Synthesis of quinoxaline derivatives from substituted acetanilides through intramolecular quaternization reactions

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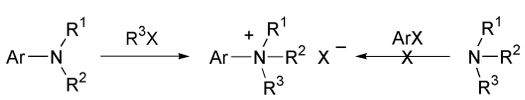
The cyclization of 2-dialkylamino-2′-halogeno- and 2-chloro-2′-(dialkylamino)acetanilides to quinoxaline derivatives has been studied in detail. These reactions proceed, respectively, through intramolecular aromatic nucleophilic or aliphatic nucleophilic substitution reactions and depending on the substituents and the experimental conditions, they lead to 3-oxoquinoxalinium salts or, after an alkyl chloride elimination, to quinoxalin-2-ones. Some new cases of the little known intramolecular quaternization of tertiary amines with aryl halides are described.

Introduction

The substitution of halogen atoms of aryl halides by NH_2, NHR, NR_2 and other nucleophilic groups is a well studied reaction. Several mechanisms are known, but the most important are the "S_NAr mechanism", operating under mild reaction conditions and usually requiring NO_2 (or other electron-withdrawing groups) activated aryl halides, and the "aryne mechanism", sometimes postulated when the reactions of unactivated aryl halides need to be carried out under strong conditions and the incoming group does not always occupy the position of the leaving group (cine-substitution).[1,2] The recent development of metal-based catalysts facilitating these substitution processes in unactivated aryl halides has increased the interest in these reactions enormously.[3] Using appropriate reactants, the substitution (sometimes, cine-substitution) of halogen atoms by nucleophilic moieties containing NH_2, NHR, SH, OH groups, *etc.*, can proceed intramolecularly affording different kinds of heterocyclic systems;[4] for example, nitrogen-containing heterocycles prepared according to this method include indoles,[5,6] indazoles,[7,8] quinolines,[5,7] quinoxalines,[7,9] *etc.*

On the other hand, the reaction of tertiary amines with alkylating agents to give quaternary ammonium salts is also a well known process (Menshutkin reaction).[10] Thus, *N*,*N*,*N*-trialkylanilinium salts **1** (Scheme 1), even those containing



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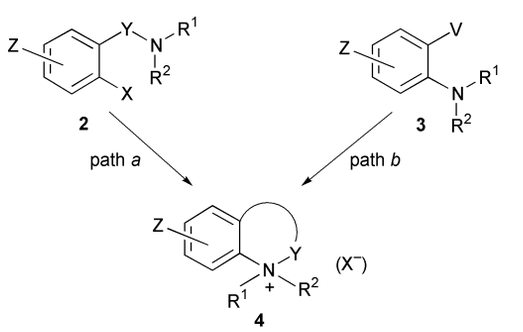
Scheme 1 Feasible and unworkable methods of synthesis of *N*,*N*,*N*-trialkylanilinium salts.

electron-withdrawing substituents in the ring, are available[11] by reaction of *N*,*N*-dialkylanilines and alkylating agents (R^3X). Nevertheless, a careful survey of the literature has shown that these salts have never been isolated from quaternization of trialkylamines with (even activated) aryl halides (ArX). In some cases the reaction does not take place at all and, in others, the expected quaternary salts, postulated as intermediates, decompose immediately by different routes.[2,12] Thus, our studies on the cyclization of *N*,*N*-disubstituted 2′-halogenophenacylamines **2** to 3-oxoindolinium halides **4** (Scheme 2, path *a*, Y = $COCH_2$, X = halogen) can be considered as the first example of such a process, showing that the quaternization of tertiary amines with aryl halides is, in some special cases, a feasible reaction.[13] Related processes (Scheme 2, path *a*)



X = halogen

Y = $COCH_2$, CONH, CH_2CONH (compounds **2**)

Y = $COCH_2$ (X = Cl, Br), CON^-, $COCH_2N^-$, SO_2N^- (compounds **4**)

V = CON_3, SO_2N_3, $COCH_2X$

Z = H, NO_2, Me

R^1,R^2 = Me, Me; $[CH_2]_n$, n = 4, 5, 6; *o*-$[CH_2]_nC_6H_4CH_2$, n = 1, 2

Scheme 2 Reported synthesis of indoxyl-, indazolinone-, cinnolinone- and benzothiadiazole-derived salts and betaines through intramolecular quaternization reactions.

are the cyclization of *N*′,*N*′-disubstituted 2-halogenobenzohydrazides[14] (**2**, Y = CONH, X = halogen) and (2-halogenophenyl)acetohydrazides[15] (**2**, Y = CH_2CONH, X = halogen) but, in these cases, the initially produced quaternary salts lose hydrogen halide yielding the corresponding indazol-1-ium-2-ide (**4**, Y = CON^-) and cinnolin-1-ium-2-ides (**4**, Y = CH_2CON^-), inner salts belonging to the chemical class of carbonyl-stabilized amine imides.[16]

An alternative cyclization method (Scheme 2, path *b*), based on the intramolecular quaternization of *N*,*N*-dialkylanilines **3** carrying a reactive chain (V = CON_3, SO_2N_3, $COCH_2X$) in the *ortho* position, has been used by other authors and by ourselves to prepare indazolinone-[17] (**4**, Y = CON^-) and benzothiadiazole-[18,19] (**4**, Y = SO_2N^-) derived amine imides as well as indoxyl-derived quaternary salts (**4**, Y = $COCH_2$, X = halogen).[13] The reactive compounds **4** prepared following these methods have been found to be useful intermediates

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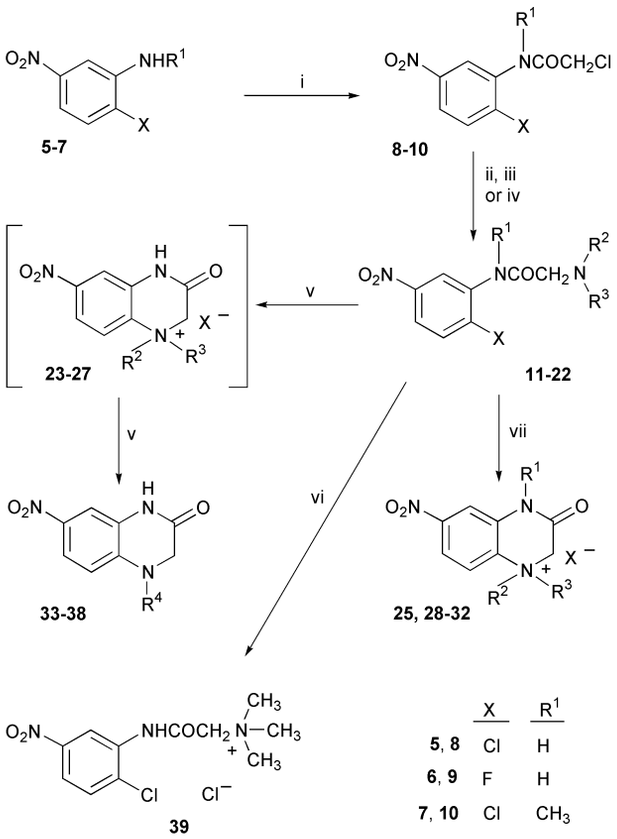
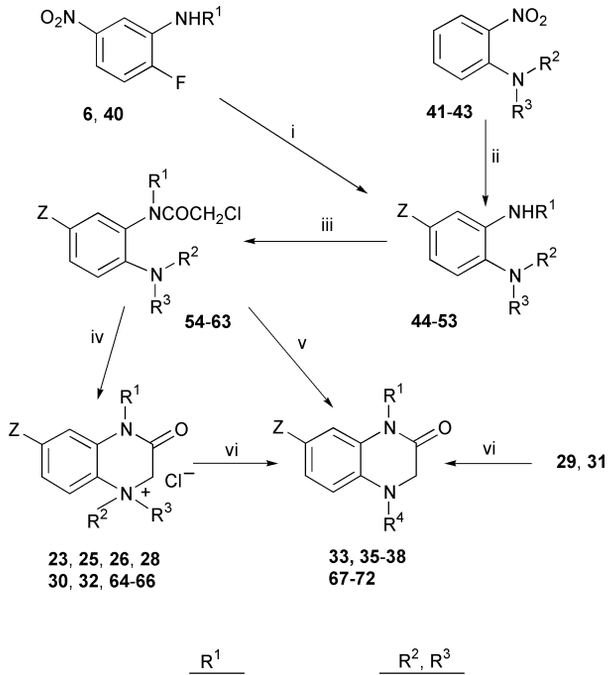


	X	R^1
5, **8**	Cl	H
6, **9**	F	H
7, **10**	Cl	CH_3

X = Cl R^1 = H	X = Cl R^1 = C H_3	R^2, R^3
11, **23**	**18**, **28**	CH_3, CH_3
12, **24**	**19**, **29**	$[CH_2]_4$
13, **25**	**20**, **30**	$[CH_2]_5$
14, **26**	**21**, **31**	$[CH_2]_6$
15, **27**	**22**, **32**	*o*-$[CH_2]_2C_6H_4CH_2$

X = F R^1 = H	R^2, R^3		R^4
16	$[CH_2]_5$	**33**	CH_3
17	*o*-$[CH_2]_2C_6H_4CH_2$	**34**	$[CH_2]_4Cl$
		35	$[CH_2]_5Cl$
		36	$[CH_2]_6Cl$
		37	*o*-$[CH_2]_2C_6H_4CH_2Cl$
		38	*o*-$[CH_2]_2C_6H_4CH_2OCH_2CH_3$

Scheme 3 *Reagents and conditions*: i, $ClCH_2COCl$–acetone, rt (for **8** and **9**) or reflux (for **10**); ii, from **8**, Me_2NH–EtOH, THF, 60–65 °C (autoclave) (for **11**) or R^2R^3NH, THF, reflux (for **12**–**15**); iii, from **9**, R^2R^3NH, THF, rt and then HBr–AcOH (for **16** and **17**, isolated as hydrobromides); iv, from **10**, Me_2NH–EtOH, acetone, rt (for **18**, not isolated) or R^2R^3NH, acetone, rt (for **19**–**22**, not isolated); v, from **11**–**15**, $MeNO_2$, reflux (for **33**–**37**); from **11**, EtOH, reflux (for **33**); from **17**, EtOH, reflux (for **38**) (salts **23**–**27** not isolated); vi, from **11**, $MeNO_2$ or EtOH, reflux (by-product); vii) from **16**, EtOH, reflux and then aq. HCl (for **25**); from **18**–**22** (not isolated), spontaneous under conditions iv (for **28**–**32**).



	R^1
6	H
40	CH_3

	R^2, R^3
41	CH_3, CH_3
42	$[CH_2]_5$
43	$[CH_2]_6$

R^1 = H Z = NO_2	R^1 = CH_3 Z = NO_2	R^2, R^3
23, **44**, **54**	**28**, **48**, **58**	CH_3, CH_3
25, **45**, **55**	**30**, **49**, **59**	$[CH_2]_5$
26, **46**, **56**		$[CH_2]_6$
27, **47**, **57**	**32**, **50**, **60**	*o*-$[CH_2]_2C_6H_4CH_2$

R^1 = H Z = H	R^2, R^3	R^1 = H Z = NO_2	R^4
51, **61**, **64**	CH_3, CH_3	**33**	CH_3
52, **62**, **65**	$[CH_2]_5$	**35**	$[CH_2]_5Cl$
53, **63**, **66**	$[CH_2]_6$	**36**	$[CH_2]_6Cl$
		37	*o*-$[CH_2]_2C_6H_4CH_2Cl$
		38	*o*-$[CH_2]_2C_6H_4CH_2OCH_2CH_3$

R^1 = CH_3 Z = NO_2	R^4		
67	CH_3	**72**	R^1 = H, R^4 = CH_3, Z = H
68	$[CH_2]_4Cl$		
69	$[CH_2]_5Cl$		
70	$[CH_2]_6Cl$		
71	*o*-$[CH_2]_2C_6H_4CH_2Cl$		

Scheme 4 *Reagents and conditions*: i, Me_2NH–EtOH, rt (for **44** and **48**) or R^2R^3NH, 110–120 °C (for **45**–**47**, **49** and **50**); ii, H_2, Pd/C, EtOH (for **51**–**53**); iii, from **44**–**50**, $ClCH_2COCl$–acetone, rt (for **54**–**60**); from **51**–**53**, $ClCH_2COCl$–Et_2O, rt (for **61**–**63**, isolated as hydrochlorides); iv, from **54**–**56** and **61**–**63**, EtOH, reflux (for **23**, **25**, **26** and **64**–**66**); from **58** and **59**, acetone, reflux (for **28** and **30**); from **60**, acetone, rt (for **32**); v, from **54**–**59**, $MeNO_2$, reflux (for **33**, **35**–**37**, **67** and **69**); from **57**, EtOH, reflux (for **38**); vi, from **23**, **25** and **28**–**32**, $MeNO_2$, reflux (for **33**, **35** and **67**–**71**); from **64**, 170–180 °C (for **72**).

for the preparation of some simple and fused indoles,[13] indazoles,[20] and related compounds, some of which have shown a remarkable *in vitro* activity against HeLa cells.[18]

In this paper we wish to report our results on the application of the above mentioned methods to the synthesis of quinoxaline derivatives (Schemes 3 and 4). Many biological properties and technical applications have been reported for quinoxalines;[21] furthermore, in recent years, quinoxalinones related to those expected from our approach have gained interest as anti-HIV agents,[22] aldose reductase inhibitors,[23] angiotensin II receptor antagonists,[24] 5-HT_3 receptor agonists[25] and, especially, as GABA/benzodiazepine receptor ligands.[22,26–28] Owing to the potential biological interest of these compounds, two different solid phase synthetic methods have been recently reported for the preparation of quinoxalin-2-one libraries.[29]

Table 1 Yields, mps and analytical data of 2-dialkylamino-2′-halogeno-5′-nitroacetanilides **11**–**17**

Compound (Formula)	Yield (%)	Mp/°C[a] (Solvent)	Found (%) (Required) C	H	N
11	95[b]	124–126	46.9	4.6	16.1
($C_{10}H_{12}ClN_3O_3$)	90[c]	(EtOH)	(46.6)	(4.7)	(16.3)
12	78	106–107	51.1	5.1	15.0
($C_{12}H_{14}ClN_3O_3$)		(EtOH)	(50.8)	(5.0)	(14.8)
13	96	154–156	52.4	5.5	14.25
($C_{13}H_{16}ClN_3O_3$)		(EtOH)	(52.4)	(5.4)	(14.1)
14	96	108–109	54.2	5.9	13.6
($C_{14}H_{18}ClN_3O_3$)		(EtOH)	(53.9)	(5.8)	(13.5)
15	98	162–164	59.3	4.5	12.3
($C_{17}H_{16}ClN_3O_3$)		(PrOH)	(59.05)	(4.7)	(12.15)
16 × HBr	78	225–230	43.35	4.65	11.4
($C_{13}H_{16}FN_3O_3$ × HBr)		(MeOH)	(43.1)	(4.7)	(11.6)
17 × HBr	71	193–195	49.9	4.15	10.2
($C_{17}H_{16}FN_3O_3$ × HBr)		(EtOH)	(49.8)	(4.2)	(10.2)

[a] Decomp. [b] For isolation method a), see Experimental section. [c] For isolation method b), see Experimental section.

Table 2 Half-lifes ($t_{1/2}$) of substituted acetanilides **11**, **54**, **58** and **61** and quinoxalinium chlorides **23**, **28** and **64** (30 mM) in different refluxing solvents

Compound	Ethanol (bp 78 °C)	Nitromethane (bp 101 °C)	Acetone (bp 56 °C)
11	10.7 h	4.6 h	–
54	1.8 h	32 min	–
58	6 min	–	30 min
61	7 min	–	1.0 h
23	4.5 h	23 min	–
28	2.0 h	<5 min	16.0 h
64	2.6 days	–	–

Results and discussion

Path *a*, based on an intramolecular aromatic nucleophilic substitution usually requires, as commented above, the presence of electron-withdrawing activated halogen atoms in the ring such as those of 2-dialkylamino-2′-halogeno-5′-nitroacetanilides **11**–**22** (Scheme 3). Related reactions seem to be very scarce. We have only found one example in the literature, that is, the unexpected (for the authors) low yield cyclization of 2′-bromoglycinanilides to 3,4-dihydro-1*H*-quinoxalin-2-ones reported by Ban and coworkers,[9] based on the nucleophilic substitution of the 2′-halogen atom by the NH–Bn or NH–Me group of the *N*-substituted glycine moiety. In our case, the starting materials were anilines **5**–**7**, which were treated with chloroacetyl chloride to yield the corresponding 2-chloroacetanilides **8**–**10** in good yield. The behaviour of these compounds towards dimethylamine and cyclic secondary amines, as well as the reactivity of the resulting acetanilides **11**–**22** seems to be very dependent on the substitution pattern. In the case of 2,2′-dichloroacetanilide **8** and 2-chloro-2′-fluoroacetanilide **9**, selective replacement of the halogen atom at position 2 yields directly the desired intermediates, isolated as free bases (**11**–**15**) or as hydrobromides (**16** and **17**) (Scheme 3, Table 1).

The reactivity of 2′-chloro-2-(dialkylamino)acetanilides **11**–**15** was studied in detail using the 2-dimethylamino derivative **11** as a model compound, its behaviour in different refluxing solvents being followed by ^{1}H NMR. According to the half-lifes reported in Table 2, it was found that the cyclization of anilide **11** to quinoxalinium chloride **23** proceeds rather slowly, while the decomposition of the latter to quinoxalinone **33** through a methyl chloride elimination seems to be easier and, thus, salt **23** does not accumulate. Working in refluxing ethanol or nitromethane 76% and 91% yields of **33** were achieved, respectively, and the maximum amounts of salt **23** detected in the reaction mixtures were 12% and *ca.* 2%, reached after 6 h and 1 h of reflux, respectively. As a by-product, we have also isolated from the cyclization of acetanilide **11** the quaternary derivative **39**. Anilide **11** can probably be quaternized to **39** by salt **23**; in fact, the alkylating ability of related 1,1-disubstituted indazolinone-derived amine imides[14] and other quaternary ammonium salts has been previously reported.[30]

Similar results were obtained from the ^{1}H NMR cyclization studies carried out with acetanilides **12**–**15**; under the conditions required for their cyclization the intermediate spiro quaternary salts **24**–**27** decomposed following the alkyl chloride elimination pattern previously observed in indazolinium[20] and anilinium[11] quaternary salts, *etc.* Thus, compounds **12**–**15** could conveniently be converted into the previously unknown 4-(ω-chloroalkyl)quinoxalin-2-ones **34**–**37** by reflux in nitromethane (Scheme 3, Table 3). In the cyclization of tetrahydroisoquinoline-derived anilide **15** only the product **37**, arising from the decomposition of intermediate salt **27** through a "benzyl chloride" (*vs.* "phenethyl chloride") elimination could be isolated, as previously observed[20] for related indazolinium salts.

On the other hand, 2-dialkylamino-2′-fluoroacetanilides **16** and **17** are more reactive than the corresponding 2′-chloro analogues **13** and **15**. After a short reflux in ethanol, piperidine-derived anilide **16** cyclized to a quinoxalinium salt, probably the fluoride (^{1}H NMR); nevertheless, owing to characterization problems, this salt was converted into the corresponding chloride **25** by treatment with hydrochloric acid. Under the same conditions, tetrahydroisoquinoline-derived anilide **17** cyclized initially to the corresponding quaternary salt (**27**), but the latter was quickly decomposed by ethanol (^{1}H NMR) yielding 2′-(ethoxymethyl)phenethyl derivative **38** as the final product of reaction.

Following path *a*, 2,2′-dichloro-*N*-methylacetanilide **10** also reacts selectively at room temperature with dimethylamine and cyclic secondary amines to afford the corresponding 2-dialkylamino derivatives **18**–**22**, easily detected by TLC. Nevertheless, the *N*-methyl group of the latter seems to enhance remarkably the reactivity of the 2′-chlorine atom, and thus

Table 3 Yields, mps and analytical data of 3,4-dihydro-1*H*-quinoxalin-2-ones **33**–**38** and **67**–**71**

Compound (formula)	Yield[a] (%)	Mp/°C (Solvent)	Found (%) (Required) C	H	N
33	91 (**11**)[b]	262–264[c]	52.35	4.6	20.45
($C_9H_9N_3O_3$)	98 (**54**)	(C_5H_5N–H_2O)	(52.2)	(4.4)	(20.3)
	95 (**23**)				
34	82 (**12**)	158–161[c]	50.95	5.1	15.0
($C_{12}H_{14}ClN_3O_3$)		($MeNO_2$)	(50.8)	(5.0)	(14.8)
35	85 (**13**)	174–176[c]	52.2	5.4	13.9
($C_{13}H_{16}ClN_3O_3$)	91 (**55**)	($MeNO_2$)	(52.4)	(5.4)	(14.1)
	93 (**25**)				
36	82 (**14**)	164–166[c]	53.7	6.0	13.2
($C_{14}H_{18}ClN_3O_3$)	90 (**56**)	($MeNO_2$)	(53.9)	(5.8)	(13.5)
37	70 (**15**)	215–217[c]	58.9	4.7	12.0
($C_{17}H_{16}ClN_3O_3$)	84 (**57**)	($PhNO_2$)	(59.05)	(4.7)	(12.15)
38	65 (**17**)	171–173[c]	64.0	5.8	11.6
($C_{19}H_{21}N_3O_4$)	75 (**57**)	(Pr^iOH)	(64.2)	(6.0)	(11.8)
67	81 (**28**)	165–168[c]	54.3	5.2	18.9
($C_{10}H_{11}N_3O_3$)	80 (**58**)	(EtOH)	(54.3)	(5.0)	(19.0)
68	79 (**29**)	121–123	52.7	5.65	14.3
($C_{13}H_{16}ClN_3O_3$)		(EtOH)	(52.4)	(5.4)	(14.1)
69	85 (**30**)	117–119	53.9	6.0	13.5
($C_{14}H_{18}ClN_3O_3$)	86 (**59**)	(EtOH)	(53.9)	(5.8)	(13.5)
70	75 (**31**)	77–78	55.5	6.0	12.9
($C_{15}H_{20}ClN_3O_3$)		(EtOH)	(55.3)	(6.2)	(12.9)
71	81 (**32**)	194–197[c]	60.3	5.2	11.8
($C_{18}H_{18}ClN_3O_3$)		($MeNO_2$)	(60.1)	(5.0)	(11.7)

[a] Starting anilide or salt in brackets. [b] $MeNO_2$ as solvent; 76% yield from anilide **11** in EtOH. [c] Decomp.

Table 4 Yields, mps and analytical data of 3-oxo-1,2,3,4-tetrahydroquinoxalinium chlorides **23**, **25**, **26**, **28**–**32** and **64**–**66**

Compound (Formula)	Yield[a] (%)	mp/°C[b] (Solvent)	Found (%) (Required) C	H	N
23	68 (**54**)	250–255	46.9	4.4	16.2
($C_{10}H_{12}ClN_3O_3$)		(H_2O–acetone)	(46.6)	(4.7)	(16.3)
25	85 (**16**)	180–182	52.25	5.7	14.3
($C_{13}H_{16}ClN_3O_3$)	80 (**55**)	(EtOH)	(52.4)	(5.4)	(14.1)
26	12 (**56**)	170–172	54.2	6.1	13.5
($C_{14}H_{18}ClN_3O_3$)		(H_2O–acetone)	(53.9)	(5.8)	(13.5)
28	96 (**10**)	169–172	48.3	5.5	15.4
($C_{11}H_{14}ClN_3O_3$)	93 (**58**)	(H_2O–acetone)	(48.6)	(5.2)	(15.5)
29	90 (**10**)	107–109	48.1	6.2	12.9
($C_{13}H_{16}ClN_3O_3$)[c]		(H_2O–acetone)	(48.1)	(5.9)	(12.9)
30	94 (**10**)	161–163	51.2	6.3	13.0
($C_{14}H_{18}ClN_3O_3$)[d]	96 (**59**)	(H_2O–acetone)	(51.0)	(6.1)	(12.7)
31	79 (**10**)	127–129	52.2	6.7	12.2
($C_{15}H_{20}ClN_3O_3$)[d]		(H_2O–acetone)	(52.4)	(6.45)	(12.2)
32	77 (**10**)	180–183	59.8	4.8	11.6
($C_{18}H_{18}ClN_3O_3$)	88 (**60**)	(H_2O–acetone)	(60.1)	(5.0)	(11.7)
64	97 (**61**)	161–163	52.0	6.8	11.8
($C_{10}H_{13}ClN_2O$)[d]		(H_2O–acetone)	(52.1)	(6.55)	(12.1)
65	98 (**62**)	176–179	61.8	7.0	10.8
($C_{13}H_{17}ClN_2O$)		(H_2O–acetone)	(61.8)	(6.8)	(11.1)
66	94 (**63**)	167–169	63.0	7.0	10.6
($C_{14}H_{19}ClN_2O$)		(Pr^iOH)	(63.0)	(7.2)	(10.5)

[a] Starting anilide in brackets. [b] Decomp. [c] ×1.5 H_2O. [d] ×H_2O.

compounds **18**–**22** cyclize spontaneously in the reaction medium to afford directly the quinoxalinium chlorides **28**–**32** in good yield (Scheme 3, Table 4).

The second approach, path *b*, has been based on the intramolecular quaternization of 2-chloro-2′-(dialkylamino)acetanilides **54**–**63** (Scheme 4). Somewhat related processes, always involving hydrogen-containing nucleophilic groups, are the cyclization of *N*-(2-chloroethyl)- and *N*-chloroacetyl-*o*-phenylenediamines to 1,2,3,4-tetrahydroquinoxalines[31] and the corresponding 2-oxo derivatives,[22,27,32] respectively. In our case the starting materials were the substituted *o*-phenylenediamines **44**–**53**, which were in turn prepared from 2-fluoro-5-nitroanilines **6** and **40** and dimethylamine or cyclic secondary amines (**44**–**50**) or by reduction of *N,N*-dialkylamino-*o*-nitroanilines **41**–**43** (**51**–**53**). Attempts to prepare compound **44** from dimethylamine and 2-chloro-5-nitroaniline **5** failed owing to the low reactivity of the chlorine atom of the latter. Treatment of compounds **44**–**50** with chloroacetyl chloride in acetone afforded 2-chloro-2′-(dialkylamino)acetanilides **54**–**60**; similar treatment of **51**–**53** with the acid chloride in diethyl ether gave acetanilides **61**–**63**, which were isolated as the hydrochlorides (Scheme 4, Table 5).

As before, a ^{1}H NMR study (the half-lifes for 2′-dimethylamino derivatives **54**, **58** and **61** are gathered in Table 2) showed that 2-chloro-2′-(dialkylamino)acetanilides **54**–**57** are rather stable, but more reactive than the respective isomeric

Table 5 Yields, mps and analytical data of 2-chloro-2′-(dialkylamino)acetanilides **54**–**63**

Compound (Formula)	Yield (%)	Mp/°C[a] (Solvent)	Found (%) (Required) C	H	N
54	97	129–131	46.9	4.7	16.3
($C_{10}H_{12}ClN_3O_3$)		(EtOH)	(46.6)	(4.7)	(16.3)
55	98	120–122	52.4	5.4	14.1
($C_{13}H_{16}ClN_3O_3$)		(EtOH)	(52.4)	(5.4)	(14.1)
56	92	118–120	53.7	5.7	13.8
($C_{14}H_{18}ClN_3O_3$)		(EtOH)	(53.9)	(5.8)	(13.5)
57	87	201–203	58.9	4.8	12.45
($C_{17}H_{16}ClN_3O_3$)		($MeNO_2$)	(59.05)	(4.7)	(12.15)
58	77	[b]		[c]	
($C_{11}H_{14}ClN_3O_3$)					
59	89	105–107[d]		[c]	
($C_{14}H_{18}ClN_3O_3$)					
60	86	89–91[d]		[c]	
($C_{18}H_{18}ClN_3O_3$)					
61 × HCl	94	121–124	48.5	5.8	11.5
($C_{10}H_{13}ClN_2O$ × HCl)		(EtOH)	(48.2)	(5.7)	(11.2)
62 × HCl	95	138–141	54.15	6.4	9.9
($C_{13}H_{17}ClN_2O$ × HCl)		(EtOH)	(54.0)	(6.3)	(9.7)
63 × HCl	95	140–143	55.7	6.9	9.3
($C_{14}H_{19}ClN_2O$ × HCl)		(EtOH)	(55.45)	(6.65)	(9.2)

[a] Decomp. [b] See Experimental. [c] Recrystallization of these compounds gave extensive decomposition to quinoxaline derivatives; analyses of crude products (homogeneous by TLC) were not carried out. [d] Mp of crude products.

2′-chloro-2-(dialkylamino)acetanilides **11** and **13**–**15**. Nevertheless, anilides **58**–**63** are unstable decomposing quickly, even at room temperature, in the solid state or in solution, to the corresponding cyclic salts. Therefore, compounds **58**–**60** could only be partially characterized, and compounds **61**–**63** were characterized as the corresponding hydrochlorides. From the ^{1}H NMR study of the cyclization reactions, a careful selection of solvents and reaction times allowed us to prepare, except in the case of tetrahydroisoquinoline-derived anilide **57**, the corresponding 3-oxoquinoxalinium chlorides (**23**, **25**, **26**, **28**, **30**, **32** and **64**–**66**) in low (**26**: 12%) to almost quantitative yield (**65**: 98%) (Scheme 4, Table 4). The ^{1}H NMR study of the reactivity of anilide **57** in refluxing ethanol showed that this compound cyclized slowly to the quaternary salt **27** and that **27** decomposed quickly through the intermediate alkyl chloride **37**, into the ethoxy derivative **38** to give the final product of the reaction.

Finally, 2-chloro-2′-(dialkylamino)acetanilides **54**–**59** as well as salts **23**, **25**, **26** and **28**–**32** (prepared following paths *a* or *b*) refluxed in nitromethane, afforded directly the corresponding quinoxalinones **33**, **35**–**37** and **67**–**71** in good yield (Scheme 4, Table 3). Salts **64**–**66** are rather stable but, for instance, **64** could be conveniently converted into the corresponding quinoxalinone **72** by heating above the melting point. 3,4-Dihydro-1*H*-quinoxalin-2-ones are rather sensitive to atmospheric oxygen in solution, on chromatographic supports (TLC), and on heating, *etc.* This process has been previously observed[9] and the mechanism of oxidation of compound **72** to the corresponding quinoxaline-2,3-dione is well documented.[33]

The structure of all compounds has been established on the basis of analytical and spectral data. NMR spectra of anilides deserve some comments; compounds **8**, **9**, **11**–**17**, **54**–**57** and **61**–**63** give simple spectra and we assume that they appear in solution as the *Z*-rotamers usually found in 2′-substituted anilides, with strong hydrogen bonds between the NH group and the eventual heteroatoms in the *ortho* position.[34] Nevertheless, the energy differences between the *Z* and *E* rotamers of *N*-methyl substituted anilides **10** and **58**–**60** must be lower and some duplicated signals, belonging to both rotamers, can be observed in their NMR spectra. *Z*/*E* rotamers ratios are *ca.* 73 : 27 in $(CD_3)_2SO$ and *ca.* 95 : 5 in $CDCl_3$ as determined by integration of ^{1}H NMR spectra signals. Furthermore, $COCH_2$ protons of both rotamers of anilides **10** and **58**–**60** are diastereotopic (AB systems), while these protons are equivalent in the remaining anilides studied.

On the other hand, in spiro salts the quaternization of the nitrogen atom hinders the conformational equilibrium of pyrrolidine, piperidine, *etc.* moieties of these compounds and thus their anisochronic NCH_2 protons can be easily distinguished. Similar effects have been previously observed in related indoxyl-,[13] indazolinone-[14] and cinnolinone-derived[15] quaternary salts and betaines. In piperidine-derived salts **25**, **30** and **65**, equatorial (H_e) and axial (H_a) protons can be distinguished owing to the different coupling patterns; in other cases, however, the assignment of the signals of these protons is not easy and they have been mentioned in the description of spectra as H_A and H_B. The spectrum for the tetrahydroisoquinoline-derived salt **32** is especially complicated and the eight hydrogen atoms of the four methylene groups present in the molecule can be distinguished.

Currently, we are studying the reactivity of the obtained quinoxaline derivatives and related compounds, especially the stabilized ammonium ylides which are easily available from 3-oxoquinoxalinium chlorides.

In conclusion, we have developed two different simple and efficient methods of synthesis of quinoxaline derivatives starting respectively from 2-dialkylamino-2′-halogenoacetanilides or from 2′-dialkylamino-2-halogenoacetanilides. Both types of acetanilide cyclize initially to 1,1-disubstituted 3-oxoquinoxalinium salts through intramolecular quaternization reactions. These salts are converted by heating, sometimes without isolation, under the conditions required for the cyclization of the corresponding acetanilides, into 4-substituted quinoxalin-2-ones.

Experimental

Mps were determined in a Gallenkamp capillary apparatus. The mps of quinoxalinium chlorides and other salts as well as those of some acetanilides are not very well defined; these compounds decompose on heating and the observed mps are frequently heating-rate dependent and previous softening is usual. IR spectra were obtained on a Perkin Elmer Spectrum One spectrophotometer. ^{1}H (200 or 300 MHz) and ^{13}C (50 or 75 MHz) NMR spectra were recorded on a Varian Gemini-200 or on a Varian XL-300 spectrometer. The chemical shifts are

reported in ppm from TMS (δ scale) but were measured against the solvent signal. J values are given in Hz. The assignments have been performed by means of different standard homonuclear and heteronuclear correlation experiments. Electron impact (EI) and electrospray (ES) mass spectra were obtained at 70 eV on a Hewlett Packard 5973 MSD spectrometer or on a Hewlett Packard 1100 MSD spectrometer, respectively. DC-Alufolien silica gel 60 PF_{254} (Merck, layer thickness 0.2 mm) and silica gel 60 PF_{254} (Merck, 20 × 20 cm plates, layer thickness 2 mm) were used, respectively, for TLC and preparative TLC (PLC). Flash column chromatography was carried out on silica gel 60 (Merck, particle size 0.040–0.063 mm). Microanalyses were performed by the Departamento de Análisis, Centro de Química Orgánica "Manuel Lora Tamayo", CSIC, Madrid, Spain.

Kinetic measurements (Table 2) were carried out by refluxing the starting compounds (1.5 mmol) in the mentioned solvents (50 cm^3) (30 mM solutions). Aliquots (1 cm^3) were collected at different times, cooled and evaporated to dryness at room temperature, and the respective residues analyzed by ^1H NMR. The cyclization of acetanilides **11**, **54**, **58** and **61** (A) followed first-order kinetics, *i.e.*, plot of ln[A] against time was linear, and k and $t_{1/2}$ ($t_{1/2} = \ln 2/k$) could be obtained from the slope. On the other hand, we have not been able to determinate the reaction order for the decomposition of salts **23**, **28** and **64** (S) to the corresponding quinoxalinones (Q); plot of 1/[S] against time was not linear, and thus the reaction does not follow, as could be expected, a second-order kinetics (first-order in quinoxalinium cation and first-order in chloride anion). In these cases half-lifes ($t_{1/2}$) were calculated from plot of [S] and [Q] against time. For comparative purposes, the decomposition of all compounds was studied at the same concentration (30 mM); nevertheless, in the case of acetanilides, $t_{1/2}$ values do not depend on the starting concentrations of reactants while for quinoxalinium chlorides such a dependence probably exists.

Preparation of 2-halogeno-*N*-methyl-5-nitroanilines 7 and 40

These compounds were prepared by methylation of the *N*-tosyl derivatives of the commercially available anilines **5** and **6** followed by hydrolysis, according to the method of Leandri *et al.*[35] but using methyl iodide in potassium carbonate–acetone instead of dimethyl sulfate in aq. sodium hydroxide as methylating agent.

2-Chloro-*N*-methyl-5-nitroaniline (7). Yield: 83% (from **5**); mp 109–111 °C (Pr^iOH) (lit., 108–109 °C,[35] 110 °C[36]).

2-Fluoro-*N*-methyl-5-nitroaniline (40). Yield: 86% (from **7**); mp 95–97 °C (Pr^iOH) (lit., 89–90 °C[37]).

Preparation of 2-chloroacetanilides 8–10

A solution of chloroacetyl chloride (5.65 g, 50 mmol) in acetone (20 cm^3) was slowly added to another solution of the corresponding aniline (**5**, **6**, **7**) (40 mmol) in the same solvent (80 cm^3). The mixture was stirred for 1 h at room temperature (for **8** and **9**) or refluxed for 3 h and allowed to reach room temperature (for **10**), and then poured in cold water (400 cm^3). The resulting suspension was stirred for 30 min and the desired anilide [homogeneous material (TLC, ^1H NMR)] isolated by filtration. In the case of anilide **9**, extraction of the filtrate with chloroform afforded a significant additional amount of product.

2,2′-Dichloro-5′-nitroacetanilide (8). Yield: 9.66 g (97%); mp 130–131 °C (EtOH) (lit., 132 °C,[38] 125 °C[39]).

2-Chloro-2′-fluoro-5′-nitroacetanilide (9). Yield: 8.93 g (96%); mp 126–127 °C (EtOH) (Found: C, 41.1; H, 2.6; N, 11.9. Calc. for $C_8H_6ClFN_2O_3$: C, 41.3; H, 2.6; N, 12.0%); ν_{max}(Nujol)/cm^{-1} 3309 and 3267 (NH), 1696 and 1680 (CO), 1551 and 1350; $\delta_H[(CD_3)_2SO]$ 10.54 (1 H, br s, NH), 8.94 (1 H, dd, $J_{H,H}$ 3, $J_{F,H}$ 7, 6′-H), 8.08 (1 H, m, 4′-H), 7.60 (1 H, dd, $J_{H,H}$ 9, $J_{F,H}$ 10, 3′-H) and 4.42 (2 H, s, 2-H); $\delta_C[(CD_3)_2SO]$ 165.88 (s, CO), 156.39 (d, $J_{C,F}$ 256, C-2′), 143.68 (d, $J_{C,F}$ 3, C-5′), 126.78 (d, $J_{C,F}$ 13, C-1′), 120.82 (d, $J_{C,F}$ 10, C-4′), 117.99 (d, $J_{C,F}$ 4, C-6′), 116.67 (d, $J_{C,F}$ 22, C-3′) and 43.10 (s, C-2); *m*/*z* (EI) 232 (M^+, 20%), 213 (1), 197 (1), 186 (1), 183 (4), 169 (3), 156 (100), 123 (9), 110 (27) and 98 (13).

2,2′-Dichloro-*N*-methyl-5′-nitroacetanilide (10). Yield: 9.79 g (93%); mp 81–83 °C (Pr^i_2O) (Found: C, 41.3; H, 3.3; N, 10.8. Calc. for $C_9H_8Cl_2N_2O_3$: C, 41.1; H, 3.1; N, 10.65%); ν_{max}(Nujol)/cm^{-1} 1694 (CO), 1519 and 1352; $\delta_H[(CD_3)_2SO]$ 8.56 (1 H, d, J 2.5, 6′-H, *Z* and *E* rot.), 8.30 (*Z* rot.) and 8.21 (*E* rot.) (1 H, both dd, J 2.5 and 9, 4′-H), 7.95 (*Z* rot.) and 7.88 (*E* rot.) (1 H, both d, J 9, 3′-H), 4.77 (2-H_A) and 4.57 (2-H_B) (both br d, J (−)14, *E* rot.) and 4.09 (2-H_A) and 3.90 (2-H_B) (both d, J (−) 14, *Z* rot.) (2 H) and 3.31 (*E* rot.) and 3.14 (*Z* rot.) (3 H, both s, CH_3) (*Z*/*E* rotamers ratio 71 : 29); $\delta_C[(CD_3)_2SO]$ 166.51 (*E* rot.) and 165.30 (*Z* rot.) (CO), 147.15 (*Z* rot.) and 146.80 (*E* rot.) (C-5′), 141.85 (*E* rot.) and 139.39 (*Z* rot.) (C-2′), 139.89 (*Z* rot.) and 138.90 (*E* rot.) (C-1′), 131.73 (*Z* rot.) and 131.20 (*E* rot.) (C-3′), 126.06 (*Z* rot.) and 124.96 (*E* rot.) (C-4′), 125.17 (*Z* rot.) and 123.95 (*E* rot.) (C-6′), 42.53 (*E* rot.) and 42.26 (*Z* rot.) (C-2) and 37.29 (*E* rot.) and 36.02 (*Z* rot.) (CH_3); *m*/*z* (EI) 262 (M^+, 0.2%), 227 (M^+ − Cl, 100), 213 (7), 186 (17), 181 (17), 140 (21), 104 (18) and 77 (28).

Preparation of 2-dialkylamino-2′-halogeno-5′-nitroacetanilides (11–17)

For 2′-chloro-2-dimethylamino derivative **11**, commercial 5.6 M dimethylamine in ethanol (4.46 cm^3) (1.13 g, 25 mmol of dimethylamine) was added to a solution of chloroacetanilide **8** (2.49 g, 10 mmol) in THF (30 cm^3) and the mixture was heated at 60–65 °C in an autoclave for 4 h. After cooling, the resulting solution was evaporated to dryness, and then water (50 cm^3) was added and the precipitated solid (2.48 g) collected by filtration. ^1H NMR analysis of the product showed that it was a mixture of the desired compound **11** and 4-methylquinoxalinone **33** in 98 : 2 molar ratio. Anilide **11** could not be purified by recrystallization and thus the mixture was separated by chromatography (a) or by selective extraction (b):

a) Column chromatography of the mixture using $CHCl_3$ as eluent afforded, following the elution order, anilide **11** (see yield in Table 1) and then quinoxalinone **33** (40 mg, 2% yield).

b) The obtained mixture was suspended in $CHCl_3$ (100 cm^3) and most of the insoluble quinoxalinone **33** (30 mg, 1.5%) was removed by filtration. The solution was then extracted with 10% aq. HCl (3 × 100 cm^3) and the resulting acidic layer neutralized with solid $NaHCO_3$. The precipitated solid was extracted with $CHCl_3$ (3 × 50 cm^3) and the solution was dried ($MgSO_4$) and evaporated to afford the desired anilide **11**.

For 2′-chloroacetanilides **12–15**, a solution of anilide **8** (2.49 g, 10 mmol) and 20 mmol of the corresponding cyclic secondary amine (pyrrolidine, piperidine, homopiperidine or 1,2,3,4-tetrahydroisoquinoline) in THF (100 cm^3) was refluxed until the reaction was complete (TLC, 6–12 h). The reaction was then cooled and the precipitated secondary amine hydrochloride separated by filtration. Evaporation of solvent, addition of water (100 cm^3) and trituration gave the desired products which were collected by filtration. Compounds **13–15** were shown to be homogeneous (TLC, ^1H NMR), but ^1H NMR analysis of crude compound **12** showed that it was a mixture of the desired compound and quinoxalinone **34** (98 : 2 molar ratio), which was removed by recrystallization from ethanol.

For 2′-fluoroacetanilides **16** and **17**, a solution of anilide **9** (2.33 g, 10 mmol) and the corresponding secondary amine

(piperidine or 1,2,3,4-tetrahydroisoquinoline, 20 mmol) in THF (50 cm^3) was stirred at rt for 24 h. The separated secondary amine hydrochloride was removed by filtration and commercial 33% HBr in AcOH (4 cm^3) was added to the filtrate. The precipitated anilide hydrobromide was collected by filtration, washed with THF (10 cm^3) and air-dried (homogeneous material, ^{1}H NMR).

The unstable free bases were prepared as follows: a mixture of the corresponding anilide hydrobromide (**16** × HBr or **17** × HBr, 2 mmol) and a solution of potassium carbonate (0.35 g, 2.5 mmol) in water (20 cm^3) was well triturated and the resulting suspension was stirred for 10 min. The solid free anilides were collected by filtration, washed with water and air-dried.

Yields, mps and analytical data of anilides **11**–**17** are gathered in Table 1.

2′-Chloro-2-dimethylamino-5′-nitroacetanilide (11). ν_{max}(Nujol)/cm^{-1} 3195br and 3123 (NH), 1691 (CO), 1534, 1514 and 1344; δ_H[$(CD_3)_2SO$] 10.03 (1 H, br s, NH), 9.06 (1 H, d, *J* 2.5, 6′-H), 7.97 (1 H, dd, *J* 2.5 and 9, 4′-H), 7.82 (1 H, d, *J* 9, 3′-H), 3.17 (2 H, s, 2-H) and 2.35 (6 H, s, $N[CH_3]_2$); δ_C[$(CD_3)_2SO$] 169.29 (CO), 146.40 (C-5′), 135.18 (C-1′), 130.28 (C-3′), 129.38 (C-2′), 119.20 (C-4′), 115.34 (C-6′), 62.77 (C-2) and 45.40 ($N[CH_3]_2$); *m*/*z* (EI) 257 (M^+, 0.3%), 199 (0.3), 196 (0.3), 185 (0.5), 171 (1), 139 (1), 125 (1), 110 (1), 90 (3), 63 (4) and 58 (100).

2′-Chloro-5′-nitro-2-pyrrolidinoacetanilide (12). δ_H[$(CD_3)_2SO$] 10.15 (1 H, br s, NH), 9.09 (1 H, d, *J* 3, 6′-H), 7.98 (1 H, dd, *J* 3 and 9, 4′-H), 7.83 (1 H, d, *J* 9, 3′-H), 3.37 (2 H, s, 2-H), 2.67 (4 H, m, 2″-, 5″-H) and 1.78 (4 H, m, 3″-, 4″-H); δ_C[$(CD_3)_2SO$] 169.48 (CO), 146.42 (C-5′), 135.18 (C-1′), 130.24 (C-3′), 129.03 (C-2′), 119.02 (C-4′), 114.80 (C-6′), 58.54 (C-2), 53.65 (C-2″, -5″) and 23.60 (C-3″, -4″); *m*/*z* (EI) 283 (M^+, 0.1%), 199 (0.2), 171 (0.6), 149 (0.4), 140 (0.5), 125 (0.7), 110 (1), 90 (2) and 84 (100).

2′-Chloro-5′-nitro-2-piperidinoacetanilide (13). ν_{max}(Nujol)/cm^{-1} 3160br and 3117 (NH), 1698 (CO), 1530, 1508 and 1346; δ_H[$(CD_3)_2SO$] 10.31 (1 H, br s, NH), 9.20 (1 H, d, *J* 3, 6′-H), 7.98 (1 H, dd, *J* 3 and 9, 4′-H), 7.84 (1 H, d, *J* 9, 3′-H), 3.18 (2 H, s, 2-H), 2.52 (4 H, m, 2″-, 6″-H), 1.59 (4 H, m, 3″-, 5″-H) and 1.44 (2 H, m, 4″-H); δ_C[$(CD_3)_2SO$] 169.54 (CO), 146.56 (C-5′), 135.23 (C-1′), 130.34 (C-3′), 128.51 (C-2′), 118.99 (C-4′), 114.29 (C-6′), 61.85 (C-2), 54.03 (C-2″, -6″), 25.89 (C-3″, -5″) and 23.18 (C-4″); *m*/*z* (EI) 297 (M^+, 0.4%), 296 (0.6), 232 (0.2), 199 (0.5), 185 (0.6), 171 (1.5), 139 (1), 125 (2), 110 (2), 98 (100) and 84 (14).

2-(1-Azepanyl)-2′-chloro-5′-nitroacetanilide (14). δ_H[$(CD_3)_2SO$] 10.26 (1 H, br s, NH), 9.21 (1 H, d, *J* 3, 6′-H), 7.95 (1 H, dd, *J* 3 and 9, 4′-H), 7.81 (1 H, d, *J* 9, 3′-H), 3.34 (2 H, s, 2-H), 2.73 (4 H, m, 2″-, 7″-H) and 1.62 (8 H, m, 3″-, 4″-, 5″-, 6″-H); δ_C[$(CD_3)_2SO$] 170.14 (CO), 146.58 (C-5′), 135.29 (C-1′), 130.37 (C-3′), 128.31 (C-2′), 118.95 (C-4′), 114.31 (C-6′), 62.47 (C-2), 56.12 (C-2″, -7″), 28.13 (C-3″, -6″) and 26.18 (C-4″, -5″); *m*/*z* (ES+) 645 (2M + Na^+, 30%), 334 (M + Na^+, 19) and 312 (MH^+, 100).

2′-Chloro-5′-nitro-2-[2-(1,2,3,4-tetrahydroisoquinolyl)]acetanilide (15). δ_H[$(CD_3)_2SO$] 10.13 (1 H, br s, NH), 9.11 (1 H, d, *J* 3, 6′-H), 7.96 (1 H, dd, *J* 3 and 9, 4′-H), 7.78 (1 H, d, *J* 9, 3′-H), 7.10 (4 H, m, 5″-, 6″-, 7″-, 8″-H), 3.80 (2 H, s, 1″-H), 3.42 (2 H, s, 2-H) and 2.89 (4 H, m, 3″-, 4″-H); δ_C[$(CD_3)_2SO$] 169.33 (CO), 146.52 (C-5′), 135.28 (C-1′), 134.12, 133.49 (C-4a″, -8a″), 130.42 (C-3′), 129.39 (C-2′), 128.59, 126.35, 126.21, 125.66 (C-5″, -6″, -7″, -8″), 119.42 (C-4′), 115.47 (C-6′), 60.94 (C-2), 55.07 (C-1″), 50.56 (C-3″) and 26.82 (C-4″); *m*/*z* (EI) 345 (M^+, 1%), 344 (2), 297 (1), 171 (3), 146 (100), 132 (95), 117 (38), 104 (15) and 91 (21).

2′-Fluoro-5′-nitro-2-piperidinoacetanilide hydrobromide (16 × HBr). ν_{max}(Nujol)/cm^{-1} 3224 and 3126 (NH), 2654br (structured band, HN^+), 1719 (CO), 1554, 1454 and 1349; δ_H[$(CD_3)_2SO$] 10.88 (1 H, br s, CONH), 9.72 (1 H, br s, NH^+), 8.94 (1 H, dd, $J_{H,H}$ 3, $J_{F,H}$ 7, 6′-H), 8.12 (1 H, m, 4′-H), 7.64 (1 H, dd, $J_{H,H}$ 9, $J_{F,H}$ 9, 3′-H), 4.23 (2 H, s, 2-H), 3.49 (2 H, m) and 3.02 (2 H, m) (2″-, 6″-H) and 1.95–1.20 (6 H, m, 3″-, 4″-, 5″-H); δ_C[$(CD_3)_2SO$] 164.35 (s, CO), 156.68 (d, $J_{C,F}$ 257, C-2′), 143.68 (d, $J_{C,F}$ 2, C-5′), 126.06 (d, $J_{C,F}$ 13, C-1′), 121.58 (d, $J_{C,F}$ 9.5, C-4′), 118.61 (d, $J_{C,F}$ 3.5, C-6′), 117.12 (d, $J_{C,F}$ 22, C-3′), 56.93 (s, C-2), 53.07 (s, C-2″, -6″), 22.22 (s, C-3″, -5″) and 21.04 (s, C-4″). Free base **16**: yield 0.52 g (92%) (from **16** × HBr); mp 100–102 °C (decomp.) (crude material, pure by TLC); ν_{max}(Nujol)/cm^{-1} 3224br and 3126 (NH), 1693 (CO), 1539, 1519 and 1349; δ_H[$(CD_3)_2SO$] 3.23 (2 H, s, 2-H), 2.55 (4 H, m, 2″-, 6″-H) and 1.70–1.30 (6 H, m, 3″-, 4″-, 5″-H); *m*/*z* (EI) 281 (M^+, 0.3%), 280 (0.7), 263 (0.6), 248 (1.3), 169 (0.6), 155 (1.6), 123 (1.5), 109 (3.5), 98 (100) and 84 (10).

2′-Fluoro-5′-nitro-2-[2-(1,2,3,4-tetrahydroisoquinolyl)]acetanilide hydrobromide (17 × HBr). δ_H[$(CD_3)_2SO$] 10.95 (1 H, br s, CONH), 10.60 (1 H, br s, NH^+), 8.98 (1 H, dd, $J_{H,H}$ 3, $J_{F,H}$ 7, 6′-H), 8.12 (1 H, m, 4′-H), 7.64 (1 H, dd, $J_{H,H}$ 9, $J_{F,H}$ 10, 3′-H), 7.26 (4 H, m, 5″-, 6″-, 7″-, 8″-H), 4.60 (2 H, s, 1″-H), 4.49 (2 H, s, 2-H), 3.68 (2 H, br s, 3″-H) and 3.13 (2 H, br s, 4″-H); δ_C[$(CD_3)_2SO$] 164.32 (s, CO), 156.57 (d, $J_{C,F}$ 257, C-2′), 143.68 (d, $J_{C,F}$ 2.5, C-5′), 131.11 (s), 128.13 (s), 126.71 (s, two superimposed signals) (C-5″, -6″, -7″, -8″), 128.60 (s), 127.78 (s) (C-4a″, -8a″), 126.13 (d, $J_{C,F}$ 14, C-1′), 121.49 (d, $J_{C,F}$ 9.5, C-4′), 118.50 (d, $J_{C,F}$ 3.5, C-6′), 117.09 (d, $J_{C,F}$ 22, C-3′), 55.92 (s, C-2), 52.83 (s), 49.73 (s) (C-1″, -3″) and 24.65 (s, C-4″). Free base **17**: yield 0.61 g (93%) (from **17** × HBr); mp 148–150 °C (decomp.) (crude material, pure by TLC); δ_H[$(CD_3)_2SO$] 3.78 (2 H, s, 1″-H), 3.44 (2 H, s, 2-H) and 2.86 (4 H, br s, 3″-, 4″-H); *m*/*z* (EI) 329 (M^+, 0.3%), 328 (0.7), 281 (0.3), 179 (0.4), 155 (1.2), 146 (100), 132 (78), 117 (24), 104 (8) and 91 (11).

Preparation of 2-(dialkylamino)anilines 44–53

Nitro derivatives **44**–**50** were prepared from 2-fluoro-5-nitroanilines **6** and **40** and the corresponding secondary amines. For dimethylamino derivatives **44** and **48**, a mixture of the required 2-fluoroaniline (**6** or **40**, 40 mmol) and 5.6 M dimethylamine in ethanol (60 cm^3, excess) was allowed to stand at room temperature; the reactions were complete (TLC) after 20 and 10 days, respectively. In the case of **44**, the solid obtained after evaporation of solvent, addition of water (100 cm^3) and trituration was collected by filtration; in the case of **48**, the solvent was evaporated to dryness and, after addition of 50 cm^3 of water, the mixture was extracted with $CHCl_3$ (3 × 50 cm^3). The organic layer was separated, dried ($MgSO_4$) and evaporated yielding the desired compound as a homogeneous (TLC, ^{1}H NMR) orange oil which was used without further purification. The reactivity of 2-chloro-5-nitroaniline **5** towards dimethylamine is very low. Under the conditions mentioned for the 2-fluoro analogue **6**, there is no reaction at all after 20 days and, when the reaction mixture is heated in an autoclave at 100 °C for 3 days, only 12% of conversion into **44** is achieved as determined by ^{1}H NMR.

For compounds **45**–**47** and **49**, **50**, derived from cyclic secondary amines, a mixture of the corresponding 2-fluoroaniline (**6** or **40**, 40 mmol) and the required amine (piperidine, homopiperidine or 1,2,3,4-tetrahydroisoquinoline, 85 mmol) was heated at 110–120 °C during 3–6 h, until consumption (TLC) of the starting aniline. The reaction was then cooled and, after addition of water (100 cm^3), the pH was adjusted to 6 by addition of acetic acid. The precipitated solid (or oil which solidifies) (homogeneous products: TLC, ^{1}H NMR) was isolated by filtration and washed with diluted acetic acid and water.

Compounds **51**–**53**, without the 5-NO_2 group, were prepared by hydrogenation [H_2 (15 psi), Pd/C, EtOH] of the known 2-nitrophenyl derivatives of dimethylamine (**41**),[40] piperidine (**42**)[41] and homopiperidine (**43**).[42] The corresponding 2-(dialkylamino)anilines **51**–**53**, obtained in almost quantitative yield, are air-sensitive and were used immediately in the further chloroacetylation step without purification.

2-Dimethylamino-5-nitroaniline (44). Yield: 7.17 g (99%); mp 59–60 °C (cyclohexane) (lit., 62 °C,[43] 60–61 °C[44]).

5-Nitro-2-piperidinoaniline (45). Yield: 8.76 g (99%); mp 82–83 °C (cyclohexane) (lit., 96 °C,[42,43] 83 °C[45]).

2-(1-Azepanyl)-5-nitroaniline (46). Yield: 9.22 g (98%); mp 65.5–66.5 °C (cyclohexane) (lit., 67–68.5 °C,[42] 67 °C[43]).

5-Nitro-2-[2-(1,2,3,4-tetrahydroisoquinolyl)]aniline (47). Yield: 10.66 g (99%); mp 132–134 °C (EtOH) (Found: C, 66.75; H, 5.9; N, 15.8. Calc. for $C_{15}H_{15}N_3O_2$: C, 66.9; H, 5.6; N, 15.6%); ν_{max}(Nujol)/cm^{-1} 3456 and 3364 (NH_2), 1619, 1502 and 1329; δ_H[$(CD_3)_2SO$] 7.58 (1 H, d, *J* 3, 6-H), 7.46 (1 H, dd, *J* 9 and 3, 4-H), 7.15 (4 H, m, 5′-, 6′-, 7′-, 8′-H), 7.07 (1 H, d, *J* 9, 3-H), 5.35 (2 H, br s, NH_2), 4.16 (2 H, s, 1′-H), 3.23 (2 H, t, *J* 6, 3′-H) and 2.97 (2 H, t, *J* 6, 4′-H); δ_C[$(CD_3)_2SO$] 144.30, 143.20, 142.79 (C-1, -2, -5), 134.31, 133.99 (C-4a′, -8a′), 128.69, 126.38, 126.28, 125.67 (C-5′, -6′, -7′, -8′), 118.67 (C-3), 112.25 (C-4), 108.33 (C-6), 51.87 (C-1′), 47.38 (C-3′) and 28.61 (C-4′); *m*/*z* (EI) 269 (M^+, 91%), 251 (11), 222 (18), 205 (6), 164 (30), 153 (15), 132 (38), 117 (100), 104 (94) and 91 (19).

2-Dimethylamino-*N*-methyl-5-nitroaniline (48). Yield: 7.65 g (98%); homogeneous (TLC, ^{1}H and ^{13}C NMR) orange oil. ν_{max}(film)/cm^{-1} 3381 (NH), 1610, 1582, 1520 and 1334; δ_H[$(CD_3)_2SO$] 7.47 (1 H, dd, *J* 2.5 and 8.5, 4-H), 7.16 (1H, d, *J* 2.5, 6-H), 6.98 (1 H, d, *J* 8.5, 3-H), 5.52 (1 H, br q, *J* 5, NH), 2.77 (3 H, d, *J* 5, NHC*H*$_3$) and 2.66 (6 H, s, N[CH_3]$_2$); δ_C[$(CD_3)_2SO$] 146.35, 143.49, 143.28 (C-1, -2, -5), 117.35 (C-3), 111.79 (C-4), 102.32 (C-6), 42.15 (N[CH_3]$_2$) and 30.06 ($NHCH_3$); *m*/*z* (EI) 195 (M^+, 100%), 180 (41), 164 (34), 149 (11), 133 (32), 119 (25), 108 (23) and 92 (25).

***N*-Methyl-5-nitro-2-piperidinoaniline (49).** Yield: 9.22 g (98%); mp 100–101 °C (*n*-hexane) (Found: C, 61.3; H, 7.4; N, 17.8. Calc. for $C_{12}H_{17}N_3O_2$: C, 61.3; H, 7.3; N, 17.9%); ν_{max}(Nujol)/cm^{-1} 3379 and 3364 (NH), 1575, 1517, 1499, 1331 and 1315; δ_H[$(CD_3)_2SO$] 7.49 (1 H, dd, *J* 3 and 9, 4-H), 7.18 (1 H, d, *J* 3, 6-H), 7.01 (1 H, d, *J* 9, 3-H), 5.29 (1 H, br q, *J* 5, NH), 2.80 (7 H, m, CH_3 and 2′-, 6′-H) and 1.78–1.45 (6 H, m, 3′-, 4′-, 5′-H); δ_C[$(CD_3)_2SO$] 146.09, 143.85, 143.69 (C-1, -2, -5), 118.08 (C-3), 111.83 (C-4), 102.37 (C-6), 51.30 (C-2′, -6′), 30.14 (CH_3), 25.60 (C-3′, -5′) and 23.78 (C-4′); *m*/*z* (EI) 235 (M^+, 100%), 220 (10), 203 (7), 189 (11), 178 (67), 167 (20), 132 (69), 118 (21), 104 (18) and 91 (14).

***N*-Methyl-5-nitro-2-[2-(1,2,3,4-tetrahydroisoquinolyl)]aniline (50).** Yield: 11.22 g (99%); mp 116–117 °C (EtOH) (Found: C, 67.55; H, 6.2; N, 15.1. Calc. for $C_{16}H_{17}N_3O_2$: C, 67.8; H, 6.05; N, 14.8%); δ_H[$(CD_3)_2SO$] 7.52 (1 H, dd, *J* 3 and 9, 4-H), 7.23 (1 H, d, *J* 3, 6-H), 7.16 (4 H, m, 5′-, 6′-, 7′-, 8′-H), 7.11 (1 H, d, *J* 9, 3-H), 5.51 (1 H, br q, *J* 5, NH), 4.13 (2 H, s, 1′-H), 3.20 (2 H, t, *J* 6, 3′-H), 2.98 (2 H, t, *J* 6, 4′-H) and 2.79 (3 H, d, *J* 5, CH_3); δ_C[$(CD_3)_2SO$] 144.88, 144.09, 144.01 (C-1, -2, -5), 134.36, 134.00 (C-4a′, -8a′), 128.66, 126.39, 126.30, 125.67 (C-5′, -6′, -7′, -8′), 118.55 (C-3), 111.81 (C-4), 102.63 (C-6), 52.21 (C-1′), 48.06 (C-3′), 30.18 (CH_3) and 28.57 (C-4′); *m*/*z* (EI) 283 (M^+, 65%), 268 (14), 251 (16), 222 (6), 205 (10), 178 (53), 167 (14), 132 (80), 117 (100), 104 (60) and 91(23).

Preparation of 2-chloro-2′-(dialkylamino)acetanilides 54–63

5′-Nitro derivatives **54**–**60** were obtained by treatment of the corresponding 2-dialkylamino-5-nitroanilines **44**–**50** (40 mmol) in acetone with chloroacetyl chloride (5.65 g, 50 mmol), following the method described above for the preparation of 2-chloroacetanilides **8** and **9**. The reaction mixtures were stirred at room temperature for 1 h (for **54**–**57**) or for 15 min (for **58**–**60**). Tetrahydroisoquinoline-derived anilide **57** is very insoluble in acetone; it precipitated in the reaction medium and was directly isolated by filtration. *N*-Methyl substituted anilides **58**–**60** are very reactive; recrystallization of these compounds gave extensive decomposition to the corresponding quinoxalinium salts **28**, **30** and **32**, and attempts to prepare the corresponding hydrochlorides failed.

For the preparation of anilides **61**–**63**, chloroacetyl chloride (1.36 g, 12 mmol) in diethyl ether (10 cm^3) was added dropwise at room temperature over a solution of the corresponding 2-(dialkylamino)aniline (**51**–**53**, 10 mmol) in 100 cm^3 of the same solvent, and the resulting suspension was stirred overnight. The precipitated solids, hygroscopic in some cases, collected by filtration and dried under vacuum over P_2O_5, were shown to be the hydrochlorides of the desired anilides (**61**–**63** × HCl). These salts are stable enough to be recrystallized and characterized, but they cyclize quickly in $(CD_3)_2SO$ solution, the NMR signals of the corresponding salts **64**–**66** appearing almost immediately.

Free anilides **61**–**63** were prepared as follows: 8 mmol of the corresponding anilide hydrochloride (**61**–**63** × HCl) was suspended in 2% aq. $NaHCO_3$ (40 cm^3), the mixture was then stirred for 5 min and the insoluble material recovered by filtration. Compounds **61**–**63**, as free bases, could not be recrystallized; they decomposed very quickly in the solid state or in solution yielding quinoxalinium salts **64**–**66**. Yields, mps and analytical data of anilides **54**–**63** are given in Table 5.

2-Chloro-2′-dimethylamino-5′-nitroacetanilide (54). ν_{max}(Nujol)/cm^{-1} 3375 (NH), 1678 (CO), 1594, 1534 and 1332; δ_H[$(CD_3)_2SO$] 9.86 (1 H, br s, NH), 8.45 (1 H, d, *J* 2, 6′-H), 7.97 (1 H, dd, *J* 2 and 9, 4′-H), 7.14 (1 H, d, *J* 9, 3′-H), 4.38 (2 H, s, 2-H) and 2.83 (6 H, s, N[CH_3]$_2$); δ_C[$(CD_3)_2SO$] 165.24 (CO), 151.74 (C-2′), 139.73 (C-5′), 127.75 (C-1′), 121.40 (C-4′), 120.14 (C-6′), 117.75 (C-3′), 43.20 (C-2) and 42.33 (N[CH_3]$_2$); *m*/*z* (EI) 257 (M^+, 52%), 220 (65), 208 (69), 193 (29), 178 (100), 162 (26), 147 (18), 132 (60), 119 (35), 106 (13) and 92 (46).

2-Chloro-5′-nitro-2′-piperidinoacetanilide (55). δ_H[$(CD_3)_2SO$] 9.49 (1 H, br s, NH), 8.72 (1 H, d, *J* 2.5, 6′-H), 7.99 (1 H, dd, *J* 2.5 and 9, 4′-H), 7.28 (1 H, d, *J* 9, 3′-H), 4.44 (2 H, s, 2-H), 2.92 (4 H, br t, *J* 4.5, 2″-, 6″-H), 1.71 (4 H, m, 3″-, 5″-H) and 1.57 (2 H, m, 4″-H); δ_C[$(CD_3)_2SO$] 164.97 (CO), 150.65 (C-2′), 141.81 (C-5′), 130.64 (C-1′), 120.67 (C-4′), 119.98 (C-3′), 116.79 (C-6′), 51.83 (C-2″, -6″), 43.28 (C-2), 25.42 (C-3″, -5″) and 23.44 (C-4″); *m*/*z* (EI) 297 (M^+, 36%), 260 (100), 232 (22), 218 (71), 205 (27), 192 (21), 174 (26), 164 (37), 145 (17), 131 (12), 118 (42), 105 (7) and 91 (14).

2′-(1-Azepanyl)-2-chloro-5′-nitroacetanilide (56). δ_H[$(CD_3)_2SO$] 9.82 (1 H, br s, NH), 8.11 (1 H, d, *J* 3, 6′-H), 7.95 (1 H, dd, *J* 3 and 9, 4′-H), 7.09 (1 H, d, *J* 9, 3′-H), 4.32 (2 H, s, 2-H), 3.41 (4 H, t, *J* 5.5, 2″-, 7″-H), 1.73 (4 H, m, 3″-, 6″-H) and 1.53 (4 H, m, 4″-, 5″-H); δ_C[$(CD_3)_2SO$] 165.30 (CO), 152.36 (C-2′), 137.91 (C-5′), 124.77 (C-1′), 123.65 (C-6′), 122.39 (C-4′), 117.28 (C-3′), 52.31 (C-2″, -7″), 42.98 (C-2), 27.67 (C-3″, -6″) and 26.57 (C-4″, -5″); *m*/*z* (EI) 311 (M^+, 51%), 275 (61), 268 (51), 246 (26), 232 (100), 219 (19), 205 (22), 192 (33), 177 (26), 164 (37), 145 (17), 132 (26), 118 (49), 104 (11) and 91 (15).

2-Chloro-5′-nitro-2′-[2-(1,2,3,4-tetrahydroisoquinolyl)]acetanilide (57). δ_H[$(CD_3)_2SO$] 9.73 (1 H, br s, NH), 8.63 (1 H, d, *J* 3,

6′-H), 8.03 (1 H, dd, *J* 3 and 9, 4′-H), 7.34 (1 H, d, *J* 9, 3′-H), 7.19 (4 H, m, 5″-, 6″-, 7″-, 8″-H), 4.39 (2 H, s, 2-H), 4.31 (2 H, s, 1″-H), 3.34 (2 H, t, *J* 6, 3″-H) and 3.00 (2 H, t, *J* 6, 4″-H); δ_C[$(CD_3)_2SO$] 165.41 (CO), 150.43 (C-2′), 141.34 (C-5′), 134.06, 133.78 (C-4a″, -8a″), 129.86 (C-1′), 128.69, 126.49, 126.43, 125.90 (C-5″, -6″, -7″, -8″), 121.19 (C-4′), 119.46 (C-3′), 119.04 (C-6′), 51.78, 49.01 (C-1″, -3″), 43.25 (C-2) and 28.34 (C-4″); *m*/*z* (EI) 345 (M^+, 4%), 309 (98), 308 (100), 292 (14), 266 (62), 251 (19), 220 (21), 164 (9), 130 (66), 117 (55), 104 (97) and 91 (32).

2-Chloro-2′-dimethylamino-*N*-methyl-5′-nitroacetanilide (58). By slow heating the mp of the crude compound **58**, pure by TLC, is 166–169 °C (decomp.); when samples of the product are introduced in the mp apparatus at prefixed temperatures, it melts at 154–156 °C, evolves MeCl and resolidifies, showing a final mp of 169–172 °C. In both cases the final observed mps are close to that of quinoxalinone **67**, final product of the thermal decomposition of anilide **58**. At room temperature compound **58** also decomposes very quickly to salt **28** in $(CD_3)_2SO$ solutions used for NMR; $CDCl_3$ solutions are somewhat more stable. ν_{max}(Nujol)/cm^{-1} 1683 (CO), 1598, 1489 and 1308; δ_H[$(CD_3)_2SO$] 8.23–7.90 (2 H, m, 4′-, 6′-H, *Z* and *E* rot.), 7.04 (1 H, m, 3′-H, *Z* and *E* rot.), 4.73 (2-H_A) and 4.52 (2-H_B) (both br d, *J* (−)14, *E* rot.) and 4.16 (2-H_A) and 4.05 (2-H_B) (both d, *J* (−)14, *Z* rot.) (2 H), 3.15 (3 H, s, NCH_3, *Z* and *E* rot.) and 2.93 (6 H, s, $N[CH_3]_2$, *Z* and *E* rot.) (*Z*/*E* rotamers ratio = 74 : 26); δ_C($CDCl_3$) (*Z* rot.) 166.48 (CO), 153.04 (C-2′), 139.19 (C-5′), 129.90 (C-1′), 125.84, 124.91 (C-4′, -6′), 116.94 (C-3′), 42.02 ($N[CH_3]_2$), 41.25 (C-2) and 37.05 (NCH_3); *m*/*z* (EI) 271 (M^+, 10%), 221 (61), 205 (6), 192 (100), 178 (48), 162 (8), 146 (90), 132 (42), 118 (16), 104 (24) and 91 (32).

2-Chloro-5′-nitro-*N*-methyl-2′-piperidinoacetanilide (59). ν_{max}(Nujol)/cm^{-1} 1680 (CO), 1598, 1489, 1330 and 1320; δ_H($CDCl_3$) [*Z* rot. (*ca.* 93%)] 8.11 (1 H, dd, *J* 2.5 and 9, 4′-H), 8.00 (1 H, d, *J* 2.5, 6′-H), 7.03 (1 H, d, *J* 9, 3′-H), 4.01 (1 H, d, J_{gem} (−)13, 2-H_A), 3.88 (1 H, d, J_{gem} (−)13, 2-H_B), 3.33 (3 H, s, CH_3), 2.92 (4 H, m, 2″-, 6″-H) and 1.65 (6 H, m, 3″-, 4″-, 5″-H); δ_C($CDCl_3$) (*Z* rot.) 166.78 (CO), 154.42 (C-2′), 141.34 (C-5′), 134.11 (C-1′), 124.84, 124.77 (C-4′, -6′), 119.52 (C-3′), 51.48 (C-2″, -6″), 41.46 (C-2), 36.87 (CH_3), 25.96 (C-3″, -5″) and 23.75 (C-4″); *m*/*z* (EI) 311 (M^+, 30%), 282 (5), 236 (5), 232 (6), 220 (100), 206 (11), 192 (100), 178 (8), 160 (26), 146 (65), 131 (45), 118 (14), 104 (22) and 91 (16).

2-Chloro-*N*-methyl-5′-nitro-2′-[2-(1,2,3,4-tetrahydroisoquinolyl)]acetanilide (60). δ_H($CDCl_3$) [*Z* rot. (*ca.* 95%)] 8.16 (1 H, dd, *J* 3 and 9, 4′-H), 8.07 (1 H, d, *J* 3, 6′-H), 7.30–7.06 (5 H, m, 3′- and 5″-, 6″-, 7″-, 8″-H), 4.48 (1 H, d, J_{gem} (−)15, 1″-H_A), 4.36 (1 H, d, J_{gem} (−)15, 1″-H_B), 3.99 (1 H, d, J_{gem} (−)13, 2-H_A), 3.91 (1 H, d, J_{gem} (−)13, 2-H_B), 3.52 (2 H, m, 3″-H), 3.39 (3 H, s, CH_3) and 2.96 (2 H, m, 4″-H); δ_C($CDCl_3$) (*Z* rot.) 166.76 (CO), 152.90 (C-2′), 141.01 (C-5′), 133.57 (C-1′), 132.84, 132.61 (C-4a″, -8a″), 128.80, 127.03, 126.47, 126.24 (C-5″, -6″, -7″, -8″), 125.38, 124.94 (C-4′, -6′), 118.79 (C-3′), 51.65, 48.57 (C-1″, -3″), 41.13 (C-2), 36.92 (CH_3) and 28.64 (C-4″); *m*/*z* (EI) 359 (M^+, 21%), 324 (2), 220 (100), 204 (4), 192 (62), 174 (7), 146 (32), 131 (12), 117 (21), 104 (12) and 91 (10).

2-Chloro-2′-dimethylaminoacetanilide hydrochloride (61 × HCl). δ_H[$(CD_3)_2SO$] 10.34 (1 H, br s, NH), 7.95–7.20 (4 H, m, aromat. H), 4.45 (2 H, s, 2-H) and 3.01 (6 H, s, $N[CH_3]_2$). Free base **61**: yield 1.55 g (91% from **61** × HCl); mp 72–74 °C (decomp.) (crude material, pure by TLC); δ_H[$CDCl_3$] 9.63 (1 H, br s, NH), 8.32 (1 H, m) and 7.13 (3 H, m) (aromat. H), 4.19 (2 H, s, 2-H) and 2.65 (6 H, s, $N[CH_3]_2$); δ_C[$CDCl_3$] 163.57 (CO), 143.26, 132.28 (C-1′, -2′), 124.83, 124.50, 119.93, 119.12 (C-3′, -4′, -5′, -6′), 44.60 ($N[CH_3]_2$) and 43.19 (C-2); *m*/*z* (EI) 212 (M^+, 35%), 175 (48), 163 (31), 148 (46), 133 (100), 119 (75), 106 (11) and 92 (23).

2-Chloro-2′-piperidinoacetanilide hydrochloride (62 × HCl). ν_{max}(Nujol)/cm^{-1} 3160 (NH), 2246br (structured band, HN^+), 1670 (CO), 1515, 1446 and 1400; δ_H[$(CD_3)_2SO$] 10.65 (1 H, br s, NH), 7.90–7.20 (4 H, m, aromat. H), 4.42 (2 H, s, 2-H), 3.25 (4 H, br s, 2″-, 6″-H), 1.92 (4 H, br s, 3″-, 5″-H) and 1.63 (2 H, br s, 4″-H). Free base **62**: yield 1.96 g (97% from **62** × HCl); mp 80–82 °C (decomp.) (crude material, pure by TLC); ν_{max}(Nujol)/cm^{-1} 3286 (NH), 1670 (CO), 1592, 1531 and 1410; δ_H[$CDCl_3$] 9.87 (1 H, br s, NH), 8.34 (1 H, m) and 7.10 (3 H, m) (aromat. H), 4.20 (2 H, s, 2-H), 2.77 (4 H, m, 2″-, 6″-H), 1.73 (4 H, m, 3″-, 5″-H) and 1.57 (2 H, m, 4″-H); δ_C[$CDCl_3$] 163.53 (CO), 143.04, 132.53 (C-1′, -2′), 124.96, 124.35, 120.61, 118.73 (C-3′, -4′, -5′, -6′), 53.72 (C-2″, -6″), 43.22 (C-2), 26.61 (C-3″, -5″) and 23.89 (C-4″); *m*/*z* (EI) 252 (M^+, 65%), 216 (81), 215 (100), 187 (33), 173 (99), 160 (42), 147 (36), 132 (24), 119 (89), 104 (7) and 92 (27).

2′-(1-Azepanyl)-2-chloroacetanilide hydrochloride (63 × HCl). δ_H[$(CD_3)_2SO$] 10.60 (1 H, br s, NH), 7.80–7.20 (4 H, m, aromat. H), 4.43 (2 H, s, 2-H), 3.38 (4 H, br s, 2″-, 7″-H), 1.91 (4 H, br s, 3″-, 6″-H) and 1.68 (4 H, br s, 4″-, 5″-H). Free base **63**: yield 2.01 g (94% from **63** × HCl); mp 92–94 °C (decomp.) (crude material, pure by TLC); δ_H[$CDCl_3$] 10.01 (1 H, br s, NH), 8.35 (1 H, m) and 7.12 (3 H, m) (aromat. H), 4.20 (2 H, s, 2-H), 2.97 (4 H, m, 2″-, 7″-H) and 1.75 (8 H, br s, 3″-, 4″-, 5″-, 6″-H); δ_C[$CDCl_3$] 163.67 (CO), 145.35, 132.74 (C-1′, -2′), 125.08, 124.57, 122.69, 118.65 (C-3′, -4′, -5′, -6′), 57.13 (C-2″, -7″), 43.16 (C-2), 29.58 (C-3″, -6″) and 26.66 (C-4″, -5″); *m*/*z* (EI) 266 (M^+, 69%), 230 (53), 223 (51), 217 (24), 201 (36), 187 (100), 174 (24), 159 (30), 146 (50), 132 (49), 119 (90), 106 (11) and 92 (28).

Preparation of 3,4-dihydro-1*H*-quinoxalin-2-ones 33–38 and 67–72

a) From 2-dialkylamino-2′-halogenoacetanilides 11–15 and 17. Starting from 2′-chloroacetanilides **11**–**15**, a solution of 4 mmol of the corresponding compound in nitromethane (10 cm^3) was refluxed under argon until the starting material was consumed (**11**: 3 days; **12**: 2 days; **13**: 14 days; **14**: 14 days; **15**: 30 days).

For quinoxalinone **33**, the precipitated orange solid was collected by filtration, washed with nitromethane (2 × 5 cm^3) and water (10 cm^3) and air-dried (homogeneous material: TLC, ^{1}H NMR). Alternatively, a solution of 4 mmol of anilide **11** in ethanol (20 cm^3) was refluxed under argon for 4 days; after cooling, the precipitated quinoxalinone **33** was collected by filtration and treated as before. In both cases, for the isolation of salt **39**, the combined filtrates from the preparation of quinoxalinone **33** were evaporated to dryness. Water (25 cm^3) was then added and the insoluble material removed by filtration. The residue obtained after evaporation to dryness of the filtrate was recrystallized from ethanol, affording salt **39**.

For quinoxalinones **34**–**37**, the solids crystallized after cooling were collected by filtration and washed with cold nitromethane (2 × 5 cm^3) (homogeneous materials: TLC, ^{1}H NMR).

In the case of 2′-fluoroacetanilide **17**, the free base (0.66 g, 2 mmol) was refluxed in ethanol (50 cm^3) for 48 h. The major product of the reaction, isolated by preparative TLC (5 plates, 2 runs) using $CHCl_3$–MeOH (30 : 1) as eluent, was shown to be the quinoxalinone **38**.

*[(2-Chloro-5-nitrophenyl)carbamoylmethyl]trimethylammonium chloride (**39**).* Yield: 86 mg (7%) (from **11** in nitromethane); 185 mg (15%) (from **11** in ethanol); mp 202–203 °C (decomp.) (EtOH) (Found: C, 42.6; H, 4.8; N, 13.5. Calc. for $C_{11}H_{15}Cl_2N_3O_3$: C, 42.9; H, 4.9; N, 13.6%); ν_{max}(Nujol)/cm^{-1} 3215 (NH), 1700 (CO), 1591, 1554 and 1345; δ_H[$(CD_3)_2SO$] 10.97 (1 H, br s, NH), 8.64 (1 H, d, *J* 2.5, 6′-H), 8.10 (1 H, dd, *J* 2.5 and 9, 4′-H), 7.86 (1 H, d, *J* 9, 3′-H), 4.57 (2 H, s, CH_2) and 3.31 (9 H, s, CH_3); δ_C[$(CD_3)_2SO$] 163.42 (CO), 146.22,

134.73, 133.97 (C-1′, -2′, -5′), 131.01, 121.73, 120.87 (C-3′, -4′, -6′), 64.03 (CH_2) and 53.39 (CH_3); *m/z* (EI) 271 (M^+ − HCl, 2%), 213 (2), 178 (2), 132 (2), 124 (2), 90 (3), 73 (6) and 58 (100).

b) From 2′-dialkylamino-2-chloroacetanilides 54–59. A solution of 4 mmol of the corresponding anilide **54**–**59** in nitromethane (10 cm^3) was refluxed under argon until the starting material was consumed (**54**: 24 h; **55**, **56**: 2 days; **57**: 3 days; **58**: 3 h; **59**: 15 h).

1-Unsubstituted quinoxalinones **33**, **35**–**37** crystallized after cooling and were collected by filtration, washed with nitromethane (5 cm^3) and air-dried. For 1-methylquinoxalinones **67** and **69**, the resulting solutions were evaporated to dryness and the residues recrystallized from ethanol.

Homogeneous materials (TLC, ^{1}H NMR) were obtained in all cases.

For the preparation of quinoxalinone **38**, anilide **57** (0.69 g, 2 mmol) in ethanol (50 cm^3) was refluxed for 20 days. The reaction was then processed as described above for the preparation of quinoxalinone **38** from 2′-fluoroacetanilide **17**.

c) From quinoxalinium chlorides 23, 25, 28–32 and 64. For quinoxalinones **33**, **35** and **67**–**71**, a suspension of 4 mmol of the required salts in nitromethane (10 cm^3) was refluxed under argon until the starting material was consumed (**23**: 7 h; **25**: 2 days; **28**: 2 h; **30**: 15 h; **29**, **31** and **32**: 4 h).

As before, 1-unsubstituted quinoxalinones **33** and **35** crystallized after cooling and were directly collected by filtration. In the case of 1-methylquinoxalinones **67**–**71**, the resulting solutions were evaporated to dryness and the residues recrystallized from ethanol (**67**–**70**) or nitromethane (**71**).

For quinoxalinone **72**, solid salt **64** (0.42 g, 2 mmol) in a sublimation apparatus connected to a water pump was heated at 170–180 °C for 3 h. The sublimated product was shown to be pure compound **72**.

Furthermore, quinoxalinones **33**, **35** and **36** have also been obtained in the preparation of quinoxalinium salts **23**, **25** and **26** following the procedure c (see below).

Yields, mps and analytical data of quinoxalinones **33**–**38** and **67**–**71** are gathered in Table 3.

*4-Methyl-7-nitro-3,4-dihydro-1H-quinoxalin-2-one (**33**).* ν_{max}(Nujol)/cm^{-1} 3189, 3140, 3080 and 3061 (NH), 1683 (CO), 1614, 1536, 1490, 1408, 1329, 1304 and 1291; δ_H[$(CD_3)_2SO$] 10.79 (1 H, br s, NH), 7.81 (1 H, dd, *J* 2.5 and 9, 6-H), 7.59 (1 H, d, *J* 2.5, 8-H), 6.74 (1 H, d, *J* 9, 5-H), 4.00 (2 H, s, 3-H) and 2.93 (3 H, s, CH_3); δ_C[$(CD_3)_2SO$] 164.16 (CO), 141.32 (C-4a), 137.05 (C-7), 125.90 (C-8a), 120.50 (C-6), 109.45, 109.28 (C-5, -8), 52.90 (C-3) and 36.89 (CH_3); *m/z* (EI) 207 (M^+, 100%), 178 (73), 161 (12), 148 (3), 132 (74), 118 (8), 104 (7) and 92 (9).

*4-(4-Chlorobutyl)-7-nitro-3,4-dihydro-1H-quinoxalin-2-one (**34**).* δ_H[$(CD_3)_2SO$] 10.79 (1 H, br s, NH), 7.77 (1 H, dd, *J* 2.5 and 9, 6-H), 7.59 (1 H, d, *J* 2.5, 8-H), 6.80 (1 H, d, *J* 9, 5-H), 4.04 (2 H, s, 3-H), 3.67 (2 H, t, *J* 6, 4′-H), 3.38 (2 H, t, *J* 7, 1′-H) and 1.74 (4 H, m, 2′-, 3′-H); δ_C[$(CD_3)_2SO$] 163.81 (CO), 140.17 (C-4a), 136.54 (C-7), 125.63 (C-8a), 120.50 (C-6), 109.68, 109.18 (C-5, -8), 50.99 (C-3), 48.38 (C-1′), 45.09 (C-4′), 29.34 (C-2′) and 22.06 (C-3′); *m/z* (EI) 283 (M^+, 30%), 206 (100), 178 (40), 160 (9), 146 (5),132 (26), 118 (12), 104 (5) and 91 (11).

*4-(5-Chloropentyl)-7-nitro-3,4-dihydro-1H-quinoxalin-2-one (**35**).* ν_{max}(KBr)/cm^{-1} 3198, 3135, 3080 and 3046 (NH), 1684 (CO), 1614, 1535, 1485 and 1314; δ_H[$(CD_3)_2SO$] 10.78 (1 H, br s, NH), 7.77 (1 H, dd, *J* 2.5 and 9, 6-H), 7.59 (1 H, d, *J* 2.5, 8-H), 6.77 (1 H, d, *J* 9, 5-H), 4.04 (2 H, s, 3-H), 3.64 (2 H, t, *J* 6.5, 5′-H), 3.35 (2 H, t, *J* 7, 1′-H) and 1.85–1.30 (6 H, m, 2′-, 3′-, 4′-H); δ_C[$(CD_3)_2SO$] 163.72 (CO), 140.13 (C-4a), 136.47 (C-7), 125.54 (C-8a), 120.46 (C-6), 109.62 (C-8), 109.10 (C-5), 50.97 (C-3), 48.95 (C-1′), 45.20 (C-5′), 31.75 (C-2′), 23.76 (C-4′) and 23.61 (C-3′); *m/z* (EI) 297 (M^+, 27%), 262 (3), 206 (100), 178 (42), 160 (9), 146 (5), 132 (27) 118 (12), 104 (5) and 91 (7).

*4-(6-Chlorohexyl)-7-nitro-3,4-dihydro-1H-quinoxalin-2-one (**36**).* δ_H[$(CD_3)_2SO$] 10.79 (1 H, br s, NH), 7.77 (1 H, dd, *J* 2.5 and 9, 6-H), 7.58 (1 H, d, *J* 2.5, 8-H), 6.75 (1 H, d, *J* 9, 5-H), 4.04 (2 H, s, 3-H), 3.62 (2 H, t, *J* 6.5, 6′-H), 3.33 (2 H, t, *J* 7, 1′-H) and 1.80–1.20 (8 H, m, 2′-, 3′-, 4′-, 5′-H); δ_C[$(CD_3)_2SO$] 163.81 (CO), 140.21 (C-4a), 136.39 (C-7), 125.56 (C-8a), 120.60 (C-6), 109.63, 109.11 (C-5, -8), 51.03 (C-3), 49.09 (C-1′), 45.32 (C-6′), 31.97 (C-2′) and 26.08, 25.48 and 24.30 (C-3′, -4′, -5′); *m/z* (EI) 311 (M^+, 40%), 282 (2), 276 (2), 206 (100), 178 (50), 160 (12), 146 (7), 132 (34), 118 (15), 104 (6) and 91 (8).

*4-[2′-(Chloromethyl)phenethyl]-7-nitro-3,4-dihydro-1H-quinoxalin-2-one (**37**).* δ_H[$(CD_3)_2SO$] 10.81 (1 H, br s, NH), 7.78 (1 H, dd, *J* 2.5 and 9, 6-H), 7.62 (1 H, d, *J* 2.5, 8-H), 7.50–7.20 (4 H, m, 3″-, 4″-. 5″-, 6″-H), 6.89 (1 H, d, *J* 9, 5-H), 4.88 (2 H, s, 2″-CH_2), 4.09 (2 H, s, 3-H), 3.63 (2 H, t, *J* 7, 1′-H) and 3.01 (2 H, t, *J* 7, 2′-H); δ_C[$(CD_3)_2SO$] 163.71 (CO), 139.85 (C-4a), 137.71, 136.66, 135.82 (C-7, -1″, -2″), 130.73, 130.45, 129.12, 127.02 (C-3″, -4″, -5″, -6″), 125.60 (C-8a), 120.58 (C-6), 109.75, 109.21 (C-5, -8), 51.17, 50.25 (C-3, -1′), 44.61 (2″-CH_2) and 26.88 (C-2′); *m/z* (EI) 345 (M^+, 16%), 206 (100), 178 (48), 160 (15), 132 (39), 117 (15), 104 (18) and 91 (12).

*4-[2′-(Ethoxymethyl)phenethyl]-7-nitro-3,4-dihydro-1H-quinoxalin-2-one (**38**).* ν_{max}(Nujol)/cm^{-1} 3193, 3140, 3070 and 3050 (NH), 1685 (CO), 1615, 1536, 1492 and 1312; δ_H[$(CD_3)_2SO$] 10.81 (1 H, br s, NH), 7.78 (1 H, dd, *J* 2.5 and 9, 6-H), 7.61 (1 H, d, *J* 2.5, 8-H), 7.40–7.15 (4 H, m, 3″-, 4″-, 5″-, 6″-H), 6.89 (1 H, d, *J* 9, 5-H), 4.52 (2 H, s, 2″-CH_2), 4.07 (2 H, s, 3-H), 3.56 (2 H, t, *J* 8, 1′-H), 3.51 (2 H, q, *J* 7, CH_2CH$_3$), 2.93 (2 H, t, *J* 8, 2′-H) and 1.15 (3 H, t, *J* 7, CH_2CH_3); δ_C[$(CD_3)_2SO$] 163.63 (CO), 139.88 (C-4a), 137.50, 136.55, 136.43 (C-7, -1″, -2″), 130.17, 129.70, 128.08, 126.35 (C-3″, -4″, -5″, -6″), 125.50 (C-8a), 120.44 (C-6), 109.71, 109.10 (C-5, -8), 70.36 (2″-CH_2), 65.06 (CH_3CH_2O), 51.14, 50.76 (C-3, -1′), 27.22 (C-2′) and 15.06 (CH_3); *m/z* (EI) 355 (M^+, 59%), 309 (27), 280 (4), 206 (100), 178 (54), 160 (17), 132 (39), 118 (20), 105 (14) and 91 (16).

*1,4-Dimethyl-7-nitro-3,4-dihydro-1H-quinoxalin-2-one (**67**).* ν_{max}(Nujol)/cm^{-1} 1682 (CO), 1496, 1309 and 1296; δ_H[$(CD_3)_2SO$] 7.91 (1 H, dd, *J* 2.5 and 9, 6-H), 7.70 (1 H, d, *J* 2.5, 8-H), 6.80 (1 H, d, *J* 9, 5-H), 4.07 (2 H, s, 3-H), 3.31 (3 H, s, 1-CH_3) and 2.94 (3 H, s, 4-CH_3); δ_C[$(CD_3)_2SO$] 163.54 (CO), 142.79 (C-4a), 137.45 (C-7), 127.96 (C-8a), 120.70 (C-6), 109.72, 109.24 (C-5, -8), 52.95 (C-3), 37.00 (4-CH_3) and 28.21 (1-CH_3); *m/z* (EI) 221 (M^+, 100%), 192 (63), 175 (7), 146 (65), 131 (12), 118 (4), 104 (9) and 91 (6).

*4-(4-Chlorobutyl)-1-methyl-7-nitro-3,4-dihydro-1H-quinoxalin-2-one (**68**).* δ_H[$(CD_3)_2SO$] 7.88 (1 H, dd, *J* 2.5 and 9, 6-H), 7.70 (1 H, d, *J* 2.5, 8-H), 6.88 (1 H, d, *J* 9, 5-H), 4.12 (2 H, s, 3-H), 3.68 (2 H, t, *J* 6, 4′-H), 3.41 (2 H, t, *J* 7, 1′-H), 3.32 (3 H, s, CH_3) and 1.75 (4 H, m, 2′-, 3′-H); δ_C[$(CD_3)_2SO$] 163.21 (CO), 141.61 (C-4a), 136.90 (C-7), 127.65 (C-8a), 120.69 (C-6), 109.61, 109.45 (C-5, -8), 51.01 (C-3), 48.44 (C-1′), 45.02 (C-4′), 29.31 (C-2′), 28.23 (CH_3) and 21.97 (C-3′); *m/z* (EI) 297 (M^+, 78%), 268 (6), 220 (100), 206 (7), 192 (90), 174 (9), 160 (15), 146 (49), 131 (25), 118 (7), 104 (11) and 91 (10).

*4-(5-Chloropentyl)-1-methyl-7-nitro-3,4-dihydro-1H-quinoxalin-2-one (**69**).* ν_{max}(Nujol)/cm^{-1} 1677 (CO), 1587, 1529, 1347, 1308, 1293 and 1282; δ_H[$(CD_3)_2SO$] 7.88 (1 H, dd, *J* 2.5 and 9, 6-H), 7.68 (1 H, d, *J* 2.5, 8-H), 6.85 (1 H, d, *J* 9, 5-H), 4.12 (2 H, s, 3-H), 3.64 (2 H, t, *J* 6.5, 5′-H), 3.37 (2 H, t, *J* 7, 1′-H), 3.31 (3 H, s, CH_3) and 1.85–1.35 (6 H, m, 2′-, 3′-, 4′-H); δ_C[$(CD_3)_2SO$] 163.24 (CO), 141.68 (C-4a), 136.82 (C-7), 127.62 (C-8a), 120.78 (C-6), 109.63, 109.47 (C-5, -8), 51.02 (C-3), 49.03 (C-1′), 45.25 (C-5′), 31.74 (C-2′), 28.23 (CH_3) and 23.69 and 23.62 (C-3′, -4′); *m/z* (EI) 311 (M^+, 79%), 276 (11), 220 (100), 206 (8), 192 (91), 174 (8), 160 (14), 146 (49), 131 (24), 118 (7), 104 (10) and 91 (6).

*4-(6-Chlorohexyl)-1-methyl-7-nitro-3,4-dihydro-1H-quinoxalin-2-one (**70**).* δ_H[$(CD_3)_2SO$] 7.89 (1 H, dd, *J* 2.5 and 9, 6-H), 7.69 (1 H, d, *J* 2.5, 8-H), 6.85 (1 H, d, *J* 9, 5-H), 4.13 (2 H, s,

3-H), 3.63 (2 H, t, *J* 6.5, 6′-H), 3.36 (2 H, t, *J* 7, 1′-H), 3.32 (3 H, s, CH_3) and 1.80–1.20 (8 H, m, 2′-, 3′-, 4′-, 5′-H); δ_C[$(CD_3)_2SO$] 163.20 (CO), 141.63 (C-4a), 136.77 (C-7), 127.57 (C-8a), 120.78 (C-6), 109.58, 109.38 (C-5, -8), 51.04 (C-3), 49.16 (C-1′), 45.27 (C-6′), 31.95 (C-2′), 28.20 (CH_3) and 26.03, 25.47 and 24.21 (C-3′, -4′, -5′); *m*/*z* (EI) 325 (M^+, 86%), 296 (6), 290 (6), 220 (100), 206 (8), 192 (92), 174 (8), 160 (16), 146 (48), 131 (23), 118 (6), 104 (10) and 91 (6).

*4-[2′-(Chloromethyl)phenethyl]-1-methyl-7-nitro-3,4-dihydro-1H-quinoxalin-2-one (**71**).* ν_{max}(Nujol)/cm^{-1} 1681 (CO), 1589, 1534, 1501 and 1313; δ_H[$(CD_3)_2SO$] 7.89 (1 H, dd, *J* 2.5 and 9, 6-H), 7.72 (1 H, d, *J* 2.5, 8-H), 7.50–7.20 (4 H, m, 3″-, 4″-. 5″-, 6″-H), 6.97 (1 H, d, *J* 9, 5-H), 4.88 (2 H, s, 2″-CH_2), 4.19 (2 H, s, 3-H), 3.66 (2 H, t, *J* 7, 1′-H), 3.33 (3 H, s, CH_3) and 3.02 (2 H, t, *J* 7, 2′-H); δ_C[$(CD_3)_2SO$] 163.24 (CO), 141.42 (C-4a), 137.66, 137.04, 135.82 (C-7, -1″, -2″), 130.73, 130.43, 129.12, 127.02 (C-3″, -4″, -5″, -6″), 127.72 (C-8a), 120.88 (C-6), 109.86, 109.58 (C-5, -8), 51.18, 50.30 (C-3, -1′), 44.63 (2″-CH_2), 28.32 (CH_3) and 26.81 (C-2′); *m*/*z* (EI) 359 (M^+, 14%), 220 (100), 192 (59), 174 (7), 146 (36), 131 (14), 115 (13), 104 (17) and 91 (13).

*4-Methyl-3,4-dihydro-1H-quinoxalin-2-one (**72**).* Yield: 0.27 g (83%) (from salt **64**). When samples of the product are introduced into the mp apparatus at prefixed temperatures, the recorded mp is 140–143 °C (decomp.) (H_2O) (lit., 144–144.5 °C,[23] 137 °C[33]). By slow heating the compound decomposes gradually and melts finally at *ca.* 285 °C; a ^1H NMR study of the process shows that when heated compound **72** is oxidized by air to 1-methyl-1,4-dihydroquinoxaline-2,3-dione (lit., mp 286–289 °C[46]).

Preparation of 3-oxo-1,2,3,4-tetrahydroquinoxalinium chlorides 23, 25, 26, 28–32 and 64–66

a) From 2′-fluoro-5′-nitro-2-piperidinoacetanilide (16). A solution of free base **16** (0.56 g, 2 mmol) was refluxed in ethanol (50 cm^3) for 7 h. After cooling and addition of 1 M HCl (5 cm^3), the reaction mixture was evaporated to dryness. The residue was triturated with acetone (10 cm^3) and the solid in suspension, collected by filtration, was shown to be 3-oxoquinoxalinium chloride **25** (homogeneous material: TLC, ^1H NMR).

b) From 2,2′-dichloro-*N*-methyl-5′-nitroacetanilide (10) and secondary amines. To a solution of acetanilide **10** (1.31 g, 5 mmol) in acetone (30 cm^3), 10 mmol of the corresponding secondary amine [dimethylamine (as the mentioned 5.6 M solution in ethanol), pyrrolidine, piperidine, homopiperidine or 1,2,3,4-tetrahydroisoquinoline] was added and the mixture was stirred at room temperature for 3 days. The precipitated solids, after being collected by filtration, were washed with acetone (4 × 10 cm^3) and $CHCl_3$ (4 × 10 cm^3) and dried under vacuum over P_2O_5, and were shown to be the corresponding quinoxalinium chlorides **28**–**32** (homogeneous materials: TLC, ^1H NMR).

c) From 2-chloro-2′-(dialkylamino)acetanilides 54–56 and 58–63. The precise conditions for the optimal cyclization of each chloroacetanilide to the corresponding quinoxalinium salt were deduced from ^1H NMR studies.

For salt **23**, anilide **54** (6.44 g, 25 mmol) in EtOH (50 cm^3) was refluxed for 3 h. Without cooling, the desired salt in suspension was collected by filtration, washed with EtOH (2 × 10 cm^3) and acetone (4 × 10 cm^3) and air-dried. The combined filtrate and washing solvents were evaporated to dryness, the residue dissolved in nitromethane (20 cm^3) and the mixture refluxed for 24 h. After cooling, the precipitated 4-methylquinoxalinone **33** was collected by filtration, washed with nitromethane (2 × 10 cm^3) and air-dried (1.45 g, 28% yield).

For salt **25**, anilide **55** (7.44 g, 25 mmol) in ethanol (50 cm^3) was refluxed for 40 h. After cooling, the precipitated salt **25** was collected by filtration and washed as before with ethanol and acetone. The residue obtained after evaporation of the filtrate was refluxed in nitromethane (15 cm^3) for 48 h and, after cooling, the crystallized 4-(5-chloropentyl)quinoxalinone **35** (1.12 g, 15% yield) was collected by filtration.

For salt **26**, anilide **56** (7.79 g, 25 mmol) in ethanol (100 cm^3) was refluxed for 30 h and then, the reaction mixture was evaporated to dryness. After addition of water (50 cm^3) and chloroform (100 cm^3) and stirring for 10 min, the organic and water layers were separated. The water phase was treated with charcoal and evaporated to dryness affording the desired salt. The organic phase was evaporated to dryness and the residue, refluxed in nitromethane for 48 h, *etc.* as described above, gave 4-(6-chlorohexyl)quinoxalinone **36** (5.61 g, 72% yield).

For salts **28** and **30**, 25 mmol of the corresponding anilide (**58** or **59**) in acetone (100 cm^3) was refluxed for 5 h. After cooling, the precipitated salts were collected by filtration, washed with acetone (2 × 30 cm^3) and air-dried.

For salt **32**, a solution of anilide **60** (9.00 g, 25 mmol) in acetone (70 cm^3) was stirred at room temperature for 10 days, and then the precipitated salt was collected by filtration.

For salts **64**–**66**, 25 mmol of the corresponding anilide (**61**–**63**, free bases) in ethanol (100 cm^3) was refluxed for 2–5 h. After evaporation of the solvent, the residue was triturated with acetone (100 cm^3) affording the corresponding salts which were collected by filtration and dried under vacuum.

Yields, mps and analytical data of quinoxalinium salts **23**, **25**, **26**, **28**–**32** and **64**–**66** are gathered in Table 4. Mass spectra (EI) of salts **25**, **26** and **29**–**32** are identical to those of the respective 4-(ω-chloroalkyl)-3,4-dihydroquinoxalin-2-ones **35**, **36** and **68**–**71**, showing the thermal decomposition of the former in the spectrometer through the alkyl chloride elimination pattern mentioned in the Results and discussion section. Therefore, we assume that the EI mass spectra reported below for salts **65** and **66** are actually those of the corresponding 4-substituted quinoxalinones.

*1,1-Dimethyl-6-nitro-3-oxo-1,2,3,4-tetrahydroquinoxalinium chloride (**23**).* ν_{max}(KBr)/cm^{-1} 3160–2650 (br structured band, NH and CH), 1709 (CO), 1546 and 1348; δ_H[$(CD_3)_2SO$] 8.24 (1 H, d, *J* 9, 8-H), 8.21 (1 H, d, *J* 2.5, 5-H), 8.09 (1 H, dd, *J* 2.5 and 9, 7-H), 4.89 (2 H, s, 2-H) and 3.73 (6 H, s, $N[CH_3]_2$); δ_C[$(CD_3)_2SO$] 160.86 (CO), 148.66 (C-6), 134.23, 133.08 (C-4a, -8a), 122.58 (C-8), 118.25 (C-7), 112.81 (C-5), 62.91 (C-2) and 53.97 ($N[CH_3]_2$); *m*/*z* (EI) 221 (M^+ − HCl, 33%), 207 (M^+ − MeCl, 100), 192 (19), 178 (71), 161 (15), 146 (19), 132 (73), 118 (10), 104 (9) and 92 (10).

*6-Nitro-3-oxo-1,2,3,4-tetrahydroquinoxaline-1-spiro-1′-piperidinium chloride (**25**).* ν_{max}(KBr)/cm^{-1} 3140–2600 (br structured band, NH and CH), 1712 (CO), 1536 and 1360; δ_H[$(CD_3)_2SO$] 12.25 (1 H, br s, NH), 8.33 (1 H, d, *J* 9, 8-H), 8.20 (1 H, d, *J* 2.5, 5-H), 8.11 (1 H, dd, *J* 2.5 and 9, 7-H), 4.91 (2 H, s, 2-H), 4.15 (2 H, m, J_{gem} (−)12, $J_{a,a}$ 10, 2′-, 6′-H_a), 3.84 (2 H, br d, J_{gem} (−)12, 2′-, 6′-H_e) and 2.35–2.02 (2 H, m) and 1.95–1.60 (4 H, m) (3′-, 4′-, 5′-H); δ_C[$(CD_3)_2SO$] 160.63 (CO), 148.52 (C-6), 134.99, 133.66 (C-4a, -8a), 122.78 (C-8), 118.23 (C-7), 113.02 (C-5), 61.66 (C-2′, -6′), 55.06 (C-2), 19.92 (C-4′) and 19.31 (C-3′, -5′).

*6-Nitro-3-oxo-1,2,3,4-tetrahydroquinoxaline-1-spiro-1′-azepanium chloride (**26**).* δ_H[$(CD_3)_2SO$] 8.29 (1 H, d, *J* 9, 8-H), 8.15 (1 H, d, *J* 2.5, 5-H), 8.07 (1 H, dd, *J* 2.5 and 9, 7-H), 4.79 (2 H, s, 2-H), 4.23 (2 H, dd, *J* 8.5 and 14, 2′-, 7′-H_A), 3.92 (2 H, dd, *J* 7 and 14, 2′-, 7′-H_B) and 2.05 (4 H, m) and 1.70 (4 H, m) (3′-, 4′-, 5′-, 6′-H); δ_C[$(CD_3)_2SO$] 160.97 (CO), 148.49 (C-6), 135.64, 133.22 (C-4a, -8a), 123.10 (C-8), 118.22 (C-7), 113.07 (C-5), 65.59 (C-2′, -7′), 60.33 (C-2), 26.79 (C-3′, -6′) and 21.63 (C-4′, -5′).

*1,1,4-Trimethyl-6-nitro-3-oxo-1,2,3,4-tetrahydroquinoxalinium chloride (**28**).* ν_{max}(Nujol)/cm^{-1} 1705 (CO), 1538, 1450 and 1357; δ_H[$(CD_3)_2SO$] 8.34–8.16 (3 H, m, aromat. H), 5.03 (2 H, s, 2-H), 3.78 (6 H, s, $N(CH_3)_2$) and 3.46 (3 H, s, NCH_3); δ_C[$(CD_3)_2SO$] 160.37 (CO), 149.09 (C-6), 135.60, 134.82 (C-4a, -8a), 122.57 (C-8), 118.85 (C-7), 112.65 (C-5), 62.86 (C-2), 53.78

($N(CH_3)_2$) and 29.66 (NCH_3); *m/z* (EI) 221 (M^+ − MeCl, 79%), 206 (2), 192 (69), 175 (10), 160 (6), 146 (100), 131 (23), 118 (8), 104 (16), 92 (9) and 91 (9).

4-Methyl-6-nitro-3-oxo-1,2,3,4-tetrahydroquinoxaline-1-spiro-1′-pyrrolidinium chloride (***29***). $\delta_H[(CD_3)_2SO]$ 8.20–8.00 (3 H, m, aromat. H), 4.92 (2 H, s, 2-H), 4.30 (2 H, m, 2′-, 5′-H_A), 4.02 (2 H, m, 2′-, 5′-H_B), 3.45 (3 H, s, CH_3) and 2.32 and 2.16 (both 2 H, both m, 3′-, 4′-H); $\delta_C[(CD_3)_2SO]$ 161.22 (CO), 149.00 (C-6), 135.35, 134.54 (C-4a, -8a), 122.84 (C-8), 118.47 (C-7), 112.79 (C-5), 65.68 (C-2′, -5′), 61.19 (C-2), 29.67 (CH_3) and 22.09 (C-3′, 4′).

4-Methyl-6-nitro-3-oxo-1,2,3,4-tetrahydroquinoxaline-1-spiro-1′-piperidinium chloride (***30***). ν_{max}(Nujol)/cm^{-1} 3433 and 3368 (H_2O), 1700 (CO), 1536 and 1351; $\delta_H[(CD_3)_2SO]$ 8.39 (1 H, d, *J* 9, 8-H), 8.21 (1 H, dd, *J* 2.5 and 9, 7-H), 8.18 (1 H, d, *J* 2.5, 5-H), 5.01 (2 H, s, 2-H), 4.18 (2 H, m, J_{gem} (−)12, $J_{a,a}$ 10, 2′-, 6′-H_a), 3.92 (2 H, br d, J_{gem} (−)12, 2′-, 6′-H_e), 3.45 (3 H, s, CH_3) and 2.35–2.04 (2 H, m) and 1.97–1.50 (4 H, m) (3′-, 4′-, 5′-H); $\delta_C[(CD_3)_2SO]$ 160.24 (CO), 148.87 (C-6), 136.46, 135.31 (C-4a, -8a), 122.93 (C-8), 118.86 (C-7), 112.73 (C-5), 61.46 (C-2′, -6′), 55.25 (C-2), 29.69 (CH_3), 19.89 (C-4′) and 19.41 (C-3′, -5′).

4-Methyl-6-nitro-3-oxo-1,2,3,4-tetrahydroquinoxaline-1-spiro-1′-azepanium chloride (***31***). $\delta_H[(CD_3)_2SO]$ 8.37 (1 H, d, *J* 10, 8-H), 8.19 (1 H, d, *J* 3, 5-H), 8.18 (1 H, dd, *J* 3 and 10, 7-H), 4.92 (2 H, s, 2-H), 4.30 (2 H, dd, *J* 9 and 13.5, 2′-, 7′-H_A), 3.95 (2 H, dd, *J* 7 and 13.5, 2′-, 7′-H_B), 3.46 (3 H, s, CH_3) and 2.10 (2 H, m), 2.00 (2 H, m) and 1.70 (4 H, m) (3′-, 4′-, 5′-, 6′-H); $\delta_C[(CD_3)_2SO]$ 160.45 (CO), 148.76 (C-6), 137.12, 135.02 (C-4a, -8a), 123.32 (C-8), 118.74 (C-7), 112.83 (C-5), 65.33 (C-2′, -7′), 60.27 (C-2), 29.70 (CH_3), 26.63 (C-3′, -6′) and 21.64 (C-4′, -5′).

4-Methyl-6-nitro-3-oxo-1,2,3,4,1′,2′,3′,4′-octahydroquinoxaline-1-spiro-2′-isoquinolinium chloride (***32***). $\delta_H[(CD_3)_2SO]$ 8.23 (1 H, d, *J* 2.5, 5-H), 8.12 (1 H, dd, *J* 2.5 and 9, 7-H), 7.75 (1 H, d, *J* 9, 8-H), 7.37 (4 H, m, 5′-, 6′-, 7′-. 8′-H), 5.44 (1 H, d, *J* (−)15, 1′-H_A), 5.30 (1 H, d, *J* (−)15, 1′-H_B), 5.02 (1 H, d, *J* (−)15, 2-H_A), 4.91 (1 H, d, *J* (−)15, 2-H_B), 4.55 (1 H, m, 3′-H_A), 4.21 (1 H, m, 3′-H_B), 3.50 (3 H, s, CH_3), 3.21 (1 H, m, 4′-H_A) and 2.80 (1 H, m, 4′-H_B); $\delta_C[(CD_3)_2SO]$ 160.26 (CO), 149.25 (C-6), 135.36, 133.34 (C-4a, -8a), 129.58, 126.90 (C-4a′, -8a′), 129.04, 128.64, 127.69, 126.15 (C-5′, -6′, -7′, -8′), 122.85 (C-8), 118.82 (C-7), 113.06 (C-5), 62.29, 60.44, 58.15 (C-2, -1′, -3′), 29.82 (CH_3) and 23.70 (C-4′).

1,1-Dimethyl-3-oxo-1,2,3,4-tetrahydroquinoxalinium chloride (***64***). ν_{max}(Nujol)/cm^{-1} 3578 and 3347 (H_2O), 3160–2600 (br structured band, NH and CH), 1694 (CO), 1615, 1502 and 1397; $\delta_H[(CD_3)_2SO]$ 7.93–7.29 (4 H, m, aromat. H), 4.74 (2 H, s, 2-H) and 3.62 (6 H, s, $N(CH_3)_2$); $\delta_C[(CD_3)_2SO]$ 161.04 (CO), 131.18, 130.28 (C-4a, -8a), 131.56, 124.05, 120.21, 118.16 (C-5, -6, -7, -8), 63.28 (C-2) and 53.79 ($N(CH_3)_2$); *m/z* (EI) 176 (M^+ − HCl, 8%), 162 (95), 147 (12), 133 (100), 118 (19) and 92 (41).

3-Oxo-1,2,3,4-tetrahydroquinoxaline-1-spiro-1′-piperidinium chloride (***65***). ν_{max}(KBr)/cm^{-1} 3150–2600 (br structured band, NH and CH), 1714 (CO), 1611, 1494 and 1397; $\delta_H[(CD_3)_2SO]$ 11.85 (1 H, br s, NH), 8.05–7.27 (4 H, m, aromat. H), 4.79 (2 H, s, 2-H), 4.04 (2 H, m, J_{gem} (−)12, $J_{a,a}$ 10, 2′-, 6′-H_a), 3.73 (2 H, br d, J_{gem} (−)12, 2′-, 6′-H_e) and 2.30–2.03 (2 H, m) and 1.93–1.55 (4 H, m) (3′-, 4′-, 5′-H); $\delta_C[(CD_3)_2SO]$ 160.76 (CO), 131.74, 131.12 (C-4a, -8a), 131.50, 124.09, 120.26, 118.46 (C-5. -6, -7, -8), 61.35 (C-2′, -6′), 55.43 (C-2), 20.04 (C-4′) and 19.40 (C-3′, -5′); *m/z* (EI) 252 (M^+, 61%), 223 (7), 217 (8), 161 (100), 147 (10), 133 (86), 119 (33), 106 (5) and 92 (34).

3-Oxo-1,2,3,4-tetrahydroquinoxaline-1-spiro-1′-azepanium chloride (***66***). ν_{max}(KBr)/cm^{-1} 3180–2600 (br structured band, NH and CH), 1723 (CO), 1610, 1499 and 1393; $\delta_H[(CD_3)_2SO]$ 11.79 (1 H, br s, NH), 7.99–7.23 (4 H, m, aromat. H), 4.70 (2 H, s, 2-H), 4.14 (2 H, dd, *J* 9 and 13, 2′-, 7′-H_A), 3.82 (2 H, dd, *J* 6.5 and 13, 2′-, 7′-H_B) and 2.00 (4 H, m) and 1.68 (4 H, m) (3′-, 4′-, 5′-, 6′-H); $\delta_C[(CD_3)_2SO]$ 161.00 (CO), 131.78, 131.21 (C-4a, -8a), 131.40, 123.92, 120.85, 118.57 (C-5. -6, -7, -8), 65.16 (C-2′, -7′), 60.79 (C-2), 26.73 (C-3′, -6′) and 21.69 (C-4′, -5′); *m/z* (EI) 266 (M^+, 82%), 237 (9), 231 (5), 201 (3), 161 (100), 147 (14), 133 (96), 119 (51), 106 (8) and 92 (51).

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