the 2.55 Å. spacing would not be equal because of the unequal effectiveness of the blocking by interaction of or competition for sites by neighboring formate molecules. As regards the second of the catalytic reactions, the deposition of cobalt on cobalt, it is known[11] that thin deposits of cobalt on copper continue the orientation, structure, and approximate lattice constants of copper. Thus the interpretation of results on the basis of the spacing of the copper crystal would apply equally well to the catalytic deposition of cobalt on the cobalt surface.

We wish to express our appreciation to Dr. Allan T. Gwathmey for his encouragement and constructive criticism.

(11) Cochrane, *Proc. Phys. Soc.* (*London*), **48**, 723 (1936).

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Synthesis and Antifungal Action of 2-Methylmercapto-1,4-naphthoquinone[1,2]

BY JOHN E. LITTLE, THOMAS J. SPROSTON AND MURRAY W. FOOTE

Many methoxyquinones are known to possess marked antibiotic activity. Among these are fumigatin, spinulosin and javanicin. Many others have been tested and found to be remarkably inhibitory to various types of organisms.[3,4,5]

Since naturally occurring 2-methoxy-1,4-naphthoquinone was found to be highly fungistatic against several plant pathogenic fungi,[6] the synthesis of the sulfur analog of this compound was carried out and its fungistatic activity measured.

A simple synthesis in good yield was developed which was based upon mercaptan addition to 1,4-naphthoquinone. The work of Fieser and Turner,[7] involving the addition of mercaptans to 2-methyl-1,4-naphthoquinone, served as a pattern for the synthesis of this new compound.

We have found that the yield can be increased markedly by the well-timed addition of ferric chloride to the reaction mixture. This material probably causes the oxidation step to proceed farther toward completion.[7] It was found that the addition of the ferric chloride increased the yield of crude product (m. p. 183°) from 27 to 56%. When the salt was added at the beginning of the reaction, no product could be obtained. The final pure crystalline product separated from alcohol as yellow needles melting at 186.5–187° (cor.).

The spectrophotometric absorption curve of this compound was obtained. The wave length and intensities of the principal maxima are as follows: 256 mμ (ϵ = 19,700), 298 mμ (ϵ = 7,700) and 407 mμ (ϵ = 3,310). The characteristic naphthoquinone maximum at 330 is evident only as a slight inflection.

The substitution of a sulfur atom for oxygen in the 2-methoxy-1,4-naphthoquinone molecule results in a marked increase in antifungal activity. The L.D.$_{50}$ value for this compound as measured against the spores of *Monolinia fructicola*[8] was found to be 1.00 part per million (0.00100 mg. per ml.) as compared to 3.65 parts per million (0.00365 mg. per ml.) for 2-methoxy-1,4-naphthoquinone[6]; an increase in potency of approximately 3.5 fold.[9]

The solubility of 2-methylmercapto-1,4-naphthoquinone determined spectrophotometrically was found to be 7.0 mg. per liter at 26°. The insoluble nature of this material would be of benefit if it were to be used as a plant fungicide.

Experimental

Preparation of 2-Methylmercapto-1,4-naphthoquinone.—16.5 g. of nearly pure naphthoquinone was dissolved in 1000 ml. of absolute alcohol by warming to 40°. The solution was cooled to room temperature and a small quantity of a dark impurity removed by filtration. The solution was then cooled in ice to 15° and 10 g. of ice-cold methyl mercaptan added suddenly while the flask was swirled.

After standing for thirty minutes at room temperature a yellow crystalline precipitate appeared; 15 ml. of 70% $FeCl_3\cdot 6H_2O$ was now added and a further crystallization observed. After standing for fifteen minutes 22 ml. more of the ferric chloride solution was added and the quantity of precipitate again increased. Further addition of ferric chloride had no effect. The suspension was now cooled to 7°, filtered and dried with petroleum ether on the funnel; 11.9 g. of yellow crystalline material was obtained, m. p. 183°. The yield was 56% of the theoretical. One recrystallization of this material from hot alcohol after treatment with norite and filtration gave 9.16 g., m. p. 186.5–187°. The over-all yield was 45%.

Anal. Calcd. for $C_{11}H_8O_2S$: C, 64.69; H, 3.95; S, 15.70. Found: C, 64.88; H, 4.06; S, 15.93.

Determination of Solubility.—Fifteen milligrams of the finely ground 2-methylmercapto-1,4-naphthoquinone (m. p. 186.5–187°) was stirred in 5 l. of distilled water for thirty-six hours at room temperature. At the end of this time, all of the material had dissolved. The optical density of this solution at the 256 mμ maximum was found to be 0.309. Comparison of this density to that obtained with a saturated solution showed the solubility to be 7.0 mg. per liter.

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(1) Printed by permission of Vermont Agricultural Experiment Station; Journal Series No. 1.

(2) We are grateful to the Herman Frasch Foundation for a grant in support of this work.

(3) Geiger, *Arch. Biochem.*, **11**, 23 (1946).

(4) Colwell and McCall, *Science*, **101**, 592 (1945).

(5) Oxford, *Chem. and Ind.*, **161**, 189 (1942).

(6) Little, Sproston and Foote, *J. Biol. Chem.*, **174**, 335 (1948).

(7) Fieser and Turner, THIS JOURNAL, **69**, 2335 (1947).

(8) Committee on Standardization of Fungicidal Tests, *Phytopathology*, **33**, 627 (1943); **37**, 354 (1947).

(9) A more detailed discussion of the fungistatic action of this and other naphthoquinones is in preparation for publication in the near future.

RECEIVED AUGUST 14, 1948

Configurations of Radicals Derived from *cis-* and *trans-*Isomers

BY FRANK R. MAYO AND KENNETH E. WILZBACH

To obtain evidence concerning the recent proposal of Kistiakowsky,[1] that radicals have a non-

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(1) Kistiakowsky, *The Indicator*, **28**, No. 3, 6 (1947), Nichols Medal Address, March 7, 1947.

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 $\mathrm{R{-}CHCl{-}\dot{C}HCl}$ 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.	$k_2 \times 10^{3a}$
cis (18.13% Cl), $[\mathrm{KI}]_0 = 0.2503$, $[C_2H_4Cl_2]_0 = 0.0342$		
24	0.0310	3.83
48	.0425	2.64
72	.0530	2.20
96	.0689	2.17
trans (19.09% Cl), $[\mathrm{KI}]_0 = 0.2503$, $[C_2H_4Cl_2] = 0.0379$		
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 $a = [\mathrm{KI}]_0$, $b = [C_2H_4Cl_2]_0$, and θ is the fraction of dichloroethylene units which have reacted. k_2 is defined by: $d[I_w]/dt = k_2[\mathrm{KI}][C_2H_4Cl_3]$.

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.

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.

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[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.

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

GENERAL LABORATORIES
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RECEIVED NOVEMBER 2, 1948

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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[2] Address: University of Kansas, Lawrence, Kansas.

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[4] Address: University of North Carolina, Chapel Hill, N. C.

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