vealed some interesting and useful properties of the acyl radical.

It is easy to produce a peroxide catalyzed chain decomposition (decarbonmonoxylation) of aldehydes

$$RCHO + P\cdot \longrightarrow RCO + PH$$
$$R\dot{C}O \longrightarrow R\cdot + CO$$
$$R\cdot + RCHO \longrightarrow RH + R\dot{C}O$$

(P· representing a free radical generated in the peroxide decomposition) similar to that observed in the gas phase photolysis.[1] Thus a mixture of 0.265 mole of β-phenylisovaleraldehyde, b. p. 86.5–87.5° (3 mm.), n^{20}D 1.5107, and 0.030 mole of di-*t*-butyl peroxide evolved 90% of the theoretical amount of carbon monoxide in five hours at 130° under reflux. Fractionation yielded 70% of an approximately 1:1 mixture of *t*-butylbenzene (monoacetamido derivative, m. p. 168.5–169.0°; perbromo derivative, m. p. 318–320°) and isobutylbenzene (monoacetamido derivative, m. p. 127.0–127.5°; perbromo derivative, m. p. 75.0–75.5°). Thus the partial rearrangement of the neophyl radical (migration of phenyl) previously reported by Kharasch and Urry[2] is confirmed.

At lower temperatures the acyl radical is considerably more stable. When the same reaction was carried out at 80° with benzoyl peroxide as catalyst, little, if any, carbon monoxide or butylbenzene was formed and 67% of the input aldehyde was recovered.

The use of carbon tetrachloride as solvent for the preceding reaction gives rise to reaction of the acyl radical with the solvent: 6.6 g. (0.04 mole) of β-phenylisovaleraldehyde and 1.0 g. (0.004 mole) of benzoyl peroxide were refluxed for twelve hours with 6.7 g. (0.05 mole) of redistilled carbon tetrachloride. No carbon monoxide was evolved. Fractionation yielded 1.6 g. (0.0135 mole) of chloroform, b. p. 60–63°, and 4.3 g. (0.0224 mole) of β-phenylisovaleryl chloride, b. p. 84.0–86.5° (3 mm.), neutral equivalent 99.0, the hydrolysis of which yielded β-phenylisovaleric acid, m. p. 58–59° (undepressed on admixture with authentic material.)

Similarly, from isovaleraldehyde was obtained isovaleryl chloride in 60% yield, b. p. 113–115°, neutral equivalent 61.1, m. p. of anilide 108.5–109.0° (undepressed on admixture with authentic isovaleranilide).

Since the yields of chloroform and acid chloride are considerably in excess of the amount of catalyst used it is evident that a chain reaction involving the aldehyde and carbon tetrachloride has been set up as follows:

$$R\dot{C}O + ClCCl_3 \longrightarrow RCOCl + Cl_3C\cdot$$
$$Cl_3C\cdot + RCHO \longrightarrow HCCl_3 + R\dot{C}O$$

An attempt to reverse the reaction by refluxing isovaleryl chloride with benzoyl peroxide and chloroform was unsuccessful.

Most of the previous interest in liquid phase radical reactions of carbon tetrachloride has been in connection with addition to the olefinic linkage.[3] The chlorination of the aldehydes represents a radical type exchange reaction, specifically the Cl–H exchange between carbon tetrachloride and a material with a uniquely active hydrogen atom (the carbonyl hydrogen atom in the aldehydes used.)

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[1] E. W. R. Steacie, "Atomic and Free Radical Reactions," Reinhold Publishing Corp., New York, N. Y., 1946, p. 184 ff.

[2] Urry and Kharasch, This Journal, **66**, 1438 (1944).

[3] Kharasch, Jensen and Urry, This Journal, **69**, 1100 (1947).

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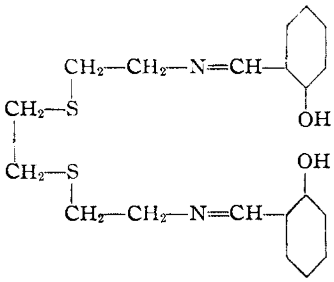
A SEXADENTATE CHELATE COMPOUND

Sir:

The dihydrochloride of 3,6-dithia-1,8-diaminooctane,[1] m. p. 186–188°, can be prepared by treating β-bromoethylphthalimide (2 moles) with ethylene dithiol in alcoholic alkali, followed by hydrolysis of the product with hydrazine and then hydrochloric acid[2] (calcd. for $C_6H_{18}N_2S_2Cl_2$: N, 11.0. Found: N, 11.2). Its hot aqueous alcoholic solution reacts with salicylaldehyde in the presence of sodium acetate to produce 3,6-dithia-1,8-bis-(salicylideneamino)-octane (I, hereafter designated SH_2), yellow leaflets, m. p. 115° (calcd. for $C_{20}H_{24}N_2O_2S_2$: C, 61.9, H, 6.2; N, 7.5. Found: C, 61.7; H, 6.3; N, 7.7).



(I)

Aerial oxidation of the orange-red solution obtained by treating I with cobaltous acetate in hot methanol, followed by dilution with water, gives a deep green solution from which potassium iodide precipitates a very dark iodide $[CoS]^+I^-$ (II), readily obtained in well-formed dark brown crystals, m. p. 245° (dec.) (calcd. for $[Co(C_{20}H_{22}N_2O_2S_2)]^+ I^-$: Co, 10.3; C, 42.0; H, 3.8; N, 4.9; I, 22.2. Found: Co, 10.3; C, 41.4; H, 3.8; N, 4.9; I, 22.2). The sparingly soluble perchlorate and the very soluble nitrate and chloride (III, $[CoS]^+Cl^-$) are also easily prepared. III forms beautifully crystalline almost black needles, m. p. 210° (dec.) (calcd. for $[Co(C_{20}H_{22}N_2O_2S_2)]^+ Cl^-\cdot H_2O$: Co, 11.7; Cl, 7.2. Found: Co, 11.7; Cl, 7.1; mol. wt. 251, cryoscopically in water).

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[1] For nomenclature *cf.* J. van Alphen, *Rec. trav. chim.*, **56**, 343 (1937), note 3.

[2] *Cf.* Ing and Manske, *J. Chem. Soc.*, 2348 (1926).

Electrical conductivity measurements indicate that III behaves in aqueous solution as a binary strong electrolyte.

The *d*-α-bromocamphor-π-sulfonate of this cobaltic complex of I can be prepared from II and silver *d*-α-bromocamphor-π-sulfonate, and separated from a mixture of methanol and ether into a sparingly soluble crystalline brown solid (IV) and a very soluble gum (V). The aqueous solution of IV is strongly levorotatory, a 0.01% solution having a specific rotation of −7,000° (Hg green line 5461). Iodides precipitate from this solution the levorotatory iodide l-$[\mathrm{CoS}]^{+}\mathrm{I}^{-}$ (found: C, 41.5; H, 3.8; N, 4.9. I, 22.0%) m. p. 268° (dec.). After six recrystallizations from 20% methanol–water, the molecular rotation (Hg green line) was −50,160°. Solutions of this salt can be boiled for twenty minutes without appreciable racemization. The aqueous solution of V is strongly dextro-rotatory. From it, after considerable difficulty the pure *d*-iodide was obtained, with molecular rotation of +50,160° (nine recrystallizations of the iodide were necessary).

Models show that I can function as a sexadentate chelate compound, occupying all six octahedrally disposed coördination positions about a six-covalent atom in one or other of two enantiomorphous strainless configurations provided that the nitrogen atoms are in *trans* positions and the sulfur atoms and oxygen atoms in *cis* positions to each other. The experimental evidence is wholly in favor of I being able to function as a sexadentate chelate compound.

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RECEIVED OCTOBER 14, 1947

α-PELTATIN, A NEW COMPOUND ISOLATED FROM *PODOPHYLLUM PELTATUM*

Sir:

The drug podophyllin N. F., prepared from the dried rhizomes and roots of *Podophyllum peltatum* L., has been shown to produce severe damage to mouse tumor cells both *in vivo*[1,2a] and *in vitro*.[2b] Chemical fractionation involving solvent extraction and chromatographic adsorption on alumina,[2a] guided by bioassay,[3] yielded two tumor-necrotizing agents in pure form. One of these was identical with the well-known podophyllotoxin; the other was a new substance which was provisionally referred to as NCI-1074.

The new compound, for which the name α-peltatin is proposed, has now been conveniently isolated from podophyllin in a yield of about 9% by chromatographic adsorption on alumina. α-Peltatin crystallizes from alcohol in colorless, transparent prisms, m. p. 230.5–232.5° (cor.) (shrinks at 222.5° and darkens at m. p.); $[\alpha]^{20}_{\mathrm{D}}$ −115° (*c* 1.0, absolute alcohol).[4] *Anal.*[5] Calcd. for $(C_{11}H_{11}O_4)_x$: C, 63.75; H, 5.35. Found: C, 63.4; H, 5.3. Calcd. for one methoxyl group per C_{11} unit: 15.0; found, 15.7. Discrepancies between the values for the molecular weight as determined by different methods make it impossible to report a true value at this time; other methods are being tried.

Solutions of the pure substance in alcohol and benzene exhibit a strong blue fluorescence under ultraviolet light, in distinction from solutions of podophyllotoxin which have only a weak blue fluorescence.

Structural, pharmacological and cytological studies with α-peltatin are in progress.

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(1) M. Belkin, *Federation Proceedings*, **6**, 308 (March, 1947).

(2) (a) J. L. Hartwell and M. J. Shear; (b) R. A. Ormsbee and I. Cornman: both papers presented before the American Association for Cancer Research, annual meeting, May 16, 1947. Abstracts in *Cancer Research*, in press.

(3) The bioassay phase of the coöperative project was carried out by Dr. Virginia Downing, Mr. A. Perrault, and Dr. M. J. Shear

(4) Through the courtesy of Dr. N. K. Richtmyer, National Institute of Health.

(5) By Mr. C. A. Kinser and Mrs. M. M. Ledyard, National Institute of Health.

NATIONAL CANCER INSTITUTE,
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ELECTROPHORETIC RESOLUTION OF HEPARIN AND RELATED POLYSACCHARIDES

Sir:

Sodium heparinate has been found to give an electrophoretic pattern indicating the presence of two components. The apparatus described by Longsworth and MacInnes[1] was used. The schlieren method was employed in photographing the moving boundaries.[2]

One per cent. solutions of the sodium salt of heparin (prepared from the crystalline barium acid salt of 500–600 Roche anticoagulent units[3] per mg.) in acetate and phosphate buffers of ionic strength 0.2 separated into two fractions under a potential gradient of 3 to 5 volts/cm. The major component migrated as an anion with a mobility at 0° of 0.8×10^{-4} to 2.4×10^{-4} cm.^{2}/sec./volt over a *p*H range of 3 to 9. The higher values were obtained in the alkaline range.

The minor component was electrically neutral and sulfate-free. From the peak areas the two fractions were found to be present in approximately a 3:2 weight ratio.

A comparison between the schlieren patterns obtained when the boundaries moved through the buffer and when they moved through the solution indicated that there was an association between the two components.

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(1) L. G. Longsworth and D. A. MacInnes, *Chem. Revs.*, **24**, 271 (1939).

(2) We are indebted to Professor W. G. France and Dr. Q. Van Winkle of this Laboratory for assistance in the electrophoretic techniques and to Hoffmann-La Roche, Inc., of Nutley, New Jersey, for the bioassays.

(3) R. H. K. Foster, *J. Lab. Clin. Med.*, **27**, 820 (1942).