0.5 g. of sodium[13] was subjected to careful fractional distillation in a column of approximately fifty theoretical plates over a period of several days. There was obtained 427 g. of distillate boiling principally at 78–79° and having $n^{20}D$ 1.366. The alcohol distillate deposited a white solid upon atmospheric exposure and therefore probably contained some ethyl borate. After the alcohol had been stripped from the reaction mixture the vapor temperature rose quickly to the boiling point of ethyl borate.

The distillation residue was freed of sodium alcoholate by rapid simple distillation at 100 mm. The crude product was fractionally distilled by E. M. Hadsell whereupon there were obtained two materials: 468 g., 3.2 moles, of ethyl borate, b.p. 120°, representing a 49% recovery of unreacted starting material; and 352 g., 1.5 moles, of *t*-butyl borate,[7] b.p. 101° at 74 mm., m.p. 18–19°, $n^{20}D$ 1.3879, representing a 45% yield based on unrecovered ethyl borate.

Anal. Calcd. for $C_{12}H_{27}O_3B$: B, 4.71. Found: B, 4.9, 4.9, 4.9, 4.8.

t-Butyl borate also was prepared by the alcoholysis of boric acid on a scale fourfold that reported.[7] There was obtained 1065 g., 58% yield of *t*-butyl borate which had b.p. 88–89° (53 mm.), $n^{20}D$ 1.3878 and an infrared spectrum (1R 4580) the same as that of the product from ethyl borate alcoholysis.

Upon exposure to atmospheric moisture for several hours *t*-butyl borate deposited a white solid, presumably boric acid. Some idea of the hydrolytic stability of the product may be gained from the method of analysis worked out by Dr. E. L. Simons. This simply involved allowing the compound to stand with an excess of 0.1 *N* HCl for about 24 hours and then potentiometrically titrating the boric acid formed. Only about 50% of the theoretical boric acid was found when the compound was allowed to stand with distilled water for 24 hours.

The infrared spectra of $(Me_3CO)_3B$ and of redistilled $(EtO)_3B$ were determined by C. A. Hirt with a Perkin–Elmer recording infrared spectrophotometer. The spectrum (1R 2309) of *t*-butyl borate showed well-defined, prominent bands at 3.39, 3.43, 3.49, 6.78, 6.87, 7.15, 7.21, 7.36, 7.45, 8.06, 8.45, 10.94, 11.04 and 13.10 μ. The spectrum (1R 2939) of ethyl borate showed well-defined, prominent bands at 3.36, 3.43, 3.53, 6.70, 6.96, 7.05, 7.27, 7.51, 7.78, 8.60, 9.07, 9.52, 11.21 and 12.37 μ.

(13) Small-scale runs made without sodium behaved capriciously. No ethanol was formed on refluxing *t*-butyl alcohol and ethyl borate (3.5:1 mole ratio) for several days through a fractional distillation column. On the other hand a similar run in a different column gave close to the theoretical amount of ethanol and about a 35% yield of *t*-butyl borate. It is unknown whether the negative result was due to poor fractionation or the positive result was due to accidental catalysis. Similar capricious behavior has been observed in the alcoholysis of ethyl silicate—D. F. Peppard, W. G. Brown and W. C. Johnson, THIS JOURNAL, **68**, 73 (1946).

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Fluorinated Amines

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The purpose of this work is the determination of the electronegative induction exerted by a CF_3 group on the amine function of a $CF_3(CH_2)_nNH_2$ series. We have observed for $CF_3(CH_2)_2NH_2$ a dissociation constant $K_B = 5 \times 10^{-6}$ and for $CF_3CH_2NH_2$ a value of 5×10^{-9}; for both unfluorinated propyl- and ethylamines we observed the accepted value 4.5×10^{-4}. A CF_3 group therefore affects the basicity of a NH_2 function adversely by a factor of 10^5 when separated by a single CH_2 group, and by a factor of only 10^2 when separated by two groups; this rapid decrease with distance characterizes induction.

It cannot be assumed that the basicity of the still unknown CF_3NH_2 can be estimated by any kind of extrapolation, because discontinuity is to be expected in $CF_3(CH_2)_nNH_2$ when n changes from 1 to 0. This is comparable to the discontinuity between benzylamine and aniline in the $C_6H_5(CH_2)_nNH_2$ series, or the break in the $CF_3(CH_2)_nH$ series where the protonic character of H increases with decreasing n, but disappears in CF_3H($n = 0$).

Degradative rearrangement of an amide (Hofmann hypohalite method) or an azide (Schmidt–Curtius reaction) were used to prepare $CF_3(CH_2)_2NH_2$ and $CF_3CH_2NH_2$. These degradations are known[1,2] not to be available for the synthesis of CF_3NH_2. The degradation of $C_3F_7CON_3$ gives a 76% yield of rearranged isocyanate C_3F_7NCO but no $C_3F_7NH_2$. This failure is not due to the rearrangement step but to the subsequent hydrolysis of the isocyanate; we believe that this hydrolysis does occur conventionally, but that the resulting $C_3F_7NH_2$ is at once hydrolyzed further with formation of a lower amide $C_2F_5CONH_2$, which we found in 10% yield in the degradation of $C_3F_7CON_3$ (in agreement with ref. 3), and regard this as a parallel to the hydrolysis of $O{=}C{-}CF_2{-}CF_2{-}CF_2O$ which does not yield $HO_2C(CF_2)_3OH$ but only $HO_2C(CF_2)_2CO_2H$.[4]

Experimental

All preparations started from $CF_3CH_2CH_2MgX$. The compound $CF_3CH_2CH_2Br$ can be made in 40% yield from $CCl_3CH_2CH_2Br$ and antimony fluoride but the reaction is complex and erratic and it is better to use the sequence $CCl_2{=}CHCH_3 \rightarrow CF_3CH_2CH_3 \rightarrow CF_3CH_2CH_2Cl$.[5,6] A conventional oxidation of the Grignard compound gave $CF_3CH_2CH_2OH$ in 50% yield, which a chromic oxidation transformed to $CF_3CH_2CO_2H$ in 80% yield. A conventional carbonation gave $CF_3(CH_2)_2CO_2H$ in 80% yield.[7] An attempted reaction with $ClNH_2$ failed to give $CF_3(CH_2)_2NH_2$.

Transformation of the acids to their chlorides was best with a 33% excess of PCl_5. The amides were obtained from them with a cold aqueous solution of ammonia kept saturated by a stream of NH_3 or with a chloroform solution of ammonia, both procedures being quite good.

The Hofmann Reaction.—The steps of the hypobromite degradation procedure[8] were standardized to ensure comparable results. Unfluorinated butyramide, $C_3H_7CONH_2$, gave 50% $C_3H_7NH_2{\cdot}HCl$, 53% CO_3, 37% $C_3H_7CO_2H$ and 47% NH_3Cl. Trifluorobutyramide, $CF_3CH_2CH_2CONH_2$, gave 35% $CF_3CH_2CH_2NH_2{\cdot}HCl$, 52% CO_2, 25% $CF_3CH_2CH_2CO_2H$, 33% NH_4Cl and some material boiling at 120–122°, $n^{20}D$ 1.4120 which could have been the intermediate $CF_3CH_2CH_2NCO$. It was concluded that the CF_3 group did not affect the rearrangement but might have slowed down the hydrolysis slightly. In contrast, trifluoropropionamide, $CF_3CH_2CONH_2$, gave a very poor yield (3%) of $CF_3CH_2NH_2{\cdot}HCl$, matched by a very small CO_2 evolution (2.5%) and there was a 27% recovery of unreacted amide, but no free acid. This was attributed to an over-riding loss of HF to the alkaline medium with formation of $CF_2{=}CHCONH_2$ and polymerization of this acrylic amide; in

(1) E. Gryszkiewicz-Trochimowski, H. Sporzynski and J. Wnuk, *Rec. trav. chim.*, **66**, 419 (1947).

(2) D. R. Husted and W. L. Kohlhase, THIS JOURNAL, **76**, 5141 (1954).

(3) A. H. Ahlbrecht and D. R. Husted, U. S. Patent 2,617,817 (1952); *C. A.*, **47**, 8774 (1953).

(4) M. Hauptschein, C. S. Stokes and A. V. Grosse, THIS JOURNAL, **74**, 1974 (1952).

(5) A. L. Henne and A. M. Whaley, *ibid.*, **64**, 1157 (1942).

(6) E. T. McBee, *ibid.*, **69**, 944 (1947).

(7) A. L. Henne and C. J. Fox, *ibid.*, **73**, 2323 (1951).

(8) K. R. S. Simon-Asher, *J. Chem. Soc.*, 2209 (1951).

support, crystals with m.p. 151–153° were isolated from the reaction mixture, which contained 69.4% of bromine and could have been the bromination product of the acrylic amide, CF_2Br–$CHBr$–$CONHBr$, 69.8% bromine. Perfluorobutyramide, $C_3F_7CONH_2$, gave a 77% yield of a crude compound boiling up to 25°, a 21% recovery of free acid and 19% of NH_4Cl; this crude compound was, at the time, assumed to be C_3F_7NCO, but according to reference 2 it is C_3F_7Br.

The Schmidt–Curtius Reaction.—The relation between the two reactions is known,[9] and we found it best to use a combination of both, *i.e.*, form the azide in the absence of an inorganic acid, separate it, then rearrange it in the presence of a mineral acid. This procedure avoids the formation of ammonium salts from an excess of NaN_3 and from decomposing HN_3; free HN_3 reacts very slowly with fluorinated acids and is preferentially decomposed in the presence of an inorganic acid.

The acyl halide (0.1 mole) was heated with NaN_3 (0.12 mole) in 100 ml. of dry benzene for 24 hours at 55–65°. After cooling, crystalline NaCl and NaN_3 excess was filtered off. The filtrate was treated with 10 ml. of concentrated sulfuric acid added dropwise at 55–65°, then refluxed about eight hours until no more gas was evolved. After pouring over ice and decanting the benzene, the aqueous layer was made alkaline and the amines so liberated were distilled into 6 *N* HCl, from which their hydrochloride was obtained by evaporation. The benzene layer was examined for recovery of any isocyanate, and the aqueous layer for recovery of any organic acid.

$CF_3(CH_2)_2COCl$ gave 81% $CF_3(CH_2)_2NH_2 \cdot HCl$; CF_3CH_2COCl gave 25% $CF_3CH_2NH_2 \cdot HCl$, which is ten times the yield of the Hofmann degradation; C_3F_7COCl gave, in addition to the expected 75% of isocyanate,[3] a 10% yield of $C_2F_5CONH_2$, m. p. 95°, no depression with an authentic sample, which is the amide of the next lower acid.

Dissociation.—The measurements were made by titration of 0.004 *N* solutions of amine with 0.05 *N* HCl, by means of a model H_2 glass electrode Beckman *p*H meter. The calculations were conventional.[10]

PHYSICAL CONSTANTS AND ANALYSES

	B.p. or m.p. °C.	Mm.	n^tD	*t*, °C.	d^t_4	Analyses, % Found	Calcd.
CF_3CH_2COCl	70.3	745	1.3382	29.5	1.422	Cl, 24.1	24.2
$CF_3CH_2CH_2COCl$	103	745	1.3610	24	1.361	Cl, 22.1	22.1
$CF_3CH_2CONH_2$	M. 108.8					F, 43.8	44.8
$CF_3CH_2CH_2CONH_2$	M. 136.4					N, 9.9	9.9
$CF_3CH_2CH_2NH_2$	67.8	744	1.3332	30	1.162		
Hydrochloride	M. 222–225					Cl, 23.7	23.7
$CF_3CH_2NH_2$[11]	36	744	1.295	30	1.245		
Hydrochloride	Sublimes					Cl, 26.3	26.2

(9) M. S. Newman and H. L. Gildenhorn, THIS JOURNAL, **70**, 317 (1948).

(10) S. Glasstone, "Introduction to Electrochemistry," D. Van Nostrand Co., Inc., New York, N. Y., 1942, pp. 322–325.

(11) H. Gilman and R. G. Jones, THIS JOURNAL, **65**, 1458 (1943).

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The Synthesis of Purines and Thymine from Methionine in the Rat[1]

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Formic acid has been shown to serve as a biological precursor of carbons 2 and 8 of the purines[2] and of the methyl group of thymine.[3] The degree to which the labile methyl group of methionine might serve as a source of these carbon atoms has been studied only to a limited extent, in spite of the suggested metabolic relationship between formic acid and methionine.[4] Brown has indicated that methionine was rather ineffective as a thymine precursor in the rat,[5] but no experimental data were provided. Sime and Johnson have recently demonstrated[6] that in the bird the methionine methyl group was readily converted to uric acid carbons 2 and 8.

The experiments to be described were performed to obtain further information on the use of methionine for the synthesis of various nucleic acid components. It was also thought desirable to obtain data which would provide a comparison of the relative utilization of formic acid and the methyl group of methionine for these processes. To attain these ends a study was made of the incorporation under comparable conditions of sodium formate-C^{14} and methionine-methyl-C^{14} into the nitrogenous bases of the deoxyribonucleic acid (DNA) of the rat.

As is illustrated in Table I, appreciable amounts of isotopic carbon appeared in the adenine, guanine and thymine of the rat DNA after injection of either labeled formate or methionine. No localization of the radioactivity in the purines was attempted. In each case, however, the methyl group of the thymine was converted to iodoform[7] which appeared to contain most of the isotopic carbon of the original thymine. Accurate measurement of the activity of the iodoform was not possible in an internal flow counter because of a quenching action of this compound on the counting rate, nor was sufficient material available for measurements with an end-window counter.

Previous work with formic acid has demonstrated that almost all of the observed activity of the purines would be found in carbons 2 and 8,[2] and that the activity of the thymine molecule would be found in the methyl group.[3] It has been assumed that the distribution of activity resulting with methionine as the precursor is similar to that obtained with formate. The low level of radioactivity found in the cytosine in all cases lends considerable support to this assumption. Certainly no non-specific precursor derived from the methionine contributed appreciable amounts of isotopic carbon to the synthesis of the various compounds.

(1) This work was supported in part under contract no. AT (11-1)-289 with the Atomic Energy Commission and in part under an All-College Research grant of Michigan State College.

(2) J. C. Sonne, J. M. Buchanan and A. M. Delluva, *J. Biol. Chem.*, **173**, 69 (1948).

(3) J. R. Totter, E. Volkin and C. E. Carter, THIS JOURNAL, **73**, 1521 (1951).

(4) P. Berg, *J. Biol. Chem.*, **205**, 145 (1953).

(5) G. B. Brown, "Phosphorus Metabolism," Vol. III, W. D. McElroy and B. Glass, eds., Johns Hopkins Press, Baltimore, Md., 1952, p. 387.

(6) J. T. Sime and B. C. Johnson, Paper No. 49, Division of Biological Chemistry, American Chemical Society, New York City Meeting, 1954.

(7) D. Elwyn and D. B. Sprinson, *J. Biol. Chem.*, **207**, 469 (1954).