In order to understand the aggregation phenomena of the vat dyestuffs on the fiber, one has to bear in mind that the sorption of the vat dyes and of the indigosols, as well as that of the direct dyes, is due to the molecular attraction between the cellulose molecule and the dye molecule. Under these circumstances, crystallization of the dye previous to oxidation is impossible because the dye-bath is not supersaturated with dye. Through oxidation, however, the vat dye becomes insoluble. Thereafter the monomolecular layer of the dye on the wall of the submicroscopic pores of the cellulose becomes unstable or metastable. Depending upon the adhesion strength and the magnitude of the tendency to crystallize, the monomolecular film will be disrupted more or less easily and form aggregates of submicroscopic or even of microscopically visible crystallites. The formation of crystalline particles in the fiber can proceed only by an enormous widening of the pores, even if the particles remain microscopically invisible.

As technically important aspects of the phenomenon, there may be mentioned changes in shade, in luster, in fastness to light and to rubbing, and in the tendency of the dye to cause deterioration of the fiber.

Summary

The particle size of commercial vat dyestuffs was investigated by photographic recording of the sedimentation during centrifuging. The average particle radius was found to be about 10^{-5} cm.

The particle size of cold-dyeing vat dyes in the leuco state and of indigosols in solution was investigated by means of diffusion measurements. The average aggregation number was found to be 3.

Crystallization phenomena of vat dyes adsorbed on the fiber were studied by means of X-ray diagrams and the dyes classified into three groups according to whether they remain amorphous, crystallize by aftertreatment, or simply by oxidation.

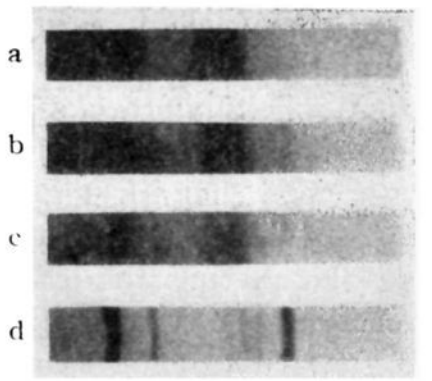

Fig. 3.—X-Ray diagrams: (a) Cuprophan film undyed; (b) Cuprophan film dyed with 9.8% indigo, after oxidation; (c) same, after oxidation and thirty-minute treatment with boiling soap solution; (d) Indigo.

MONTREAL, CANADA RECEIVED JANUARY 24, 1941

[CONTRIBUTION FROM THE DANIEL SIEFF RESEARCH INSTITUTE]

Synthesis of Lipophilic Chemotherapeuticals. III.[1] Remarks on the Properties of Halogen-acylureas, Amides and Related Compounds

BY F. BERGMANN AND L. HASKELBERG

Pearl and Dehn[2] recently reported the physical characteristics of the halogen-acetylureas. We have studied the toxicological and pharmacological properties of chlorinated acetylureas and related compounds, and in view of their general interest we should like to give a brief report of our results.

From Table I it is evident that in the different series of compounds studied, the monochloroacetyl derivatives always show the greatest toxicity while the toxicity of the dichloro compound is less than or equal to that of the trichloroacetyl derivative. No general correlation can be established, therefore, between the halogen content and the poisonous effect; the behavior of the trichloroacroyl derivatives confirms this view.

As the introduction of halogen atoms increases fat-solubility, one should expect in the series of amides a similar "central" effect as in diethyl chloro- and bromo-acetamide[3] and the corresponding diethylamide. The narcotic influence of the chlorine atoms appears to be much less than that of bromine. The dichloroacetamide exhibits a slight narcotic action, the trichloro derivative

(1) Original manuscript received April 26, 1940. Part I, *J. Chem. Soc.*, 1 (1939); II, *ibid.*, 576 (1940).

(2) Pearl and Dehn, THIS JOURNAL, **61**, 1377 (1939).

(3) *Chem. Zentr.*, **95**, II, 1485 (1924); Fuchs, *Z. angew. Chem.*, **17**, 1505 (1904).

a powerful one, which falls in line with that of chloroform and chloral. The trichloroacetyldiethylamide,[4] however, only provokes symptoms of central intoxication (clonic convulsion). On the other hand, we found that trichloroacroyl amide has no hypnotic action although it would have been probable that the unsaturated bond would favor such an action. The O-halogen-acylsalicylic acids showed a toxicity greater than or equal to that of acetylsalicylic acid.

The toxicity tests were made on white mice, weighing about 20 g.; the solutions were injected intraperitoneally. The study of the hypnotic effect of trichloroacetamide has been made on Syrian hamsters and on rats.

TABLE I

Substance	Solution used	DTM[a]	DLM[b]
Acetamide	10% aqueous	12.0	15.0
Chloroacetamide	2% aqueous	0.1	0.15
Dichloroacetamide	2% aqueous	1.5	1.75
Trichloroacetamide[c]	2% aqueous	1.0	1.1
Trichloroacetyldiethylamide[d]	2% arachis oil	0.9	1.0
Trichloroacroylamide[e]	2% aqueous	0.2	0.3
Acetylurea	2% aqueous	3.0	3.5
Chloroacetylurea[g]	2% aqueous	0.175	0.2
Dichloroacetylurea	2% aqueous	1.25	1.5
Trichloroacetylurea	1% aqueous	0.25	0.3
Trichloroacroylurea[f]	0.5% aqueous	.05	0.075
11,12-Dibromoundecanoylurea	2% arachis oil	.175	0.2
Acetanilide[g]	2% arachis oil	.9	1.0
N-Chloroacetanilide[h]	0.5% arachis oil	.05	0.1
N-Dichloroacetanilide	4% arachis oil	.7	0.8
N-Trichloroacetanilide	4% arachis oil	.9	1.0
N-Trichloroacroylanilide	4% arachis oil	.2	0.3
O-Acetylsalicylic acid[i]	2% aqueous	.4	.5
O-Chloroacetylsalicylic acid	1% aqueous	.175	.2
O-Dichloroacetylsalicylic acid	1% aqueous	.2	.3
O-Trichloroacroylsalicylic acid	1% aqueous	.6	.7

[a] DTM means dosis tolerata maxim. (g. per kg. of body weight). [b] DLM = dosis lethalis minim. [c] In high doses, 0.7–1.0, the substance causes deep sleep, lasting for two to three hours. [d] This substance (b. p. 109° (9 mm.), $n^{24}D$ 1.4900) causes a burning taste on the tongue, followed by anesthesia. [e] Our preparation yielded a substance of m. p. 87°, whereas Böeseken[6] reports a m. p. of 20°. [f] 0.5–0.7 g./kg. causes deep sleep ten minutes after injection. The mice awake from it many hours before death occurs. [g] This proved to be the only one of all the acetanilides tried, which has a narcotic effect on white mice. Curiously enough, no indication of such an action was detected with the chloroacylanilides. [h] For their preparation see Votoček and Burda.[5] [i] For the toxicity test of salicylic acids, the sodium salt was used.

(4) v. Braun, *Ber.*, **62**, 411 (1929).

(5) Votoček and Burda, *ibid.*, **48**, 1002 (1915).

Experimental Part

Acid Chlorides.—10,11-Dibromoundecanoyl chloride was prepared from the acid and thionyl chloride. The excess of the thionyl chloride was evaporated *in vacuo* and the reaction product used as such.

Trichloroacroyl Chloride.—For the preparation of the required large quantities of trichloroacrylic acid the following convenient method was worked out.[6] Tetrachloroethylene (166 g.) in chloroform (230 g.) was cooled to −10° and powdered aluminum chloride (33 g.) was added under constant stirring. After one hour, the mixture was heated to 100° for six hours and then poured into water. The 1,1,1,2,2,3,3-heptachloropropane was isolated, washed, dried and distilled at 122° (25 mm.), (m. p. 30°, yield 85%).

Hexachloropropylene was obtained in 92% yield by treating heptachloropropane (282 g.) with 225 ml. of a 25% methyl alcoholic potassium hydroxide solution, at a temperature between 0–10°. After washing and drying the hexachloropropylene was distilled at 100° (45 mm.); b. p. 210° at 759 mm.

Trichloroacrylic Acid.—Hexachloropropylene (246 g.) was mixed with concd. sulfuric acid (206 g.) and a solution of aluminum sulfate (2 g.) in water (20 cc.) added. The mixture was slowly heated in a 3-liter flask, fitted with a reflux condenser and an efficient stirrer. Within the first four hours a temperature of more than 110° must be avoided; otherwise, violent explosion occurs. Then it was heated for another six to eight hours to a temperature of 110–130°. The reaction mixture was cooled to 0° and mixed with an equal volume of water. The trichloroacrylic acid was filtered off and the mother liquor extracted with ether. Recrystallized from petroleum ether (40–60°), it forms rhombohedra, m. p. 76°; yield 140 g. The acid chloride is prepared by heating the acid with 4 moles of thionyl chloride for twenty-four hours.

10,11-Dibromoundecanoylurea.—The crude acid chloride (36 g.) and urea (12 g.) were cautiously heated to 100° when an exothermic reaction took place, the temperature rising to 130°. The product was heated for ten minutes more, triturated with water, collected and washed with alcohol and ether; from alcohol, needles, m. p. 161°; yield 30 g.

Anal. Calcd. for $C_{12}H_{22}O_2N_2Br_2$: C, 37.3; H, 5.7; N, 7.3. Found: C, 37.2; H, 5.9; N, 8.0.

N-Trichloroacroylanilide.—To aniline (45 g.) in chloroform (100 cc.), trichloroacroyl chloride (48 g.) in chloroform (100 cc.) was added dropwise at 0°. After twelve hours of standing, 70 cc. of the solvent was distilled off and the reaction product separated on cooling; from petroleum ether (80–100°) clusters of needles, m. p. 98°, yield 48 g.

Anal. Calcd. for $C_9H_6ONCl_3$: C, 43.1; H, 2.4; N, 5.6. Found: C, 42.9; H, 2.0; N, 5.9.

(6) Böeseken and Dujardin, *Rec. trav. chim.*, **32**, 98 (1913); **34**, 179 (1935); Prins, *Chem. Zentr.*, **84**, II, 394 (1913).

O-Halogen-acylsalicylic acids were prepared from the corresponding halogen-acyl chlorides and salicylic acid in a mixture of chloroform and pyridine at 0°: O-chloroacetylsalicylic acid,[7] m. p. 134–135° (needles, from 50% acetic acid).

Anal. Calcd. for $C_9H_7O_4Cl$: C, 50.5; H, 3.3. Found: C, 50.6; H, 3.6.

O-Dichloroacetylsalicylic acid, m. p. 126–127° (from benzene).

Anal. Calcd. for $C_9H_6O_4Cl_2$: C, 43.4; H, 2.4. Found: C, 43.1; H, 2.6.

(7) Barnett and Cook [*J. Chem. Soc.*, 797 (1922)], could not isolate this compound in a crystalline form. In our working conditions, the chloroacetylsalicylic acid crystallized directly from the chloroform solution.

O-Trichloroacetylsalicylic acid, m. p. 138–139° (from benzene).

Anal. Calcd. for $C_{10}H_5O_4Cl_3$: C, 40.6; H, 1.7. Found: C, 40.9; H, 1.8.

Summary

Introduction of chlorine into the acyl radical of acetylurea increases its toxicity, the dichloroacetyl compound being less toxic than the mono- and trichloro- compounds. In the parallel series of acylanilides and O-acylsalicylic acids, however, the dichloro- compound does not show this peculiar behavior.

REHOVOTH, PALESTINE RECEIVED FEBRUARY 27, 1941

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF IOWA STATE COLLEGE]

Reversible Metal–Metal Interconversions Involving Lithium and Magnesium[1]

BY HENRY GILMAN AND R. G. JONES

Earlier investigations have shown that metal–metal interconversions take place with organolithium and with organomagnesium compounds. The other organometallic compounds involved in these exchanges have been those of mercury,[2] bismuth[3a] and lead.[3b] A typical reaction is: $2C_2H_5Li + (CH_3)_2Hg \longrightarrow 2CH_3Li + (C_2H_5)_2Hg$. We are now presenting evidence for the reversibility of some of these interconversions.

Mercury–Lithium.—A mixture of phenyllithium and di-*p*-tolylmercury in ether undergoes the following transformation:

$$2C_6H_5Li + (p\text{-}CH_3C_6H_4)_2Hg \leftrightarrows (C_6H_5)_2Hg + 2p\text{-}CH_3C_6H_4Li \quad [I]$$

The procedure was to carbonate the mixture after a measured time interval, and then isolate the two mercurials. Both diphenylmercury and di-*p*-tolylmercury were obtained by starting with either phenyllithium and di-*p*-tolylmercury or *p*-tolyllithium and diphenylmercury.

Reactions of *n*-butyllithium with diphenylmercury and di-*p*-tolylmercury proceeded very rapidly in ether at room temperature with no appreciable heat effects. However, with these combinations the equilibria appear to be displaced largely in one direction, for no unchanged diphenylmercury or di-*p*-tolylmercury was recovered, and high yields of benzoic and *p*-toluic acids, respectively, were obtained.

$$(C_6H_5)_2Hg + 2n\text{-}C_4H_9Li \leftrightarrows 2C_6H_5Li + (n\text{-}C_4H_9)_2Hg$$

The di-*n*-butylmercury formed in these reactions underwent a further change, for some *n*-butylmercuric bromide was isolated. The bromine necessary for this product undoubtedly came from lithium bromide which was formed incidental to the preparation of *n*-butyllithium from *n*-butyl bromide and lithium. On the basis of other studies, it appears that *n*-butylmercuric bromide owes its formation to the following reaction:

$$(n\text{-}C_4H_9)_2Hg + LiBr \leftrightarrows n\text{-}C_4H_9HgBr + n\text{-}C_4H_9Li$$

Mercury–Magnesium.—Interconversions between organomercury compounds and Grignard reagents take place readily in ether solution, but at a much slower rate than related reactions between R_2Hg and R'Li compounds. The rates of interconversion may be correlated with the relative reactivities of organometallic compounds for no exchange was noted between *n*-butylmagnesium bromide and tetraphenyllead even on extended refluxing.[3b]

A reaction similar to [I] also takes place with Grignard reagents, for both benzoic and *p*-toluic acids were obtained subsequent to carbonation of a mixture of either diphenylmercury and *p*-

(1) Paper XXXVI in the series: "Relative reactivities of organometallic compounds." The preceding paper is in THIS JOURNAL, **63**, 839 (1941).

(2) Schlenk and Holtz, *Ber.*, **50**, 262 (1917). Hein, Petzchner, Wagler and Segitz, *Z. anorg. allgem. Chem.*, **141**, 161 (1925). Ziegler and Schäfer, *Ann.*, **479**, 150 (1930).

(3) (a) Gilman, Yablunky and Svigoon, THIS JOURNAL, **61**, 1170 (1939). (b) Gilman and Moore, *ibid.*, **62**, 3206 (1940). References to other metal–metal interconversions are contained in the series of comprehensive studies by Calingaert and co-workers; the most recent account is to be found in *ibid.*, **62**, 1542 (1940).