was then obtained by subtraction from the corrected initial volume. The percentage completion of the reaction was calculated by dividing the total volume evolved into the volume evolved at the time of the reading.

The 2-allyloxy- and 2-crotyloxy-3,5-dichlorobenzoic acids were samples which had been prepared by Dr. J. W. Wilson.[2]

ROCHESTER, N. Y. RECEIVED SEPTEMBER 1, 1950

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[20] Young and Lane, THIS JOURNAL, **59**, 2051 (1937). The crotyl alcohol was obtained readily by lithium aluminum hydride reduction of crotonaldehyde (Nystrom and Brown, *ibid.*, **69**, 1197 (1949)).

[21] Vorländer, *Z. anal. Chem.*, **77**, 247 (1929).

[22] Claisen and Tietze, *Ann.*, **449**, 81 (1926).

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF CALIFORNIA]

The *cis*-Decahydro-2-naphthoic Acids and their Relationship to the *cis*-2-Decalols and *cis*-2-Decalylamines

BY WILLIAM G. DAUBEN AND EARL HOERGER

The two *cis*-decahydro-2-naphthoic acids and their amides have been prepared in pure form. Each acid has been degraded, with stereochemical retention, to a *cis*-2-decalol and a *cis*-2-decalylamine. The steric relationship postulated by Hückel for these latter compounds has been found to be inverted.

The preparation of the isomeric decahydro-2-naphthoic acids and their derivatives has been reported by various workers over the past twenty-five years. The results of such investigations are tabulated in Table I. Kay and Stuart[1] isolated the four possible isomers, as the amides, by the reduction of 5,6,7,8-tetrahydro-2-naphthoic acid. The amides of acids obtained by sodium and ethanol reduction were assigned a *cis*-decalin configuration whereas the products isolated when the reduction was conducted in amyl alcohol were given the *trans*-decalin structure. The ring-juncture configuration of one of the *cis* amides and of one of the *trans* amides has been established by the preparation of the acids (and their amides) form known *cis*- and *trans*-decalins[2] or decalols.[3]

TABLE I

Ring config.	Acid m.p., °C.	Amide m.p., °C.	Method of preparation	Ref.
cis	80–90	171	Reduction[a]	1
cis		140	Reduction[a]	1
cis	98	168	Grignard[c]	2, 3
cis	81	145	Hydrogenation	4, 5
trans	65–75	174	Reduction[b]	1
trans		196	Reduction[b]	1
trans	109	201	Grignard[c]	2, 3

[a] Sodium and ethanol. [b] Sodium and amyl alcohol. [c] The starting *cis*- and *trans*-chlorodecalins were prepared from the corresponding decalins and decalols.

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[1] F. W. Kay and N. Stuart, *J. Chem. Soc.*, 3038 (1926).

[2] W. Borsche and E. Lange, *Ann.*, **434**, 219 (1923).

[3] G. Tsatsas, *Ann. chim.*, **19**, **217** (1944).

[4] V. Ipatieff, *Ber.*, **42**, 2097 (1909).

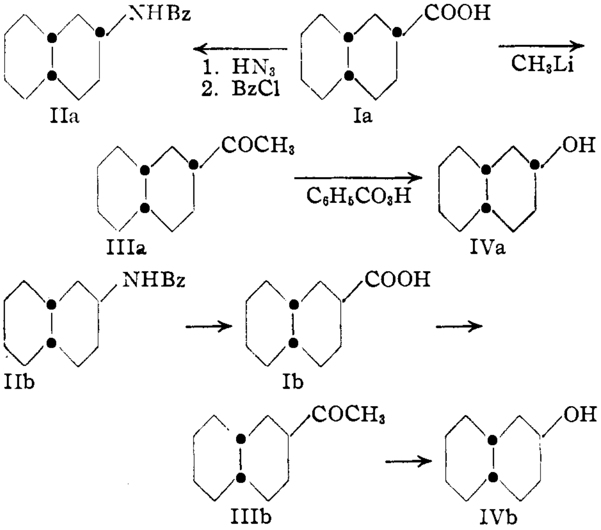
The second *cis* isomer of Kay and Stuart has been prepared by Ranedo and Leon[5] from 2-naphthoic acid by catalytic hydrogenation under conditions which usually yield *cis* isomers.

With reference to the relative configurations of the carboxyl group and the ring-juncture hydrogen atoms, a relationship seemingly well-established by Hückel[6] for the decalols and decalylamines, Tsatsas[3] has suggested that the acid obtained by the Grignard method[7] is related to that decalol of Hückel which is thought to have all the hydrogen atoms on asymmetric centers *cis* to each other. In view of the questionable steric orientation of the Grignard reagent employed, such an assignment seems of doubtful significance and, in fact, the acid obtained by Ranedo and Leon[5] by hydrogenation would appear more likely to have the suggested all *cis* configuration.

In connection with other work in this laboratory, such a stereochemical relationship became of interest and the above preparations have been repeated with this in mind. 2-Naphthoic acid was hydrogenated in acetic acid over platinum at low pressure and at room temperature and a pure decahydro-2-naphthoic acid, m.p. 80-81°, was obtained in about 70% yield. This isomer appears to be the same as the one previously obtained by catalytic hydrogenation. The amide, however, was found to melt at 179-180° which is in direct contrast to a value of 145° reported by the previous investigators[4]. It is possible that these latter workers prepared the amide under conditions which could have brought about partial inversion of the carboxyl-substituted center; such inversions have been shown to be possible when care is not taken in the preparation of an acid chloride.[8] The amide in the present work was prepared under conditions which Gutsche[8] found not to produce such an isomerization. As a further confirmation of the purity of this higher melting amide, it was hydrolyzed under controlled conditions with nitrous acid[9] and the original acid was recovered in pure form in a yield of 90%.

The second *cis* acid was obtained from *cis*-2-decalol (m.p. 104°) via the bromide and the Grignard reagent. Although the crude acid was obtained in 56% yield, a pure acid, m.p. 92-94°, was isolated in only 11% yield. This isomer also agrees closely with that previously reported to have been obtained by this method. Again it was found that the amide melts higher than previously reported, our value being 186-187° as compared to 171°. Such a result is not surprising since the earlier workers[2,3] reported heating the acid chloride. It was also found that treatment of this amide with nitrous acid yielded the starting acid in high yield. In view of the fact that no inversion was found to occur when either isomeric amide was treated with nitrous acid, it can safely be assumed that such treatment does not affect the asymmetric center to which the carboxyl group is attached.

The lower-melting acid, prepared by catalytic hydrogenation, should have a *cis*-*cis* structure (Ia)[10] in view of its method of preparation. In related work, Linstead and co-workers[11] have shown that the predominant product (>75%) formed by catalytic hydrogenation under mild conditions of an aromatic ring always has an all *cis* configuration. It follows that the acid prepared from the decalol then must have the *cis*-*trans* structure (Ib). In order to further confirm these suggested configurations and to correlate them with the previously prepared isomeric *cis*-2-decalols and *cis*-2-decalylamines of Hückel,[6] the acids have been converted to these latter compounds by a sequence of reactions known to progress with retention of configuration, namely, the peracid oxidation of methyl ketones[12] and the Schmidt reaction.[13]



The products obtained by catalytic hydrogenation or sodium and ethanol reduction of 2-naphthol, *cis*-2-decalone and *cis*-2-decalone oxime have been divided by Hückel[6] into two groups with respect to the relative configurations of hydrogen atoms at asymmetric centers. A *cis*-*cis* structure[14] was

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[5] J. Ranedo and A. Leon, *Anales soc. espan. fis. quim.*, **25**, 421 (1927).

[6] W. Hückel, *Ann.*, **441**, 1 (1925); **451**, 109 (1926); **533**, 1 (1938); W. Hückel and C. Kuhn, *Ber.*, **70**, 2479 (1937).

[7] This suggestion was based upon the observation that the Grignard reagents prepared from the isomeric decalyl chlorides yielded upon oxidation only that decalol from which the original chloride was derived. Such a specificity in the steric orientation of the Grignard reagent is, indeed, open to question in view of the present knowledge of the mechanism of formation and the reaction of such a compound; *cf.* H. S. Gilman, "Organic Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1943, p. 516.

[8] C. D. Gutsche, THIS JOURNAL, **70**, 4150 (1948).

[9] G. Heyl and V. Meyer, *Ber.*, **28**, 2776 (1895).

[10] All configurational assignments are in terms of the relative positions of the hydrogen atoms at C_9, C_{10} and C_9, C_2. The positions of the hydrogen atoms are represented in the formulas by black dots, a dot indicating that a hydrogen atom is above the plane of the molecule. A dot is always placed at C_9.

[11] R. P. Linstead, W. E. Doering, S. B. Davis, P. Levine and R. Whetstone, THIS JOURNAL, **64**, 1985 (1942), and subsequent papers; *J. Chem. Soc.*, 1423 (1950).

[12] R. B. Turner, THIS JOURNAL, **72**, 878 (1950).

[13] A. Campbell and J. Kenyon (*J. Chem. Soc.*, 25 (1946)) have shown that the Hofmann, Lossen, Curtius and Schmidt reactions exhibit the same specificity of reaction. Since the Hofmann and Curtius reactions (E. S. Wallis and J. F. Lane in "Organic Reactions," John Wiley and Sons, Inc., New York, N. Y., 1947, Vol. III, p. 272) have been shown to not involve a Walden inversion, it can be concluded that the same is true of the Schmidt reaction.

[14] This structure was called series I by Hückel and the *cis*-*trans*, series II.

suggested for the decalol melting at 105° (hydrogen phthalate, m.p. 116°) and the decalylbenzamide melting at 204°. A *cis–trans* structure was given to the decalol melting at 18° (hydrogen phthalate, m.p. 153°) and the 128° decalylbenzamide.

The *cis–cis* acid (Ia) was converted into methyl ketone IIIa by the use of methyl lithium. The resulting decalyl methyl ketone was oxidized with perbenzoic acid[12] and the *cis–cis*-2-decalol, m.p. 104°, was isolated in good yield. No trace of the other isomer could be detected. When the acid was degraded by means of the Schmidt reaction[13] with hydrazoic acid, the crude amine was isolated as the decalylbenzamide (IIa). The amide melts at 128° and in direct contrast to the foregoing decalol had been assigned a *cis–trans* structure by Hückel. Furthermore, degradation of the isomeric *cis–trans* acid (Ib) yielded the alcohol IVb (hydrogen phthalate, m.p. 153°) and the benzdecalylamide IIb (m.p. 204°); that is the alcohol of series I of Hückel and the amine of series II.

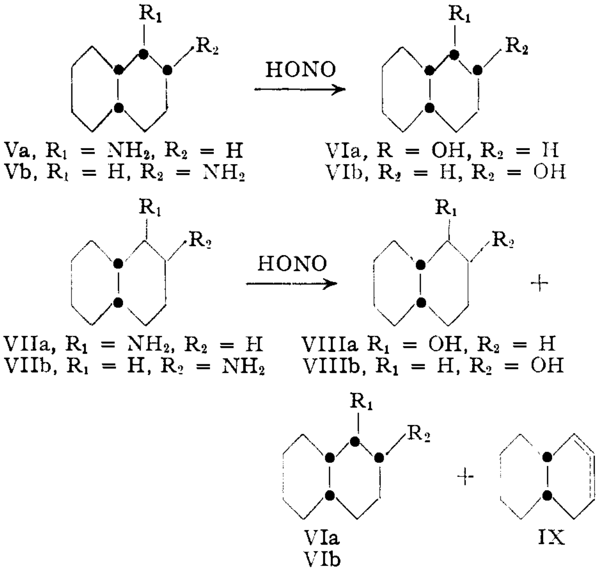
Regardless of the assumed configuration of the starting acids, if no isomerization had occurred in these degradations, both the amine and the alcohol obtained from the same acid should belong to the same series (*i.e.*, *cis–cis* or *cis–trans*). Of the three reactions employed, the Schmidt, the peracid and the methyl lithium reactions, the first two have been shown to proceed by complete retention.[12,13] Only the ketone preparation is under suspicion. The usual methods of preparation of methyl ketones progressing through an acid chloride were not employed in order to circumvent possible isomerizations. To establish the fact that the methyl lithium method produced no inversions, *cis*-2-methyl-1-acetylcyclohexane[12] was prepared from the known *cis*-2-methylcyclohexane carboxylic acid[15] and complete retention was found. As a further check on the Schmidt reaction, this same *cis* acid was degraded to the known *cis*-2-methylcyclohexylamine.[16] Thus, it must be concluded that in the substituted-2-decalin series, the stereochemical relationship postulated by Hückel between the 2-decalols and 2-decalylamines is incorrect and that the amine of series II belongs with the alcohol of series I and *vice versa* as summarized in Table II.

TABLE II

Configuration C_9, C_{10}	C_9, C_2	Melting point, °C. Acid	Amide	Decalol	Decalyl acid phthalate	Decalylbenzamide
cis	*cis*	81	180	105	116	128
cis	*trans*	98	187	18	153	204

It was thought that a possible explanation for this inverted relationship arrived at by Hückel might be that the amine actually isolated was not that amine originally formed by catalytic hydrogenation, namely, the *cis–cis* amine formed on hydrogenation was unstable and under the conditions of the reaction passed over to the more stable *cis–trans* amine. To test this hypothesis, the isomeric amines were prepared and subjected to the hydrogenation conditions employed by Hückel, and it was found that no such epimerization occurred. In view of this result, the hydrogenation of *cis*-2-decalone oxime was reinvestigated. Following the method outlined by Hückel, it was found that the hydrogenation did not go well, volatile amines being isolated in only 40% yield. The crude amine obtained was benzoylated and the benzamide fractionally crystallized. In contrast to the reported results, it was found that both isomeric amines were formed in about equal but small yield (~9%). From such a result it would appear quite difficult to make a decision as to the relative stereochemistry of the two products as was done by Hückel.

In view of the reassignment of the configuration of the *cis*-2-decalylamines, it is of interest to examine the work of Hückel on the nitrous acid reaction with these amines. In the *cis*-1-decalylamine series, it was found that the *cis–cis* compound Va (series I) gave only *cis–cis*-1-decalol VIa (retention) whereas the isomeric *cis–trans* (series II) amine VIIa yielded about 25% octalin (IX) in addition to the alcohols. These alcohols were found to consist of 90% of the *cis–trans* product VIIIa (retention) and about 10% of the *cis–cis* decalol VIa (inversion). In the *cis*-2-decalylamine group, just the opposite was reported, *i.e.*, his series I amine gave octalin and mainly decalol VIIIb and his series II amine yielded only decalol VIb. Both of these decalols were thought to have been formed by inversion. Such different results were not to be expected since agreement had been found within each stereochemical series of the *trans*-decalins. In light of the previously proposed revisions of the configurational assignment of the *cis*-2-decalylamines (Vb, *cis–cis* and VIIb, *cis–trans*), it is seen that such disagreement is corrected and consistency is found within each isomeric series.



Va, $R_1 = NH_2, R_2 = H$
Vb, $R_1 = H, R_2 = NH_2$

VIa, $R = OH, R_2 = H$
VIb, $R_2 = H, R_2 = OH$

VIIa, $R_1 = NH_2, R_2 = H$
VIIb, $R_1 = H, R_2 = NH_2$

VIIIa $R_1 = OH, R_2 = H$
VIIIb, $R_1 = H, R_2 = OH$

VIa
VIb

IX

Although no absolute proof is available at this time for the *cis–cis* structure assigned to the acid obtained by hydrogenation in this work, the above correlations strongly indicate such an arrangement.

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(15) A. K. Macbeth, J. A. Mills and D. H. Simmonds, *J. Chem. Soc.*, 1011 (1949).

(16) A. Skita, *Ber.*, **56**, 1010 (1923); *Ann.*, **427**, 266 (1923).

Experimental[17]

Decahydro-2-naphthoic Acid. (a) *cis–cis* **Acid.**—A mixture of 2.00 g. of 2-naphthoic acid in 40 ml. of glacial acetic acid and 0.50 g. of platinum oxide was hydrogenated at room temperature and pressure. After the theoretical amount of hydrogen had been absorbed,[18] the catalyst was filtered, the filtrate made nearly neutral with 50% potassium hydroxide and then extracted with three portions of hexane. The solvent was removed under reduced pressure and the residual sirup stored in a vacuum desiccator to constant weight. Upon standing at room temperature, the product crystallized to a waxy solid, m.p. 52–75°. The solid acid was recrystallized from 2.5 ml. of hexane; yield 1.4 g., m.p. 72.0–79.5°. Two additional recrystallizations from 5 ml. of hexane gave 0.7 g. of pure acid, m.p. 80.0–81.5°. Further recrystallization did not affect the melting point. Reworking of the mother-liquors yielded an additional 0.7 g. of material of the same purity. The total yield was 66%.

In a similar hydrogenation starting with 15 g. of naphthoic acid, 10.3 g. (65%) of material was obtained.

Anal. Calcd. for $C_{11}H_{18}O_2$: C, 72.49; H, 9.95. Found: C, 72.24; H, 9.85.

(b) *cis–trans* **Acid.**—*cis*-2-Decalol (30 g.) was refluxed with 100 ml. of acetic acid saturated with hydrogen bromide for one hour, the mixture diluted with water and the bromide extracted with ether. The ethereal solution was washed with aqueous sodium carbonate solution, the solvent removed and the product distilled through an efficient column, b.p. 106° (5 mm.), $n^{25}D$ 1.5226, yield 31 g. (73%).

Anal. Calcd. for $C_{10}H_{17}Br$: C, 55.30; H, 7.89; Br, 36.80. Found: C, 55.06; H, 7.95; Br, 37.08.

A solution of 30 g. (0.14 mole) of *cis*-2-decalyl bromide in 100 ml. of anhydrous ether was added slowly to 3.3 g. (0.14 mole) of magnesium turnings and 50 ml. of ether. After the addition was complete, the mixture was refluxed for an additional four hours and then cooled to −5° in an ice-salt bath. The resulting Grignard reagent was carbonated by introducing a stream of carbon dioxide above the surface of the ether. The rate of addition was controlled so that the temperature did not rise above +5°. The reaction appeared to be complete after ten minutes as indicated by the drop in temperature to −5° but the process was continued for an additional twenty minutes. The mixture was then decomposed and the acid formed extracted from the ether layer with 3 *N* sodium hydroxide. Acidification of the alkaline extract yielded 14.2 g. of material which was dissolved in a few ml. of hexane and cooled to 0°. Crystallization was induced by occasionally scratching the walls of the flask. After the appearance of a semi-solid material, more cold hexane was added to enable the separation of the resulting solid from the thick residual oil. The solid melted in the range 75–92°. Two recrystallizations from small volumes of hexane yielded the pure *cis–trans* acid as hard granular crystals, m.p. 92–94°, and further recrystallization failed to raise the melting point. Extensive recrystallizations of the mother-liquors yielded additional pure acid. The total yield was 2.72 g. or 19% of the mixture of acids obtained from the Grignard reaction or 8% over-all yield from the decalol.

Anal. Found: C, 72.32; H, 9.90.

Decahydro-2-naphthamide. (a) *cis–cis* **Amide.**—A mixture of 2.0 g. of *cis–cis*-decahydro-2-naphthoic acid, 5 ml. of purified thionyl chloride, 5 ml. of dry benzene and one drop of pyridine were warmed slowly to 40°. After stirring for thirty minutes at this temperature, the excess thionyl chloride and benzene were removed under reduced pressure (bath at 50°). The crude acid chloride was then added dropwise, with stirring, to 20 ml. of ammonia cooled in an ice-bath. The resulting solid was filtered, washed well with water and dried. The crude material melted at 175–179°. The amide was recrystallized twice from aqueous ethanol, m.p. 179–180°, yield 1.84 g. (93%).

Anal. Calcd. for $C_{11}H_{19}ON$: C, 72.88; H, 10.56; N, 7.73. Found: C, 72.96; H, 10.50; N, 7.59.

(b) *cis–trans* **Amide.**—Following the procedure described above, 0.36 g. of *cis–trans*-decahydro-2-naphthoic acid yielded 0.32 g. (88%) of pure amide melting at 186–187°. An equal weight mixture of these two amides melted at 157–170°.

Anal. Found: C, 72.84; H, 10.55; N, 7.73.

(c) **Mixed Amides by Heating of Acid Chloride.**—The *cis–cis* acid (0.2 g.) was refluxed with 5 ml. of thionyl chloride for ninety minutes, the excess reagent removed under reduced pressure and the acid chloride mixed with 10 ml. of ammonia (without any special cooling). The crude product (0.11 g.) melted at 167–173° which is considerably lower than that reported for the crude product prepared with greater care. The amide was shown to be a mixture by fractional crystallization from aqueous ethanol. The first fraction (0.06 g.) melted at 172–176° and after two additional recrystallizations (0.04 g.) at 176–178°. A second fraction (0.03 g.) melted at 168–172°.

Hydrolysis of Amides. (a) **Alkaline Hydrolysis of** *cis–cis*-**Decahydro-2-naphthamide.**—The amide (100 mg.) was refluxed for eight hours in a nitrogen atmosphere with 10 ml. of 25% potassium hydroxide in 1:1 ethanol-water. A nearly quantitative yield of acid was obtained. The material, however, was a mixture of isomers and only 34 mg. (34%) of the pure *cis–cis* acid could be obtained after repeated crystallization from hexane.

(b) **Reaction of** *cis–cis*-**Decahydro-2-naphthamide with Nitrous Acid.**—An ice-cold solution of 1.0 g. of sodium nitrite in 5 ml. of water was added dropwise to a stirred ice-cold solution of 290 mg. (1.6 mmoles) of the amide in 5 ml. of concentrated sulfuric acid. When the addition was complete, the blue-green mixture was gradually warmed on a steam-bath with the resultant evolution of nitrogen. After keeping the solution at 100° for five minutes, it was cooled and diluted with water. The acid which separated melted at 78.5–80.5°, yield 270 mg. The crude material was dissolved in cold alkali, the solution filtered (7 mg. of amide) and the acid regenerated. Recrystallization from hexane gave 259 mg. (89%) of product melting at 79.5–81°.

(c) **Reaction of** *cis–trans*-**Decahydro-2-naphthamide with Nitrous Acid.**—Following the method described above, 91 mg. (0.5 mmole) of the *cis–trans* amide yielded crude acid which melts from 88–91°. Alkali treatment gave 8 mg. of amide and the purified acid after one crystallization from hexane melted at 91–94°; yield 78%.

Schmidt Reaction with Acids. (a) *cis–cis*-**Decahydro-2-naphthylamine.**—Powdered sodium azide (100 mg., 1.5 mmoles) was added in small portions with stirring over a period of thirty minutes to a solution of 182 mg. (1 mmole) of *cis–cis*-decahydro-2-naphthoic acid in 5 ml. of chloroform and 2 ml. of concentrated sulfuric acid at 40°. The mixture was stirred for an additional thirty minutes at 50° and then poured onto ice. Sufficient water was added to dissolve all the salts and the aqueous and chloroform layers were separated. Only 16 mg. of material was recovered from the chloroform layer. The aqueous layer was made alkaline and the generated amine extracted with three portions of ether. The combined ethereal extracts were washed with water, dried and the ether removed. The crude amine isolated (121 mg., 79%) was benzoylated with 0.25 ml. of benzoyl chloride and 3 ml. of 1 *N* sodium hydroxide. The crude product was recrystallized from an ethanol-water mixture (1:1) to yield 162 mg. (63% based on acid) of N-(*cis–cis*-decahydro-2-naphthyl)-benzamide, m.p. 125–127° (lit.[6] 128°).

(b) *cis–trans*-**Decahydro-2-naphthylamine.**—As described above, 364 mg. (2 mmoles) of *cis–trans*-decahydro-2-naphthoic acid was degraded with hydrozoic acid and the amine was obtained in high yield. This product was converted to the benzamide by the Schotten–Baumann method and recrystallization of the crude product from ethanol-water (6:1) gave 451 mg. (88% based on acid) of N-(*cis–trans*-decahydro-2-naphthyl)-benzamide, m.p. 201–202° (lit.[6] 204°).

2-Acetyldecalin. (a) *cis–cis* **Ketone.**—A solution of 3.6 g. (0.02 mole) of *cis–cis*-decahydro-2-naphthoic acid in 6 ml. of ether was added dropwise with stirring to 100 ml. of a 0.51 *M* solution of methyl lithium in ether.[19] Following the addition, the mixture was stirred for an additional ten minutes, then poured onto ice and the ether layer sepa-

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[17] Analyses by the Microanalytical Laboratory of the Department of Chemistry, University of California. All melting points are corrected.

[18] The presence of a few per cent. of the tetrahydro acid makes the isolation of the pure decahydro product quite difficult.

[19] D. A. Van Dorp and J. F. Arens, *Rec. trav. chim.*, **65**, 338 (1946).

rated. After processing in the usual manner, the product was distilled, b.p. 132–133° (12 mm.), yield 3.2 g. (90%).

(b) *cis–trans* **Ketone.**—By a procedure similar to that above, 0.91 g. (5 mmoles) of *cis–trans*-decahydro-2-naphthoic acid was treated with methyl lithium. The methyl ketone was not distilled but used directly in the perbenzoic acid oxidation.

Perbenzoic Acid Oxidation of Ketones. (a) *cis–cis*-**2-Decalol.**—*cis–cis*-2-Acetyldecalin (2.4 g., 0.013 mole) was allowed to react with 2.6 g. of 85% perbenzoic acid (0.016 mole of peracid) in 15 ml. of chloroform for seven days at room temperature. At the end of this time, the mixture was diluted with ether and washed thoroughly with dilute sodium hydroxide solution to remove all the benzoic and perbenzoic acid. The ethereal solution was concentrated and the residue was treated with Girard Reagent T. The neutral non-ketonic fraction was saponified by refluxing (for two hours) with 20 ml. of 1 *N* aqueous sodium hydroxide in methanol. The decalol was removed by steam distillation. The steam distillate, containing solid decalol, was extracted with ether and the recovered decalol was recrystallized from hexane, m.p. 103–104°, yield 1.35 g. (66%). About 0.3 g. of oil was recovered from the foregoing crystallization liquors and was treated with phthalic anhydride at 130° for two hours. The cooled mixture was diluted with hexane but no solid phthalate ester was formed, indicating the absence of the isomeric *cis–trans*-decalol.

(b) *cis–trans*-**2-Decalol.**—The crude *cis–trans*-2-acetyldecalin prepared above was treated with perbenzoic acid and the resulting mixture separated into a neutral and an acidic fraction. The neutral fraction, after saponification, was heated for three hours with phthalic anhydride at 135°. The ketone and any unreacted decalol was removed by ether extraction of an alkaline solution of the reaction mixture. Acidification of the alkaline solution yielded a phthalate which rapidly solidified. The solid was extracted with ether, the ether removed and the residue melts 143–149°; yield 714 mg. (45% from acid). Recrystallization from ether–hexane yielded 691 mg. (37% from acid) of *cis–trans*-2-decalyl acid phthalate, m.p. 152–153° (lit.[6] 153°).

cis-**2-Methylcyclohexane Carboxylic Acid.**—*o*-Toluic acid was hydrogenated and purified as described by Macbeth, Mills and Simmonds,[15] b.p. 126° (11 mm.), $n^{20}\text{D}$ 1.4635 (lit.[15] b.p. 119° (11 mm.), $n^{20}\text{D}$ 1.4644). The *p*-bromophenacyl ester melted at 81–82° (lit.[15] 81–82°).

cis-**2-Methylcyclohexylamine.**—*cis*-2-Methylcyclohexane carboxylic acid (1.42 g., 0.01 mole) was degraded by the Schmidt reaction as described previously and the crude amine was isolated as the benzamide. Recrystallization from both ethanol and ligroin gave pure material; yield 1.45 g. (68.1%), m.p. 110.5–111.5° (lit.[16] 107°).

cis-**2-Methyl-1-acetylcyclohexane.**—*cis*-2-Methylcyclohexane carboxylic acid (9.0 g., 0.064 mole) was allowed to react with 0.16 mole of methyl lithium reagent as described above. A sample of the crude ketone was converted to a semicarbazone, m.p. 182.0–182.5° (lit.[12] 182.0–182.5°). The major portion of the reaction product was distilled through an 18-inch Podbielniak spiral wire column, b.p. 71.6–72.6° (10 mm.), $n^{25}\text{D}$ 1.4538, yield 5.5 g. (61.8%). Turner[12] reports b.p. 67–68° (10 mm.), $n^{25}\text{D}$ 1.4532.

Hydrogenation of *cis*-**2-Decalone Oxime.**—The oxime (22.0 g., 0.132 mole) was hydrogenated in 75 ml. of acetic acid, 125 ml. of water and 25 ml. of concentrated hydrochloric acid over 2.0 g. of platinum oxide. The catalyst was filtered, the filtrate made alkaline and the amine isolated by steam distillation; yield 8.0 g. The recovered oxime amounted to 46%. The crude amine was benzoylated in the usual fashion and fractionally crystallized from ethanol to yield 2.6 g. (7.7%) of the amide melting from 200–202° and 3.0 g. (8.8%) of the amide melting from 124.5–126°. Hückel[6] reports 204° and 128°, respectively.

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[CONTRIBUTION FROM THE BIOLOGY DIVISION, OAK RIDGE NATIONAL LABORATORY]

Partial Purification of a Non-phosphorylytic Uridine Nucleosidase from Yeast

BY C. E. CARTER

From yeast plasmolysates an enzyme has been partially purified by ammonium sulfate fractionation which degrades uridine to uracil and ribose in the absence of inorganic phosphate or arsenate, and which does not hydrolyze other ribosides.

The phosphorylytic cleavage of the riboside linkage in inosine and guanosine by an enzyme purified from rat liver,[1] and in several purine and pyrimidine ribo- and desoxyribonucleosides by cell-free extracts of microörganisms[2] suggests a general phosphorylytic mechanism for the enzymatic degradation of ribosides. In this paper an exception to such a generalization is reported involving an enzyme system purified from yeast by ammonium sulfate fractionation which hydrolyzes the pyrimidine riboside uridine in the absence of phosphate, arsenate or activating cations.

Experimental

Materials.—Uridine was purchased from Schwarz and Company and purified by recrystallization from 75% ethanol. The compound chromatographed as a single component and showed no contamination with uracil, cytidine or cytosine.[3]

Preparation of Enzyme.—Three pounds of Fleischmann yeast was plasmolyzed in toluene according to Kunitz.[4] To the clear plasmolysate, solid ammonium sulfate was added to a concentration of 445 g. per liter. After standing 1 hour the precipitate was collected by centrifugation, dissolved in distilled water, and dialyzed against distilled water. To 350 ml. of this solution, 385 ml. of saturated ammonium sulfate was added, and after standing 1 hour, the precipitate was collected by centrifugation, dissolved in distilled water, and dialyzed against distilled water with frequent changes for 48 hours. This fraction was then adjusted to *p*H 4.7 and the precipitate, collected by centrifugation, was discarded. The supernatant solution, adjusted to *p*H 7.0 with dilute sodium hydroxide contained about 60% of the original activity and represented about ten- to fifteen-fold purification when assayed as described below. It contained 0–2.5 γ P/ml. and 2.0–2.5 mg. protein/ml. All operations were conducted at 4–10°.

Enzymatic Assay.—Two methods, both based on the differential spectrophotometry of uridine and uracil solutions, were employed. In the first method, employed during fractionation procedures, where a rapid, sensitive test for enzymatic hydrolysis of uridine was required, the great difference in the extinction coefficient at 290 mμ in 0.01 *N* NaOH of uracil (E_{M} 5.4 $\times 10^3$) and uridine (E_{M} 30) was applied.[5] In this procedure 0.1 ml. of enzyme solution, 0.025 ml. of a uridine solution containing 20 mg. of uridine/ml. and 0.2 ml. of buffer *p*H 7.0 (phosphate, borate, glycine or veronal) were incubated for 30 minutes at 38°. Four ml. of 0.01 *N* NaOH was then added and the solution read at 290 mμ in the Beckman spectrophotometer. The increment in absorption at this wave length read against a zero time blank is a measure of the uracil formed. The ratio of

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