

849. *Alkylation-Bromination of Fluoreneamines with Alkyl and Aralkyl Bromides in Dimethyl Sulphoxide*

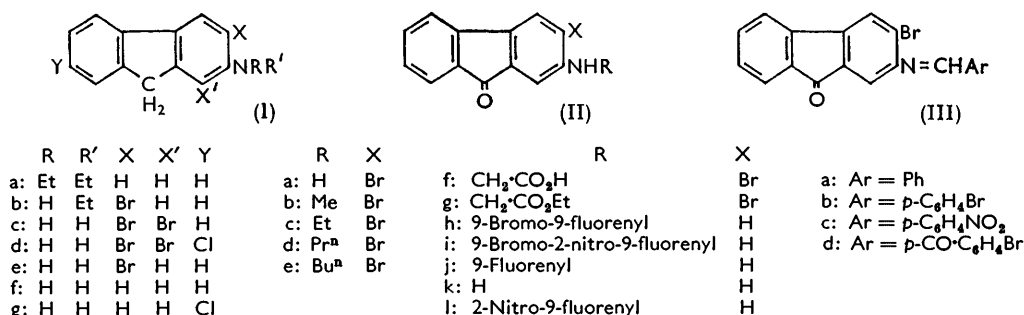
By T. LLOYD FLETCHER and HSI-LUNG PAN

WE have mentioned¹ ring brominations, *N*-alkylations and aralkylations, alkyl carbon bromination (in ArNHCH₂Ar') and dehydrobromination of the latter to azomethines by the use of dimethyl sulphoxide (DMSO). We now describe extensions of this work and some results which give clues to the mechanism.

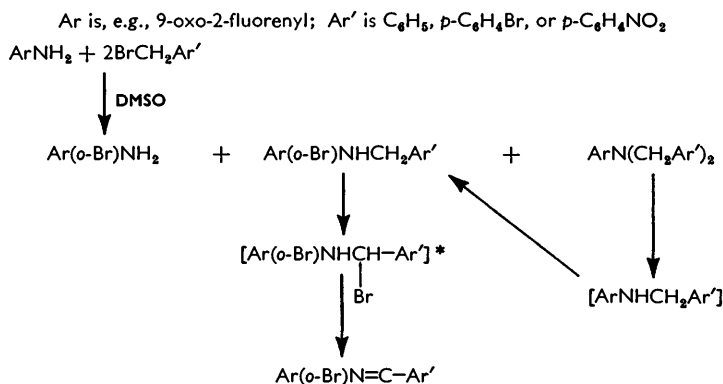
Reports that hydrobromic acid, a likely by-product in the reactions, reduces DMSO

¹ (a) T. L. Fletcher and H.-L. Pan, *J. Amer. Chem. Soc.*, 1956, **78**, 4812; (b) T. L. Fletcher, M. J. Namkung, and H. L. Pan, *Chem. and Ind.*, 1957, 660; (c) T. L. Fletcher and H. L. Pan, *J. Org. Chem.*, 1959, **24**, 141.

and its analogues to the sulphide have appeared.² The suggestion that "halogenation might be effected with water-soluble aliphatic sulphoxides and hydrohalic acids" was first made by Gilman and Eisch;³ our work shows the validity of this with alkyl and aralkyl bromides in the presence of arylamines. It first seemed^{1a, b} that DMSO, offering a favourable environment for alkylation of amines with RBr, reacts with the eliminated hydrobromic acid to give $\text{Me}_2\text{SBr}^+\text{Br}^-$. The observation of a by-product, 2-*N*-methylamino-3-bromofluorenone (IIb) (see Table), in the reaction between ethyl bromide and 2-amino-



fluorenone, and the fact that ring bromination is more rapid than *N*-alkylation, indicate that another mechanism also takes place, perhaps exclusively with ArCH_2Br . With the latter, the brominated primary amine builds up more rapidly than the other products;



* Isolated when Ar' is *o,o'*-diphenylene.

the yield of *N*-aralkylbromoamine then increases at the expense of the first-named product. DMSO and the bromide appear to form a fast-acting brominating agent. With ethyl bromide, the only source of the methyl group is DMSO. Smith and Winstein,⁴ using DMSO and methyl iodide, showed that both DMSO^+Me^- and $\text{DMS}^+\text{O}^-\text{Me}$ are formed.

Similar substances may be formed with ethyl bromide, and the mixture may contain a small amount of $\text{Et}(\text{Me})\text{S}^+\text{O}^-\text{Me}^-$ Br^- , as well as of DMSO^+Et^- Br^- , thus accounting for the *N*-methyl derivative.

² (a) E. Fromm, *Angew. Chem.*, 1912, **24**, 1125; (b) I. M. Hunsberger and J. M. Tien, *Chem. and Ind.*, 1959, 88; (c) B. Iselin, *Helv. Chim. Acta*, 1961, **44**, 61.

³ H. Gilman and J. Eisch, *J. Amer. Chem. Soc.*, 1955, **77**, 3862.

⁴ S. G. Smith and S. Winstein, *Tetrahedron*, 1958, **3**, 317.

Oxidation of ArCH_2Br to the aldehyde⁵ does not play any appreciable role in the formation of azomethines. With one equivalent of aralkyl bromide, and one of amine, no azomethine is found; with two equivalents of the former, azomethine is formed, but none unbrominated. With 2-*N*-aralkylaminofluorenes and 48% hydrobromic acid in DMSO, high yields of brominated azomethine are formed. When the bromide is 9-bromofluorene the reaction stops at the stage at which the α -carbon is brominated.

The Scheme indicates the products in one of the more complicated reactions.

Experimental.—General procedure for aryl bromination and/or *N*-alkylation of fluorenamines with alkyl bromides or 48% hydrobromic acid. The amine (1 equiv.) was dissolved in DMSO, and alkyl bromide (or 48% hydrobromic acid) (2 equiv.) was added. The mixture was heated under reflux at 150–155° for 1–2 hr., cooled, triturated with dilute ammonium hydroxide, filtered off, and recrystallised or chromatographed (alumina).

Reaction of 2-aminofluorenone with ethyl bromide in DMSO. 2-Aminofluorenone (39 g.), ethyl bromide (43.6 g.), and DMSO (70 ml.) were allowed to react for 1.5 hr. as described above. The product (55.7 g.) was chromatographed (alumina) in benzene giving 55% of 3-bromo-2-*N*-ethylaminofluorenone^{1a} (IIc), and 32% of 2-amino-3-bromofluorenone^{1a} (IIa). When the mixture was heated for 4 hr., 50% of compound (IIc), 12% of compound (IIa), and 5% of 3-bromo-2-*N*-methylaminofluorenone (IIb), m. p. 177–178° (lit.,⁶ 177–178°) were obtained.

*Reaction of 2-*N*-*p*-nitrobenzylaminofluorenone with 48% hydrobromic acid in DMSO.* 2-*N*-*p*-Nitrobenzylaminofluorenone⁶ was heated at 100–105° with 48% hydrogen bromide

Bromination and/or *N*-alkylation of fluorenamines with RBr in dimethyl sulphoxide

Amine (If)	R in RBr	Molar ratio	Product(s) (% yield)	M. p.	Formula	Found (%)				Required (%)			
						C	H	N	Br	C	H	N	Br
	Et	2	(Ia) * (10), (Ib) (30)	149.5— 150.5°	$\text{C}_{15}\text{H}_{14}\text{BrN}$	62.7	4.7	4.8	27.4	62.5	4.9	4.9	27.7
	Bu [†]	3	(Ie) † (15), (Ic) (60)	185.5— 186.5	$\text{C}_{13}\text{H}_9\text{Br}_2\text{N}, \text{H}_2\text{O}$				44.4				44.7
(Ig)	H ‡	2.2	(Id) (88)	198— 199	$\text{C}_{13}\text{H}_8\text{Br}_2\text{ClN}$				42.5				42.8
(IIk)	Pr ^a	2	(IIa) § (18), (IIc) (26)	108— 108.5	$\text{C}_{16}\text{H}_{14}\text{BrNO}$				25.5				25.3
	Bu ^a	2	(IIa) § (17), (IIe) (25)	97— 97.5	$\text{C}_{17}\text{H}_{16}\text{BrNO}$	61.8	5.0			61.8	4.9		
	$\text{CH}_2\text{-CO}_2\text{H}$	1.1	(IIa) § (25), (IIf) (34)	231— 235 ¶	$\text{C}_{15}\text{H}_{10}\text{BrNO}_3$	54.0	3.3	4.2	24.3	54.2	3.0	4.2	24.1
	$\text{CH}_2\text{-CO}_2\text{Et}$	1	(IIa) § (20), (IIg) (24)	186— 187	$\text{C}_{17}\text{H}_{14}\text{BrNO}$	56.5	4.2	3.7	22.3	56.7	3.9	3.9	22.2
	Ph- CH_2	2	(IIa) § (34), (IIIa) (46)	193.5— 194.5	$\text{C}_{20}\text{H}_{11}\text{BrNO}$	66.0	3.7	3.6	21.8	66.3	3.4	3.9	22.1
	<i>p</i> - $\text{CH}_2\text{-C}_6\text{H}_4\text{Br}$	2	(IIIb) (80)	195— 196	$\text{C}_{20}\text{H}_{12}\text{Br}_2\text{NO}$	54.5	2.8	3.1	35.7	54.5	2.5	3.2	36.2
	<i>p</i> - $\text{CH}_2\text{-C}_6\text{H}_4\text{NO}_2$	2	(IIIc) (76)	252— 253	$\text{C}_{20}\text{H}_{11}\text{BrN}_2\text{O}_3$	58.9	2.7	7.0	20.3	59.0	2.7	6.9	19.6
	<i>p</i> - $\text{CH}_2\text{-CO-C}_6\text{H}_4\text{Br}$	1	(IIIId) (61)	274.5— 275.5 ¶	$\text{C}_{21}\text{H}_{11}\text{Br}_2\text{NO}_2$	54.0	2.5	3.0	33.9	53.8	2.4	3.0	34.1
	9-Fluorenyl	1	(IIa) § (20), (IIj) (4), (IIh) (55)	218— 221	$\text{C}_{26}\text{H}_{16}\text{BrNO}$	71.4	3.9	3.5	18.4	71.2	3.7	3.2	18.2
(III)	H ‡	1	(IIi) (52)	272— 272.5	$\text{C}_{26}\text{H}_{15}\text{BrN}_2\text{O}_3$	64.3	3.1	5.8	17.1	64.6	3.1	5.8	16.5

* T. L. Fletcher, M. E. Taylor, and A. W. Dahl, *J. Org. Chem.*, 1955, **20**, 1021. † Ref.^{1b}.
‡ Aqueous 48% hydrobromic acid. § Ref.^{1a}. ¶ Decomp. || Ref.⁶

(2 equiv.) in DMSO for 1.5 hr. and then diluted with ammonium hydroxide. The solid was recrystallised from benzene–ethanol giving 80% of 3-bromo-2-*p*-nitrobenzylidenaminofluorenone (IIIc).

General procedure for N-alkylation, aryl bromination, and arylidenamine formation of amino-fluorenes with aralkyl bromides. A mixture of the aminofluorenone (1 equiv.) and aralkyl

⁵ N. Kornblum, W. J. Jones, and G. J. Anderson, *J. Amer. Chem. Soc.*, 1959, **81**, 4113.

⁶ H. L. Pan and T. L. Fletcher, *J. Org. Chem.*, 1962, **27**, 3639.

bromide (1—2 equiv.) was dissolved in DMSO (20 ml. per 0.01—0.03 mol. of amine) and heated at 95—105°. Ammonium hydroxide was then added and the precipitate filtered off. The following are typical:

(a) A mixture of 2-aminofluorenone (5.9 g.), *p*-bromobenzyl bromide (7.5 g., 1 equiv.), and DMSO (10 ml.) was set aside at 25° for 1 hr., then heated under reflux at 95—100° for 1 hr. and stirred into dilute ammonium hydroxide. The solid (13.2 g.) was isolated and chromatographed (alumina) in benzene-chloroform (2 : 1) giving 15% of 2-*NN*-di-*p*-bromobenzylaminofluorenone,⁶ 20% of 3-bromo-2-*N*-*p*-bromobenzylaminofluorenone,⁶ and 56% of 3-bromo-2-aminofluorenone ^{1a} (IIc).

(b) 2-Aminofluorenone (3.9 g.), *p*-bromobenzyl bromide (10 g., 2 equiv.), and DMSO (10 ml.) were heated at 100—105° for 1.5 hr., diluted with ice-water, and the solid recrystallised from methanol-chloroform, giving 80% of 3-bromo-2-*p*-bromobenzylidenaminofluorenone (IIIb).

2-*N*-(9-*Bromo-9*-fluorenyl)aminofluorenone (IIh). (a) A mixture of 2-aminofluorenone (5.9 g.), 9-bromofluorene (7.4 g.), and DMSO (10 ml.) was heated for 1.5 hr. and worked up as above; recrystallisation twice from chloroform-methanol gave 7.3 g. (55%), m. p. 217.5—220°. This was twice chromatographed with benzene as eluent (m. p. 218—221°). The liquor was evaporated giving compound (IIa) (20%) from benzene. A second crop, recrystallised twice from carbon tetrachloride, proved to be 2-*N*-(9-fluorenyl)aminofluorenone ⁶ (4%).

(b) A mixture of 48% hydrobromic acid (1 equiv.) and DMSO (5 ml.) was heated at 110° (bath) for 10 min. and cooled to ~50°. 2-*N*-(9-Fluorenyl)aminofluorenone ⁶ (1.8 g.) was added. The mixture was heated for 1.5 hr., cooled, triturated with dilute ammonium hydroxide, and worked up to give 1.6 g. (73%) of the product.

(c) 2-*N*-(9-Fluorenyl)aminofluorenone (1.8 g.) was brominated in carbon tetrachloride (80 ml.) with *N*-bromosuccinimide (1 g.) and irradiated by two 100-w light bulbs and a G.E. 250-w Purple-X bulb. Recrystallisation yielded 1.7 g. (79%) of the product obtained in (b).

2-*N*-(9-*Bromo-2-nitro-9*-fluorenyl)aminofluorenone (IIi). (a) 2-Aminofluorenone (3.9 g.), 9-bromo-2-nitrofluorene (5.8 g., 1 equiv.), and DMSO (15 ml.) were heated as described above to give 4 g. (41%) of vermilion needles.

With two equivalents of 9-bromo-2-nitrofluorene, 27% of this product was obtained. In addition, 2-nitrofluorenone (31%) was isolated.

(b) A mixture of 48% hydrobromic acid (0.005 mol.) and DMSO (5 ml.) was heated at 110° for 10 min. then cooled to 50°. To the solution was added 2-*N*-(2-*nitro-9*-fluorenyl)aminofluorenone (2 g., 0.005 mol.), m. p. 224.5—225.5° (Found: C, 77.4; H, 4.1; N, 7.1. C₂₆H₁₆N₂O₃ requires C, 77.2; H, 4.0; N, 6.9%) was added. (The latter was prepared from 2-aminofluorenone and 9-bromo-2-nitrofluorene in triethyl phosphate⁶). The mixture was heated at 100—105° for 1.5 hr., cooled, and diluted with ammonium hydroxide. Recrystallisation gave 1.3 g. (52%) of the product.

(c) 2-*N*-(2-Nitro-9-fluorenyl)aminofluorenone (2 g.) was heated under reflux in a mixture of carbon tetrachloride (60 ml.) and benzene (160 ml.) and irradiated for 30 min. *N*-Bromosuccinimide (1 g., 1.1 equiv.) was added to the solution. The mixture was refluxed for 2 hr. and the solvent distilled off. The residue was recrystallised from chloroform-methanol giving an 80% yield of the product.

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