much higher conversion to the aldehyde was observed. The results are tabulated in Table I. This reaction is not as useful since the thioanilides are less accessible than the thioamides.

The action of lithium aluminum hydride on thiobenzamide was briefly investigated. The products isolated point to an elimination of hydrogen sulfide to give the nitrile followed by reduction of the nitrile to the amine. It has been observed[6] that heating thioacetamide with sodium ethoxide will bring about elimination of hydrogen sulfide to give acetonitrile.

TABLE I

DESULFURATION OF THIOANILIDES[a]

Thioanilide	Conversion, % (DNP)	Aldehyde
Thiobenzanilide[b]	28[c]	
	84	61
p-Methoxythiobenzanilide[b]	96	68
p-Hydroxythiobenzanilide[b]	78[d]	
Thiobutyranilide	32[e]	
Thioisovaleranilide	32[e]	

[a] The solutions were stirred in refluxing acetone for one hour with 15 g. of nickel per gram of thioanilide. After the removal of the nickel and the acetone the anil was hydrolyzed and the aldehyde was steam distilled from an acid solution. The nickel used was deactivated by refluxing in acetone, C. B. Spero, A. V. McIntosh, R. H. Levin, THIS JOURNAL, **70**, 1907 (1948). [b] Prepared from phenyl isocyanate and benzene by the method of A. Friedmann and L. Gattermann, *Ber.*, **35**, 3525 (1892). When the thiobenzanilide was prepared by the action of P_2S_5 on benzanilide it always contained some unreacted benzanilide. [c] Stirred two hours at room temperature, 70% thiobenzanilide recovered. [d] The anil was relatively stable to the refluxing 5% hydrochloric acid and was isolated directly. [e] The crude thioanilide from the reaction of P_2S_5 with the anilide was used. The yield is over-all for the two reactions.

Lithium Aluminum Hydride with Thiobenzamide. a.—To a solution of 5.0 g. of thiobenzamide in 200 ml. of ether cooled in Dry Ice and acetone was added 1.75 g. of lithium aluminum hydride in 25 ml. of ether. The solution gradually warmed to 20° during three hours and upon hydrolysis of the reaction product with sodium potassium tartrate there was obtained 2.5 g. (64%) of benzylamine benzenesulfonamide, m.p. 86–87°.

b.—A mixture of 3.0 g. of thiobenzamide and 0.45 g. of lithium aluminum hydride in 200 ml. of ether was kept at −60° for 15 minutes. The solution was then warmed slowly and at −20 to −10° a solid separated. After coming to room temperature the mixture was worked up as before and there was obtained 1.0 g. (33%) of unreacted thiobenzamide, 0.65 g. (30%) of benzonitrile n^{20}_{D} 1.5280, and 0.2 g. (8%) of benzylamine.

---

[6] C. V. Jorgensen, *J. prakt. Chem.*, [2] **66**, 33 (1902).

DEPARTMENT OF CHEMISTRY AND CHEMICAL ENGINEERING
UNIVERSITY OF CALIFORNIA
BERKELEY 4, CALIFORNIA

The Solubility of Aromatic Hydrocarbons in Water

BY W. F. CLAUSSEN[1]

RECEIVED MARCH 7, 1952

In a recent note, Herington[2] has criticized the conclusions drawn by Bohon and Claussen[3] from their data on the solubility of aromatic hydrocarbons in water. He suggests that by the choosing of the vapor as the standard state the abnormalities of the water solution disappear. There is of course no objection to the choice of the vapor as the standard state, but it must be obvious that, since benzene is a normal liquid, no abnormality would be cancelled out by this manipulation.

If one chooses the standard state of the pure hydrocarbon as vapor at 1 mm. pressure and the standard state of the solution when the mole fraction of the dissolved hydrocarbon (N_2) equals unity, then

$$\Delta F^\circ = RT \ln (p_0/N_2) \tag{1}$$

represents the standard free energy of hydration,[4] where p_0 is the saturated vapor pressure of the liquid hydrocarbon in equilibrium with the saturated water solution and the temperature T is in degrees Kelvin. Then

$$\Delta S^\circ = -(\mathrm{d}\Delta F^\circ/\mathrm{d}T) \tag{2}$$

represents the standard entropy change for the solution process. Combining equations (1) and (2), one obtains

$$\Delta S^\circ = \frac{\Delta H_{\mathrm{T(sol)}}}{T} - \frac{\Delta H_{\mathrm{T(vap)}}}{T} - R \ln \frac{p_0}{N_2} \tag{3}$$

where $\Delta H_{\mathrm{T(sol)}}$ is the heat of solution of the liquid hydrocarbon in water as used by Bohon and Claussen and $\Delta H_{\mathrm{T(vap)}}$ is the heat of vaporization of the liquid hydrocarbon. Both of these heats change with temperature and may be subject to an analytical expression of the form

$$\Delta H_{\mathrm{T}} = \Delta H_{298} + \Delta C_{\mathrm{p}}(T - 298^\circ\mathrm{K.}) \tag{4}$$

by which the heats are referred to a standard temperature of 298°K. and the ΔC_{p} term is the difference between the molar hydrocarbon heat capacities of the solution (or vapor) and the liquid hydrocarbon. Substituting equation (4) in (3) and then differentiating will yield

$$\mathrm{d}\Delta S^\circ/\mathrm{d}T = \Delta C_{\mathrm{p}}/T \tag{5}$$

where

$$\Delta C_{\mathrm{p}} = \Delta C_{\mathrm{p(sol)}} - \Delta C_{\mathrm{p(vap)}} \tag{6}$$

$\Delta C_{\mathrm{p(sol)}}$ is the value for the solution of liquid hydrocarbon in water; the average value for all of the aromatics studied by Bohon and Claussen is about 70 cal./mole deg.[5]

The import of these equations is illustrated by the thermochemical changes accompanying the solution of toluene in water. A plot of the standard free energy of solution *versus* T for toluene is shown in Fig. 1. The plot is a *curved* line; the straight line shown in the figure is for comparison. The change in slope with temperature of the curved line which might connect the points in Fig. 1 is equal to $\Delta C_{\mathrm{p}}/T$, by equation 5. ΔC_{p} was approximately calculated using the standard free energy data for three temperatures (316.0, 298.8 and 276.8°K.) and was found to be 91 cal./mole deg. For the vaporization of toluene, ΔC_{p} was found to be about −18 cal./mole deg. Thus, by equation 6, the $\Delta C_{\mathrm{p(sol)}}$ for the liquid toluene in water should be about 73 cal./mole deg., in fairly good agreement with the average value of 70 cal./mole deg.

---

[1] Corning Glass Works, Corning, New York.

[2] E. F. G. Herington, THIS JOURNAL, **73**, 5883 (1951).

[3] R. L. Bohon and W. F. Claussen, *ibid.*, **73**, 1571 (1951).

[4] J. A. V. Butler, "Chemical Thermodynamics," 4th ed. (1 Vol), The Macmillan Co., London, 1946, p. 389.

[5] The value of 108 cal./deg. mole given by Bohon and Claussen in their Fig. 4 is in error.

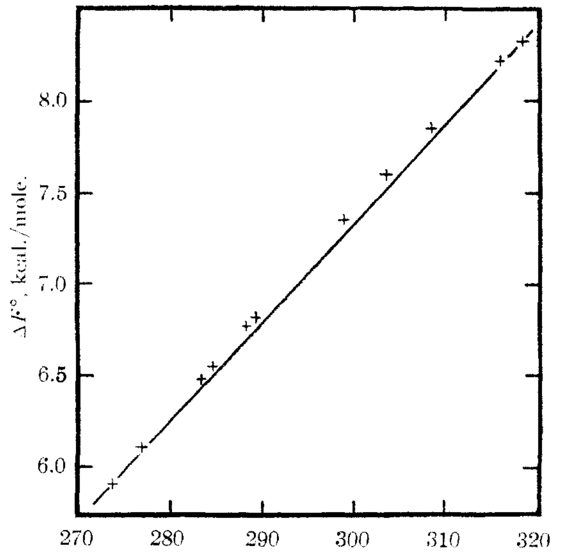

Fig. 1.—Free energy of hydration of toluene in water, $\Delta F°$, plotted against temperature, T, in degrees absolute.

for all of the lower liquid aromatic hydrocarbons as a group.

Thus, the two ways of handling the solubility data, which ways differ in the selection of the standard states of the components, give identical results. It is therefore felt that the conclusions reached by Bohon and Claussen still form a good working hypothesis for further research.

This work was sponsored by the ONR and the USPHS at the Illinois State Water Survey.

CORNING, NEW YORK

The Formation of Steroid Azines by Reaction of Ketosteroids with Girard Reagents[1]

BY HERMAN COHEN,[2] ROBERT W. BATES AND SEYMOUR LIEBERMAN[3]

RECEIVED JANUARY 28, 1952

The introduction of Girard reagents T and P for the separation of ketosteroids,[4] has greatly facilitated the isolation of estrone as well as other ketosteroids from biological sources. Since these reagents are widely employed, it will be of interest to report that during the reaction of these hydrazides, especially reagent P, with steroid ketones small amounts of azines are simultaneously formed. These azines in contrast to the usual Girard complexes are not water soluble and therefore appear in the non-ketonic fraction.

In the course of the commercial isolation of ketonic estrogens from pregnant mares' urine, the phenolic fraction is separated into ketonic and non-ketonic components by means of Girard reagent P. During one such separation a crystalline precipitate was formed in an alcoholic solution of the non-ketonic fraction resulting from the treatment of a urinary, phenolic fraction with reagent P. The crystalline material was isolated and identified as estrone azine (I).

That azines may be formed during the treatment of aldehydes with Girard reagents T or P has already been noted by Lederer,[5] who reported that aldazines are produced in 3–33% yield when various aromatic aldehydes are treated with these reagents. Assuming that the azines were formed because of the presence of free hydrazine in the Girard reagent, Lederer considered it possible to avoid this side reaction by using reagent free of the base. Miescher and Schmidlin[6] isolated an unsaturated aldazine (of β,β-diphenylacrolein) during the Girard separation of the ketones produced by oxidation of $\Delta^{4,20,23}$-3-keto-24,24-diphenylcholatriene. They assumed that an unusual splitting of the Girard complex during the hydrolysis step resulted in the formation of the azine instead of the expected carbonyl compound.

In order to study further the formation of estrone azine during the isolation of urinary estrogens by reagent P several model experiments were performed. After refluxing an ethanolic solution of crystalline estrone with the reagent for two hours, 6% of estrone azine was isolated from the non-ketonic fraction. The yield of azine was not decreased by using a freshly recrystallized sample of the reagent which gave a negative test for free hydrazine with the Pesez reagent.[7] The yield of azine was increased to 36% when the time of reflux was lengthened to 24 hours. These results indicate that free hydrazine in the reagent was not responsible for the formation of the azine and suggests that the hydrazine arises by decomposition of the excess reagent. This suggestion was confirmed by refluxing an acetic acid–ethanolic solution of reagent P alone for 24 hours. At the end of this period estrone was added and the heating continued for two additional hours. The yield of azine found in the non-ketonic fraction was 36%. The expected yield of azine formed when estrone and reagent P are refluxed together for two hours is 6–7%.

It can be shown that the formation of the azine is not due to an unusual mode of acid cleavage of the Girard–estrone complex because the azine will precipitate directly from the cooled reaction mixture before either water or acid is added. Addition of water to the reaction mixture did not appear to alter the yield of azine.

These model experiments suggest that the azines are formed by the action of hydrazine arising from the excess reagent P by hydrolysis or alcoholysis. The hydrazine so liberated can then react either with the ketone or react directly with the complex to displace the Girard hydrazide yielding the hydrazone. Under acidic conditions hydrazones are known to be rapidly converted to azines.[8]

It has also been found that other ketosteroids

---

[1] Presented at the Meeting of the American Chemical Society at Chicago, Ill., September, 1950, Abstracts page 29C.

[2] Princeton Laboratories, Princeton, N. J.

[3] Departments of Biochemistry and of Obstetrics & Gynecology, College of Physicians and Surgeons, Columbia University, New York City.

[4] A. Girard and G. Sandulesco, *Helv. Chim. Acta*, **19**, 1095 (1936).

[5] E. Lederer, *Bull. soc. chim.*, 1149 (1942); 172 (1946); 400 (1949).

[6] K. Miescher and J. Schmidlin, *Helv. Chim. Acta*, **30**, 1405 (1947).

[7] M. Pesez and A. Petit, *Bull. soc. chim.*, 122 (1947).

[8] H. H. Szmant and C. McGinnis, THIS JOURNAL, **72**, 2890 (1950).