After evaporation of the trifluoroacetic acid, the oily residue was dissolved in 100 ml. of methanol, neutralized with alcoholic potassium hydroxide, and then treated with 4 molar equivalents of alkali in 100 ml. of methanol. The mixture was refluxed for 1 hr., concentrated under reduced pressure, poured into water, and extracted with methylene chloride. All organic extracts were combined, washed with water, dried, and evaporated. Acetic anhydride (525 ml.) was added to the residue and refluxed for 2 hr. Hydrolysis of the anhydride in 5 l. of water left a gummy material which was filtered off with the aid of Super-cel. The clear filtrate was made basic with sodium hydroxide and extracted with methylene chloride. Evaporation of the dried solution and recrystallization of the residue (128 g.) from alcohol gave 104 g. (36% over-all) of 3β-acetoxy-5α-conanine-11-one, m.p. 185.5–189°.

Derivatives of Fluorene. XVII. Alkyl Phosphates, Phosphites, and Phosphonates with Lithium Halides or Alkyl Halides in the N-Alkylation of Fluorenamines

HSI-LUNG PAN AND T. LLOYD FLETCHER[1,2]

Chemistry Research Laboratory of the Department of Surgery, University of Washington School of Medicine, Seattle 5, Washington

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Lithium halides, especially lithium bromide, together with trialkyl phosphates, trialkyl phosphites, or dialkyl alkylphosphonates, have conveniently given good yields of a variety of alkylaminofluorenes. The alkylating agent was either the phosphorus acid ester itself or alkyl halide, generated by the dealkylating action of lithium halides on the acid esters, or both. Also, triethyl phosphate was found to be an excellent medium for the alkylation of aromatic amines with alkyl and aralkyl bromides and iodides. A number of new N-mono- and N,N-dialkyl(and aralkyl)aminofluorenes and 9-oxofluorenes were prepared.

After finding that lithium bromide promoted good yields of 2-N-ethylaminofluorenone from 2-aminofluorenone with triethyl phosphate,[3] we have used lithium halide and phosphorus acid ester combinations, extensively in the alkylation of aromatic amines, especially fluorenamines. This is part of a general study of certain metabolites and modifications of the carcinogen, 2-acetamidofluorene. Certain esters of phosphorous and phosphoric acids containing sufficiently electrophilic α-CH_2 groups, were reported to undergo anionic cleavage of the α-carbon from the CH_2—OP linkage in the presence of an anion such as the chloride ion of lithium chloride.[4,5] In the alkylation of weak amines with trialkyl phosphates, this reaction takes place readily when certain halides, such as lithium bromide, are present, as shown in this investigation, whereas in the absence of this salt the reaction requires a higher temperature to give a much poorer yield, or does not take place at all.[6] Therefore the presence of such halides produces a more reactive alkylating system, *i.e.*, an alkyl halide in the presence of a phosphate ester, than the alkyl phosphate alone. This, in turn, produces hydrogen halide from the alkylation of the amine, and the hydrogen halide itself is capable of dealkylating the phosphorus acid esters,[7] thus providing a still higher concentration of alkyl halide in the reaction. The outline of the alkylating system of trialkyl phosphate–lithium halide is as follows

$$(Li^+)X^- + R\overset{\delta+}{-}CH_2-O-P(O)(OCH_2R)_2 \longrightarrow R-CH_2X + {}^-O-P(O)(OCH_2R)_2 \quad \text{(a)}$$

X = Cl, Br, I[8]

$$R-CH_2X + Ar-NH_2 \longrightarrow Ar-NH-CH_2-R + HX \quad \text{(b)}$$

$$H^+X^- + R\overset{\delta+}{-}CH_2-O-P(O)(OCH_2R)_2 \longrightarrow R-CH_2X \longrightarrow HOP(O)(OCH_2R)_2 \quad \text{(c)}$$

This outline would appear to be true also of the trialkyl phosphite–lithium halide system except

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(2) For the previous paper in this series, see *J. Org. Chem.*, **26**, 2244 (1961).

(3) T. L. Fletcher, M. E. Taylor, and A. W. Dahl, *ibid.*, **20**, 1021 (1955).

(4) V. M. Clark and A. R. Todd, *J. Chem. Soc.*, 2031 (1950).

(5) J. Lecocq and A. R. Todd, *ibid.*, 2381 (1954).

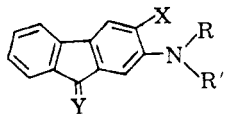
(6) D. G. Thomas, J. H. Billman, and C. E. Davis, *J. Am. Chem. Soc.*, **68**, 895 (1946), reported that *p*-nitroaniline did not undergo alkylation with triethyl phosphate. With the use of lithium bromide in this reaction we were able to obtain about 35% yields of mono-N-ethylated *p*-nitroaniline with evidence of a small amount of the di-N,N-ethylamine.

(7) W. Gerrard, *J. Chem. Soc.*, 1464 (1940); W. Gerrard, *ibid.*, 85 (1944); W. Gerrard, *ibid.*, 848 (1945); W. Gerrard, W. J. Green, and R. A. Nutkins, *ibid.*, 4076 (1952).

(8) Our experiments show that, refluxed in triethyl or tripropyl phosphate, lithium chloride, bromide, and iodide produce the corresponding halide in decreasing yields, with decreasing speeds, in the above order. The ethyl halides, in trialkyl phosphates, however, in the presence of amines, were increasingly effective alkylating agents in the above order. Both phenomena, taking place in the system trialkyl phosphate–lithium halide–amine, gave results indicating that lithium bromide was the best of the three in the promotion of alkylation.

TABLE I

ALKYLATION OF FLUORENAMINES WITH ESTERS OF PHOSPHORUS ACIDS AND LITHIUM HALIDES



(A, R = R′ = H)

A: X	A: Y	B (R =)	A:B:LiX (molar ratio)	Reaction temp.[a]	Products: R	Products: R′	Yield, %	M.p., °C.	Compound no.[c]
				Alkylating agent (B) = $(RO)_3PO$					
H	H_2	C_2H_5	1:2:2[d,e]	145–150	C_2H_5	C_2H_5	97	84.5–85[f]	XXX
H	H_2	n-C_3H_7	3:1:0[g]	185–190	n-C_3H_7	H	18	85–85.5	I
H	H_2	n-C_3H_7	1:2:0[g]	185–190	n-C_3H_7	n-C_3H_7	72	75.5–76	IV
H	O	CH_3	1:2:2[d,e]	135–140	CH_3	CH_3	52	166–167[f]	XXXII
H	O	C_2H_5	1:2:2[d,e]	140	C_2H_5	C_2H_5	24	101.5–102.5[h]	XXXIII
					C_2H_5	H	42	153–154[f]	XXXI
H	O	n-C_3H_7	1:1:1[d,e]	150–155	n-C_3H_7	H	31	132–133[p]	VIII
Br	O	CH_3	1:15:1.2[d,e]	135–140	CH_3	H	55	177–178	XX
					CH_3	CH_3	25	128.5–129.5	XXV
Br	O	C_2H_5	1:10:2[d,e]	145–150[i]	C_2H_5	H	44 (73[j])	164.5–165.5[k]	XXXIV
F	H_2	CH_3	5:4:0[g]	190–195	CH_3	CH_3	60	109–110[l]	VII
F	O	CH_3	1:2:2[d,e]	120–125	CH_3	CH_3	54	95.5–96.5[l]	XXVIII
				Alkylating agent (B) = $(RO)_3P$					
H	H_2	C_2H_5	1:2:2[d,e]	145–150	C_2H_5	C_2H_5	90		XXX
H	H_2	n-C_4H_9	3:1:0[g]	195–200	n-C_4H_9	H	52		II
H	H_2	n-C_6H_{13}	3:1:0[g]	200–205	n-C_6H_{13}	H	33	61.5–62.5	III
H	H_2	n-C_6H_{13}	1:2:0[g]	195–200	n-C_6H_{13}	n-C_6H_{13}	27	123.5–124 (picrate)	VI
				Alkylating agent (B) = $RP(O)(OR)_2$					
H	H_2	n-C_4H_9	1:1:0[g]	180–185	n-C_4H_9	H	50	81–81.5	II
H	H_2	n-C_4H_9	1:2:0[g]	190–195	n-C_4H_9	n-C_4H_9	10[m]	29–30.5 176.5–177 (picrate)	V
H	H_2	n-C_4H_9	1:1:1[d,e]	180–190	n-C_4H_9	H	11		II
H	O	C_2H_5	1:1:1[d,e]	160–165	C_2H_5	H	34		XXXI
H	O	C_2H_5	1:2:2[d,e]	150–155	C_2H_5	H	70		XXXI
H	O	n-C_4H_9	1:2:0[g]	195–200	n-C_4H_9	H	0		IX
H	O	n-C_4H_9	1:2:1[d,e]	150–160	n-C_4H_9	H	55	127.5–128.5[p]	IX
H	O	n-C_4H_9	1:2:2[d,e]	150–160	n-C_4H_9	H	59		IX
H	O	n-C_4H_9	1:1:1[n,e]	165	n-C_4H_9	H	25		IX
H	O	n-C_4H_9	1:1:1[o,e]	155–165	n-C_4H_9	H	17		IX
				Alkylating agent (B) = $(RO)_2P(O)H$					
H	H_2	CH_3	1:3:0[g]	175–180	CH_3	CH_3	24	180–180.5[f]	XXIX

[a] Bath temperature. [b] Melting points were taken on a Fisher-Johns block and corrected to standards. [c] See Table III for analyses of the new compounds with the corresponding number (I–XXVII). Several numbers appear more than once in Tables I and II if the product was made by more than one procedure. [d] Lithium bromide. [e] Procedure I (see Experimental). [f] Ref. 3. [g] Procedure II (see Experimental). [h] M. E. Taylor, formerly of this laboratory, first prepared this compound by alkylating the amine with ethyl sulfate in 95% yield, m.p. 102–103°. Calcd. for $C_{17}H_{17}NO$: N, 5.57. Found: N, 5.65. [i] Heated 4 hr. [j] Based on the amount of 2-amino-3-bromofluorenone consumed. The unchanged amine was recovered. [k] T. L. Fletcher and H. L. Pan, *J. Am. Chem. Soc.*, **78**, 4812 (1956). [l] T. L. Fletcher, M. J. Namkung, W. H. Wetzel, and H. L. Pan, *J. Org. Chem.*, **25**, 1342 (1960). [m] 41% of a less pure product was obtained by using 3 moles of the phosphonate. [n] Lithium chloride. [o] Lithium iodide. [p] We have reported the melting point for this compound, but not the synthesis or analyses, previously; see H. L. Pan and T. L. Fletcher, *J. Org. Chem.*, **23**, 799 (1958), Table I.

that phosphite to phosphonate transformation also takes place[9]:

$$(RO)_3P + R'X \longrightarrow (RO)_2P(O)R' + RX \qquad (d)$$

The dialkyl alkylphosphonate, thus formed, also reacts with the halide ion, to produce more alkyl halide:

$$(RO)_2P(O)R + X^- \longrightarrow ROP(O)R + RX \qquad (e)$$

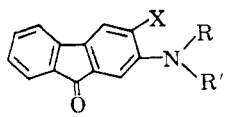
(9) G. M. Kosolapoff, *J. Am. Chem. Soc.*, **66**, 109 (1944); A. E. Arbuzov and K. V. Nikonorov, *J. Gen. Chem.* (USSR), **17**, 2139 (1947) (*Chem. Abstr.*, **42**, 4546 (1948)).

Dialkyl alkylphosphonates, alone, are good alkylating agents for relatively strong aromatic amines such as 2-aminofluorene. However, like trialkyl phosphates, these phosphonates fail to alkylate weaker amines such as 2-amino-9-oxofluorene in appreciable yield except in the presence of a promoter such as lithium bromide (see Table I).

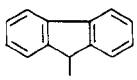
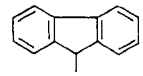
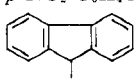
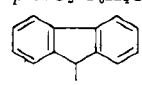
Trialkyl phosphates, in addition to being good solvents for the aromatic amines used in this study, are excellent media for the alkylation of weak amines with the corresponding alkyl bromide or

TABLE II

ALKYLATION AND ARALKYLATION OF 9-OXOFLUORENAMINES WITH ALKYL AND ARALKYLBROMIDES IN TRIETHYL PHOSPHATE



(A, R = R′ = H)

A (X =)	B (R =)	A:B:-NaHCO₃ (molar ratio)[a]	Reaction temp.[b]	Products R	Products R′	Yield, %	M.p., °C.[c]	Compound no.[d]
			Alkylating agent (B) = RBr					
H	n-C_4H_9[e]	1:2:2	150–155	n-C_4H_9	H	60		IX
H		1:2:2	150–155		H	37	164–165[i]	X
H	$C_6H_5CH_2$[f]	1:1:1	40–50	$C_6H_5CH_2$	$C_6H_5CH_2$	6		XVI
				$C_6H_5CH_2$	H	83	149.5–150.5[i]	XI
H	$C_6H_5CH_2$	1:2:2	100–105	$C_6H_5CH_2$	$C_6H_5CH_2$	90	139–140[i]	XVI
H	p-Br-$C_6H_4CH_2$	1:1:1	80–85	p-Br-$C_6H_4CH_2$	H	75	192–193	XII
				p-Br-$C_6H_4CH_2$	p-Br-$C_6H_4CH_2$	10		XVII
H	p-Br-$C_6H_4CH_2$	1:2:2	95–100	p-Br-$C_6H_4CH_2$	p-Br-$C_6H_4CH_2$	99	186–187[i]	XVII
H	p-CH_3-$C_6H_4CH_2$	1:1:1	100–105	p-CH_3-$C_6H_4CH_2$	H	41	148.5–149.5	XIII
H	p-CH_3-$C_6H_4CH_2$	1:2:2	100–105	p-CH_3-$C_6H_4CH_2$	p-CH_3-$C_6H_4CH_2$	52	129–130	XVIII
H	p-NO_2-$C_6H_4CH_2$	1:1:1	r.t. first then 150–155	p-NO_2-$C_6H_4CH_2$	H	75	206–207[i]	XIV
H	p-NO_2-$C_6H_4CH_2$	1:2:2	150–155	p-NO_2-$C_6H_4CH_2$	p-NO_2-$C_6H_4CH_2$	84	212–213[i]	XIX
H		1:1:1	150–155		H	83	214.5–215.5	XV
Br	C_2H_5	1:2:1	150–155	C_2H_5	H	50	164.5–165.5[g]	XXXIV
Br	$C_6H_5CH_2$	1:2:2	100–105	$C_6H_5CH_2$	H	64	139–140[i]	XXI
				$C_6H_5CH_2$	$C_6H_5CH_2$	10	163.5–164.5	XXVI
Br	p-Br-$C_6H_4CH_2$	1:1:1	100–105	p-Br-$C_6H_4CH_2$	H	68 (77[h])	159–160[i]	XXII
Br	p-Br-$C_6H_4CH_2$	1:2:2	95–100	p-Br-$C_6H_4CH_2$	p-Br-$C_6H_4CH_2$	25	179.5–180.5	XXVII
Br	p-NO_2-$C_6H_4CH_2$	1:1:1	105–110	p-NO_2-$C_6H_4CH_2$	H	33	185–186[i]	XXIII
Br		1:1:1	95–100		H	23	216–217	XXIV

[a] Procedure III (see Experimental). [b] See Table I, footnote *a*. [c] See Table I, footnote *b*. [d] See Table I, footnote *c*. [e] In tri-*n*-butyl phosphate. [f] The alkylating agent was added dropwise over a period of 80 min., then the reaction mixture was allowed to stand at room temperature overnight. A high yield of water-soluble product was formed, possibly a fluorenyl phosphonate or phosphoramide. [g] See Table I, footnote *k*. [h] See Table I, footnote *j*. [i] See Table I, footnote *p*.

iodide. In the case of very reactive halides, such as the aralkyl halides used (see Table II), the small amount of ethyl halide, produced by the hydrogen halide (reaction C) released in the aralkylation, did not give enough mono-N-ethylamine to interfere with the main reaction. This side reaction could be suppressed altogether by addition of an equivalent of sodium bicarbonate (see Experimental, procedure III). For example, ethyl bromide in tributyl phosphate was a good ethylation medium; butyl bromide in triethyl phosphate without sodium bicarbonate gave a mixture, however, because of the release by hydrogen bromide of ethyl bromide, and the relatively rapid alkylation by the latter as compared with butyl bromide. With an equivalent of sodium bicarbonate in the latter mixture, a successful butylation was achieved.

We also investigated some other solvents in the alkylation of amines with alkyl halides under conditions comparable to those in triethyl phosphate. Among these were dimethyl phthalate, phenol, tetralin, and pyridine. The only one of the foregoing giving yields at all appreciable was phenol, which in one case gave almost two thirds of the yield of alkylated amine obtained in triethyl phosphate.

Our experiences using dimethyl sulfoxide were novel and have been noted in three preliminary publications.[10]

2-Amino-7-nitrofluorene proved particularly difficult to alkylate. Dimethylation in about 5% yield was achieved with either trimethyl phosphate or methyl iodide alone, or in 10–15% yields in our improved trimethyl phosphate–lithium bromide reaction.[11] Good yields of the dimethylamino derivative were obtained, however, when trimethyl phosphate and methyl iodide were used together (see Experimental). Reduction of 2-N,N-di-

(10) T. L. Fletcher and H. L. Pan, *J. Am. Chem. Soc.*, **78**, 4812 (1956); T. L. Fletcher, M. J. Namkung, and H. L. Pan, *Chem. Ind.* (London), 660 (1957); T. L. Fletcher and H. L. Pan, *J. Org. Chem.*, **24**, 141 (1959).

(11) Unpublished work done by W. H. Wetzel and M. J. Namkung of this laboratory.

TABLE III

NEW ALKYL AND ARALKYLAMINOFLUORENES

Compound no.	Fluorene derivative	Formula	Calcd.[a] C	Calcd.[a] H	Calcd.[a] N	Calcd.[a] Br	Found[a] C	Found[a] H	Found[a] N	Found[a] Br
I	2-N-*n*-Propylamino-	$C_{16}H_{17}N$	86.05	7.67	6.27		86.26	7.44	6.14	
II	2-N-*n*-Butylamino-	$C_{17}H_{19}N$	86.03	8.07	5.90		86.26	7.59	6.10	
III	2-N-*n*-Hexylamino-	$C_{19}H_{23}N$	85.98	8.74	5.28		86.30	8.60	5.46	
IV	2-N,N-Di-*n*-Propylamino-	$C_{19}H_{23}N$	85.98	8.74	5.28		86.10	8.40	5.48	
V	2-N,N-Di-*n*-Butylamino-	$C_{27}H_{30}N_4O_7$ (picrate)	62.06	5.79			62.13	5.64		
VI	2-N,N-Di-*n*-Hexylamino-	$C_{31}H_{38}N_4O_7$ (picrate)	64.34	6.62	9.68		65.09	6.69	9.05	
VII	3-Fluoro-2-N,N-dimethylamino-	$C_{15}H_{14}FN$[b]								
VIII	9-Oxo-2-N-*n*-propylamino-	$C_{16}H_{15}NO$	80.98	6.37	5.90		80.75	6.37	5.82	
IX	9-Oxo-2-N-*n*-butylamino-	$C_{17}H_{17}NO$	81.24	6.82	5.57		81.17	7.06	5.74	
X	9-Oxo-2-N-cyclopentylamino-	$C_{18}H_{17}NO$	82.10	6.51	5.32		82.20	6.57	5.28	
XX	3-Bromo-9-oxo-2-N-methylamino-	$C_{14}H_{10}BrNO$	58.35	3.50	4.86		58.28	3.40	4.80	
XXI	3-Bromo-9-oxo-2-N-benzylamino-	$C_{20}H_{14}BrNO$	65.96	3.87	3.85	21.94	66.14	4.10	3.57	21.90
XXII	3-Bromo-9-oxo-2-N-*p*-bromobenzylamino-	$C_{20}H_{13}Br_2NO$	54.20	2.96	3.16	36.07	54.48	3.30	3.59	36.10
XXIII	3-Bromo-9-oxo-2-N-*p*-nitrobenzylamino-	$C_{20}H_{13}BrN_2O_3$	58.70	3.20	6.85	19.53	59.07	3.20	7.00	19.82
XXIV	3-Bromo-9-oxo-2-N-(9′-fluorenyl)amino-	$C_{26}H_{16}BrNO$	71.24	3.68	3.20	18.23	71.35	3.90	3.35	18.27
XXV	3-Bromo-9-oxo-2-N,N-dimethylamino-	$C_{15}H_{12}BrNO$	59.62	4.00	4.64		59.19	4.65	4.66	
XXVI	3-Bromo-9-oxo-2-N,N-dibenzylamino-	$C_{27}H_{20}BrNO$	71.37	4.44	3.08	17.59	71.25	4.36	2.91	17.50
XXVII	3-Bromo-9-oxo-2-N,N-(di-*p*-bromobenzyl)amino-	$C_{27}H_{18}Br_3NO$	52.97	2.96	2.29	39.16	53.12	3.02	2.36	39.57
XI	9-Oxo-2-N-benzylamino-	$C_{20}H_{15}NO$	84.18	5.30	4.91		84.16	5.48	4.60	
XII	9-Oxo-2-N-*p*-bromobenzylamino-	$C_{20}H_{14}BrNO$	65.95	3.87	3.85		65.79	4.10	3.77	
XIII	9-Oxo-2-N-*p*-xylylamino-	$C_{21}H_{16}BrNO$			3.70				3.70	
XIV	9-Oxo-2-N-*p*-nitrobenzylamino-	$C_{20}H_{14}N_2O_3$	72.72	4.27	8.48		72.96	4.38	8.63	
XV	9-Oxo-2-N-(9′-fluorenyl)-amino	$C_{26}H_{17}NO$	86.88	4.77	3.90		86.85	4.89	3.93	
XVI	9-Oxo-2-N,N-dibenzylamino	$C_{27}H_{21}NO$	86.37	5.64	3.73		86.25	5.67	3.59	
XVII	9-Oxo-2-N,N-(di-*p*-bromobenzyl)amino-	$C_{27}H_{19}Br_2NO$	60.81	3.59	2.63	29.97	60.54	3.69	2.85	30.20
XVIII	9-Oxo-2-N,N-(di-*p*-xylyl)-amino	$C_{29}H_{25}NO$	86.32	6.25	3.47		85.80	6.35	3.41	
XIX	9-Oxo-2-N,N-(di-*p*-nitrobenzyl)amino-	$C_{27}H_{19}N_3O_5$	69.67	4.11	9.03		69.72	4.08	9.21	

[a] Performed by Weiler and Strauss, Oxford; W. Manser, Zurich; Schwarzkopf Microanalytical Laboratory, Woodside, N. Y.; and M. E. Taylor, formerly of this laboratory. [b] See Table I, footnote *l*.

methylamino-7-nitrofluorene gave 2-N,N-dimethylamino-7-aminofluorene.[12] Monoacetylation of the latter gave a compound with acceptable molecular weight, nitrogen and hydrogen values, but the percentage of carbon was variable as shown by repeated duplicate analyses on several samples.

Experimental[13]

Procedure I.—The amine was heated with an appropriate amount of trialkyl phosphate or other phosphorus acid ester to effect solution. To the hot mixture anhydrous[14] lithium bromide was added as a powder in one portion with shaking or thorough stirring. The mixture was heated under reflux for 0.5–2 hr., then sufficient 10% aqueous sodium hydroxide was added to make the mixture strongly alkaline. Refluxing was continued for 15–30 min. and the mixture was diluted with water. Filtration and drying of the product were followed by recrystallization from an appropriate solvent, *e.g.*, carbon tetrachloride, benzene, methanol, ethanol, etc.

Example: 2-N-Ethylamino-3-bromo-9-oxofluorene.—2-Amino-3-bromo-9-oxofluorene (see[10] ref. 1) (8.2 g., 0.03 mole) was dissolved in warm triethyl phosphate (55 g., 0.3 mole). Anhydrous powdered lithium bromide (5.2 g., 0.06 mole) was added in one portion with shaking. The mixture was heated under reflux at 145–150° (bath) for 4 hr. with occasional shaking, then cooled to ~100°. To the

(12) T. L. Fletcher and M. J. Namkung, *J. Org. Chem.*, **23**, 680 (1958), see footnote *e* under Table I.

(13) See Table I, footnote *b*.

(14) We have recently alkylated in the presence of lithium bromide which is not completely dry, with no adverse effect on the reaction (M. J. Namkung, this laboratory).

mixture 10% aqueous sodium hydroxide (50 ml.) was added. Refluxing was continued for 15 min. and the mixture was stirred into cold water. The product was filtered and chromatographed in chloroform on alumina. From the fast moving band there was obtained 4 g. (44%) of the product. The slow moving band gave unchanged 2-amino-3-bromofluorenone, 3.2 g. (40%), m.p. and mixture m.p. 215–216° (see[10] ref. 1).

Procedure II.—A mixture of the amine and the trialkyl phosphate or other phosphorus acid ester was heated under reflux for several hours then treated with 10% aqueous sodium hydroxide. The product was isolated and purified as above.

Example: 2-N-*n*-Butylaminofluorene.—2-Aminofluorene (5.4 g., 0.03 mole), m.p. 127–128°, was heated with stirring at 195–200° (bath) while tri-*n*-butyl phosphite (2.5 g., 0.01 mole) was introduced dropwise over a period of 1.5 hr. Heating under reflux was continued at the same temperature for another 1.5 hr. After cooling to 100°, 10% aqueous sodium hydroxide (30 ml.) was added and the mixture refluxed for 0.5 hr. and stirred into ice water. The solidified product was recrystallized from 95% ethanol (Darco) giving 3.7 g. (52%), m.p. 81.5–82.5°.

Procedure III.—The alkyl- or aralkyl halide was mixed with the amine, sodium bicarbonate, and an excess of triethyl phosphate. The mixture was heated under reflux with occasional agitation for 0.5–2 hr. (a longer reaction time was used for *ortho*-substituted amines or secondary alkyl halides, *e.g.*, 9-bromofluorene). The reaction mixture was stirred into cold water. The product or mixture of products was purified by recrystallization or by chromatography through an alumina column.

Example: 2-N-(9′-Fluorenyl)amino-9-oxofluorene.—9-Bromofluorene (7.4 g., 0.03 mole), m.p. 103–104°, was mixed thoroughly with 2-aminofluorenone (5.9 g., 0.03 mole), m.p. 159–160°, sodium bicarbonate (2.5 g., 0.03 mole), and triethyl phosphate (15 ml.). The mixture was heated under reflux at 150–155° (bath) for 1 hr. and cooled to room temperature. After water dilution the product was filtered off and recrystallized from chloroform–methanol giving 8.9 g. (83%) of glistening reddish violet needles, m.p. 214.5–215.5°.

N-(9-Fluorenyl)-*p*-nitroaniline.—A mixture of *p*-nitroaniline (6.9 g., 0.05 mole), 9-bromofluorene (12.3 g., 0.05 mole), sodium bicarbonate (4.2 g., 0.05 mole), and triethyl phosphate (30 ml.) was heated under reflux at 120–125° (bath) for 2 hr., then cooled to room temperature. The mixture was stirred into 9 *N* hydrochloric acid (200 ml.) and cooled in ice water. The precipitate was filtered, washed with concentrated ammonium hydroxide, air-dried, and recrystallized from chloroform–methanol giving 10.1 g. (67%), m.p. 212.5–213.5° (lit., m.p. 225°[15]).

Anal. Calcd. for $C_{19}H_{14}N_2O_2$: C, 75.48; H, 4.67; N, 9.25. Found: C, 75.64; H, 4.78; N, 9.29.

2-N,N-Dimethylamino-7-nitrofluorene.—2-Amino-7-nitrofluorene (30 g.), m.p. 234–235°, anhydrous sodium carbonate (16 g.) and trimethyl phosphate (90 ml.) were placed in a 500-ml. three-necked flask equipped with a mechanical stirrer and distilling condenser. The mixture was stirred while methyl iodide (30 ml.) was introduced in one portion. This was then heated (Glas-col) until all the excess methyl iodide was distilled and the temperature of the reaction mixture reached 160°. The mixture was then cooled in an ice water bath to <40° and the recovered methyl iodide was again added to the reaction flask. Heating was resumed and this operation twice repeated. Finally the hot (160°) reaction mixture was cooled to room temperature and diluted with concentrated ammonium hydroxide (100 ml.). The solid was filtered, washed twice with 25-ml. portions of 5% aqueous sodium carbonate, and dried (38 g.).

The crude product was boiled in *o*-dichlorobenzene (80 ml.) until the volume was reduced to one-half, and cooled. The solid mass was taken up in boiling acetone (3–4 l.), filtered, and the filtrate concentrated to 600 ml. and cooled, giving 20 g. (59%) of pure dimethylamino-7-nitrofluorene, m.p. 231–232° (lit., 229–230°[12]).

N-2-(7-N′,N′-Dimethylamino)fluorenylacetamide.—Acetylation of the corresponding amine[12] in the usual manner gave a product which after crystallization from methanol melted at 202.5–203.5°. Another preparation using pyridine gave material almost as good analytically, but with m.p. 203.5–207°. If put on the plate at 190–198° this melted and at once resolidified, remelting as above.

Anal. Calcd. for $C_{17}H_{18}N_2O$: C, 76.66; H, 6.81; N, 10.52; mol. wt., 266.3. Found: C, 74.01; H, 6.99; N, 10.33; mol. wt., 255.

Preparation of Anhydrous Lithium Bromide.—The Lithium Corp. of America generously donated 50% aqueous lithium bromide. This was evaporated first on a steam bath then heated with stirring on a hot plate until the dihydrate (m.p. ~44°) was formed. This was pulverized and reheated at a higher temperature until water of hydration was eliminated. The anhydrous salt was stored over phosphorus pentoxide in a vacuum.[14]

Lithium Diethyl Phosphate.—Triethyl phosphate (91 g., 0.5 mole) and lithium bromide (anhydrous) (43.5 g., 0.5 mole) were heated at 155 ± 2° (bath) for 5 hr. The ethyl bromide formed was collected in a cold trap and weighed (40.8 g., 75%). The white solid in the reaction vessel was triturated with dry ether, filtered, washed with ether, and dried over phosphorus pentoxide in a vacuum giving 60.6 g. (76%) of the product as snow-white needles which did not melt up to 310°.

An analytical sample was prepared by further ether extraction in a Soxhlet extractor and drying.

Anal. Calcd. for $C_4H_{10}LiO_4P$: C, 30.02; H, 6.30; P, 19.36. Found: C, 29.77; H, 6.18; P, 18.94.

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(15) C. Courtot and P. Petitcolas, *Compt. rend.*, **180**, 297 (1925).