Ritchie[2] was able to reduce 6-methylphenanthridine to its dihydro derivative with tin and hydrochloric acid in the same manner that Pictet and Ankersmit[3] reduced phenanthridine. Using catalytic reduction, it was found that under moderately low pressures at room temperature in the presence of platinum, 6-methylphenanthridine is readily reduced to its dihydro derivatives. The 6-methyl-5,6-dihydrophenanthridine was characterized by the preparation of its toluenesulfonamide.

If the reduction is carried out in acetic acid at 100° and 1000 lb. pressure, 6-methyloctahydrophenanthridine is obtained. This substance is a colorless crystalline compound melting at 57–58°, sublimes *in vacuo* at 110°, and forms a picrate. Tentatively, it is assumed that the ring vicinal to the nitrogen atom is reduced. In this connection it was interesting to observe that Albert, Brown and Duell[4] obtained hexahydrophenanthridine upon reduction of phenanthridone with sodium amalgam at 85° under carbon dioxide.

Following the procedure employed by Pictet and Patry[5] for the N-alkylation of 5,6-dihydrophenanthridine, the alkylation of 6-methyl-5,6-dihydrophenanthridine goes easily. On heating β-diethylaminoethyl chloride with the dihydro compound at 100°, 5-(β-diethylaminoethyl)-6-methyl-5,6-dihydrophenanthridine was obtained. For simple N-alkylations it was found that the preparation of a 5,6-dihydrophenanthridine was unnecessary. For example, 5-ethyl-6-methyl-5,6-dihydrophenanthridine was obtained by first preparing the ethyl *p*-toluenesulfonate quaternary salt followed by hydrogenation.

Acknowledgment.—The authors are indebted to Dr. John Lee for suggesting the problem and to Dr. Al Steyermark and his associates for the microanalyses.

Experimental

6-Methylphenanthridine can be obtained readily by the elegant method of Morgan and Walls[6] by dehydrating acetyl-*o*-xenylamine.

5-*p*-Toluenesulfonamido-6-methyl-5,6-dihydrophenanthridine.—A solution of 5 g. of 6-methylphenanthridine in 25 cc. of alcohol was reduced under 350 lb. pressure in the presence of platinum oxide. The initial drop in pressure was rapid and gradually slowed down until the reduction was completed. After filtering off the catalyst, the alcohol was removed by distillation and the residue treated with *p*-toluenesulfonyl chloride in aqueous alkali in the usual manner. The sulfonamide was purified by recrystallization from alcohol, m. p. 166–168°.

Anal. Calcd. for $C_{21}H_{19}NSO_2$: C, 72.18; H, 5.48; N, 4.01. Found: C, 72.16; H, 5.80; N, 4.00.

6-Methyloctahydrophenanthridine.—A solution of 20 g. of 6-methylphenanthridine in 55 cc. of acetic acid was hydrogenated at 100° and 1000 lb. pressure in the presence of platinum to completion. Approximately four moles of hydrogen were absorbed. After filtering and diluting with water, the solution was concentrated to a small volume *in vacuo* under nitrogen. Upon making alkaline with dilute sodium hydroxide, a precipitate was obtained. After purification by sublimation *in vacuo* at 110°, the product was obtained as long, colorless needles, m. p. 57–58°.

Anal. Calcd. for $C_{14}H_{19}N$: C, 83.55; H, 9.51; N, 6.95. Found: C, 83.17; H, 9.53; N, 6.92.

The picrate was prepared and recrystallized from hot methanol–butyl ether mixture, m. p. 137–138°.

Anal. Calcd. for $C_{14}H_{19}N\cdot C_6H_2OH(NO_2)_3$: C, 55.80; H, 5.16; N, 13.01. Found: C, 55.69; H, 5.02; N, 13.14.

5-(β-Diethylaminoethyl)-6-methyl-5,6-dihydrophenanthridine.—A mixture of 5 g. of 6-methyl-5,6-dihydrophenanthridine and 4 g. of β-diethylaminoethyl chloride was heated in a sealed tube at 100° for five hours. After cooling, dilute hydrochloric acid was added, and the unreacted phenanthridine was removed as its insoluble hydrochloride. The filtrate was made alkaline, and the resultant oil was extracted with ether and dried over potassium hydroxide. The dried ethereal solution was saturated with dry hydrogen chloride to obtain the salt; yield, 4 g. The compound was recrystallized from dioxane and dried *in vacuo* at 110°, m. p. 186–187°.

Anal. Calcd. for $C_{20}H_{26}N_2\cdot HCl\cdot {}^1/_2H_2O$: C, 70.67; H, 8.25; N, 8.24. Found: C, 70.43; H, 7.82; N, 8.49.

5-Ethyl-6-methyl-5,6-dihydrophenanthridine.—A mixture of 10 g. of 6-methylphenanthridine and 11 g. of ethyl *p*-toluenesulfonate was heated at 100° for three days. The melt was dissolved in 65 cc. of methanol and hydrogenated at room temperature under 1000 lb. pressure in the presence of platinum until one equivalent of hydrogen was absorbed. The methanol was removed by distillation and the residue treated with dilute sodium hydroxide. The precipitate was extracted with ether, dried, and the solution saturated with dry hydrogen chloride to produce the colorless hydrochloride; yield, 7.5 g. A small amount of 6-methylphenanthridine was separated when recrystallization from alcohol–ether was attempted. After removal, the alcohol–ether filtrate was concentrated and the residue made alkaline with ammonia. The oil was then extracted with ether, dried over potassium hydroxide, and saturated with hydrogen chloride. The hydrochloride now obtained was recrystallized from ethyl acetate–ether mixture, m. p. 148–149°.

Anal. Calcd. for $C_{16}H_{17}N\cdot HCl$: C, 73.98; H, 6.99; N, 5.39. Found: C, 73.70; H, 7.09; N, 5.21.

NUTLEY, N. J. RECEIVED JANUARY 23, 1950

(2) Ritchie, *J. Proc. R. S. N. S. W.*, **78**, 184 (1945).
(3) Pictet and Ankersmit, *Ber.*, **22**, 3339 (1889).
(4) Albert, Brown and Duell, *J. Chem. Soc.*, 1284 (1948).
(5) Pictet and Patry, *Ber.*, **35**, 2535 (1902).
(6) Morgan and Walls, *J. Chem. Soc.*, 2447 (1931).

Free-Radical Initiated Dimerizations

BY CHARLES E. FRANK AND ANGUS U. BLACKHAM[1]

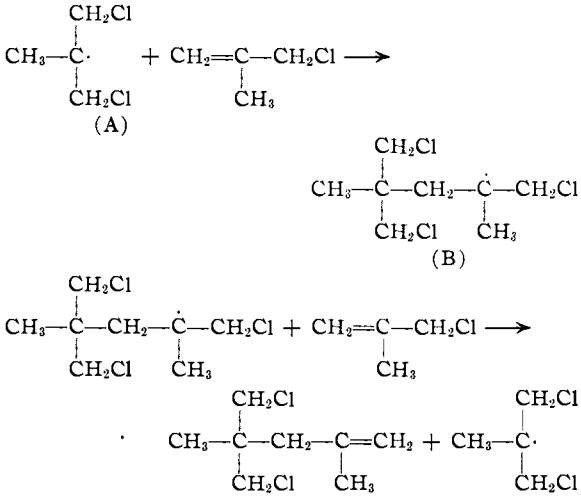
A number of unsaturated compounds have been reported to yield largely dimers rather than higher molecular weight products when subjected to conditions favoring polymerization. Compounds of this type include methallyl chloride,[2] trichloroethylene[3a] and *sym*-dichloroethylene.[3b] Wilzbach, Mayo and Van Meter[4] recently determined the structure of methallyl chloride dimer, and suggested the following mechanism to account for the selective formation of this product.

(1) Abstracted from the thesis of A. U. Blackham submitted in partial fulfillment of the requirements for the M.S. degree at the University of Cincinnati. Presented at the Philadelphia Meeting of the A. C. S., April, 1950.
(2) Bauer and Gotz, U. S. Patent 2,338,893.
(3) (a) Mugden and Wimmer, U. S. Patent 2,161,078; (b) Bauer, U. S. Patent 2,267,712.
(4) Wilzbach, Mayo and Van Meter, THIS JOURNAL, **70**, 4069 (1948).

TABLE I

POLYMERIZATION PRODUCTS OF CHLORINATED OLEFINS (1.2 MOLE % Bz_2O_2)

Monomer	Probable dimer radical	At reflux temp., 96 hr. Reacn. temp., °C.	Total yield, %	Wt. ratio dimer: higher polymer	At 70°, 72 hr. Total yield, %	Wt. ratio dimer: higher polymer
Methallyl chloride	(B)	73–99	63.5	4.3	54.5	3.8
Trichloroethylene	$CHCl_2CCl_2CHClCCl_2\cdot$ (I)	87–115	68.3	9.0	28.0	3.5
cis-Dichloroethylene	$CHCl_2CHClCHClCHCl\cdot$ (II)	61–78.4	57.2	2.2	55.7	2.2
trans-Dichloroethylene	(II)	49–64.4	53.5	0.56	71.0	1.1
Allyl chloride	$CH_2ClCH(CH_2Cl)CH_2\dot{C}HCH_2Cl$ (III)	45.6–47	14.9	0.0	82.1	0.01
Isocrotyl chloride	$CHCl_2C(CH_3)_2CHCl\dot{C}(CH_3)CH_3$	68.3–69.3	1.7	..	2.1	..



Kharasch and Buchi[5] have found allyl bromide similarly yields a dimer on reaction with acetyl peroxide, though the efficiency of the reaction is lower than that observed with the other monomers listed; the structure determined for the allyl bromide dimer, and the mechanism proposed for its formation, are in agreement with the results obtained[4] on the methallyl chloride reaction.

In the present study, the relative tendencies toward the formation of dimers and higher polymers have been investigated for a series of six monomers; these are listed in Table I along with the dimer radicals corresponding to radical B derived from methallyl chloride. The ratio of dimer to higher polymer from any given monomer is dependent upon the reactivity of the intermediate dimer radical; the more reactive radicals yield more high molecular weight products, the less reactive yield more dimer through loss of a chlorine atom. An additional factor affecting the ratio of dimer to higher polymer is temperature; an increase in temperature increases the dimer:higher polymer ratio markedly, apparently because of reduced stability of the dimer radical.

The ratios dimer:higher polymer obtained at 70° show the effect of structure upon the relative reactivities of the radicals B, I, II and III. Under these conditions, the reactivity of isocrotyl chloride was too slight to yield sufficient product for similar evaluation. There is reason to believe that trichloroethylene with its slower reaction rate should yield a larger dimer:higher polymer ratio than methallyl chloride; the slightly lower value obtained here may be explained by the greater difficulty of cleanly separating the trichloroethylene products. The difference observed between the relative tendencies of the *cis* and *trans* dichloroethylenes toward dimerization affords an interesting extension of the observations of Lewis and Mayo[6] regarding the copolymerization tendencies of *cis* and *trans* isomers. In our work also, the *trans* isomer was found to react more rapidly than the *cis;* the *cis* yielded a dimer:higher polymer ratio over twice that of the *trans*, in line with the general observation that the radical of the least reactive monomer has more opportunity to lose a chlorine atom by transfer.

The marked effect of temperature upon the dimer:higher polymer ratios apparent in Table I prompted us to attempt the dimerization of allyl chloride at elevated temperatures. Allyl chloride was heated at 130 and 165° in a stainless steel reactor (1.2 mole per cent. di-*t*-butyl peroxide initiator) for eight and twenty-two hours, respectively. At 130° the yield amounted to 17% with a dimer:higher polymer ratio of 0.19; at 165° the yield was 52% with a dimer:higher polymer ratio of 0.32.

The dimers of methallyl chloride and *sym*-dichloroethylene are reported to be 2-methyl-4,4-bis-(chloromethyl)-1-pentene[4] and 1,3,4,4-tetrachloro-1-butene,[3] respectively. If, as we believe, the dimerizations of allyl chloride and trichloroethylene follow a similar course, the dimers of these two compounds are 5-chloro-(4-chloromethyl)-1-pentene and 1,1,3,3,4,4-hexachloro-1-butene, respectively.

TABLE II

PROPERTIES OF THE DIMERS

Parent momomer	B. p., °C.	Mm.	$n^{20}D$	d^{20}_{20}	Anal., % Cl Calcd.	Found
Methallyl chloride	82.4	10	1.4773	1.0711	39.2	39.3
Trichloroethylene	104.4	10	1.5461	1.6790	81.0	81.2
sym-Dichloroethylene	88.0	20	1.5150	1.4759	73.2	72.7
Allyl chloride	66–67	21	1.4681	1.1034	46.3	46.4

Experimental

Materials.—Methallyl and allyl chlorides (Shell Chemical Company) and trichloroethylene (E. I. du Pont de

(5) Kharasch and Buchi, *J. Org. Chem.*, **14**, 84 (1949).

(6) Lewis and Mayo, THIS JOURNAL, **70**, 1533 (1948).

Nemours and Company) were purified by fractionation through a 90-cm. column packed with glass helices. *cis*- and *trans*-dichloroethylenes were prepared by dechlorination of tetrachloroethane with zinc dust, and fractionation of the mixed product; *cis*, b. p. 59.7° (740 mm.); *trans*, b. p. 47.3° (740 mm.). Isocrotyl chloride was prepared by dehydrochlorination of isobutylidene dichloride prepared from isobutyraldehyde and phosphorus pentachloride; b. p. 67.1° (740 mm.), $n^{20}D$ 1.4224.

Dimerizations.—The preparation of trichloroethylene dimer illustrates the general procedure. Trichloroethylene (4 moles) was refluxed for ninety-six hours in the presence of 1.2 mole % of benzoyl peroxide added in 20 portions. During this period the temperature of the refluxing solution rose from 87 to 115°, half of this rise occurring during the last thirty hours of reaction. At the close of the reaction the volatile portion of the product was distilled from the flask under reduced pressure into a Dry Ice cooled receiver, thereby freeing the monomer and dimer from higher polymeric and peroxide residues before fractionation. The distillate then was fractionated through a 90-cm. helices-packed column, the dimer distilling at 76° (1.2 mm.). Material recovered here amounted to 154 g. (29.2%) trichloroethylene, 324 g. (61.5%) dimer and 36 g. (6.8%) of higher polymers. In calculating these yields, the weight of peroxide residues was assumed roughly equal to 75% of the original peroxide.

The dimerizations at constant temperature were carried out by placing each monomer (with 1.2 mole % peroxide) in a polymerization bottle which was rotated end-over-end for seventy-two hours in a water-bath at 70°. Separation of the reaction mixture was effected in the manner described above.

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Preparation of I^{131} Labelled Iodoacetamide and N-Iodoacetyl Amino Acids

BY ORRIE M. FRIEDMAN AND ALEXANDER M. RUTENBURG

A study of N-iodoacetyl derivatives of L-tryptophan, L-leucine and DL-phenylalanine in experimental animals was undertaken because of interest in the possible usefulness of toxically substituted metabolites for inhibition of tumor growth. Control observations with iodoacetamide were necessary for assessment of general toxicity and specific toxicity for tumor tissue. Since preliminary results[1] indicated that tumor growth inhibitory effect of the four compounds bears little quantitative relationship to their systemic toxicity, tissue distribution studies of their radioactive analogs were of interest.

N-Iodoacetyl derivatives of L-tryptophan[2] and DL-leucine[3] had been prepared previously by use of iodoacetyl chloride. A more convenient method for the preparation of the required iodoacetyl derivatives in this instance was by treatment of the appropriate bromoacetyl or chloroacetyl amino acids with sodium iodide in acetone. For the preparation of isotopically labelled analogs NaI^{131} was used.[4,5] Radioactive iodoacetamide was similarly prepared from chloroacetamide.

Experimental[6]

Isotopic N-Iodoacetyl-L-tryptophan.—A mixture of 44 mg. of chloroacetyl-L-tryptophan prepared according to Aberhalden and Kempe[7] and 25 mg. of NaI^{131} containing one to two millicuries of I^{131} [7a] in 10 cc. of reagent acetone was heated under reflux for fifteen minutes. The sodium chloride that separated was removed on a filter, 0.5 cc. of water was added to the filtrate which was then evaporated until it became cloudy. On cooling, the product precipitated as white flaky crystals, 39 mg., m.p. 180–182°; after recrystallization from methanol–water, m.p. 185–187°.

A macro modification of this method with non-radioactive sodium iodide gave **N-iodoacetyl-L-tryptophan**, m.p. 186–188°. (Aberhalden and Baumann[2] reported m.p. 175–176°, previous dec.) *Anal.* Calcd. for $C_{13}H_{13}N_2O_3I$: N, 7.52. Found: N, 7.43.

N-Bromoacetyl-L-leucine.—This compound was obtained from L-leucine with bromoacetyl bromide by the method of Aberhalden and Zeisset[8] for the preparation of N-bromoacetyl-DL-leucine, in 80% yield, m.p. 149–151°. *Anal.* Calcd. for $C_8H_{14}O_3NBr$: C, 38.05; H, 5.56. Found: C, 38.15, 38.10; H, 5.60; 5.77.

Isotopic N-Iodoacetyl-L-leucine.—A mixture of 44 mg. N-bromoacetyl-L-leucine and 25 mg. of NaI^{131} (one to two millicuries activity)[7a] in 10 cc. of reagent acetone was heated under reflux for ten minutes. The precipitate of sodium bromide was separated on a filter and the filtrate after addition of 0.5 cc. of water was heated to drive off the acetone. The aqueous solution remaining when cooled and seeded precipitated 37 mg. of crystalline product m.p. 164–165°.

A macro modification of this method with non-radioactive sodium iodide gave **N-iodoacetyl-L-leucine**, m.p. 165–166°. *Anal.* Calcd. for $C_8H_{14}O_3NI$: C, 32.12; H, 4.77. Found: C, 32.18; H, 4.36.

Isotopic N-Iodoacetyl-DL-phenylalanine.—A solution of 49 mg. of chloroacetyl-DL-phenylalanine prepared according to Leuchs and Suzuki[9] and 35 mg. of NaI^{131} (one to two millicuries activity)[7a] in 5 cc. of acetone was heated under reflux for 30 minutes. After removal of the precipitate of sodium chloride the reaction mixture was concentrated and after dilution with five drops of water further concentrated on the steam cone till cloudiness resulted. The precipitate obtained on cooling the solution in ice was transferred to a filter and after washing with a minimum of cold water was dried in a desiccator. A white, flaky crystalline product was obtained, 55 mg., m.p. 137–139°.

A macro modification of this method with non-radioactive sodium iodide gave **N-iodoacetyl-DL-phenylalanine** which after recrystallization from water melted 138–139°. *Anal.* Calcd. for $C_{11}H_{12}O_3NI$: C, 39.65; H, 3.60. Found: C, 39.67; H, 3.66.

Isotopic Iodoacetamide.—The required chloroacetamide was prepared according to Scholl[10] from ethyl chloroacetate and ammonia. A solution of 15 mg. of chloroacetamide and 25 mg. of NaI^{131} (one to two millicuries activity)[7a] in 5 cc. of acetone was heated under reflux for fifteen minutes. The precipitate of sodium chloride was removed by filtra-

(1) Friedman and Rutenberg, to be published.
(2) Aberhalden and Baumann, *Ber.*, **41**, 2857 (1908).
(3) Aberhalden and Aberhalden, *Ferment*, **16**, 48 (1938).
(4) Seligman, Rutenberg and Friedman, *J. Nat. Cancer Instit.*, **9**, 261 (1949).
(5) Seligman, Friedman and Rutenberg, *Cancer*, **3**, 342 (1950)
(6) Microanalyses by Shirley R. Golden, all melting points are corrected.
(7) Aberhalden and Kempe, *Ber.*, **40**, 2737 (1907).
(7a) Prepared by evaporation to dryness of an aqueous solution containing the required amount of sodium iodide and one to two millicuries of carrier free I^{131} as the sodium salt. Carrier free I^{131} was obtained from the chain-reacting pile at Oak Ridge, Tenn.
(8) Aberhalden and Zeisset, *Ferment*, **11**, 174 (1930).
(9) Leuchs and Suzuki, *Ber.*, **37**, 3313 (1904).
(10) Scholl, *ibid.*, **29**, 2417 (1896).