1*H*-4,5,6,7-Tetrahydro-1,3-diazepines. Part I: Synthesis, Spectral and Chemical Properties of 1,2-Diaryl Derivatives

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The synthesis of several 1,2-diaryl-1*H*-4,5,6,7-tetrahydro-1,3-diazepines **1** by cyclization of *N*-aryl-*N'*-benzoyltetramethylenediamines **2** is described. Two alternative synthetic routes to obtain precursors **2** are discussed, being that which employes pyrrolidine as starting material the most convenient. Nucleophilic attack of compounds **1** on methyl iodide affords 1,2-diaryl-1*H*-4,5,6,7-tetrahydro-1,3-diazepinium iodides **3**. ^{1}H-nmr spectra of these compounds are unequivocally assigned by means of NOESY experiments. ^{1}H-nmr spectra of compounds **1** and **3** are analyzed and compared *inter se* and with those of compounds **1** run in the presence of trifluoroacetic acid-*d*. Reduction of compounds **1** with borane leads regiospecifically to *N*-aralkyl-*N'*-aryltetramethylenediamines **7**.

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Introduction.

Many 1*H*-4,5,6,7-tetrahydro-1,3-diazepines have been compounds of interest, due to their different biological activity. Thus, they have been tested as antispasmodics [1,2], hypoglycemiants [3-6], antiinflamatories [6], diuretics [3,4,6] and natriuretics [5].

Since synthetic methods to afford these seven-membered cyclic amidines employing ring expansion have not been succesful, most emphasis has been placed on their synthesis from acyclic precursors [7]. Thus, literature describes synthetic routes for 1*H*-4,5,6,7-tetrahydro-1,3-diazepines substituted at C2 with alkyl [1-4,7-12], and aryl [5,7-10,12-14] groups, which involve reaction of 1,4-butanediamine (putrescine) with carboxylic acids or their derivatives. There is only one synthesis reported for 1,2-diaryl derivatives (**1**, Scheme 1), where substituents on N1 are nitrophenyl groups [15]. Such synthetic method employs cyclodehydration of the corresponding *N*-aroyl-*N'*-aryltetramethylenediamines **2**, obtained by the reaction of the corresponding chloronitrobenzene with 1,4-butanediamine, followed by benzoylation in Schotten-Baumann conditions. However, when the aryl group on N1 is not substituted, or when it is substituted with electron donor or lightly withdrawing groups, this method to obtain precursors **2** is not suitable.

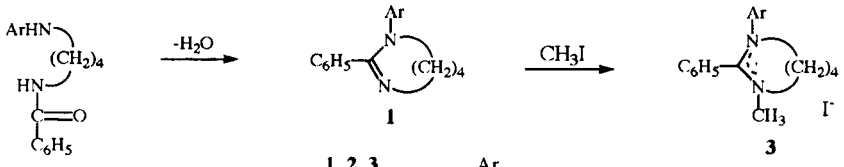
In this work, a series of 1-aryl-2-phenyl-1*H*-4,5,6,7-tetrahydro-1,3-diazepines **1a-d** are obtained from **2** (Scheme 1). Two synthetic routes to afford precursors **2** are discussed, and the most convenient one (employing pyrrolidine as starting material) is described.

We also explore certain properties of the synthesized compounds **1**, such as their nucleophilic character, behaviour under reducing conditions and spectroscopic features. Thus, synthesis of 1,2-diaryl-3-methyl-1*H*-4,5,6,7-tetrahydro-1,3-diazepinium iodides **3a-d** by reaction of the corresponding diazepine **1** with methyl iodide (Scheme 1) is described, and ^{1}H-nmr spectra of both series of compounds are analyzed and compared *inter se* and with the cationic form of compounds **1** (**1D**$^+$).

Synthesis.

Attempts to obtain precursors **2** adapting the synthetic route described for inferior homologues [16,17], failed. This route involves the synthesis of the corresponding *N*-(ω-bromoalkyl)benzamide from the ω-bromoalkylamine hydrobromide by a Schotten-Baumann acylation, followed by reaction with an arylamine (Scheme 2, Route a). However, when starting from 4-bromobutylamine hydrobromide **4**, the basic media necessary for the benzoylation reaction induces intramolecular aminolysis

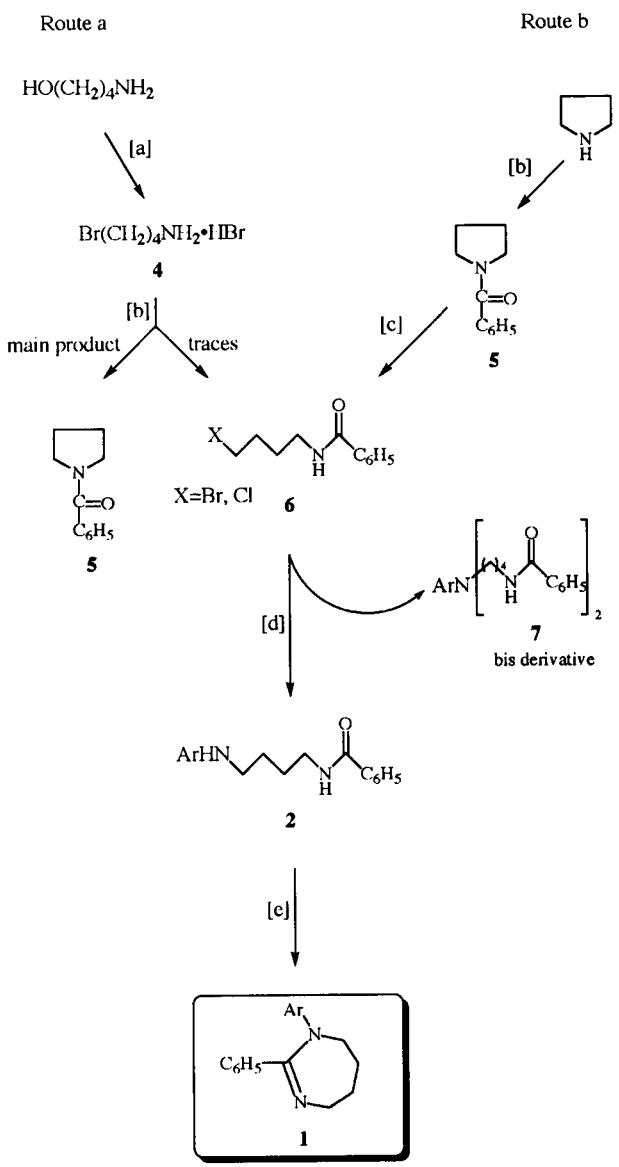
Scheme 1



2 **1** **3**

1, 2, 3	Ar
a	C_6H_5
b	*p*-$CH_3C_6H_4$
c	*p*-$CH_3OC_6H_4$
d	*p*-ClC_6H_4

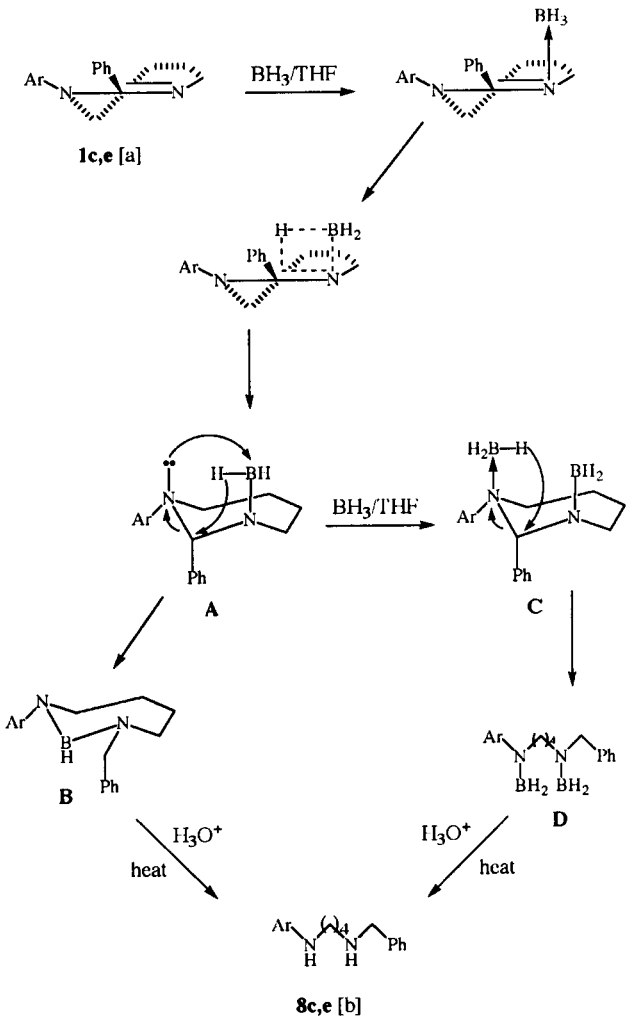
Scheme 2



[a] HBr/Benzene Deak-Stark Trap 2 hours, reflux; [b] C_6H_5COCl/HO^-/-0 °C; [c] PCl_5, 1 hour, reflux; [d] $ArNH_2$, reflux; [e] EPP, reflux.

to give *N*-benzoylpyrrolidine **5**, and only traces of the desired *N*-(4-bromobutyl)benzamide (**6**, X = Br) are obtained. This trouble could not be solved even by adding in a first step the benzoyl chloride, and then dropping the diluted base, as described by Fones *et al.* [18]. Better results in the synthesis of *N*-(4-chlorobutyl)benzamide (**6**, X=Cl), were obtained by reaction of *N*-benzoylpyrrolidine **5** with phosphorous pentachloride (von Braun reaction) [19] (Scheme II, Route b). Subsequent reaction of compounds **6** with arylamines leads to the expected *N*-aryl-*N'*-benzoyltetramethylenediamines **2a-d** (Table 1),

Scheme 3



[a] Substituent Ar in **1e** corresponds to *p*-$NO_2C_6H_4$, synthesized by Perillo *et al.* [16]. [b] Substituent Ar correspond to those indicated for compounds **1**.

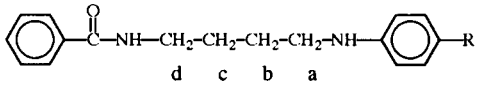
accompanied with the bis derivative **7**. In order to minimize bis derivative formation, reaction was assayed under different conditions (in toluene, without solvent and at different temperatures), reaching the best results employing absence of solvent and reflux at 120-130 °C. Ring closure of compounds **2** with a chloroform solution of ethyl polyphosphate (EPP) yielded 1,2-diaryl-1*H*-4,5,6,7-tetrahydro-1,3-diazepines **1a-d** (55-64%). Elemental analyses and spectroscopic properties (as described below) are presented in Table II and confirmed the proposed structures.

Chemical Properties.

As it arises from their easy quaternization in reactions with alkyl halides, heterocycles **1** have strong nucleophilic character. This behaviour is similar to that observed for inferior homologues, 4,5-dihydroimidazoles [20-22] and 1,4,5,6-tetrahydropyrimidines [23], and agrees with the typical cyclic amidine structure of compounds **1**. Thus,

Table 1

N-Aryl-*N'*-benzoyltetramethylenediamines **2a-d**



d c b a

Compound N°	Mp (°C)	Yield (%)	Formula	Analyses Calcd./Found %C	%H	%N	Mass (M+·) m/z	δ (ppm)	^{1}H-NMR Multiplicity	Assignment
2a	76	65	$C_{17}H_{20}N_2O$	76.09	7.51	10.44	268	7.75	dd	COC_6H_5 (2 *ortho* H)
				75.97	7.47	10.40		7.40-6.95	m	COC_6H_5 (2 *meta* and *para* H) and NC_6H_5 (2 *meta* and *para* H)
								6.45	m	NC_6H_5 (2 *ortho* H)
								6.28	s [a]	N*H*CO
								3.30	q [b]	CH_2 d
								2.90	t	CH_2 a
								[c]		N*H*C_6H_5
								1.70-1.50	m	CH_2 b and c
2b	84	86	$C_{18}H_{22}N_2O$	76.56	7.85	9.92	282	7.71	dd	C_6H_5 (2 *ortho* H)
				76.61	7.82	9.94		7.51-7.37	m	C_6H_5 (2 *meta* and *para* H)
								6.94	dd	*p*-$CH_3C_6H_4$ (2 *meta* H)
								6.55	dd	*p*-$CH_3C_6H_4$ (2 *ortho* H)
								6.30	bs [a]	NHCO
								3.52	q [b]	CH_2 d
								3.15	t	CH_2 a
								2.24	s	CH_3
								[c]		*p*-$CH_3C_6H_4$N*H*
								1.75-1.72	m	CH_2 b and c
2c	104	82	$C_{18}H_{22}N_2O_2$	72.46	7.43	9.39	298	7.72	dd	C_6H_5 (2 *ortho* H)
				72.60	7.40	9.45		7.50-7.36	m	C_6H_5 (2 *meta* and *para* H)
								6.78	dd	*p*-$CH_3OC_6H_4$ (2 *meta* H)
								6.60	dd	*p*-$CH_3OC_6H_4$ (2 *ortho* H)
								6.36	bs [a]	NHCO
								3.75	s	CH_3O
								3.51	q [b]	CH_2 d
								3.15	t	CH_2 a
								[c]	bs [a]	*p*-$CH_3OC_6H_4$N*H*
								1.76-1.42	m	CH_2 b and c
2d	72	88	$C_{17}H_{19}N_2ClO$	67.43	6.32	9.25	302	7.70	dd	C_6H_5 (2 *ortho* H)
				67.34	6.35	9.29		7.50-7.20	m	C_6H_5 (2 *meta* and *para* H)
								6.95	dd	*p*-ClC_6H_4 (2 *meta* H)
								6.45	dd	*p*-ClC_6H_4 (2 *ortho* H)
								6.36	bs [a]	NHCO
								3.45	q [b]	CH_2 d
								3.05	t	CH_2 a
								[c]	s [a]	*p*-ClC_6H_4N*H*
								1.85-1.60	m	CH_2 b and c

[a] Exchangeable. [b] Upon deuteration the quartet collapsed into a triplet. [c] Overlapped with signal corresponding to methylene a.

Scheme 4

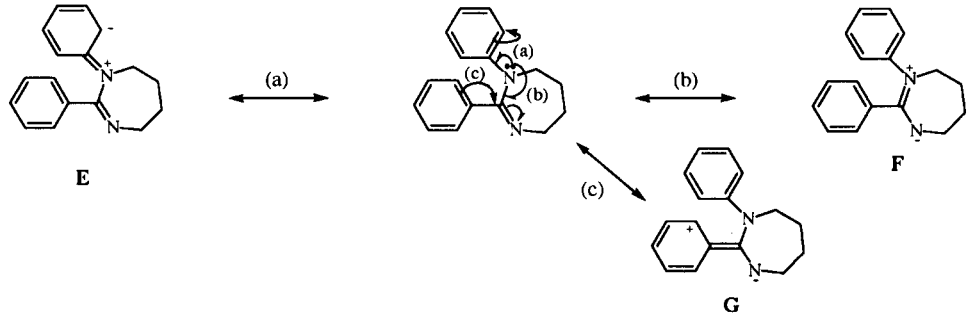
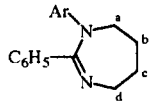


Table 2

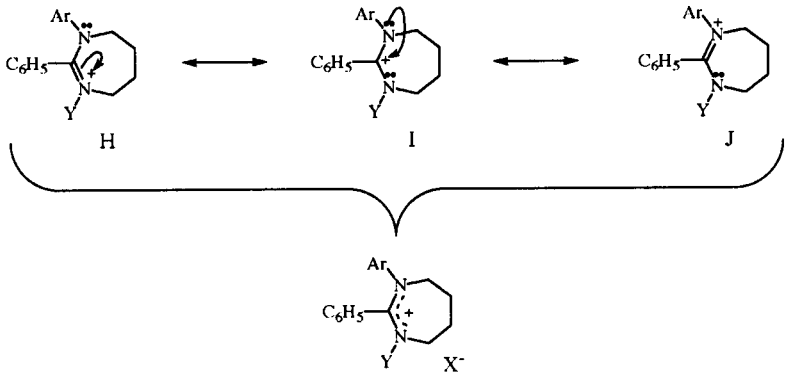
1-Aryl-2-phenyl-1*H*-4,5,6,7-tetrahydro-1,3-diazepines **1a-d**



Compound N°	Mp (°C)	Yield (%)	Formula	Analyses (Calcd./Found) %C	%H	%N	Mass ($M^{+\cdot}$) m/z	δ (ppm)	^{1}H-NMR Multiplicity	Assignment
1a	107	64	$C_{17}H_{18}N_2$	81.56	7.25	11.19	250	7.57	dd	CC_6H_5 (2 *ortho* H) [b]
	[a]			81.45	7.30	11.09		7.19	t	CC_6H_5 (*para* H) [b]
								7.15	t	CC_6H_5 (2 *meta* H) [b]
								7.05	m	NC_6H_5 (2 *meta* H)[b]
								6.75	t	NC_6H_5 (*para* H) [b]
								6.65	d	NC_6H_5 (2 *ortho* H) [b]
								3.85-3.78	m	CH_2 a and d
								1.80 and 1.70	[c]	CH_2 b and c
1b	110	68	$C_{18}H_{20}N_2$	81.78	7.63	10.60	264	7.60	t	C_6H_5 (2 *ortho* H)
	[a]			81.59	7.68	10.52		7.25-7.23	m	C_6H_5 (2 *meta H* and *para* H)
								6.90	dd	*p*-$CH_3C_6H_4$ (2 *meta* H)
								6.63	dd	*p*-$CH_3C_6H_4$ (2 *ortho* H)
								3.82-3.76	m	CH_2 a and d
								2.19	s	CH_3
								1.77-1.90	m	CH_2 b and c
1c	121	60	$C_{18}H_{20}N_2O$	77.11	7.19	9.99	280	7.60	dd	C_6H_5 (2 *ortho* H)
	[a]			77.05	7.14	9.96		7.26-7.24	m	C_6H_5 (2 *meta* and *para* H)
								6.73 and	dd	*p*-$CH_3OC_6H_4$ (2 *ortho* H
								6.68	dd	and 2 *meta* H)
								3.82-3.76	m	CH_2 a and d
								3.70	s	OCH_3
								1.77-1.90	m	CH_2 b and c
1d	95	55	$C_{17}H_{17}N_2Cl$	71.70	6.02	9.84	284	7.58	dd	C_6H_5 (2 *ortho* H)
	[d]			71.54	6.05	9.77		7.26-7.23	m	C_6H_5 (2 *meta* and *para* H)
								7.07	dd	*p*-ClC_6H_4 (2 *meta* H)
								6.61	dd	*p*-ClC_6H_4 (2 *ortho* H)
								3.78 and 3.73	[e]	CH_2 a and d
								1.89 and 1.75	[c]	CH_2 b and c

[a] Recrystallized from cyclohexane. [b] Signals unequivocally assigned by HMQC and HMBC experiments. [c] Two pentuplets partially overlapped. [d] The final product was an oil which did not crystallize from cyclohexane. When it was dissolved in a mixture of 5% hydrochloric acid-ethanol (1:10), **1d** precipitated by adding 5% sodium hydroxide to *p*H 14. [e] Two triplets partially overlapped.

Scheme 5

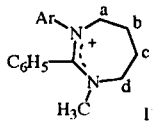


H I J

3 (Y = CH_3)
1D$^+$ (Y = D)

Table 3

1-Aryl-3-methyl-2-phenyl-1*H*-4,5,6,7-tetrahydro-1,3-diazepinium Iodides **3a-d**



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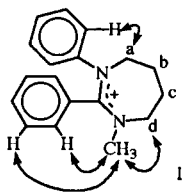
Compound N°	Mp (°C)	Yield (%)	Formula	Analyses (Calcd./Found) %C	%H	%N	δ (ppm)	^{1}H-NMR Multiplicity	Assignment
3a	260	90	$C_{18}H_{21}IN_2$	55.11	5.40	7.14	7.69	dd	CC_6H_5 (2 *ortho* H) [a]
				55.14	5.42	7.05	7.30	m	NC_6H_5 (2 *ortho* H) [a]
							7.25-7.11	m	NC_6H_5 (2 *meta* and *para* H) and CC_6H_5 (2 *meta* and *para* H)
							4.65	t	CH_2 a [a]
							4.25	t	CH_2 d [a]
							3.23	s	CH_3
							2.45	p	CH_2 c [a]
							2.05	p	CH_2 b [a]
3b	161	85	$C_{19}H_{23}IN_2$	56.17	5.71	6.89	7.80	dd	C_6H_5 (2 *ortho* H)
				56.28	5.69	6.93	7.20-7.23	m	C_6H_5 (2 *meta* and *para* H)
							7.10	dd	*p*-$CH_3C_6H_4$ (2 *ortho* H)
							6.95	dd	*p*-$CH_3C_6H_4$ (2 *meta* H)
							4.65	t	CH_2 a
							4.20	t	CH_2 d
							3.12	s	CH_3N
							2.35	p	CH_2 c
							2.19	s	$CH_3C_6H_4$
							2.10	p	CH_2 b
3c	170	92	$C_{19}H_{23}IN_2O$	54.04	5.49	6.63	7.60	dd	C_6H_5 (2 *ortho* H)
				54.08	5.45	6.60	7.30-7.24	m	C_6H_5 (2 *meta* and *para* H)
							7.15	dd	*p*-$CH_3OC_6H_4$ (2 *ortho* H)
							6.80	dd	*p*-$CH_3OC_6H_4$ (2 *meta* H)
							4.55	t	CH_2 a
							4.25	t	CH_2 d
							3.70	s	$CH_3OC_6H_4$
							3.18	s	CH_3N
							2.42 and	p	
							2.05	p	CH_2 b and c
3d	174	81	$C_{18}H_{20}ClIN_2$	50.66	4.72	6.56	7.65	dd	C_6H_5 (2 *ortho* H)
				50.52	4.70	6.53	7.55	dd	*p*-ClC_6H_4 (2 *ortho* H)
							7.26-7.23	m	C_6H_5 (2 *meta* and *para* H)
							7.15	dd	*p*-ClC_6H_4 (2 *meta* H)
							4.35	t	CH_2 a
							4.15	t	CH_2 d
							3.05	s	CH_3
							2.17 and	p	
							1.99	p	CH_2 b and c

[a] Signals unequivocally assigned by NOESY experiments. In the other compounds, assignments were made by comparison.

Scheme 6



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reaction of compounds **1a-d** with methyl iodide in chloroform solution afforded the corresponding 1,2-diaryl-3-methyl-1*H*-4,5,6,7-tetrahydro-1,3-diazepinium iodides **3a-d** (Scheme 1). Analytical and spectroscopic data of methiodides **3** are shown in Table 3. Ir spectrum of compounds **3a-d** confirmed their ionic structure, as it can be seen from the strong amidinium band at *ca.* 1590-1640 cm^{-1}.

Reduction of compounds **1c** and **1e** (**1**, Ar = *p*-$NO_2C_6H_4$) [16] with borane/tetrahydrofuran lead regiospecifically to unsymmetrical *N,N'*-disubstituted putrescines **8c,e** with good yields (81% and 78% respectively) (Scheme 3). We propose for this reaction, initial hydroboration of the C=N double bond leading to the intermediate **A**. This *N*-monoborane adduct may undergo rearrangement with selective reductive cleavage of N1-C2 bond, to form borodiazepines **B** [24]. Subsequent decomposition of **B** in the hydrolytic reaction medium leads to tetramethylenediamines **8c,e**. Alternatively, selective N1-C2 cleavage could be explained by means of diadduct **C**, formed from **A** and another equivalent of borane. In this case, reductive cleavage of the heterocyclic ring would occur through a hydride ion transfer from the second borane molecule, leading to boranediamine **D** [26]. Further hydrolysis of **D** would originate compounds **8c,e**.

Spectral properties.

^{1}H-nmr spectra of compounds **1** show that both hydrogen atoms on each carbon of the tetramethylene chain become isochronous, being the spectrum similar to that of an acyclic compound. This is probably due to the rapid ring and/or nitrogen inversion processes at room temperature. In order to evaluate the effect of introducing a substituent on N1, spectra of compounds **1a-d** were compared with that of 2-aryl derivatives [12,13].

Methylene hydrogens a and d in compounds **1a-d**, appear like partially or completely overlapped multiplets at 3.73-3.85 ppm, showing a paramagnetic shift with respect to those of 2-aryl-1*H*-4,5,6,7-tetrahydro-1,3-diazepines [12,13] ($\Delta\delta$ = 0.23-0.35 ppm). Deshielding of the methylene moiety, as well as the shielding observed for aromatic hydrogens at N1 [28] respect to benzene, may be explained by the contribution of mesomeric structure **E** or an equivalent structure with the negative charge on *para* position (a, Scheme 4).

Ortho hydrogens of phenyl on C2 (7.57-7.63 ppm) show no difference with the values obtained for 1-unsubstituted derivative [12], while aryl groups on N1 shifted *meta* and *para* hydrogen signals of 2-phenyl from 7.37 ppm in 2-phenyl-1*H*-4,5,6,7-tetrahydro-1,3-diazepine [13], to 7.15 and 7.19 ppm respectively in compound **1a**. The observed shielding effect cannot be thought in terms of mesomeric effects (Scheme 4). As it was pointed before, aryl substituent on N1 originates a mesomeric effect (a), which decrease donation of N1 lone pair to the amidine system (b), and resonance involving phenyl on C2 (c) would become more meaningful deshielding 2-phenyl *ortho* and *para* hydrogens. Instead, the observed selective shielding of *meta* and *para* hydrogens may be thought in terms of anisotropy effects: the steric tension caused by the presence of two vicinal aryl groups, could determine the twisting of aromatic rings from the amidine moiety, thus causing 2-phenyl *meta* and *para* hydrogen atoms to be within the protection region of the 1-aryl group.

Spectra of methiodides **3** in deuteriochloroform, showed strong differences with compounds **1** in polymethylene chain signals (Table 3). Thus, four differenciable signals were obtained for methylene hydrogens a-d, at *ca.* 4.60, 4.20, 2.25, 2.15 ppm, and unequivocal assignments were made by means of NOESY experiment for compound **3a**. Correlation between non adjacent hydrogens is shown in Scheme 4.

Comparing spectra of compounds **1** and **3**, we found certain remarkable facts: (i) a, b, c and d methylene hydrogen signals are sharply differentiated in compounds **3**, being all signals deshielded with respect to the values of compounds **1**, in agreement with the cationic character of the amidinium system. Methylene a was the most affected by quaternization, thus proving the great contribution of mesomeric structure J (Scheme 5, Y = CH_3); (ii) a significant deshielding effect in compounds **3** is observed on 1-aryl *ortho* hydrogens ($\Delta\delta$ *ca.* 0.46 ppm) as well as on *meta* hydrogens (*ca.* 0.1 ppm), also coherent with the contribution of structure J; and (iii) a slight deshielding effect of 2-phenyl *ortho* hydrogens is observed, probably due to contribution of structure I.

^{1}H-nmr spectra of compounds **1** in deuteriochloroform-trifluoroacetic acid-*d*, were run and analyzed. In general, all aromatic hydrogens suffered downfield shift on going from **1** to deuteronated **1D$^+$**, due to the cationic character of these species (Scheme 5, Y = D). Four signals are observed for methylene hydrogens (two triplets at *ca.* 4.00 and 4.35 ppm, and two pentuplets at *ca.* 2.15 and 2.30 ppm), being deshielding effects opperating in **1D$^+$**, qualitative similar to those present in methiodides **3**. However, deshielding effects and peak separation are less in species **1D$^+$** than in methiodides **3**, suggesting that these effects are quantitatively lower in **1D$^+$**, and hence *N*-protonation would confer a slightly less cationic character than *N*-methylation to the amidinium system. This could be explained taking into account that protonation involves an acid/base equilibrium, where both **1D$^+$** and the free base **1** are present. This is not the case of compounds **3**, where methyl group is irreversibly bonded to N3.

EXPERIMENTAL

Melting points were taken on a Büchi capillary apparatus and are uncorrected. Ir spectra were taken on a Beckman 180A spectrometer. Samples were run as potassium bromide pellets. ^{1}H-nmr spectra were obtained on a Bruker MSL 300 MHz spectrometer using deuteriochloroform as the solvent. NOESY experiment was performed on a Bruker ACE-200 MHz. Chemical shifts are reported in parts per million (δ) downfield from an internal TMS reference. Signals are quoted as: s (singlet), d (doublet), dd (double doublet), t (triplet), q (quartet), p (pentuplet), m (multiplet) and bs (broad signal). The presence of exchangeable protons was confirmed by use of deuterium oxide. Mass spectra were recorded on a MS Shimadzu QP-1000 instrument at 20 eV. Analytical tlc was carried out on aluminium sheets Silica Gel 60

F_{254} using ethyl acetate, benzene/methanol (9:1) and chloroform/methanol (9:1) as solvents. Column chromatography were performed on Silica Gel 60 (230-400 mesh) with typically 30-50 g of stationary phase per gram of substance. Reagents, solvents and starting materials were purchased from standard sources and purified according to literature procedures.

4-Bromobutylamine Hydrobromide (**4**).

A mixture of 4-aminobutanol (0.01mole), hydrobromic acid 47 % (2.5 ml, 0.02 mole pure hydrogen bromide) and benzene (4.6 ml) was heated under reflux employing a Dean-Stark trap. After 2 hours, azeotropic distillation was concluded (care must be taken over the end of the reaction, in order to avoid product destruction). The residue consisted of highly hygroscopic white crystals of 4-bromobutylamine hydrobromide **4** (70%), mp 155-157 °C (acetone); lit [29] mp 157-158 °C.

Reaction of 4-Bromobutylamine Hydrobromide (**4**) with Benzoyl Chloride.

To a mixture of 4-bromobutylamine hydrobromide **4** (0.01 mole) and benzoyl chloride (0.015 mole), 10% sodium hydroxide (10 ml) were added dropwise, with continuous stirring on an ice bath. Once addition was finished, a white solid and an amber oil were obtained. The white solid, *N*-(4-bromobutyl)-benzamide **6** (X = Br), (5%), was purified by recrystallization from ethanol/water, mp 50-51 °C. The oily phase was dissolved in chloroform, washed with 10% hydrochloric acid (10 ml), and then with water until neutral *p*H, dried with anhydrous sodium sulphate, filtered and concentrated *in vacuo*. The compound proved to be *N*-benzoylpyrrolidine **5** (67%), by comparison with an authentical sample obtained from pyrrolidine and benzoyl chloride [19]. Similar results were previously obtained by Fones *et al.* [18] in the reaction of 4-iodobutylamine hydrobromide with benzoyl chloride.

N-(4-Chlorobutyl)benzamide (**6**, X = Cl).

To *N*-benzoylpyrrolidine [19] (0.042 mole), phosphorous pentachloride (0.047 mole) was added slowly in small portions on an ice bath. When addition was finished, the mixture was heated under reflux at 80° C until phosphorous pentachloride was dissolved. The amber solution was then heated at 140 °C for one hour. The reaction mixture was slowly poured into a water-ice bath, and a dark oil separated. It was decanted and after a steam distillation, the residue was taken with methylene chloride (30 ml), washed with 10% sodium hydroxide (20 ml) and then with water until neutral *p*H, dried with anhydrous sodium sulphate, filtered and concentrated *in vacuo*. The dark brown residue was purified by recrystallization from cyclohexane yielding white needles of *N*-(4-chlorobutyl)benzamide **6** (X = Cl) (60%), mp 65 °C, (lit [20], mp 58 °C); ms: m/z 211 ($M^{+\cdot}$); ^{1}H-nmr: δ 1.30-1.70 (4H, m, $CH_2CH_2CH_2CH_2$), 3.00-3.50 (4H, m, $CH_2CH_2CH_2CH_2$), 6.50 (1H, bs, exchangeable, NH), 7.10-7.50 (3H, m, C_6H_5, 2 *meta* H and *para* H), 7.75 (dd, 2H, C_6H_5, 2 *ortho* H).

N-Aryl-*N'*-benzoyltetramethylenediamines **2a-d**.

General Procedure.

A mixture of *N*-(4-chlorobutyl)benzamide **6** (X = Cl) (0.02 mole) and the corresponding arylamine (0.04 mole) was heated for 1 hour under reflux in an oil bath at 120 °C. After cooling, the crude material was treated with 10 ml of hot water in order to extract the arylamine hydrochloride, and then heated for 5 minutes with 10% hydrochloric acid (10 ml) and filtered before cooling. The filtrate was alkalinized with 10% sodium hydroxide to *p*H 14. When product precipitated, it was filtered, dried and recrystallized from cyclohexane. In other cases, the solution became turbid, so it was extracted with chloroform (3 x 20 ml). The organic layer was washed with 5% hydrochloric acid and then with water until neutral *p*H, dried with anhydrous sodium sulphate, filtered and evaporated *in vacuo*. The residue was purified by recrystallization from cyclohexane, affording compounds **2**. Melting points, yields, elemental analysis and spectroscopic data of the compounds are given in Table 1.

In the crude product, before recrystallization, a spot of higher R_f (*ca.* 0.50) is observed accompanying product **2** (R_f *ca.* 0.30). In the case of reaction of **6** with aniline, it was isolated by column chromatography yielding *N,N*-bis(4-benzamidobutyl)aniline (**7**, Ar = C_6H_5) as an oil, 35% yield; ^{1}H-nmr: δ 7.75 (4H, dd, C_6H_5CO, 4 *ortho* H), 7.47-7.26 (8H, m, C_6H_5CO, 4 *meta* and 2 *para* H, and C_6H_5N, 2 *meta* H), 7.17 (1H, t, C_6H_5N, 1 *para* H), 6.58 (2H, C_6H_5N, 2 *ortho* H), 6.55 (1H, broad signal, NHCO, ex), 3.45-3.47 (4H, q, collapse into a triplet by addition of D_2O, $CONHCH_2$), 3.35 (4H, t, $C_6H_5NCH_2$), 1.60-1.75 (8H, m, $CH_2CH_2CH_2CH_2$).

Anal. Calcd. for $C_{28}H_{33}N_3O_2$: C, 75.82; H, 7.50; N, 9.47. Found: C, 75.90; H, 7.51; N, 9.45.

1-Aryl-2-phenyl-1*H*-4,5,6,7-tetrahydro-1,3-diazepines **1a-d**.

General Procedure.

The corresponding *N*-aryl-*N'*-benzoyltetramethylenediamine **2** (1 g) was dissolved in a chloroform solution of ethyl polyphosphate [30] and heated under reflux for 12 hours. The solution was cooled and extracted with water (4 x 20 ml). Aqueous phases were pooled and made alkaline with 10% sodium hydroxide to *p*H 14. When product precipitated, the resulting solid was filtered. In other cases, it was necessary to extract the aqueous phase with methylene chloride (3 x 20 ml). The organic layer was washed with water until neutral *p*H, dried with anhydrous sodium sulphate, filtered and evaporated *in vacuo* affording compounds **1**. Melting points, yields, elemental analysis and spectroscopic data of the compounds are given in Table 2.

^{1}H-nmr spectra of compounds **1a-c** run in the presence of trifluoroacetic acid-*d* (named as **1aD$^+$-1cD$^+$**), showed the following signals (unequivocal assignment performed for **3a** was extrapolated to deuteronated species): **1aD$^+$**: δ 7.70 (2H, dd, CC_6H_5 2 *ortho* H), 7.60-7.10 (m, 8H, CC_6H_5, 2 *meta* and *para* H, NC_6H_5), 4.45 (t, 2H, $C_6H_5NCH_2$), 3.99 (t, 2H, CH_3NCH_2), 2.34 (2H, p, $CH_3NCH_2CH_2$), 2.14 (2H, p, $C_6H_5NCH_2CH_2$). **1bD$^+$**: δ 7.46-7.25 (5H, m, C_6H_5), 7.10 (dd, 2H, *p*-$CH_3C_6H_4$, 2 *ortho* H), 6.95 (dd, 2H, *p*-$CH_3C_6H_4$, 2 *meta* H), 4.40 (t, 2H, *p*-$CH_3C_6H_4NCH_2$), 3.98 (t, 2H, CH_3NCH_2), 2.27 (2H, p, $CH_3NCH_2CH_2$), 2.25 (3H, s, CH_3), 2.14 (2H, p, *p*-$CH_3C_6H_4NCH_2CH_2$). **1cD$^+$**: δ 7.48-7.26 (5H, m, C_6H_5), 7.02 (dd, 2H, *p*-$CH_3OC_6H_4$, 2 *ortho* H), 6.76 (dd, 2H, *p*-$CH_3OC_6H_4$, 2 *meta* H), 4.37 (t, 2H, *p*-$CH_3OC_6H_4NCH_2$), 3.98 (t, 2H, CH_3NCH_2), 3.75 (3H, s, CH_3), 2.30 (2H, p, $CH_3NCH_2CH_2$), 2.18 (2H, p, *p*-$CH_3OC_6H_4NCH_2CH_2$).

1,2-Diaryl-4,5,6,7-tetrahydro-1*H*-1,3-diazepinium Iodides **3a-d**.

General Procedure.

A solution of compound **1** (0.003 mole) in anhydrous tetrahydrofuran (20 ml) was refluxed protected from moisture with methyl iodide (0.05 mole) until disappearance of compound **1** checked by tlc. The solid was filtered and recrystallized from anhydrous 2-propanol, affording salts **3** as white crystals. Melting points, yields, elemental analysis and spectroscopic data of the compounds are given in Table 3.

N-Aryl-*N'*-benzyltetramethylenediamines **8c,e**.

General Procedure.

Compounds **1c,e** (0.01 mole) were treated with borane/tetrahydrofuran (20 ml saturated solution) [31] and heated under reflux in a nitrogen atmosphere for 5 hours. The solvent was removed *in vacuo* and the residue boiled with concentrated hydrochloric acid (20 ml) for one hour. Solution was cooled, diluted with water (10 ml) and made alkaline (*p*H=14) with sodium hydroxide pellets. The mixture was extracted with chloroform (3 x 20 ml) and the organic layer washed with water (10 ml) and dried with anhydrous sodium sulphate. The solution was concentrated *in vacuo* and products were purified by column chromatography on Silica Gel (chloroform/methanol 9:1), affording *N*-(*p*-methoxyphenyl)-*N'*-benzyltetramethylenediamine (**8c**) [32] (81%) and *N*-(*p*-nitrophenyl)-*N'*-benzyltetramethylenediamine (**8e**) (78%) [32].

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