

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

CRYSTALLINE SOLVATES OF ROTENONE

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Rotenone ($C_{23}H_{22}O_6$, m. p. 163°) as ordinarily crystallized from alcohol or ether separates as well-formed, thin plates of rather characteristic hexagonal outline. These crystals may be heated at 105° under atmospheric, or even under reduced, pressure for an extended period of time without loss in weight, indicating that they contain no solvent of crystallization.

Tattersfield and Roach¹ have reported that rotenone separates from certain solvents with solvent of crystallization. Thus they obtained from benzene needle-like crystals which contained 23 and 16% of benzene in two determinations. These investigators also obtained from alcohol needle-like crystals which contained about 3% of alcohol of crystallization. In a previous paper² the present author reported that rotenone separates from some other solutions as crystalline solvates.³ Thus it was found that the long, needle-like crystals obtained from carbon tetrachloride lost weight on heating, evidently owing to the expulsion of solvent of crystallization.

In order to determine the composition of the compounds formed, two rather simple methods were adopted. In the first of these the crystals were obtained by cooling warm solutions containing rotenone in excess of that soluble at room temperature. The separated crystalline material was filtered and placed in a desiccator containing a 50-50 mixture of the solvent and petroleum oil⁴ until the material came to constant weight. A definite amount of this was then weighed and allowed to stand in air for some time to determine its stability, after which it was heated in an electric oven at 105° to constant weight. The total loss in weight was considered to be the amount of solvent of crystallization.

In the other method a weighed quantity of rotenone was dissolved in the solvent, the excess solvent evaporated by placing the dish in a draft of air at room temperature, and the solid material allowed to stand in the solvent-petroleum oil desiccator until it had come to constant weight. The increase in weight was considered to be the solvent added to the rotenone in the solvate compound. Blanks were run on the solvents alone to determine the residue on evaporation, and a suitable correction was made. The material was then allowed to stand in the air to determine roughly its

¹ Tattersfield and Roach, *Ann. Appl. Biol.*, 10, 1 (1923).

² Jones and Smith, *THIS JOURNAL*, 52, 2554 (1930).

³ The term "solvate" as used in this paper is intended to apply only to solid materials containing solvent of crystallization.

⁴ Such mixtures were used arbitrarily in an effort to insure the evaporation of the mother liquor without decomposition of the compound. In the case of the acetic acid compound, 50-50 glycerin and acetic acid was used.

rate of loss of solvent, and finally heated to constant weight at 105°. In the case of solvates this loss in weight should equal the gain in weight on evaporation and should again be the amount of solvent of crystallization.

In the paper² previously referred to it was reported that rotenone crystallized from acetic acid, benzene, carbon tetrachloride, chlorobenzene, chloroform, *sym.*- β -dichloroethyl ether, ethylene dichloride and sometimes from toluene and trichloroethylene in the form of needles, and it was thought that all these might be solvates. In the present determinations *sym.*- β -dichloroethyl ether, toluene and trichloroethylene were not tested because they will be little used as solvents for rotenone. On the other hand, acetone, ethyl acetate and ethyl alcohol were used to prove that these solvents do not form crystalline solvates of rotenone.

The high solvent power of chloroform for rotenone made it impossible to use the procedures outlined, because concentrated, sirupy solutions were formed from which it was difficult to obtain crystalline material. Accordingly a modification of the first method was adopted. A solution of rotenone in chloroform was prepared at a concentration considerably below the saturation value, this solution was warmed, and four to five times its volume of warm petroleum ether added slowly. On cooling, long, needle-like crystals separated. This crystalline material was then filtered and treated as outlined in the first procedure. It was established that this solvate did not contain petroleum ether.

The results obtained are given in Table I. As will be noted acetone, chlorobenzene, ethyl acetate, ethyl alcohol and ethylene dichloride, under the conditions of the experiment, did not form solid solvates. Since Tattersfield's results with alcohol would require a compound with the unusually high proportion of about four molecules of rotenone to one of alcohol, it is probable that his result was incorrect and was due to retained mother liquor. Acetic acid forms a crystalline compound containing two molecules of rotenone to one of acetic acid. These crystals lost only 0.2% of their weight on standing in the air for forty-eight hours, showing efflorescence to be extremely slow. Benzene, carbon tetrachloride and chloroform form crystalline compounds containing one molecule of rotenone to one of solvent. The benzene result agrees with one of the analyses by Tattersfield. These benzene crystals effloresced appreciably in air, losing 1.2% of their original weight on standing for forty-eight hours in the air at room temperature. The chloroform crystals lost about 1.5% in the same time. The crystals containing carbon tetrachloride, however, were fairly stable in air, losing only 0.5% in the same time. On warming these crystalline solvates the odor of the solvent was readily detected.

Attempts were made to determine the melting points of these materials. All lose their solvent of crystallization gradually at a rate dependent on the rate of heating, and then melt at temperatures ranging between 171 and

TABLE I
 CRYSTALLINE SOLVATES OF ROTENONE

Solvent	Crystallization method		Evaporation method		Formula of compound and theoretical percentage, solvent
	Cryst. matl., g. After heating, g.	Percentage solvent of compound (from loss in wt.)	Rotenone, g. Evapd. matl., g. After heating, g.	Percentage of compound (from increase in wt.)	
Acetic acid	0.419		1.000		$2C_{23}H_{22}O_6 \cdot CH_3COOH$ 7.1
	.389	7.2	1.076	7.1	
			...		
Acetone	1.120		1.000	
	1.120	None	1.000	None	
			0.997		
Benzene	1.220		1.000		$C_{23}H_{22}O_6 \cdot C_6H_6$ 16.5
	1.021	16.3	1.195	16.3	
			1.001		
Carbon tetrachloride	0.825		0.500		$C_{23}H_{22}O_6 \cdot CCl_4$ 28.1
	.598	27.5	.694	28.0	
			.501		
Chlorobenzene	0.285		1.000	
	.282	None	1.003	None	
			1.002		
Chloroform	0.268				$C_{23}H_{22}O_6 \cdot CHCl_3$ 23.2
	.208	22.5	
Ethyl acetate	1.125		1.000	
	1.124	None	1.004	None	
			1.002		
Ethyl alcohol	0.411		0.500	
	.411	None	.503	None	
			.500		
Ethylene dichloride	1.462		1.000	
	1.461	None	1.011 ^a	None	
			1.006		

^a The rotenone underwent some oxidation in this case.

179°, which is above the melting point of ordinary rotenone. On cooling and remelting all give about the same melting points. These temperatures are in the region of the melting point given by Butenandt⁵ for a polymorphic form of rotenone (m. p. 176°) which he obtained by grinding ordinary rotenone in a mortar.

All of these solvates separate in the form of rod-like crystals except the acetic acid compound, which is lath-like in appearance. The crystals all have high birefringence, parallel extinction and negative elongation. Crystals of rotenone obtained from ethyl acetate, although not a solvate, are lozenge-shaped instead of hexagonal in outline. We have found this of value as a diagnostic feature in the microscopic examination of crystalline material for rotenone.

⁵ Butenandt and Hildebrandt, *Ann.*, **477**, 245 (1930).

The formation of the solvates may also be of value as diagnostic features of rotenone and may be of some application in analytical procedures. Thus in the extraction of derris root with carbon tetrachloride, the rotenone-solvent compound crystallizes from the evaporated extract and may be separated, dried and weighed in the air without heating in the oven, the weight being calculated to that of rotenone.

Summary

Under ordinary conditions rotenone forms with benzene, carbon tetrachloride and chloroform crystalline solvates containing one molecule of rotenone to one of solvent, and with acetic acid a solvate containing two molecules of rotenone to one of solvent.

No crystalline solvates were formed with acetone, chlorobenzene, ethyl acetate, ethyl alcohol and ethylene dichloride.

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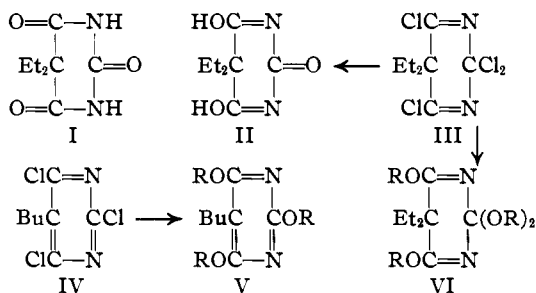
OXYGEN ETHERS OF BARBITAL

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The formula commonly assigned to barbital (5,5-diethylbarbituric acid) represents the keto-lactam structure (I). On theoretical grounds this structure should be more stable than the isomeric enol-lactim (II). At least one of the lactam groupings has the properties of an imide, since a monosodium salt can be prepared which reacts with alkyl halides to form N-alkylated barbital. If the sodium salt exists as the tautomeric enol, it should yield an oxygen ether, but no such oxygen ethers have thus been obtained. After alkylation of one lactam the resulting 1,5,5-trialkylbarbituric acid again behaves as an imide, the remaining lactam forming a sodium salt which reacts as before. It is thus possible to prepare a 1,3,5,5-tetraalkylbarbituric acid.¹



¹ Dox and Jones, *THIS JOURNAL*, **51**, 316 (1929).