The ability to form mixed crystals (solid solutions) is common to all hydrocarbons having low heats and entropies of fusion, as has 1,1-dimethylcyclohexane. Such molecules rotate in the solid phase below their melting points and possess considerable mobility of structure, enabling solute molecules of similar size and shape to be accommodated in the crystal lattice without fusion of the crystal. Solute molecules such as *n*-heptane and *n*-butylcyclohexane which would interfere with the rotation cannot be incorporated into the crystal lattice of 1,1-dimethylcyclohexane, hence, solid solution formation does not occur, and normal cryoscopic behavior is observed. The fact that abnormal behavior occurs when 2,2,3-trimethylbutane is used as the solute confirms the idea that it is the over-all size and shape of the molecule rather than its molecular species which determines whether or not a solid solution will result.

Experimental

Hydrocarbons.—The 1,1-dimethylcyclohexane and the hydrocarbons used as "impurities" were materials taken from the stock of the American Petroleum Institute Research Project 45 and were of good purity (99.0 mole % ± 0.5). When practicable, the 1,1-dimethylcyclohexane was separated from the "impurity" by fractional distillation at about 25-plate efficiency and re-used (after its freezing point had been checked) in the next determination, otherwise fresh solvent was used.

Apparatus.—The apparatus used in determining freezing points was essentially that described by Glasgow, Streiff and Rossini.[7] Temperatures were measured by means of a platinum resistance thermometer in connection with a Mueller resistance bridge (Leeds and Northrup, Type G-2). This thermometer was calibrated at the National Bureau of Standards.

Acknowledgment.—Grateful acknowledgment is made for the criticisms and suggestions of Drs. F. D. Rossini of the National Bureau of Standards and M. R. Cines of the Phillips Petroleum Company.

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[7] Glasgow, Streiff and Rossini, *J. Research Natl. Bur. Standards*, **35**, 355 (1945).

DEPARTMENT OF CHEMISTRY
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The Reaction of Diazonium Salts with Some 2-Thiouracils

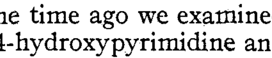
BY ELVIRA A. FALCO, GEORGE H. HITCHINGS AND PETER B. RUSSELL

Lythgoe, Todd and Topham[1] showed that pyrimidines suitably substituted in the 2,4-, 4,6- or 2,4,6-positions would undergo coupling with diazotized anilines in sodium carbonate or bicarbonate solution giving 5-phenylazo derivatives. They also investigated the structural conditions governing the coupling of pyrimidine derivatives. For this last purpose the dyes were not isolated, color being taken as an indication of coupling. They reported that 2-thiol-4,6-dihydroxy-, 2-thiol-4,6-diamino- and 2-thiol-4-hydroxy-6-methyl-pyrimidine underwent coupling.

In a recent paper Polonovski and Pesson[2] re-examined the reaction and arrived at the same general conclusions as the English authors regarding the nature of the products and the structural limitations of the reaction. They were, however, unable to couple 2-thiol-4-hydroxy-6-methylpyrimidine with diazonium salts, although they synthesized the brownish red 2-thiol-4-hydroxy-5-phenylazo-6-methylpyrimidine by condensation of thiourea with ethyl phenylazoacetoacetate.

Some time ago we examined the reactions of 2-thiol-4-hydroxypyrimidine and 2-thiol-4-hydroxy-6-methylpyrimidine with diazotized *p*-chloroaniline. When either of these compounds was allowed to react with the diazonium salt in carbonate or bicarbonate solution the following sequence of changes occurred. The solution turned pinkish red, solid separated and nitrogen was evolved. Examination of the solids revealed that they were not the expected 5-phenylazo compounds since on recrystallization from alcohol they were obtained colorless.

The product from 2-thiol-4-hydroxypyrimidine analyzed for $C_{10}H_7ON_2SCl$, while that from 2-thiol-4-hydroxy-6-methylpyrimidine gave analytical figures which agreed with the formula $C_{11}H_9ON_2SCl$. On heating with concentrated hydrochloric acid at 100° these compounds gave *p*-chlorothiophenol and uracil or 6-methyluracil, respectively. We concluded therefore that they were 2-(*p*-chlorophenylthio)-4-hydroxypyrimidine (I) and 2-(*p*-chlorophenylthio)-4-hydroxy-6-methylpyrimidine (II).



I, $R = H$
II, $R = CH_3$

The formation of *p*-chlorophenyl ethers of 2-thiolpyrimidines by this method is analogous to the formation of unsymmetrical diaryl and alkylaryl sulfides by the reaction of diazonium salts with the sodium salts of thiophenols or mercaptans.[3] In this instance the reaction proceeds *via* the diazosulfide (III) (R = alkyl or aryl). We did not isolate any product corresponding to III from the reaction of 2-thiolpyrimidines with diazonium salts. The fact that nitrogen is evolved in the cold would indicate that the 2-diazosulfides of pyrimidines are less stable than their aryl or alkyl analogs.

$$ArN_2^+X^- + RSNa \longrightarrow \underset{\text{III}}{ArN{=}NSR} \longrightarrow ArSR + N_2$$

Unfortunately Polonovski's paper, no doubt unintentionally, gives the impression that previous students of the coupling reaction have been content to observe the appearance or non-appearance of a color reaction. In fact, Todd[1] demon-

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[1] Lythgoe, Todd and Topham, *J. Chem. Soc.*, 315 (1944).

[2] Polonovski and Pesson, *Bull. soc. chim.*, [5] **15**, 688 (1948).

[3] Stadler, *Ber.*, **17**, 2675 (1884); Ziegler, *Ber.*, **23**, 2469 (1890).

strated by isolation and synthesis by alternative routes the nature of the coupling products in several instances and established the structural requirements for the occurrence of the reaction. Polonovski and Pesson have usefully extended these observations, but have failed to mention the considerable use to which the reaction already has been put in synthetic work.[4,5,6,7,8]

Experimental

2-(*p*-Chlorophenylthiol)-4-hydroxypyrimidine.—Five grams of *p*-chloroaniline in 100 ml. of *N* hydrochloric acid was diazotized with 3.0 g. of sodium nitrite at 0°. Seven and one-half grams of sodium bicarbonate was added to the solution and then the whole was added rapidly with stirring to a solution of 5 g. of 2-thiol-4-hydroxypyrimidine in 4 l. of water. When the addition of the diazonium solution was complete, 10 ml. of a 15% solution of sodium carbonate was added. The solution turned pinkish in color, some gas was evolved and a solid began to form. After standing two hours the solution was neutralized with acetic acid and the solid filtered off. The pinkish powder (5.4 g.), after recrystallization from alcohol containing a little pyridine gave colorless octahedra, m. p. 243–245°.

Anal. Calcd. for $C_{10}H_7ON_2SCl$: C, 50.4; H, 3.0; N, 11.7. Found: C, 50.4; H, 2.9; N, 11.5.

2-(*p*-Chlorophenylthio)-4-hydroxy-6-methylpyrimidine.—To a solution of 5 g. of 2-thiol-4-hydroxy-6-methylpyrimidine in 3 l. of water was added a diazonium solution prepared from 8.9 g. *p*-chloroaniline (2 moles), followed by 16.6 ml. of a 15% solution of sodium carbonate. After standing for two hours, the solution was neutralized with acetic acid and the reddish solid was filtered off (8.3 g.). After washing with warm ethanol to remove some red material the substance was recrystallized from boiling ethanol. It formed colorless rectangular prisms, m. p. 223.5°.

Anal. Calcd. for $C_{11}H_9ON_2SCl$: N, 11.1. Found: N, 11.3.

Hydrolysis of *p*-Chlorophenylthioethers with Hydrochloric Acid.—One gram of each of the above compounds was refluxed with 25 ml. of 6 *N* hydrochloric acid for three hours. Steam distillation gave *p*-chlorothiophenol in about 75% yield, m. p. 53–54°; benzoyl derivative, m. p. 74–74.5°.[9] The acid solution on evaporation gave uracil or 6-methyluracil, according to the starting material, in about 80% yield. The compounds were identified by melting points, ultraviolet absorption spectra and analyses.

Anal. Calcd. for $C_4H_4N_2O_2$: C, 42.8; H, 3.6. Found: C, 42.5; H, 3.6. Calcd. for $C_5H_6N_2O_2$: C, 47.7; H, 4.8. Found: C, 47.6; H, 4.4.

The authors are indebted to Samuel W. Blackman for the microanalyses reported here.

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[4] Baddiley, Lythgoe and Todd, *J. Chem. Soc.*, 318 (1944).

[5] Kenner, Lythgoe and Todd, *ibid.*, 652 (1944).

[6] Todd, *ibid.*, 647 (1946).

[7] King and King, *ibid.*, 731, 943 (1947).

[8] King, King and Spensley, *ibid.*, 1247 (1947).

[9] Daccomo, *Chem. Centr.*, **62**, II, 657 (1891).

THE WELLCOME RESEARCH LABORATORIES
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The Surface Area of Vermiculite

BY B. L. HARRIS

The surface area of vermiculite before and after exfoliation was measured by adsorption of nitrogen at −195° by the method of Brunauer, Emmett and Teller[1] in order to ascertain whether the area was large enough that the material might be used as a catalyst support. The area of the unexfoliated sample was measured by nitrogen adsorption and found to be 0.52 sq. m./g., giving a calculated average thickness of the platelets of 1.8 microns when the theoretical density of 2.13 is assumed. This indicates that the material was thoroughly fissured before exfoliation.

A sample of the vermiculite was exfoliated by heating for five minutes at 950°, resulting in a silvery-white accordion-like structure. The loss in weight on exfoliation was 19.6%. The surface area of this sample was 10.35 sq. m./g., giving a calculated platelet thickness of 0.091 micron. The structure of vermiculite consists of sheets of $(OH)_4Mg_6(Si, Al)_8O_{20}$ of 9.26 Å. thickness with alternate layers of 8 H_2O spaced the order of 4.8 Å.[2] It was hoped that the platelet spacing might approximate this order of magnitude, resulting in a very large surface area. The smaller area, corresponding to a thickness some 200 times as great, agrees with the conclusion of Gruner that the structure collapses above 750° and that exfoliation is mechanical, due to the formation of steam.

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[1] S. Brunauer, P. H. Emmett and Edward Teller, THIS JOURNAL, **60**, 309 (1938).

[2] J. W. Gruner, *Am. Mineral.*, **19**, 557 (1934).

DEPARTMENT OF CHEMICAL ENGINEERING
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The Interaction of Purified Antibody with Homologous Hapten. Antibody Valence and Binding Constant

BY HERMAN N. EISEN[1] AND FRED KARUSH[2]

As part of a study of the relation between protein structure and specificity we are investigating the properties of soluble complexes formed between purified antibody and homologous haptens. Rabbits were immunized with sheep serum coupled with diazotized *p*-arsanilic acid. Purified antibody, homologous to *p*-azophenylarsonic acid (R), was obtained[3] by treating pooled antisera with human erythrocyte stromata coupled with diazotized *p*-arsanilic acid (R-stromata). After several washings with 0.16 *M* sodium chloride, the antibody was eluted from R-stromata by acidification (*p*H 3.8) with acetic acid. The R-stromata was removed by centrifugation and the supernate, which contained the antibody, was neutralized. In the antibody solutions thus prepared at least 90% of the protein was specifically precipitable with R-stromata, in agreement

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[1] Research Fellow, National Institute of Health.

[2] Investigation conducted during tenure of a Fellowship in Cancer Research of the American Cancer Society, recommended by the Committee on Growth of the National Research Council.

[3] K. Landsteiner and J. van der Scheer, *J. Exp. Med.*, **63**, 325 (1936).