planar configuration, some copolymerization experiments with *cis*- and *trans*-dichloroethylenes have been carried out. If a monomer added to each isomer in the same way, *i. e.*, predominantly *cis* or *trans*, and if the configuration of the resulting radical was maintained until addition to another monomer occurred, stereoisomeric dichlorides would be produced. In view of the conclusions of Young and Dillon[2] that the stereoisomeric 2,3-dibromobutanes react with potassium iodide at widely different rates, it seemed probable that the steroisomeric dichloroethylene copolymers would also show a difference in rate of reaction with potassium iodide. Since no difference was found, and if it is assumed that addition to both isomers is predominantly *cis* or predominantly *trans*, then the results show that the R–CHCl–ĊHCl radicals involved have either a planar configuration or else a pyramidal configuration which inverts or racemizes faster than the radicals add to vinyl acetate. Racemization, indeed, might be anticipated from the racemization of optically active hydrocarbons during chlorination with sulfuryl chloride.[3]

Copolymers of vinyl acetate with *cis*- and *trans*-1,2-dichloroethylene, containing about four vinyl acetate units per dichloroethylene unit, were prepared[4] at 15% conversion at 60° and the rates of reaction of these copolymers with potassium iodide were followed at 100°.

TABLE I

RATE OF IODINE LIBERATION FROM COPOLYMERS OF *cis*- AND *trans*-DICHLOROETHYLENE WITH VINYL ACETATE AT 100°

t, hours	I_2 formed, milliequiv in 20 ml.	$k_2 \times 10^3$[a]
cis (18.13% Cl), $[KI]_0 = 0.2503$, $[C_2H_4Cl_2]_0 = 0.0342$		
24	0.0310	3.83
48	.0425	2.64
72	.0530	2.20
96	.0689	2.17
trans (19.09% Cl), $[KI]_0 = 0.2503$, $[C_2H_4Cl_2] = 0.0379$		
24	0.0320	3.56
48	.0493	2.77
72	.0594	2.24
96	.0719	2.10

[a] $k_2 = \frac{2.303}{t(a-2b)} \log \frac{a-2b\theta}{a(1-\theta)}$ where $a = [KI]_0$, $b = [C_2H_4Cl_2]_0$, and θ is the fraction of dichloroethylene units which have reacted. k_2 is defined by: $d[I_w]/dt = k_2[KI]\cdot[C_2H_4Cl_2]$.

The results in Table I show that, although the reactions do not follow the simple second order kinetics found[2] for the dibromobutanes, there is no significant difference in the rates of iodine liberation from the two copolymers.

(2) Dillon, Young and Lucas, THIS JOURNAL, **52**, 1953 (1930).

(3) Brown, Kharasch and Chao, *ibid.*, **62**, 3435 (1940).

(4) Lewis and Mayo, *ibid.*, **70**, 1533 (1948), present data from which the feeds required for preparation of these polymers can be calculated.

Experimental

The polymers were prepared in evacuated tubes from carefully fractionated monomers and were isolated by the frozen benzene technique.[5] Methanol was distilled from potassium hydroxide before use. Tubes of 30-ml. capacity containing 5 milliequivalents of potassium iodide and sufficient polymer to provide about 1.5 milliequivalents of available iodine in 20 ml. of 96% methanol were sealed in vacuum and heated at 100° from one to four days. The contents of the tubes were then poured into 75 ml. of water containing 2 g. of potassium iodide and a known slight excess of sodium thiosulfate to prevent occlusion of iodine by the polymers as they precipitated in the aqueous solution. The solutions were then titrated to the starch end-point with 0.05 *N* iodine solution. A weighed amount of iodine added to one of two otherwise identical tubes required the calculated additional thiosulfate, showing that the titration was valid and a correction factor was unnecessary.

(5) Lewis and Mayo, *Ind. Eng. Chem., Anal. Ed.*, **17**, 134 (1945).

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Synthesis of 2- and 6-Fluoronicotinamides[1]

BY JOHN T. MINOR,[2] G. F. HAWKINS,[3] CALVIN A. VANDERWERF[2] AND ARTHUR ROE[4]

The current hypothesis which attributes the antimetabolite activity of such compounds as sulfanilamide and pyridine-3-sulfonic acid to the structural similarity but functional dissimilarity of these compounds to essential metabolites, suggests that a study of the physiological activity of various fluorine substituted vitamins should be of considerable interest.

Of the non-metallic elements, other than hydrogen, which commonly form single covalent bonds, fluorine is the one which most closely approximates hydrogen in atomic size and weight. The question of whether the substitution of a fluorine for a hydrogen atom in the molecules of various vitamins will lead to derivatives which possess vitamin or anti-vitamin activity is, therefore, a significant one. Of interest in this connection, is the observation of Mitchell and Niemann[5] that 3-fluorotyrosine and 3-fluorophenylalanine act as growth inhibitors for *Neurospora crassa* 8815-3a.

As part of a broad study, we have completed the synthesis of two compounds of this type, 2- and 6-fluoronicotinamides. The critical steps in these syntheses, the replacement of the amino-group by the fluorine atom in the commercially available compounds 2-amino-3-methylpyridine and 2-amino-5-methylpyridine, proceeded only in low yields when the amines were diazotized in anhydrous hydrogen fluoride and the resulting diazonium fluorides decomposed, and also when the conventional Schiemann reaction was employed. The modification of the Schiemann reaction de-

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(5) Mitchell and Niemann, THIS JOURNAL, **69**, 1232 (1947).

veloped by two of the present authors,[6] however, gave good results. Antimetabolite tests showed no inhibition of growth of *E. coli, Staph. aureus,* or *Strep. varidans in vitro* by 1:2000 dilution of either 2- or 6-fluoronicotinic acid. These tests were carried out by the Lilly Research Laboratories. Testing of the fluoronicotinamides is in progress.

Experimental

2-Fluoro-3-methylpyridine.—To a solution of 80 g. (0.74 mole) of redistilled 2-amino-3-methylpyridine[7] in 310 g. of 40% fluoboric acid contained in an ice-cooled 1500 ml. beaker, 51 g. (0.74 mole) of sodium nitrite was gradually added in small portions with mechanical stirring. When the addition was complete, the solution was stirred for an additional thirty minutes at ice-bath temperature, and was then warmed to 45° to ensure complete decomposition. The solution was neutralized with sodium carbonate and steam-distilled. The yellow oil which separated from the distillate was removed and the remaining water layer extracted with ether. The oil and ether extracts were combined, dried over anhydrous sodium sulfate, and the ether removed. Distillation of the residue gave 39.5 g. (48%) of 2-fluoro-3-methylpyridine, b. p. 150.5–151.0° at 757 mm.

Anal. Calcd. for C_6H_6NF: C, 64.9; H, 5.4; N, 12.6. Found: C, 64.7; H, 5.6; N, 12.5.

2-Fluoronicotinic Acid.—A mixture of 38 g. (0.33 mole) of 2-fluoro-3-methylpyridine, 126 g. (0.80 mole) of potassium permanganate, and 1.5 l. of water contained in a 3-liter three-necked flask, fitted with condenser and sealed stirrer, was refluxed gently for four hours. The mixture was first steam-distilled to remove unreacted 2-fluoro-3-methylpyridine (8.0 g.) and then filtered hot. The resulting solution was evaporated to approximately 700 ml., cooled in an ice-bath, and acidified with concentrated hydrochloric acid. The precipitate which formed was filtered, dried, and recrystallized from water to yield 23.0 g. (49% based on starting methyl compound or 63% based on amount reacted) of 2-fluoronicotinic acid, m. p. 164–165°,[8] with decomposition.

Anal. Calcd. for $C_6H_4O_2NF$: C, 51.1; H, 2.9; N, 9.9; F, 13.5. Found: C, 51.2; H, 3.1; N, 9.9; F, 13.7.

2-Fluoronicotinamide.—A solution of 28.2 g. (0.20 mole) of 2-fluoronicotinic acid in 250 ml. of thionyl chloride was refluxed for forty-five hours. The excess thionyl chloride was then removed under reduced pressure, and the residue of 2-fluoronicotinyl chloride, b. p. 84.0–85.0° at 4 mm., was dissolved at once in 115 ml. of dry benzene. Dry ammonia was bubbled through the solution for thirty minutes and the solids formed were removed by filtration. These were extracted with dry acetone, the solvent was taken off, and the remaining yellow crystals were recrystallized from water. The yield of pure 2-fluoronicotinamide, m. p. 120.9–122.0° was 67.5%.

Anal. Calcd. for $C_6H_5ON_2F$: C, 51.4; H, 3.6; N, 20.0. Found: C, 51.4; H, 3.5; N, 19.8.

Approximately the same yield was obtained when the acid chloride was prepared by reaction of the acid with phosphorus pentachloride in phosphorus oxychloride solvent.

2-Fluoro-5-methylpyridine.—This compound was prepared according to the directions given for 2-fluoro-3-methylpyridine, except that 2-amino-5-methylpyridine was the starting material. A 46% yield of pure product, b. p. 155–156° at 752 mm., was obtained.

Anal. Calcd. for C_6H_6NF: C, 65.0; H, 5.4; N, 12.6. Found: C, 64.7; H, 5.5; N, 12.8.

(6) Roe and Hawkins, THIS JOURNAL, **69**, 2443 (1947).

(7) Obtained from the Reilly Tar and Chemical Corporation.

(8) Melting points are corrected.

6-Fluoronicotinic Acid.—This product was obtained in 60% yield, based on starting 2-fluoro-5-methylpyridine (71% based on that reacted), according to the method described for the preparation of the 2-fluoro-isomer. It was purified by sublimation and melted at 146–147° with decomposition.

Anal. Calcd. for $C_6H_4O_2NF$: C, 51.1; H, 2.9; N, 9.9; F, 13.5. Found: C, 51.0; H, 3.1; N, 9.8; F, 13.8.

6-Fluoronicotinamide.—Prepared in 65% yield from 6-fluoronicotinic acid by the method described for the 2-fluoro-isomer, this compound melted at 166.2–167.0°, after recrystallization from water.

Anal. Calcd. for $C_6H_5ON_2F$: C, 51.4; H, 3.6; N, 20.0. Found: C, 51.4; H, 3.8; N, 19.7.

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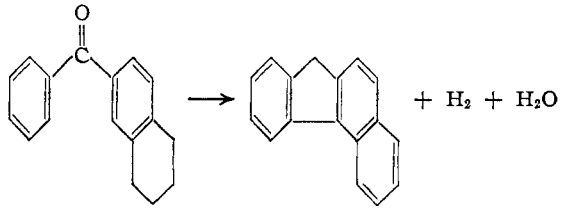
Aromatic Cyclodehydrogenation. VIII. Experiments with 2-Benzoyl-5,6,7,8-tetrahydronaphthalene[1]

BY MILTON ORCHIN,[2] E. O. WOOLFOLK[2] AND LESLIE REGGEL[2]

A possible convenient two-step synthesis of 3,4-benzfluorene, II, consists of its formation by direct cyclization of 2-benzoyl-5,6,7,8-tetrahydronaphthalene, I. The latter is readily available,



I II

since acylating agents substitute exclusively at the 6-position of 1,2,3,4-tetrahydronaphthalene. In the respect that the conversion would involve a cyclization of a diaryl ketone, accompanied by loss of water, the reaction bears a superficial resemblance to the Elbs reaction. Although no suitable catalyst has been found for the Elbs reaction,[3] it seemed reasonable to expect, in the present instance, that a chromia-on-alumina catalyst would combine dehydration and cyclization activity. It has been found that vapor-phase treatment of I over such a catalyst at 450-470° gave, as a major product, 2-benzylnaphthalene. Only a little of the expected 3,4-benzfluorene was formed, accompanied by a small quantity of 2,3-benzfluorene. Both benzfluorenes were probably formed *via* 2-benzylnaphthalene, the former by cyclization into the 1-position and the latter by closure at the 3-position.

Liquid-phase treatment of 2-benzoyl-5,6,7,8-

(1) Article not copyrighted.

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(3) For a review of this reaction see Fieser in "Organic Reactions," John Wiley & Sons, N. Y., Vol. I, p. 129.