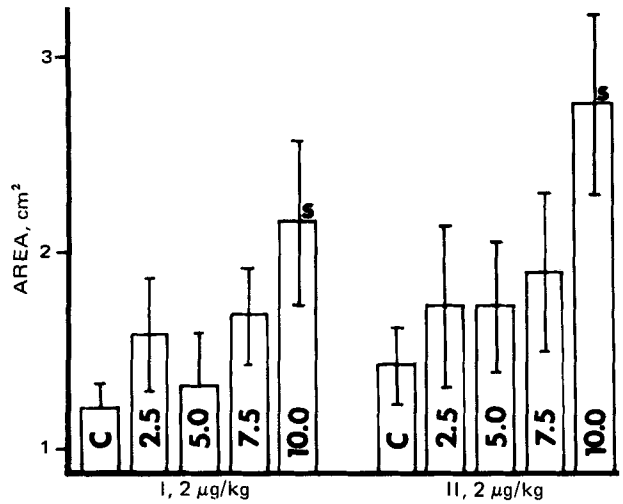

Figure 2—*Effect of intravenous pentazocine (milligrams per kilogram shown in the bars) on the pressor responses to I and II. At a dose of 10 mg/kg, pentazocine significantly (S) potentiated the pressor response to I and II when compared to the control (C) at* $p < 0.05$.

times. No autopotentiation was found; in fact, the responses tended to decrease after the agonist had been administered several times[5].

Tammisto *et al.* (6) reported a marked increase in plasma catecholamine levels after an intravenous injection of pentazocine, 1.2 mg/kg, in humans. The rise in plasma catecholamine levels was concomitant with the rise in blood pressure and heart rate in the same patients. It was concluded that the rise in circulating catecholamines was due to peripheral release of epinephrine and levarterenol caused by central sympathetic stimulation by pentazocine. These investigators also suggested that the pentazocine-induced increase in plasma catecholamines was not due to an inhibition of reuptake or of enzymatic degradation of the catecholamines since pentazocine did not potentiate the pressor responses of exogenous epinephrine or levarterenol.

The results presented in this study do not agree with those of Tammisto *et al.* (6). Pentazocine potentiated the pressor responses of exogenous amines. It is tempting to suggest that one possible explanation for the pentazocine–pressor amine interaction would be a pentazocine-induced alteration of the physiological disposition of the neurotransmitters by interaction with the sympathetic nervous system.

Investigations into the actions of pentazocine on neural function in the central nervous system support the hypothesis that pentazocine may alter adrenergic function.

Holtzman and Jewett (7) demonstrated that pentazocine, at a wide range of doses, significantly lowered rat brain norepinephrine and theorized that the drop in brain norepinephrine content might be related to a pentazocine-induced release of the adrenergic transmitter. Likewise, Paalzow *et al.* (8) reported a drop in rat brain norepinephrine after pentazocine treatment. They also showed that pentazocine accelerated the depletion of the adrenergic neurotransmitter in the brain after tyrosine hydroxylase or dopamine β-hydroxylase was inhibited, thereby indicating that the turnover of norepinephrine was increased.

[5] Unpublished results.

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Synthesis and Hydrolysis of Fluorene-9-spiro-2′-(*N*-aryl-3′,3′-dichloroaziridines)

MAGID ABOU-GHARBIA and MADELEINE M. JOULLIÉ [x]

Abstract □ The synthesis of eight fluorene-9-spiro-2′-(*N*-aryl-3′,3′-dichloroaziridines) was achieved *via* the reaction of dichlorocarbene with the appropriately substituted *N*-fluorenylideneanilines. Hydrolysis of the spirofluorenes afforded the corresponding 9-chlorofluorene-9-carboxanilides in excellent yields.

Keyphrases □ Fluorene-9-spiro-2′-aziridines, various—synthesized, hydrolyzed to 9-chlorofluorene-9-carboxanilides □ Aziridines, fluorene-9-spiro—synthesized, hydrolyzed to 9-chlorofluorene-9-carboxanilides □ Hydrolysis—various fluorene-9-spiro-2′-aziridines to 9-chlorofluorene-9-carboxanilides □ Spiro compounds—various fluorene-9-spiro-2′-aziridines synthesized, hydrolyzed to 9-chlorofluorene-9-carboxanilides

The synthesis of aziridines from imines has been accomplished either by the reactions of imines with dimethylsulfoxonium methylide in dimethyl sulfoxide (1) or by the insertion of carbenes in the carbon–nitrogen double bond of imines (2, 3).

The reaction of *N*-fluorenylideneanilines (I) with dimethylsulfoxonium methylide afforded a mixture of the starting imine and fluorenone instead of the expected spiroaziridines. However, the reactions of I with dichlorocarbene, generated by the reaction of chloroform with

Table I—*N*-Fluorenylideneanilines

Compound[a]	R	Yield, %	Melting Point	Molecular Formula		Analysis, % Calc.	Found	IR Spectra, cm^{-1} (C=N)
Id[b]	C_2H_5	80	88–89°	$C_{21}H_{17}N$	C	89.00	89.21	1640
					H	6.04	5.86	
					N	4.94	5.15	
Ig	Br	100	140–141°	$C_{19}H_{12}BrN$	C	68.27	68.36	1650
					H	3.62	3.58	
					Br	23.91	24.13	
					N	4.19	4.15	
Ih	I	100	133–135°	$C_{19}H_{12}IN$	C	59.85	54.89	1635
					H	3.17	3.13	
					I	33.29	32.99	
					N	3.67	3.64	

[a] All compounds were recrystallized from ethanol–chloroform. [b] NMR: δ 1.15–1.45 (t, 3H), 2.55–2.95 (q, 2H), and 6.6–8.0 (m, 12H) ppm.

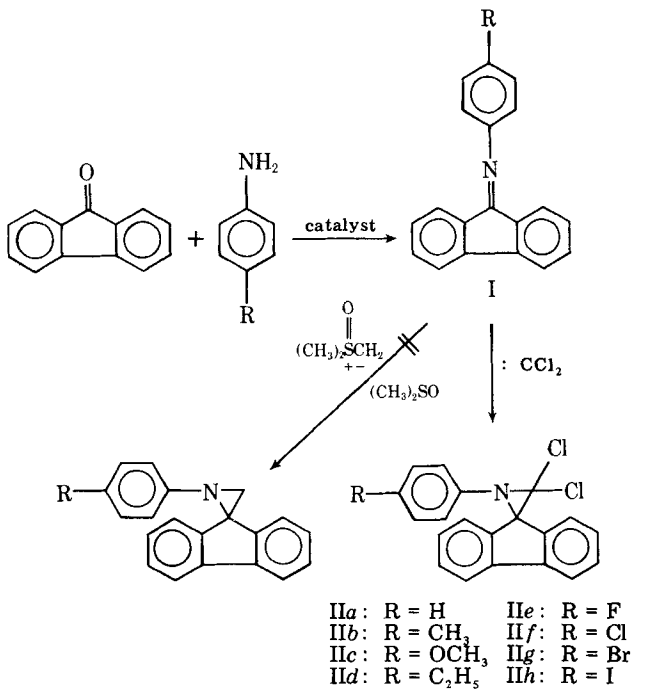
Table II—Fluorene-9-spiro-2′-(*N*-aryl-3′,3′-dichloroaziridines)

Compound	Yield, %	Melting Point	Molecular Formula		Analysis, % Calc.	Found
IIa	81	98–99°	$C_{20}H_{13}Cl_2N$	C	71.01	71.29
				H	3.87	3.95
				Cl	20.96	21.28
				N	4.14	4.09
IIb[a]	88	135–136°	$C_{21}H_{15}Cl_2N$	C	71.60	71.50
				H	4.29	4.26
				Cl	20.13	19.92
				N	3.97	3.76
IIc[b]	83	108–109°	$C_{21}H_{15}Cl_2NO$	C	68.48	68.62
				H	4.10	4.09
				Cl	19.25	19.25
				N	3.80	3.81
IId[c]	86[d]	82–84°	$C_{22}H_{17}Cl_2N$	C	72.13	72.94
				H	4.67	4.95
				N	3.82	3.87
IIe	80	111–112°	$C_{20}H_{12}Cl_2FN$	C	67.43	67.53
				H	3.39	3.35
				Cl	19.90	20.10
				F	5.33	5.33
				N	3.93	3.96
IIf	80	134–135°	$C_{20}H_{12}Cl_3N$	C	64.45	64.69
				H	3.24	3.29
				Cl	28.54	28.26
				N	3.75	3.79
IIg	89	145–147°	$C_{20}H_{12}BrCl_2N$	C	57.58	57.60
				H	2.90	2.90
				Br	16.99	17.10
				Cl	19.15	19.34
				N	3.35	3.30
IIh	75	113–115°	$C_{20}H_{12}Cl_2IN$	C	51.75	51.47
				H	2.60	2.87
				Cl	15.27	15.34
				I	27.34	27.20
				N	3.01	3.07

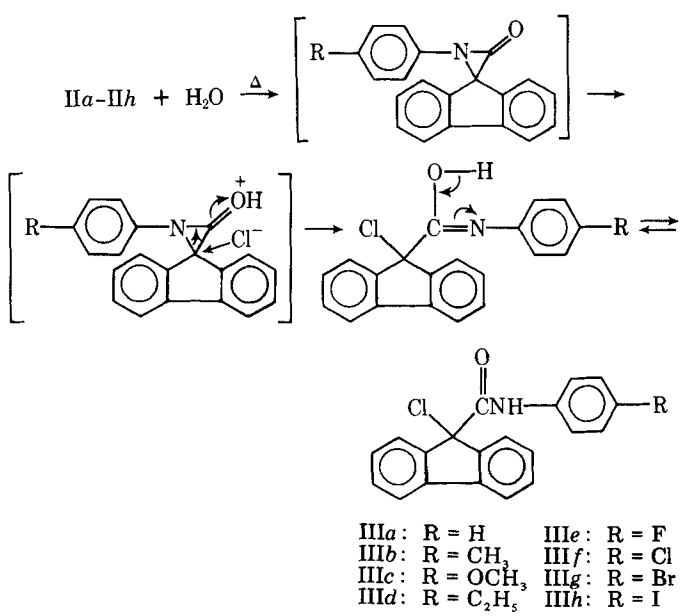
[a] NMR: δ 2.29 (s, 3H) and 6.85–7.85 (m, 12H) ppm. Mass spectrum: M^+ 353. [b] NMR: δ 3.8 (s, 3H) and 6.95–7.9 (m, 12H) ppm. [c] NMR: δ 1.1–1.35 (t, 3H), 2.4–2.8 (q, 2H), and 6.85–7.85 (m, 12H) ppm. [d] Only 45% of this material could be isolated as a crystalline solid since it becomes an oil on standing.

potassium *tert*-butoxide, afforded the corresponding spirodichloroaziridines (IIa–IIh) in 75–90% yields (Scheme I).

The hydrolysis of IIa–IIh occurred rapidly in boiling water to afford 9-chlorofluorene-9-carboxanilides (IIIa–IIIh) in excellent yields (Scheme II).



Scheme I



Scheme II

EXPERIMENTAL[1]

***N*-Fluorenylideneanilines (I)**—These imines were prepared by the

[1] Melting points are uncorrected. IR spectra were recorded on a Perkin-Elmer model 137B spectrophotometer calibrated with polystyrene. Samples were determined as potassium bromide disks. NMR spectra were determined on a Varian A-60 spectrometer using tetramethylsilane as an internal standard. Samples were dissolved in deuterochloroform unless otherwise noted. Elemental analyses were performed by Midwest Microlab, Indianapolis, IN 46226. Mass spectra were obtained on a Finnigan model F-3300 with a data system 6000 mass spectrometer, with an ionizing potential of 30 ev.

Table III—9-Chlorofluorene-9-carboxanilides

Compound	Yield, %	Melting Point	Molecular Formula		Analysis, % Calc.	Found	IR Spectra, cm^{-1} (NH and C=O)
III*a*	100	164–165°	$C_{19}H_{14}ClNO$	C	75.11	75.00	3300
				H	4.41	5.00	1675
				Cl	11.08	10.83	
				N	4.38	4.41	
III*b*[a]	100	282–284°	$C_{21}H_{16}ClNO$	C	75.55	75.47	3200
				H	4.83	4.77	1660
				Cl	10.62	10.50	
				N	4.19	4.08	
III*c*[b]	88	134–135°	$C_{21}H_{16}ClNO_2$	C	72.10	72.43	3310
				H	4.61	4.77	1670
				Cl	10.13	9.98	
				N	4.00	4.03	
III*d*[c]	93	123–124°	$C_{22}H_{18}ClNO$	C	75.96	75.98	3250
				H	5.21	5.13	1655
				Cl	10.19	10.37	
				N	4.02	3.94	
III*e*	80	157–159°	$C_{20}H_{13}ClFNO$	C	71.11	71.16	3200
				H	3.87	3.85	1650
				Cl	10.49	10.60	
				F	5.62	5.73	
				N	4.14	4.03	
III*f*	95	199–201°	$C_{20}H_{13}Cl_2NO$	C	67.81	67.64	3280
				H	3.64	3.76	1660
				Cl	20.01	19.86	
				N	3.95	3.96	
III*g*	89	208–210°	$C_{20}H_{13}BrClNO$	C	60.24	60.34	3280
				H	3.28	3.26	1660
				Br	20.04	19.79	
				Cl	8.89	8.73	
				N	3.51	3.43	
III*h*	88	202–204°	$C_{20}H_{13}ClINO$	C	53.89	54.15	3230
				H	2.93	2.99	1660
				Cl	7.95	7.98	
				I	28.47	28.75	
				N	3.14	3.07	

[a] NMR (dimethyl sulfoxide): δ 2.29 (s, 3H) and 7.15–7.9 (m, 13H) ppm. Mass spectrum: M^+ 333. [b] NMR: δ 3.85 (s, 3H) and 6.75–7.8 (m, 13H) ppm. [c] NMR: δ 1.05–1.35 (t, 3H), 2.4–2.8 (q, 2H), and 7–7.9 (m, 13H) ppm.

reaction of fluorenone with the appropriate substituted anilines in the presence of either zinc chloride (4) or boron trifluoride etherate (5) as the catalyst. All compounds shown in Table I were prepared using boron trifluoride etherate.

Fluorene-9-spiro-2′-(*N*-aryl-3′,3′-dichloroaziridines) (II*a*–II*h*)—Dry chloroform (47.8 g, 0.4 mole) was added slowly to a stirred slurry of 0.1 mole of the *N*-fluorenylideneaniline derivative, 60 g (0.5 mole) of potassium *tert*-butoxide, and 250 ml of hexane. The reaction was stirred at room temperature for 16 hr. The mixture was filtered, and the residue was collected and washed three times with hot hexane. The combined filtrates were concentrated *in vacuo* to afford a crystalline product. The aziridine derivatives were recrystallized from hexane (Table II).

9-Chlorofluorene-9-carboxanilides (III*a*–III*h*)—These compounds were obtained in excellent yields by allowing the spirodichloroaziridine derivatives to remain in contact with excess water at 25° for 24 hr. Compounds III*a*–III*h* were recrystallized from aqueous ethanol (Table III).

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