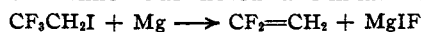Trifluoroethyl iodide reacted readily with magnesium, but no Grignard reagent was obtained. Instead, the iodine atom and one fluorine atom were extracted, and 1,1-difluoroethylene was formed. Henne[2] has noted a similar reaction

$$CF_3CH_2I + Mg \longrightarrow CF_2{=}CH_2 + MgIF$$

between 2,2-difluoroethyl iodide and magnesium, sodium, or potassium, the organic product being fluoroethylene.

These reactions illustrate the difficulty of preparing a Grignard reagent from a 1,2-dihalogen compound. It is possible that trifluoroethyllithium can be prepared by a halogen–metal interconversion reaction[3] using ethyllithium at low temperatures.

Experimental

2,2,2-Trifluoroethyl Iodide.—Free trifluorodiazoethane was prepared as described previously.[1a] A solution made by dissolving 12.7 g. (0.115 mole) of the diazo compound in 25 cc. of toluene at −75°, was gently stirred, and to it was added dropwise a solution of 15 g. (0.117 mole) of pure hydrogen iodide in 25 cc. of toluene also cooled to −75°. The addition of the hydrogen iodide solution was conveniently made by means of a small pipet to which was attached a rubber bulb for filling. The reaction was violent even at −75°, and the mixture was soon colored with free iodine. This iodine color persisted after all of the hydrogen iodide solution had been added and the mixture had stood in the "dry-ice"–acetone bath for twelve hours. However, when the reaction mixture was allowed to warm up to room temperature, the iodine color quickly faded, and this indicated that some unreacted trifluorodiazoethane was still present. The mixture was therefore cooled again to −75° and treated with another 2 g. of hydrogen iodide dissolved in 5 cc. of toluene.

The reaction mixture was distilled through a small packed column and the first fraction, boiling from 50 to 105°, was collected. This fraction was redistilled through the same column to yield 16.0 g. of pure 2,2,2-trifluoroethyl iodide, b. p. 54.5–55° (730 mm.); d^{23}_4 1.989.

Anal. Calcd. for CF_3CH_2I: I, 60.46. Found: I, 60.15, 60.52.

An additional 2.5 g. of liquid was obtained which boiled from 55 to 57°, and this was probably slightly impure trifluoroethyl iodide. This made a total yield of 18.5 g. (77%). The compound is a colorless liquid with an odor similar to ethyl iodide or bromide.

Action of Phosphorus and Iodine on Trifluoroethanol.— A mixture of 48 g. (0.48 mole) of 2,2,2-trifluoroethanol[1b] and 8 g. (0.26 atom) of dry red phosphorus was placed in a 100-cc. flask carrying an efficient reflux condenser. Dry powdered iodine (65 g., 0.5 atom) was added through the condenser in small portions while the flask was kept in a water-bath at 75°. After all of the iodine had been added, the mixture was refluxed for one and a half hours. Hydrogen iodide was copiously evolved. The reaction mixture was distilled, and a white, porous, solid residue remained.

(2) Henne, This Journal, **60**, 2275 (1938).

(3) Gilman and Jones, *ibid.*, **63**, 1441 (1941).

The distillate was shaken with 100 cc. of water, and the heavy non-aqueous layer (12 g.) was separated and dried over potassium carbonate. Upon distillation of this liquid, 5.1 g. (5%) of crude trifluoroethyl iodide was obtained (b. p. 55–58°). The aqueous solution was extracted with three 30-cc. portions of ether. This extract was washed with sodium thiosulfate solution, dried over calcium chloride, and fractionated to yield 19 g. (40%) of unchanged trifluoroethanol.

The white solid residue in the original reaction flask was treated with 50 cc. of water, and the mixture was distilled by heating with an open flame. Five grams of unreacted phosphorus remained. The distillate, consisting of two liquid phases, was extracted with 25 cc. of ether. After drying this extract and removing the ether, the residual liquid (8 g.) boiled at 181–183°. It has not been identified.

In another experiment a mixture of 20 g. (0.20 mole) of trifluoroethanol, 6.2 g. (0.20 atom) of phosphorus, and 127 g. (1.0 atom) of iodine was heated at 50° for four hours, 75° for two hours, 100° for a few minutes. Large quantities of hydrogen iodide were evolved. From this reaction were isolated 1.8 g. (4% yield) of crude trifluoroethyl iodide; 5 g. (25%) of unchanged trifluoroethanol; and 10 g. of a white wax-like solid which has not been identified.

Reaction of Trifluoroethyl Iodide with Magnesium.—A 100-cc. three-necked flask, provided with a mechanical stirrer, dropping funnel, and reflux condenser, was thoroughly dried and swept out with nitrogen. In the flask was placed 1.50 g. (0.062 atom) of fine magnesium turnings, 15 cc. of dry ether, and 1.0 g. (0.008 atom) of iodine. When all of the iodine had reacted, a solution of 10.5 g. (0.050 mole) of pure trifluoroethyl iodide in 20 cc. of dry ether was added dropwise to the well-stirred mixture in the flask. Reaction took place immediately, and gas was evolved which was collected over water. As soon as all of the trifluoroethyl iodide had been added the gas evolution stopped. A color test[4] with Michler ketone on a 1-cc. portion of the reaction mixture was negative. This indicated that no Grignard reagent was present. Analysis was made on an aliquot portion of the gas which was found to contain 0.045 mole of an ethylenic compound. The remainder of the gas was bubbled very slowly into 8 g. of bromine which absorbed all but a small portion. Upon distillation of the reaction product, 7.0 g. of colorless liquid was obtained which had the following constants: b. p. 91° (740 mm.), d^{27}_4 2.141. Swarts[5] has described the reaction of 1,1-difluoroethylene with bromine to yield 1,1-difluoro-1,2-dibromoethane, b. p. 93°, d^{12}_4 2.242. The ethylenic gas was therefore assumed to be 1,1-difluoroethylene, and the yield was 90%.

(4) Gilman and Schulze, *ibid.*, **47**, 2002 (1925).

(5) Swarts, *Bull. Acad. Roy. Belg.*, 383 (1901).

A Note on 10-Iodohydroquinines

BY ALICE G. RENFREW, C. L. BUTLER AND
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The addition of hydrogen iodide to β-isoquinine is reported below. Saturation of the semi-cyclic

ethylidene bond of isoquinine takes place more slowly than similar addition to the vinyl group of quinine.

Although the reduction of isoquinine has been studied,[1] the use of an unsymmetrical molecule as an addendum has not been described. From the material available we were not able to identify epimeric C-3 derivatives as Henry and co-workers[1] did with dihydroquinine. Subsequent removal of halogen from iodohydroquinine (prepared from isoquinine) regenerated isoquinine and gave some niquine.

The separation of the α and α' isomers[2] of 10-iodohydroquinine by recrystallization from benzene had been carried out in this Laboratory prior to the publication of Reyman and Suszko[3]; the specific rotations observed ($-218°$ and $-19°$) were practically identical with the values reported by the Polish investigators. $[\alpha] - 19°$ is the value for α'-iodohydroquinine, having one mole of benzene of crystallization. When benzene was removed by evaporating an ether solution to dryness, the product melted at 130° and $[\alpha]_D$ was $-22.3°$. The $-218°$ fraction was most advantageously crystallized from acetone or alcohol for final purification.

The strongly levorotatory α-isomer loses hydrogen iodide to give predominantly niquine, and the α'-isomer gives predominantly isoquinine.[3,4] In our experience it was not possible to get the exclusive transformation Suszko reported. During storage for a number of months, the more levo of the isomeric iodohydroquinines appears to be the less stable, and this fact has been noted previously for the quinidine series in the case of bromodihydroquinidine.[5]

Iodohydroquinine from Isoquinine.—Ten-gram portions of isoquinine, heated on a water-bath for two hours with 60 g. of hydriodic acid[6] (d. 1.7), gave only a 35% yield of the yellow crystalline iodohydroquinine dihydriodide. Continued heating for thirty minutes increased the yield to 50%. Unchanged isoquinine, recovered from the final liquor, accounted for 25–30% of the original isoquinine. This slow reaction rate is in contrast to the 70% yield obtained in two hours when quinine was the starting

(1) Henry, Solomon and Gibbs, *J. Chem. Soc.*, 592 (1937).

(2) In the absence of a uniform scheme of nomenclature, we have followed the method of Goodson, who arbitrarily used the prefix α for the isomer of higher rotation and α' for the other isomer: Goodson. *ibid.*, 1094 (1935).

(3) Reyman and Suszko, *Bull. Intern. Acad. Polonaise*, **A**, 360 (1935).

(4) Podlewski and Suszko. *Rec. trav. chim.*, **55**, 892 (1936).

(5) Gibbs and Henry, *J. Chem. Soc.*, 240 (1939).

(6) Skraup, *Monatsh.*, **14**, 428 (1893); Rosenmund and Kittler, *Arch. Pharm.*, **262**, 18 (1924).

material. The specific rotation of the iodohydroquinine base in alcohol was $-150°$.

Anal. Calcd. for $C_{20}H_{25}N_2O_2I \cdot C_6H_6$: I, 24.0. Found: I, 24.4.

On treating this sample of iodohydroquinine with alcoholic potassium hydroxide, isoquinine and a small amount of niquine were obtained.

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The Role of Glycine in Protein Structure

BY HANS NEURATH

Recent discussions of protein structure have emphasized the importance of the amino acid side chains in determining the structure of fibrous and globular proteins.[1-4] The position of the side chains along a polypeptide chain is determinant for the types of lateral bonds and the extent of internal rotation of polypeptide chains. A skeletal polypeptide chain, stripped of side chains, is endowed with a considerable degree of internal rotation about single valence bonds of the constituent carbon and nitrogen atoms. However, in a genuine polypeptide chain, equipped with the full complement of side chains, internal rotation is greatly restricted due to the space requirements of the amino acid residues. Various configurations, previously proposed for folded polypeptide chains and chain net-works, had, accordingly, to be excluded, since they resulted in an excessive crowding of component atoms and groups.[1,5] Such steric limitations apply equally to fully extended polypeptide chains, if they be made up of a combination of alternating d- and l-amino acids, but not to polypeptides comprised of less than four amino acid residues. In the latter, terminal side chains are free to branch out and, by virtue of rotation about the α,β carbon bond, to orient themselves as demanded by their space requirements.

The space requirements of amino acids depend on their average chain length and their cross-sectional area beyond the α-carbon atom.[1] The amino acid with the smallest cross-sectional area is glycine, since at the place where other amino acids carry a side chain, glycine has merely a hydrogen atom of about 4 sq. Å. cross-sectional

(1) Neurath, *J. Phys. Chem.*, **44**, 296 (1940).

(2) Bull, "Advances in Enzymology," Vol. I, Interscience Publishers, New York, N. Y., p. 1 *et seq.*

(3) Astbury and Bell, *Nature*, **147**, 696 (1941).

(4) Chibnall, *Proc. Roy. Soc.* (London), **B131**, 136 (1942).

(5) Mack, *Ohio J. Sci.*, **41**, 183 (1941); Huggins, *Ann. Rev. Biochem.*, **11**, 32 (1942).