However, when several residues have added, this configuration becomes unstable and following a transitional period the D residues take up their own stable configuration, the mirror image of the L peptide helix.[9]

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DEPARTMENT OF CHEMISTRY
HARVARD UNIVERSITY PAUL DOTY
CAMBRIDGE, MASSACHUSETTS R. D. LUNDBERG*
*Public Health Service Research Fellow (1955-56).

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N-MONOALKYLATION AND ARYL BROMINATION OF CERTAIN AMINES WITH ETHYL BROMIDE IN DIMETHYL SULFOXIDE[1]

Sir:

In a study of alkylation of certain weak aromatic amines by alkyl phosphates and phosphonates,[2] we found that alkyl bromides in trialkyl phosphates gave good yields, for example, of N-monoalkylated 2-aminofluorenone.[3] We have therefore tried a limited number of other solvents, with other reaction conditions unchanged, finding none as good as the phosphates (or phosphonates), until use of dimethyl sulfoxide (generously donated by the Stepan Chemical Co., Chicago) resulted in a novel reaction which we wish to report briefly.

From 2-aminofluorenone and ethyl bromide in dimethyl sulfoxide, kept under reflux at a bath temperature of 150° for 1.5 hours, stirred into cold water and purified, there was obtained a product in crude yields of 50–60%, which we have identified as 2-N-ethylamino-3-bromofluorenone (I), m.p.[4] (of analytical sample) 164.5–165.5°. *Anal.* Calcd. for $C_{15}H_{12}BrNO$: C, 59.62; H, 4.00; Br, 26.45; N, 4.64. Found: C, 59.65; H, 3.98; Br, 26.63; N, 4.91. About 8–15% of 2-amino-3-bromofluorenone (II) was also isolated, m.p. 215.5–216°. *Anal.* Calcd. for $C_{13}H_8BrNO$; N, 5.11. Found: N, 5.04.

A similar reaction with *p*-nitroaniline gave 2-bromo-4-nitro-N-ethylaniline, m.p. 66.5–68° (reported[5] m.p. 65–66°), and 2-bromo-4-nitroaniline, m.p. 103.5–104.5° (m.p.[6] 104.5°). *Anal.* Calcd. for $C_6H_5BrN_2O_2$: N, 12.91. Found: N, 12.92.

Finding no report of direct bromination of 2-aminofluorenone, we attempted this reaction at 20° in acetic acid, obtaining 80–85% of a crude product (III), m.p. (after two crystallizations from benzene) 215.5–216°; the mixture m.p. with II was not depressed. *Anal.* Calcd. for $C_{13}H_8BrNO$: N, 5.11. Found: N, 5.09. Monoethylation[2] of III gave I (m.p. and mixture m.p.). Diazotization of III and treatment with hypophosphorous acid[7] (1°) for 22 hours gave 3-bromofluorenone (IV), m.p. 165.5–166° (reported m.p. 162°,[8a] 165.5°[8c]). *Anal.* Calcd. for $C_{13}H_7BrO$: C, 60.26; H, 2.72; Br, 30.84. Found: C, 60.34; H, 2.91; Br, 30.90. Reduction of the latter compound with sodium borohydride[9] gave 3-bromofluorenol, m.p. 169.5–170.5° (reported[8b] m.p. 142–145°). *Anal.* Calcd. for $C_{13}H_9BrO$: C, 59.79; H, 3.47; Br, 30.61. Found: C, 60.00; H, 3.71; Br, 30.73. This upon further reduction with phosphorus and iodine[8b] yielded 3-bromofluorene (V), m.p. 89–90° (reported[8b] m.p. 90–91°).

For further confirmation, acetylation of III (*i.e.*, II) followed by reduction with sodium borohydride[9] to the corresponding 9–01 and further reduction with phosphorus and iodine[8b] gave 3-bromo-2-acetamidofluorene, m.p. 208–209° (after melting, this substance solidified with pressure and remelted 210–211°). *Anal.* Calcd. for $C_{15}H_{12}BrNO$: C, 59.62; H, 4.00; Br, 26.45; N, 4.64. Found: C, 59.70; H, 3.86; Br, 26.50; N, 4.30. Bell and Mulholland[10] report isolation of "3 (or 1)-bromo-2-acetamidofluorene," m.p. 206–207°. In support of evidence in the preceding paragraph our substance cannot be the 1-bromo derivative since diazotization of III would have given 1-bromofluorenone which is reported to melt at 134–134.3°.[11] It is also highly unlikely that the 1-position would be attacked in this reaction to the exclusion of significant amounts of other isomers.

It would appear that dimethyl sulfoxide, offering a favorable environment for alkylation with ethyl bromide, reacts with eliminated hydrogen bromide, giving $(CH_3)_2SBr_2$.[12] The latter then effects ring bromination of the N-alkylated amine (or the free amine remaining) and is finally released as dimethyl sulfide, a supposition which is in agreement with the odor of the filtrate after aqueous treatment of the crude reaction product.

(1) This work was supported in part by a research grant (C-1744) from the National Cancer Institute of the National Institutes of Health, Public Health Service.

(2) Mention of the effect of lithium bromide on alkyl phosphate alkylations of 2-aminofluorenone was included in T. L. Fletcher, M. E. Taylor and A. W. Dahl, *J. Org. Chem.*, **20**, 1021 (1955).

(3) Included in a further report which will be presented shortly by this Laboratory.

(4) All melting points are corrected, and were taken on a Fisher–Johns apparatus. We wish to thank Mr. Murray E. Taylor of this Laboratory for nitrogen microanalyses.

(5) M. S. Kharasch and I. M. Jacobson, THIS JOURNAL, **43**, 1894 (1921).

(6) B. H. Nicolet and W. L. Ray, *ibid.*, **49**, 1801 (1927).

(7) N. Kornblum, in "Organic Reactions," Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1944, p. 277.

(8) (a) H. F. Miller and G. B. Bachman, THIS JOURNAL, **57**, 2443 (1935); (b) H. F. Miller and G. B. Bachman, *ibid.*, **57**, 2447 (1935). The wide m.p. reported for 3-bromofluorenol may have resulted from impurity. Reported Br analysis 30.45 (no C or H). A small amount of IV remaining in the reduction product would change this analysis only slightly. Our melting points for IV and V agree with the literature; (c) P. J. Montagne and J. M. v. Charante, *Rec. trav. chim.*, **32**, 164 (1913).

(9) The reduction of approximately fifteen fluorenone derivatives in high yield has been carried out in this Laboratory and forms part of a paper in preparation.

(10) F. Bell and D. B. Mulholland, *J. Chem. Soc.*, 2020 (1949).

(11) E. H. Huntress, K. Pfister, 3rd, and K. H. T. Pfister, THIS JOURNAL, **64**, 2845 (1942).

(12) See, for example, R. Connor in "Organic Chemistry, An Advanced Treatise," ed. H. Gilman, Vol. I, 2nd ed., John Wiley and Sons, Inc., New York, N. Y., p. 872.

CHEMISTRY RESEARCH LABORATORY
DEPARTMENT OF SURGERY T. LLOYD FLETCHER
UNIVERSITY OF WASHINGTON HSI-LUNG PAN
SCHOOL OF MEDICINE
SEATTLE 5, WASHINGTON

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21-FLUORO DERIVATIVES OF 9α-FLUORO- AND 1-DEHYDROCORTICOIDS

Sir:

The preparation of a series of 21-fluorinated steroids by the action of silver fluoride on 21-iodo-