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.

Acknowledgment.—The authors are indebted to the Stephen H. Wilder Foundation for a Fellowship Grant which made this work possible.

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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).

tion and the acetone distilled from the filtrate. The residue was crystallized by solution in 5 drops of ethyl acetate which was cooled in ice and diluted with a few drops of benzin. The supernatant fluid was decanted from the precipitate that formed and the process of recrystallization repeated. The product was obtained as white flaky crystals, 15 mg., m.p. 93–95°.

Acknowledgment.—This investigation was aided by a research grant from the National Cancer Institute, National Institute of Health, Public Health Service.

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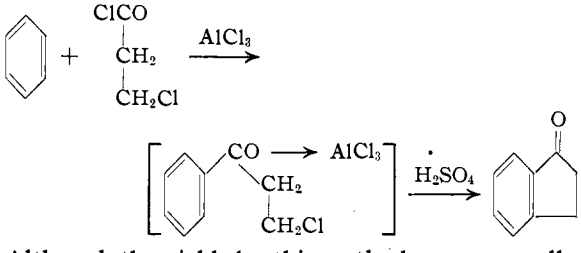
BETH ISRAEL HOSPITAL
BOSTON, MASSACHUSETTS RECEIVED JANUARY 17, 1950

Acylation–Alkylation Studies. I[1]

BY ROBERT T. HART AND R. F. TEBBE[2]

The purpose of this investigation has been to effect the condensation of a bifunctional molecule with an aromatic nucleus to produce a number of indanones in a one-step reaction involving acylation and alkylation of the nucleus.

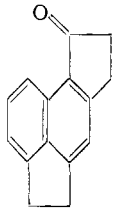
In general, two methods were employed: (a) a modification of the classical procedure involving a simplification of manipulation, *i.e.*, the regular Friedel–Crafts acylation is carried out and, after removal of solvent, the oily complex is heated with concentrated sulfuric acid at 80–100° for thirty to forty-five minutes before being poured onto crushed ice. In this procedure the acid not only decomposes the aluminum chloride–ketone complex but simultaneously causes intramolecular ring closure by cycli-alkylation



Although the yields by this method were generally somewhat lower than by the conventional two-step procedure in which the intermediary product of acylation was isolated, the present method affords an improvement in that the ketones are thus produced more easily and quickly. (b) The hydrogen fluoride method of Fieser and Hershberg[3] was extended to cover three additional cases.

For the bifunctional condensation of unsaturated acids and unsaturated acid chlorides with the aromatic nucleus, method (a) was found to be inferior to other methods previously reported.[4,5] Also, although method (b) gave excellent results in effecting the bifunctional condensation of unsaturated acids with the aromatic nucleus, it was found to be unsuccessful for the bifunctional condensation of β-chloropropionyl chloride, β-chloropropionic acid, β-propiolactone, acrylyl chloride, acrylic acid and hydracrylic acid with the aromatic nucleus, large amounts of intractable tars being formed.

An interesting exception was found when β-chloropropionyl chloride was condensed with a particularly reactive aromatic nucleus, acenaphthene. When this reaction was carried out at room temperature for eighteen hours followed by three hours of reaction at 90°, 29.7% of a chlorine-free ketone, m. p. 160–161°, which gave a correct analysis for $C_{15}H_{12}O$, was isolated indicating that bifunctional condensation had occurred. It is clear that this condensation did not occur across the peri positions of acenaphthene since the compound which would have resulted in such a case, 3,4-aceperinaphthane-7-one, m. p. 102.6–103.4°, has been reported previously.[6] It is therefore probable that the compound was formed by initial acylation in the α-position followed by cyclization into the β-position to give α-acenaphthindane-1-one (I). A compound having this probable structure was reported by Greune[7] to melt at 162–163°. Also, it should be noted that this structure is analogous to that obtained by Fieser and Hershberg[8] who found that acenaphthene reacts smoothly with crotonic acid in the presence of anhydrous hydrogen fluoride to give 1′-methyl-3′-keto-2,3-cyclopentenoacenaphthene.



I

Experimental

β-Chloropropionyl Chloride.—A mixture of 174 g. (2.42 moles) of β-propiolactone and 346 g. (2.9 moles) of thionyl chloride was allowed to react according to the method of Gresham and Shaver.[8] The chloride was obtained by distillation at the water-pump, 218 g. (71%), b. p. 80–83° (100 mm.).

Method (a): 4,7-Dimethyl-indanone-1.—A solution of 26.6 g. (0.21 mole) of β-chloropropionyl chloride and 21.2 g. (0.20 mole) of *p*-xylene in 25 cc. of carbon disulfide was added over forty-five minutes to 32 g. (0.24 mole) of anhydrous aluminum chloride covered with 125 cc. of carbon disulfide in a 1-liter three-necked round-bottomed flask fitted with condenser, stirrer, and addition tube. After

(1) Project NR 055-166 of the Office of Naval Research.

(2) Present address: Gordon College, Rawalpindi, N. W. Pakistan, India.

(3) Fieser and Hershberg, THIS JOURNAL, **61**, 1272 (1939).

(4) Plattner and Furst, *Helv. Chim. Acta*, **28**, 1636 (1945).

(5) Koelsch, THIS JOURNAL, **65**, 59 (1943).

(6) Fieser and Jones, *ibid.*, **64**, 1666 (1942).

(7) Greune, *Chem. Zentr.*, **103**, II, 2238 (1932).

(8) Gresham and Shaver, U. S. Patent 2,411,875 (Dec. 3, 1946).