Solubility of Water in Diethyl Ether at 25°

BY H. H. ROWLEY AND WM. R. REED[1]

During the course of another research problem it became necessary to know the correct solubility relationships of diethyl ether and water at 25°. Numerous values were found in the literature, but the agreement was poor and many of the methods of doubtful accuracy. The volumetric method of Hill[2] and Kablukov and Malischeva[3] appears to be the most reliable but, even using the same method, their results are not in good agreement. It was, therefore, decided to determine the value for the solubility of water in diethyl ether at 25° using the Karl Fischer reagent for the determination of water.

Experimental

The Karl Fischer reagent was prepared by accepted methods,[4-7] standardized against weighed samples of water and used to standardize a methanol–water solution. The dead-stop end-point method[8,9] was used with mechanical stirring for all standardizations and analysis of samples. When analyzing a sample for water, it was found that more precise results were obtained if the sample was added to a measured excess volume of Karl Fischer reagent. The excess Karl Fischer reagent was titrated with the methanol-water standard solution.

All systems of purified diethyl ether and water were brought to equilibrium in a water-bath at 25 ± 0.05° by means of a motor-driven stirrer with two agitators at different levels to ensure true equilibrium conditions. It was found that equilibrium was established within four hours under the conditions of the experiment. The system was allowed to stand unstirred for an additional hour to allow for complete separation of the two layers before analysis.

A desired volume of sample was drawn into a cooled, weighed pipet of suitable design and removed from the system. After sealing, to prevent loss of sample, the pipet and contents were weighed. The sample was then transferred quantitatively into excess Karl Fischer reagent and analyzed.

A number of diethyl ether–water systems were prepared and at least two independent samples were analyzed for each system. The average weight per cent. of water in diethyl ether was found to be 1.468%. The standard deviation of the mean for twelve determinations was 0.003. The average weight per cent. of diethyl ether is 98.532% by difference.

Discussion.—Many workers[2,3,10-14] have investigated the solubility of water in diethyl ether. The methods used were different and the values obtained for the system at 25° range from 1.19 to 2.66%. The reliability of the present work is based on the specific and quantitative reaction of the Karl Fischer reagent with water in the presence of many organic and inorganic reagents.[6] The fairly good precision for the per cent. water in the diethyl ether layer shows that the sampling method was good enough to give uniform samples of the system. Since the method used would keep the diethyl ether from evaporating from the sample before it is weighed or transferred, the precision also indicates that the average value obtained is more nearly correct than previously reported values.

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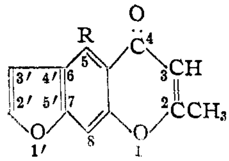
Khellin from Visnagin

BY ALEXANDER SCHÖNBERG AND NASRY BADRAN

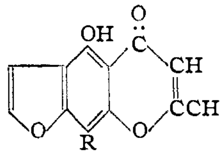
Khellin (IVb) occurs together with visnagin (Ia) in the fruits of *Ammi visnaga* (L). Visnagin is a by-product in the manufacture of khellin. Because of the attention which khellin has attracted in the medical profession, it becomes more than a matter of academic interest to find a method by which visnagin can be converted into khellin. The following scheme shows how this can be done. Attention is drawn to the change Ia → Ib by dilute hydrochloric acid.

$$\text{Ia} \xrightarrow[\text{dilute}]{\text{HCl}} \text{Ib} \xrightarrow{\text{HNO}_3} \text{IIa} \xrightarrow[\text{HCl}]{\text{Sn}} \text{IIb} \xrightarrow{\text{chromic acid}}$$

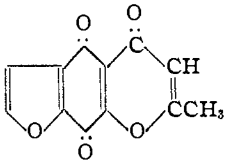
$$\text{III} \xrightarrow[\text{water}]{\text{SO}_2} \text{IVa} \xrightarrow{\text{CH}_3\text{I}} \text{IVb}$$



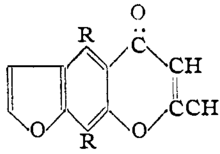
(I) (a) R = OCH_3
(b) R = OH



(II) (a) R = NO_2
(b) R = NH_2



(III)



(IV) (a) R = OH
(b) R = OCH_3

Experimental

2-Methyl-5-hydroxyfuro-4',5'-6,7-chromone (Ib).—A mixture of visnagin (Ia), 1.0 g., 15 ml. of hydrochloric acid (sp. gr. 1.16) and 15 ml. of distilled water was refluxed for one hour. The chromone dissolved and after about 20 minutes a precipitate began to form, increasing gradually in amount. The mixture was left to cool to room temperature and then filtered. The crystalline product weighed 0.8 g. and was recrystallized from glacial acetic acid giving yellowish crystals which melted at 156–158°.

The ferric chloride reaction was green; this was carried out by adding aqueous ferric chloride to an alcoholic solution of the substance. (Ib) when treated with methyl iodide in acetone, in the presence of potassium carbonate as described in the case of (IVa) (see below), yielded visnagin (Ia) (m.p. and mixed m.p.).

Anal. Calcd. for $C_{12}H_8O_4$: C, 66.7; H, 3.7. Found: C, 66.3; H, 3.8.

2-Methyl-5-hydroxy-8-nitrofuro-4',5'-6,7-chromone (IIa).—(Ib), 1.0 g., was dissolved in 20 ml. of acetone and to the solution 10 ml. of nitric acid (obtained by adding 35 ml. of water to 50 g. of nitric acid sp. gr. 1.42) was added and the mixture was allowed to stand for 30 minutes; the reaction proceeded with evolution of heat. Yellow crystals (0.6 g.) separated, m.p. 260–262° with decomposition. The ferric chloride reaction in alcohol gave a brown color turning red after a few minutes.

Anal. Calcd. for $C_{12}H_7NO_6$: C, 55.2; H, 2.7; N, 5.3. Found: C, 54.9; H, 2.9; N, 5.2.

2-Methyl-5-hydroxy-8-aminofuro-4′,5′-6,7-chromone (IIb).—(IIa), 1.0 g., 30 ml. of hydrochloric acid (sp. gr. 1.18) and 5.0 g. of tin (added gradually) were heated with continual stirring on a boiling water-bath until all the tin went into solution (about two hours). Twenty ml. of distilled water was then added, the solution boiled for about one minute and filtered hot (sintered glass filter). The deep yellow filtrate was cooled, left overnight in the ice-chest and then filtered. The yellow, crystalline precipitate of the tin hydrochloride complex of (IIb), which melted at about 245° with strong evolution of gas, was dissolved in 20 ml. of distilled water, 10 ml. of a 20% solution of sodium acetate was then added, followed by the gradual addition of 10% aqueous sodium hydroxide, until the *p*H of the solution was adjusted between 6.5 and 7.0. (IIb) came down as a cream colored crystalline precipitate, which was filtered off. Recrystallized from acetone the product gave 0.5 g. of yellowish crystals which melted at 225°.

Anal. Calcd. for $C_{12}H_9NO_4$: C, 62.3; H, 3.9; N, 6.1. Found: C, 62.6; H, 3.8; N, 6.4.

2-Methyl-furo-4′,5′-6,7-chromone-5,8-quinone (III).—(IIb), 1.0 g., was dissolved in a hot mixture of 5 ml. of sulfuric acid (sp. gr. 1.8) and 30 ml. of distilled water. After cooling to room temperature, the mixture was treated drop by drop (continuous stirring) with a solution of 2.0 g. of sodium dichromate in 20 ml. of distilled water, then left to stand at room temperature for about one hour and filtered. Recrystallized from acetone the product weighed 0.3 g. and melted at about 239° with decomposition.

(III) gives no color reaction with ferric chloride; it dissolves in sulfuric acid (sp. gr. 1.8) with an orange color and in 10% aqueous sodium hydroxide to give a violet solution.

Anal. Calcd. for $C_{12}H_6O_5$: C, 62.6; H, 2.6. Found: C, 63.1; H, 2.6.

2-Methyl-5,8-dihydroxyfuro-4′,5′-6,7-chromone (IVa).—(III), 1.0 g., was dissolved in 20 ml. of a 10% sodium bisulfite solution, and the mixture treated at room temperature with 2 ml. of hydrochloric acid, and then heated on the water-bath to free it completely of sulfur dioxide. The mixture was cooled and filtered; the yellow crystalline product obtained weighed 0.8 g. and melted at 278°. This was identical with the product obtained from khellin by demethylation.[1]

Anal. Calcd. for $C_{12}H_8O_5$: C, 62.1; H, 3.4. Found: C, 62.0; H, 3.7.

2-Methyl-5,8-dimethoxyfuro-4′,5′-6,7-chromone (IVb) (Khellin).—A mixture of (IVa), 1.0 g., 100 ml. of acetone, 6.0 g. of potassium carbonate and 5 ml. of methyl iodide was refluxed for 24 hours, then cooled and filtered. The potassium salts were washed twice with hot acetone, and the washings added to the main acetone solution. The acetone was evaporated, the residue boiled with 300 ml. of water and the aqueous solution filtered hot. On cooling 0.5 g. of almost colorless needles was obtained, which when recrystallized from alcohol melted at 153–154° and proved to be khellin by a mixed melting point determination and the color reaction with potassium hydroxide pellets.

Anal. Calcd. for $C_{14}H_{12}O_5$: C, 64.6; H, 4.6. Found: C, 64.9; H, 4.4.

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Gramine Methiodide

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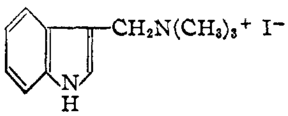
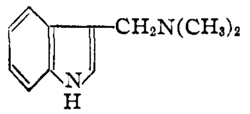
During the course of an investigation involving the synthesis of certain indole derivatives, it was necessary to prepare gramine methiodide (I).



I

Kühn and Stein[2] obtained this compound by adding methyl iodide to an alcoholic solution of gramine (II), and reported that the product, in a melting



II

point determination, turned brown at 175° but did not melt when heated to 350°. Snyder[3] used the procedure of Kühn and Stein but did not report a melting point for their methiodide. Wieland and Hsing[4] prepared the same compound in methanol solution and reported similar results, but they expressed some doubt concerning the identity of their product in light of the work of Orechoff and Norkina.[5] These latter authors claimed a melting point of 176–177° for gramine methiodide prepared in ethanol from the alkaloid Donaxin. On the other hand, Wieland and Hsing, although suspecting a case of dimorphism, did not find it possible to prepare the 176–177° product. No attempt has been made to reconcile these results.

It has been found possible to obtain both methiodides depending upon the reaction conditions used. When gramine reacted with methyl iodide in cold absolute *ethanol*, the methiodide melting at 172–173° was obtained and this was found to be a metastable or "labile" modification. The reaction of the same gramine with methyl iodide in *methanol* solution yielded the "stable," non-melting isomer. When the low-melting product was recrystallized from ethanol, the stable isomer was obtained. No change in melting point (172–173°) was observed when the labile isomer was recrystallized from methanol. It was not possible to convert the stable modification into the metastable one. Both compounds behaved in identical fashion in subsequent reactions.

Experimental

Gramine.—This compound was prepared according to the method of Kühn and Stein.[2]

Gramine Methiodide. Metastable Isomer.—Forty grams of gramine was dissolved in 280 cc. of absolute ethanol. This represented an almost saturated solution. The alcoholic solution was stirred with a mechanical stirrer, and 37.8 g. of methyl iodide was added over a period of one-half hour. Cold water was used to control the reaction during this addition. Crystals of the methiodide separated within a short time. It was thereby possible to obtain 62.6 g. (86%) of pure white needles, m.p. 172–173°. Recrystallization from methanol did not change the melting point.

Gramine Methiodide. Stable Isomer.—A solution of 1.0 g. of gramine in 5 cc. of methanol was treated with 0.8 g. of methyl iodide. The methiodide (1.6 g.) crystallized almost immediately. In a melting point determination, this mate-

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