was prepared in accordance with the directions of Gilman, Brown and Jones[13] and 41.5 g. (0.25 mole) of it was nitrated after the procedure described for the nitration of furylacrylic acid. The mixture was stirred for three hours and during this time a yellow precipitate separated. When the temperature reached 0°, the reaction product was removed by filtration and washed several times with cold water. The yield of ethyl nitrofurylacrylate, melting at 123°, was 27 g. or 51%. When recrystallized from benzene, it melted at 125°.

Anal. Calcd. for $C_9H_9O_5N$: C, 51.18; H, 4.30. Found: C, 50.68; H, 4.43.

The ester is unusually stable, being quite resistant to thionyl chloride and phosphorus pentachloride. It may be hydrolyzed with 65% sulfuric acid by heating until solution is completed, to give the nitrofurylacrylic acid. The identity of this acid, like the other compounds described in this paper, was confirmed by a mixed melting-point determination, in this case with the acids obtained in the Perkin condensation and in the nitration of furylacrylic acid.

The authors gratefully acknowledge assistance from W. M. Selby for a part of the experimental work.

Summary

The first nitrofurfural has been prepared by the hydrolysis of nitrofurfural diacetate obtained by nitrating furfural diacetate. The mechanism of its formation is probably unlike that of nitrofurylacrylic acid and ethyl nitrofurylacrylate, which were obtained by direct nitration of furylacrylic acid and ethyl furylacrylate, respectively. The nitro group markedly increases the stability of the furan nucleus.

AMES, IOWA

[CONTRIBUTION FROM THE INSECTICIDE DIVISION, BUREAU OF CHEMISTRY AND SOILS]

THE SOLUBILITY OF ROTENONE. I. SOLUBILITY AND OPTICAL ROTATION IN CERTAIN ORGANIC SOLVENTS AT 20°

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RECEIVED MARCH 18, 1930 PUBLISHED JUNE 6, 1930

Introduction

The root of *Derris elliptica* has long been used by the natives of the Malay Peninsula and the East Indies as a fish poison. One of the active insecticidal principles of this root is a white, crystalline material with a melting point of 163°. This material, now known as rotenone, crystallizes from alcohol in the form of six-sided plates apparently belonging to the orthorhombic system. The empirical formula $C_{23}H_{22}O_6$, now generally accepted, was first proposed by Takei and later substantiated by Butenandt. Much work has been done to determine its constitution but at present its structure is still unknown.

Rotenone is known to be practically insoluble in water, Gimlette stating its solubility to be of the order of one part in six million.[1] Numerous quali-

[13] Gilman, Brown and Jones, *Iowa State College J. of Science*, **2**, 317 (1928).

[1] Gimlette, "Malay Poisons and Charm Cures," London, **1923**, 2d ed.

tative statements as to its solubility in organic solvents are found in the literature,[2,3,4,5] but few quantitative data are available. The present investigation had as its object the finding of solvents suitable for use in extracting rotenone and for the preparation of spray mixtures. This paper treats of its solubility in some organic solvents at 20°. A later paper will deal with other solvents and with some mixed solvents, both at 20° and at higher temperatures.

Materials and General Procedure

The rotenone used consisted of several samples prepared by H. V. Claborn of this Laboratory from the root of *Derris elliptica* by extraction of the ground root with ether. The rotenone crystallizes from the concentrated extract and is purified by recrystallization from alcohol. The purity of each lot was checked by determinations of melting point and by microscopical examination. Only rotenone passing a 70-mesh sieve was used.

Twenty-one solvents, representing the more common classes of organic compounds, were used. These were, in general, of chemically pure grade, except in those cases in which a commercial grade was more readily available.

The method used for determining solubility was based on the optical activity of the compound, and was suggested by the fact that the specific rotation of rotenone was given by Kariyone, Atsumi and Shimada[6] as $[\alpha]_D^{20}$ $-244°$ and by Ishikawa[7] as $[\alpha]_D^{29.5}$ $-225.2°$ in benzene solution. The specific rotation of rotenone in the various solvents was first determined by the use of solutions of known concentration. Then saturated solutions were prepared, their rotations measured and the concentrations (or solubility) obtained by extrapolation.

The solvents were all tested for optical rotation, but in only one was any observed. The commercial *n*-butyl alcohol used was very slightly levorotatory and a corresponding correction was made in the readings. The specific gravities of the solvents and of the saturated solutions were obtained in order to permit the results to be stated in several units. All determinations were carried out in a constant-temperature room kept at 20°.

Determination of Specific Rotation.—Solutions of known concentrations were made by weighing the rotenone accurately into volumetric

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[2] Ishikawa, *Tokyo Igakkwai Zasshi*, **30**, 45 (1916); *C. A.*, **11**, 2370 (1917).

[3] Van Hasselt, *Proc. Roy. Acad. Sci.* (*Amsterdam*), [Pt. 2] **13**, 688 (1911) (in English).

[4] Lenz, *Arch. Pharm.*, **249**, 298 (1911).

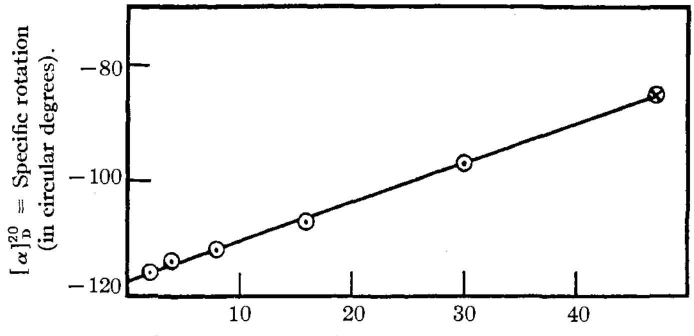
[5] Moeller and Thoms (Editors), "Real-Enzyklopadie der gesamten Pharmazie," **1905**, 2d ed., Vol. IV.

[6] Kariyone, Atsumi and Shimada, *J. Pharm. Soc.* (*Japan*), No. 500, 739 (1923); *C. A.*, **18**, 408 (1924).

[7] Ishikawa, *J. med. Ges. Tokio*, **31**, No. 4, 180 (1917); [abstracted by Takei, *Biochem. Z.*, **157**, 2 (1925)].

flasks and making to volume at 20° with the solvent. After considerable shaking a careful inspection was made to see whether any material remained undissolved; if so, the solution was diluted to a larger known volume, until the rotenone went into complete solution. Because of this, the concentrations are expressed as "grams of rotenone per 100 cc. of solvent" throughout the calculations. The making of these solutions also gave a rough estimate of the solubility of rotenone in each solvent.

The light used was obtained from an ordinary electric light bulb by filtration through a bichromate cell containing a solution giving an optical path equivalent to 9 mg. of $K_2Cr_2O_7$ per square centimeter. This light was therefore made up of wave lengths centering rather closely around that of the "D" line of sodium. The readings of this instrument, in Ventzke degrees, were converted to circular degrees by multiplying by the factor 0.3466. The specific rotation was then calculated by means of the formula



⊙, Observed values; ⊗, extrapolated value for saturated solution.
Equation of line $[\alpha]^{20°}_{D} = 0.67C - 117$

Fig. 1.—Specific rotation–concentration. Rotenone in chloroform at 20°.

$$[\alpha]^{20}_{D} = \frac{\text{Ventzke degrees} \times 0.3466 \times 100}{\underset{\text{(in decimeters)}}{\text{Length tube}} \times \underset{\text{(in g./100 cc. soln.)}}{\text{concentration of solution}}} \qquad (1)$$

With practically all solvents solutions of different concentrations were measured in order to determine whether there was any variation of the rotation with change in concentration. The specific rotations obtained for the various concentrations are given in Table I, Col. 3.

In those cases in which no variation with concentration was evident, the specific rotation was assumed to be a constant and its most probable value obtained by taking a weighted average of the values for specific rotation at the different concentrations, giving each the relative weight of the actual Ventzke readings.

With those solvents which gave more concentrated solutions, a definite decrease of specific rotation with increase in concentration was found.

In two other cases this same decrease was noted although the range of concentration was not as great. The results for these solvents were represented graphically by plotting the specific rotation against concentration. The variation was found to be linear within the limits of error of the measurements, and the straight line which seemed best to fit the points was drawn. The parameters of the equation for this line were obtained graphically, and from the expression obtained the value for specific rotation at any concentration may be calculated. The graph obtained for chloroform is shown in Fig. 1 and is typical of those obtained with the other solvents.

The final values adopted for specific rotation are given in Table I, Col. 4.

TABLE I

OPTICAL ROTATION OF ROTENONE AT 20°

(1) Solvent and sp. gr. at 20°	(2) Concn. (C) of soln. in g. of solute per 100 cc. of soln.	(3) Sp. rotation of soln. in circular degrees	(4) Sp. rota.[b] $[\alpha]_D^{20}$ in circular degrees (weighted av. or equation)
Acetone[a]	1	−106	−105
0.791	2	−107	
	3	−109	
	5	−103	
Acetic acid[a]	1	−131	−129
1.049	1.5	−128	
	2	−129	
Alcohol, *n*-butyl	0.1	−105	−105
0.811			
Alcohol, ethyl (absolute)[a]	0.0625	−111	−124
0.789	0.1	−121	
	0.125	−132	
Alcohol, isopropyl	0.1	−126	−126
0.786			
Alcohol, methyl[a]	0.1	−156	−156
0.791	0.2	−156	
Amyl acetate	0.75	− 92	− 93
0.867	1.4	− 93	
Benzene[a]	2	−230	$[\alpha]_D^{20} = 1.8C - 233$
0.879	4	−225	
	8	−219	
Carbon disulfide[a]	1	− 96	− 96
1.263	1.5	− 99	
	2[c]	− 95	
Carbon tetrachloride[a]	0.25	−107	−108
1.594	0.375	−104	
	0.5	−111	
Chlorobenzene	4	−168	$[\alpha]_D^{20} = 1.7C - 175$
1.107	8	−162	
	10	−158	

TABLE I (*Concluded*)

(1) Solvent and sp. gr. at 20°	(2) Concn. (C) of soln. in g. of solute per 100 cc. of soln.	(3) Sp. rotation of soln. in circular degrees	(4) Sp. rota.[b] $[\alpha]^{20}_{D}$ in circular degrees (weighted av. or equation)
Chloroform[a] 1.489	2	−116	$[\alpha]^{20}_{D} = 0.67C-117$
	4	−114	
	8	−112	
	16	−107	
	30	− 97	
s-β-Dichloro-ethyl ether[a] 1.208	1	− 85	$[\alpha]^{20}_{D} = 0.53C - 85$
	3	− 83	
	6	− 82	
Ether, ethyl (anhydrous)[a] 0.714	0.1	−147	−136
	0.25	−139	
	0.3	−130	
Ethyl acetate[a] 0.901	0.5	−106	−107
	1	−106	
	1.5	−107	
	3	−107	
Ethylene chlorohydrin 1.203	2	−103	$[\alpha]^{20}_{D} = 0.35C-104$
	4	−102	
	7	−102	
	10	−100	
Ethylene dichloride 1.256	6	− 74	$[\alpha]^{20}_{D} = 0.44C- 77$
	15	− 71	
	25	− 66	
n-Propyl formate 0.896	1	−108	−106
	4	−106	
	5	−106	
Toluene[a] 0.866	3	−210	−209
	5	−211	
	6	−206	
Trichloro-ethylene 1.469	5	−100	$[\alpha]^{20}_{D} = 0.77C-104$
	10	− 96	
	14	− 93	
Xylene 0.864	1	−213	$[\alpha]^{20}_{D} = 4.0C-217$
	2	−210	
	3	−205	

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[a] Solvents of "Chemically Pure" grade. The specific gravity of each of these was obtained from the "International Critical Tables," Vol. III. All other solvents were less pure and their specific gravities were determined by pycnometer.

[b] Although the specific rotation is quoted as $[\alpha]^{20}_{D}$ it does not refer as accurately to the wave length of "D" light as do measurements made with strictly monochromatic sodium light.

[c] This solution is apparently supersaturated. Upon addition of more rotenone and shaking for four hours the concentration is reduced to that of the saturated solution.

An inspection of Table I shows that rotenone is levorotatory in all solvents and at all concentrations tested. In ten of the solvents the specific rotation lies between −90 and −110°. In only two is it below this, while in the remainder it is appreciably higher, with benzene and its homologs forming a rather distinct group above −200°. The specific rotation definitely decreases with increasing concentration in the six solvents in which rotenone is most soluble, and also seems to do so in two other solvents in which it is moderately soluble.

The values for specific rotation do not all have the same degree of accuracy due to the fact that in those solvents giving only low concentrations it was impossible to get large readings on the instrument. This is indicated in Table I by the smaller size of the third digit in the cases of the alcohols, ether and carbon tetrachloride. In the cases of benzene and its homologs it was evident that the rotation dispersion was not fully compensated, but this caused practically no difficulty in making the readings.

Preparation and Optical Rotation of Saturated Solutions.—In obtaining saturated solutions of rotenone in the various solvents, the following procedure was adopted. An approximately weighed amount of rotenone[8] was introduced into ordinary test-tubes of about 30-cc. capacity. The solvent was added (25 cc. or less, depending on the amount of solid present) and the tubes tightly stoppered with cork stoppers. These tubes were placed in a shaking machine consisting of a vertical wooden disk (diameter, 16 inches) to which the tubes were held in a radial position, the disk being rotated by an electric motor at a speed of about 25 to 30 r. p. m. The shaking was continued through a period of seven hours, which trial experiments had shown to be sufficient for the attainment of equilibrium. The tubes were then removed from the shaker and allowed to stand upright overnight. In the morning the tubes were well shaken by hand and filtered directly into polariscope tubes of suitable length and the optical rotations of the clear solutions determined immediately in the saccharimeter already described. This entire operation was carried out in a constant-temperature room maintained at 20°.

At least two determinations were made with each solvent; the average results are given in Table II, Col. 4. The readings are given in Ventzke degrees, and for the sake of uniformity are calculated to a 1-decimeter tube, although in some cases longer tubes were used so that the actual reading could be made more accurately on the instrument.

Crystals Obtained from Solution.—In the preparation of saturated solutions in benzene, carbon tetrachloride and chloroform it was found that the solution could be supersaturated with rotenone but when an excess of rotenone was added an almost solid mat of needle-like crystals immediately separated. For this reason it was thought necessary to make a brief study of the crystals obtained from solutions of rotenone in some of the solvents used. To accomplish this, small amounts of rather concentrated solutions were evaporated at room temperature in a draft of air until crystallization

[8] The relative amounts of rotenone and solvent were adjusted so that from 25 to 50% rotenone in excess of that required to saturate the solution was present, as judged from trial experiments.

TABLE II

SOLUBILITY DATA FOR ROTENONE AT 20°

(1)	(2)	(3)	(4) Optical rotation of satd. soln.		(5) Soly. at 20° (concn. of satd. soln.) in g. of rotenone		
Solvent	Sp. gr. of satd. soln. at 20°	Crystals obtd. from soln.	No. of detns.	Av. reading in Ventzke deg. for a 1-dm. tube	per 100 cc. of soln.	per 100 g. of soln.	per 100 cc. of solvent
Acetone	0.825	Hexag. and lozenge-shaped plates	3	− 20.0	6.6	8.0	6.9
Acetic acid	1.057	Needles and lath-like plates	2	− 8.8	2.4	2.2	2.4
Alcohol, *n*-butyl	0.814	Hexagonal-shaped plates	2	− 0.75	0.2	0.3	0.2
Alcohol, ethyl (absolute)	.792	Hexagonal-shaped plates	2	− .80	.2	.3	.2
Alcohol, isopropyl	.790	Hexagonal-shaped plates	2	− .55	.2	.2	.2
Alcohol, methyl	.796	Hexagonal-shaped plates	2	− 1.1	.2	.3	.2
Amyl acetate	.872	Hexagonal-shaped plates	2	− 4.3	1.6	1.8	1.6
Benzene	.908	Needles	4	− 50.4	8.0	8.8	8.5
Carbon disulfide	1.270	Hexagonal-shaped plates	3	− 4.5	1.6	1.3	1.6
Carbon tetrachloride	1.587	Fine needles	3	− 2.0	0.6	0.4	0.6
Chlorobenzene	1.127	Elongated, almost needle-like hexagons	2	− 59.4	13.5	12.0	15.1
Chloroform	1.430	Needles	4	−116.4	47.2	33.0	73.4
s-β-Dichloro-ethyl ether	1.228	Fine needles	2	− 17.6	7.5	6.1	7.9
Ether, ethyl (anhydrous)	0.721	Hexagonal-shaped plates	2	− 1.5	0.4	0.5	0.4
Ethyl acetate	.916	Lozenge-shaped plates	3	− 14.7	4.8	5.2	4.9
Ethylene chlorohydrin	1.210	Hexagonal-shaped plates	2	− 33.0	11.4	9.4	12.5
Ethylene dichloride	1.270	Needles	4	− 59.7	33.1	26.1	44.3
n-Propyl formate	0.915	Hexagonal-shaped plates	2	− 18.4	6.0	6.6	6.3
Toluene	.890	Hexagonal and lozenge-shaped plates; also elongated hexagons and needles	2	− 38.6	6.4	7.2	6.7
Trichloro-ethylene	1.447	Hexagonal and lozenge-shaped plates; also fine needles	2	− 43.3	16.5	11.4	19.0
Xylene	0.878	Hexagonal-shaped plates	2	− 19.8	3.4	3.8	3.5

occurred. These crystals were examined under the microscope and their general appearance noted. The results are given in Table II, Col. 3. It will be noted that rotenone crystallizes from the majority of these solvents in the form of hexagonal-shaped plates. In some cases, however, distinctly needle-shaped crystals were obtained.

It has been reported by Tattersfield and Roach[9] that the needle crystals obtained from benzene contain solvent of crystallization. Certain preliminary experiments made in this Laboratory substantiate this result, and indicate that some other solvents form similar crystalline products. In any such case it is, of course, the addition product which is in equilibrium with the saturated solution, but in the absence of more complete information the final results for solubility have been expressed in terms of rotenone.

Calculation of Solubility.—In the cases of those solvents showing no decided variation of specific rotation with change in concentration the calculation is fairly simple. After the optical rotation of the saturated solution has been obtained the corresponding concentration (in grams of rotenone per 100 cc. of solution) may be calculated from a rearrangement of Formula 1, the appropriate specific rotation being used.

$$\underset{\text{(g./100 cc. soln.)}}{\text{Concentration}} = \frac{\text{Ventzke reading of satd. soln.} \times 0.3466 \times 100}{\text{Length tube (in dm.)} \times [\alpha]^{20}_{\text{D}}} \qquad (2)$$

In those cases in which the specific rotation was found to vary with the concentration, the concentrations of the saturated solutions were calculated from the equations given in Table I, Col. 4, for the specific rotation–concentration graph. This was done by substituting for the specific rotation its value in terms of the known Ventzke reading of the saturated solution (Table II, Col. 4) and the unknown concentration ("*C*"), and solving for the latter.

The values obtained from these calculations give the solubility, or concentration of the saturated solution, in terms of "grams of rotenone per 100 cc. of solution." By the use of the specific gravities of the solvent and of the saturated solution these values have been converted to "grams of rotenone per 100 g. of solution" and "grams of rotenone per 100 cc. of solvent." The solubility of rotenone, in terms of these three units, is given in Table II, Col. 5.

Discussion of Solubility Data

In general, it appears that rotenone is most soluble in the chloro products, with the exception of carbon tetrachloride. Benzene is also a good solvent, but the addition of aliphatic residues, as in toluene and xylene, seems to lower the solvent power, while the addition of chlorine, as in chlorobenzene, increases the solubility. Acetone is a fair solvent, as are also acetic acid and the three esters tested. The alcohols and ether, contrary to state-

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[9] Tattersfield and Roach, *Ann. appl. biol.*, **10**, No. 1, 1 (1923).

ments found in the literature, are rather poor solvents for rotenone. However, at higher temperature their solvent powers may increase considerably. For example, it was found in trial experiments that absolute ethyl alcohol, at its boiling point, will dissolve as much as 4 g. of rotenone per 100 cc. of solution, and it is this large temperature gradient which makes it useful in the recrystallization of rotenone.

An attempt was made to determine the solubility of rotenone in certain oils by the method outlined above, but, due to extremely low solubility in some cases and to difficulties caused by high optical rotation of the solvent in other cases, the method was found to be not applicable. It may be stated with some degree of certainty, as the result of trial experiments, that the solubility of rotenone in petroleum ether, gasoline, kerosene, "Nujol" and rectified oil of turpentine is less than one-tenth of one per cent. at 20°. Rotenone, however, appears to be appreciably soluble in Menhaden fish oil and in steam-distilled pine oil.

Since this article was written an interesting reference has been brought to the attention of the authors. Geoffroy[10] in 1895 isolated from the plant *Robinia nicou* now known as *Lonchocarpus nicou* (one of the species locally called "cube"), a material which he named "nicouline." The properties of this material indicate that he was dealing with what we now know as rotenone. This is substantiated by the fact that Clark[11] has recently found rotenone in "cube" roots.

Among other properties Geoffroy made a quantitative study of the solubility of "nicouline" in various solvents and obtained values markedly higher than those given in this paper, but bearing the same general relationship to each other. The temperature at which these measurements were made is not specified and if higher than 20° might account for the higher values.

Summary

The optical rotation at 20° of rotenone in twenty-one organic solvents has been determined and found to range from -66 to $-230°$.

The solubility at 20° of rotenone has been determined in these same solvents and found to range from 0.2 to 33%.

The solubility is very low in petroleum hydrocarbons, which are used extensively for spraying purposes.

WASHINGTON, D. C.

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[10] Geoffroy, *Annales de L'Institut Colonial de Marseille*, **2**, 1-86 (1895).

[11] Clark, *Science*, **70**, 478 (1929).