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ARYNIC AND SNAr REACTIONS OF POLYHALOGENOBENZENES—VI[1,2]

STUDY OF POLYFLUOROBENZENES

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Abstract—Condensations of diethylamine and piperidine with *ortho* and *para* difluorobenzenes and several dialkylaminofluorobenzenes were performed in two basic media: "$NaNH_2$, HMPT–THF" and "$NaNH_2$–t-AmONa, THF". The mechanisms involved depend on the base, the amine and the halogeno compound.

We have previously shown[3] that fluoroaromatic compounds without electron-withdrawing groups can be substituted by nucleophilic reagents in the presence of sodamide in the mixture THF–HMPA, or in THF alone in the presence of the complex base $NaNH_2$–t-AmONa. These reactions are direct substitutions or arynic ones, and the mechanisms which occur depend upon the nucleophile and the basic medium used. This mechanism duality has also been found with polychlorobenzenes.[2b,c] Concerning the behaviour of polyfluorobenzenes we report the condensation of amines with *ortho* and *para* difluorobenzenes.

RESULTS AND DISCUSSION

Taking into account our first work,[3] we limited our study to the condensation of two amines: diethylamine and piperidine. For each of these and each of the fluoro compounds, we performed two kinds of experiments. In the first one, amines and fluorobenzenes were used in equivalent quantities in such a way that monosubstitution was favoured. In the second case the amine was in excess and disubstitution the chief reaction

Monocondensation with ortho *and* para *difluorobenzenes*

The results obtained according to the amine and the medium used, are summarized in Table 1.

The overall yields of these reactions were not very good. This was due to the formation of tar and disubstituted compounds. The latter were formed by further condensation of the amines with **3**, **4** and **6** (v.i.).

With *o*-difluorobenzene, we again found[3] that direct substitution was highly favoured in HMPA–THF in the presence of $NaNH_2$ (runs 1 and 3), in contrast with the complex base in THF which permitted formation of an aryne, as seen by the presence of the *meta* isomer **4**. The intervention of this arynic mechanism was important with diethylamine (run 2); but with piperidine (run 4) direct substitution was the main reaction, because of the more necleophilic character of this amine, and the autoactivation of the F atoms. Such an observation has also been made with 1,2,3-trichlorobenzene.[2c]

In all cases we verified that the ratios **3**/**4** did not change during the course of the condensations.

With *p*-difluorobenzene, the results obtained with $NaNH_2$ (runs 5 and 7) were in agreement with what we expected. (Here also the ratios **4**/**6** were constant during the condensations). However, the reactions observed with the complex base (runs 6 and 8) were in contradiction with our first results. The products of direct substitution were formed almost exclusively, though *p*-difluorobenzene should have given arynic reactions more easily than the *ortho* isomer. In fact, when the condensations were followed in time, we observed that the ratios **4**/**6** were not constant: At the beginning of the reaction (5 min after the addition of the halogeno compound) the ratio **4**/**6** was 37/63 with diethylamine and 30/70 with piperidine. This fact is explained by the high reactivity of isomers **4** with amines in the complex base-THF medium (due to the strong acidity of the H atom located between the amino group and the F atom), hence they disappear faster than **6**, to give diamines **9**. The initial values of **4**/**6** were in agreement with those found by Roberts *et al.*[4] and de Graaf *et al.*[5] for the amination of *p*-bromofluorobenzene by KNH_2 in liquid ammonia. This last reaction is of the arynic type. Thus we confirmed that the complex base in THF is particularly efficient for cinesubstitution.

Evolution of the ortho *and* para *amino fluorobenzenes*

As mono substitutions were always accompanied by disubstitutions, we decided to investigate the behaviour of the *o*- and *p*-fluoroamines given in Table 1. The evolution of *m*-fluoro compounds is not considered here, since it is very easy to predict. Indeed a direct substitution will give *m*-diaminobenzenes. These will also be formed by an arynic reaction: the H atom between the amino group and the F atom is far more acidic than the others; thus the benzyne formed will be 3-amino dehydrobenzene **11** which condenses with a nucleophilic reagent only on the *meta* position.[6]

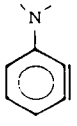

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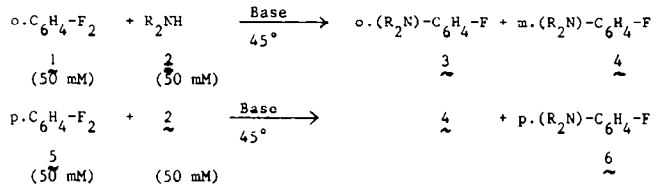
Table 1.

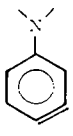


Run n°	Halogeno compound	R	Solvent (ml)	Base (M)	Time (h)	3 (%)	4 (%)	6 (%)	Yield (%)
1	1	C_2H_5	HMPA-THF (30 - 10)	$NaNH_2$ (0,1)	15	98	2		32
2	1	C_2H_5	THF (40)	$NaNH_2$(0,1) t-AmONa(0,05)	8	20	80		35
3	1	$(CH_2)_5$	HMPA-THF (30 - 10)	$NaNH_2$ (0,1)	15	100	-		45
4	1	$(CH_2)_5$	THF (40)	$NaNH_2$(0,1) t-AmONa(0,05)	8	85	15		48
5	5	C_2H_5	HMPA-THF (30 - 10)	$NaNH_2$ (0,1)	15		2	98	37
6	5	C_2H_5	THF (40)	$NaNH_2$(0,1) t-AmONa(0,05)	8		3	97	38
7	5	$(CH_2)_5$	HMPA-THF (30 - 10)	$NaNH_2$ (0,1)	15		-	100	52
8	5	$(CH_2)_5$	THF (40)	$NaNH_2$(0,1) t-AmONa(0,05)	8		3	97	45

The results obtained are given in Table 2. With the amines of type **3**, it is noteworthy that in run 9, a substantial quantity of *meta* isomer **9** was formed. This fact demonstrated the formation of benzyne **11** competing for the direct substitution. This elimination-addition in $NaNH_2$, HMPA-THF medium, is recorded for the first time.[3] We think that it is the result of steric hindrance of the "Et_2N" group (of the fluoro compound and of the condensed amine), which impedes the direct substitution; moreover diethylamine is not nucleophilic enough to compensate for this steric effect.

These hypotheses were verified by runs 11 and 13 in which we diminished steric crowding and increased amine nucleophilicity; also in run 15 where only the steric hindrance was diminished. In the presence of the complex base (runs 10, 12, 14, 16) cinesubstitution, by way of aryne **11**) was the only reaction observed (formation of *meta* isomer).

Concerning fluoroamines **6**, the literature reports[5] the condensation of a nucleophilic compound on aryne **12** yielding a mixture of *meta* and *para* isomers with 65–70% of the *meta* derivative.



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Examination of the results obtained in HMPA-THF (runs 17, 19, 21 and 23) shows that the action of piperidine results only in direct substitution products, whereas with diethylamine, there is some intervention of the arynic mechanism. Comparison with analogous reactions performed with *ortho* aminofluorobenzenes (runs 9 and 15) shows the role of steric hindrance with these latter compounds and it is noteworthy that the arynic mechanism intervenes. We think that the stimultaneous presence of the amino group and fluorine on the ring enhances the acidity of the H atom and the mobility of fluorine sufficiently to allow the elimination resulting in **12**.

Note. We verified that for all the direct substitutions encountered here, $NaNH_2$ is needed. In other words, the amines, in HMPA-THF but without a base, are unreactive. The same observation has been made previously[3] and we proposed the intervention of an "arynoide" as an explanation.

Finally, in the presence of the complex base (runs 18, 20, 22 and 24) it was clear that the mechanism was chiefly of the arynic type.[5] The ratios of the isomers were in agreement with what we expected.

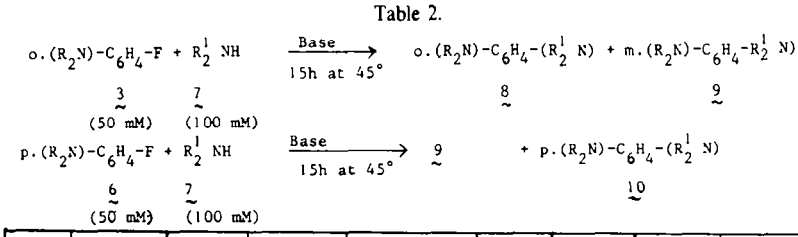
Dicondensation with ortho *and* para *difluorobenzenes*

We used the same base-solvent systems as in first part but with larger amounts of amine and base relative to the halogeno compound. Our main results are summarized in Table 3. The relative proportions of the diamines obtained were in agreement with the results of Tables 1 and 2 taking into account that:

(1) *m*-Aminofluorobenzenes **4** gave only *meta* diamines **9**.

(2) Under the conditions of runs 6 and 8 (Table 1) the starting ratios **4/6** were about 40/60 and 30/70. These observations explain the ratios **9/10** in runs 30 and 32.

Table 2.



Run n°	Halogeno compound (R)	R^1	Solvent (ml)	Base (M)	8 (%)	9 (%)	10 (%)	Yield (%)
9	3 (C_2H_5)	C_2H_5	HMPA-THF (30 - 10)	$NaNH_2$ (0,2)	48	52		68
10	3 (C_2H_5)	C_2H_5	THF (40)	$NaNH_2$(0,2) t-AmONa(0,1)	-	100		68
11	3 (C_2H_5)	$(CH_2)_5$	HMPA-THF (30 - 10)	$NaNH_2$ (0,2)	96	4		72
12	3 (C_2H_5)	$(CH_2)_5$	THF (40)	$NaNH_2$(0,2) t-AmONa(0,1)	-	100		72
13	3 ($CH_2)_5$	$(CH_2)_5$	HMPA-THF (30 - 10)	$NaNH_2$ (0,2)	96	4		75
14	3 ($CH_2)_5$	$(CH_2)_5$	THF (40)	$NaNH_2$(0,2) t-AmONa(0,1)	-	100		73
15	3 ($CH_2)_5$	C_2H_5	HMPA-THF (30 - 10)	$NaNH_2$ (0,2)	73	27		70
16	3 ($CH_2)_5$	C_2H_5	THF (40)	$NaNH_2$(0,2) t-AmONa(0,1)	-	100		68
17	6 (C_2H_5)	C_2H_5	HMPA-THF (30 - 10)	$NaNH_2$ (0,2)		9	91	63
18	6 (C_2H_5)	C_2H_5	THF (40)	$NaNH_2$(0,2) t-AmONa(0,1)		65	35	62
19	6 (C_2H_5)	$(CH_2)_5$	HMPA-THF (30 - 10)	$NaNH_2$ (0,2)		-	100	65
20	6 (C_2H_5)	$(CH_2)_5$	THF (40)	$NaNH_2$(0,2) t-AmONa(0,1)		63	37	63
21	6 ($CH_2)_5$	$(CH_2)_5$	HMPA-THF (30 - 10)	$NaNH_2$ (0,2)		-	100	67
22	6 ($CH_2)_5$	$(CH_2)_5$	THF (40)	$NaNH_2$(0,2) t-AmONa(0,1)		55	45	67
23	6 ($CH_2)_5$	C_2H_5	HMPA-THF (30 - 10)	$NaNH_2$ (0,2)		12	88	62
24	6 ($CH_2)_5$	C_2H_5	THF (40)	$NaNH_2$ (0,2) t-AmONa(0,1)		55	45	58

CONCLUSION

This work shows that it is possible to realize arynic substitution on difluorobenzenes if, as in the case of monofluorobenzenes,[3] the complex base "$NaNH_2$, t-AmONa" and THF, are used. Note that very few systems generate benzyne from a fluoroaromatic derivative.

We have also shown that in the mixture HMPA-THF in the presence of $NaNH_2$, the observed reactions appear to be SNAr as far as the results are concerned, but they need sodamide. Moreover an arynic mechanism can compete if steric hindrance prevents direct substitution, and if the condensed amine is not sufficiently nucleophilic.

Lastly, the experimental conditions outlined favour the synthesis of several fluoroaromatic derivatives. This work is being continued with the aim of generalising and improving these results.

EXPERIMENTAL

IR spectra were recorded with a Perkin–Elmer R-257 spectrophotometer; NMR spectra were carried out with varian A-60 and JEOL C-60 HL instruments, using TMS as internal standard; the chemical shifts (δ) are expressed in ppm. Analytical VPC analyses were carried out with a Techmation Tracor MT 220 instrument, flame ionization detector, with Carbowax 20 M 10% and SE-30 5% columns (chromosorb W DMCS). We used Fluka sodium amide, washed several times and finely ground in a mortar, under THF. M.ps are instantaneous. All reactions were carried out under N_2. The yields were calculated with reference to the fluoro derivative used in the reaction. All the compounds described gave satisfactory C, H, N microanalyses.

Table 3.

$$\underset{(50\ mM)}{1} + \underset{(150\ mM)}{2} \xrightarrow[15h\ at\ 45°]{Base} o.(R_2N)_2\text{-}C_6H_4 \underset{8}{(R = R^1)} + m.(R_2N)_2\text{-}C_6H_4 \underset{9}{(R = R^1)}$$

$$\underset{(50\ mM)}{5} + \underset{(150\ mM)}{2} \xrightarrow[15h\ at\ 45°]{Base} \underset{9}{(R = R^1)} + p.(R_2N)_2\text{-}C_6H_4 \underset{10}{(R = R^1)}$$

Run n°	Halogeno compound	R	Solvent (ml)	Base (M)	8 (%)	9 (%)	10 (%)	Yield (%)
25	1	C_2H_5	HMPA-THF (30 - 10)	$NaNH_2$ (0,2)	52	48		65
26	1	C_2H_5	THF (40)	$NaNH_2$(0,2) t-AmONa(0,1)	-	100		67
27	1	$(CH_2)_5$	HMPA-THF (30 - 10)	$NaNH_2$ (0,2)	96	4		73
28	1	$(CH_2)_5$	THF (40)	$NaNH_2$(0,2) t-AmONa(0,1)	-	100		73
29	5	C_2H_5	HMPA-THF (30 - 10)	$NaNH_2$ (0,2)		12	88	63
30	5	C_2H_5	THF (40)	$NaNH_2$(0,2) t-AmONa(0,1)		85	15	60
31	5	$(CH_2)_5$	HMPA-THF (30 - 10)			-	100	65
32	5	$(CH_2)_5$	THF (40)	$NaNH_2$(0,2) t-AmONa(0,1)		65	35	65

General procedure. The quantities involved as well as reaction times and temp, are indicated in Tables 1–3.

Reactions carried out in HMPA-THF *in the presence of* $NaNH_2$

To a suspension of $NaNH_2$ (50 or 100 mM) in HMPA-THF (30 ml–10 ml) was added the amine (50, 100 or 150 mM); the mixture was heated at 45–50° for 1 hr; the halogenobenzene (50 mM) dissolved in THF (5 ml) and the remaining $NaNH_2$ (50 or 100 mM) were then added; the mixture was heated to the desired temp. After the end of the reaction, the mass was poured onto ice, extracted with ether, and dried over K_2CO_3. After evaporation of the solvent under ordinary pressure, the residue was washed with a large excess of water (elimination of HMPA), extracted with ether, dried (K_2CO_3) and distilled under reduced pressure.

Reactions carried out in THF *in the presence of* $NaNH_2$–t-*AmOHa*

To a suspension of $NaNH_2$ (150 or 300 mM) in THF (30 ml) was added dropwise a soln of t-AmOH (50 or 100 mM) in THF (5 ml); the mixture was heated at 45° for 2 hr. The amine (50 or 100 mM) in THF (5 ml) was added at room temp., and the mass heated at 45° for 1 hr. The soln of halogenobenzene (50 mM) in THF (5 ml) was then added, and the mixture heated to the desired temp. After the end of the reaction, the mass was poured onto ice, extracted with ether, and dried over K_2CO_3. After evaporation of the solvent, the residue was distilled under reduced pressure.

Monocondensation of **2** *with* o-*difluorobenzene* **1** (Table 1)

Condensation of diethylamine ($R = C_2H_5$). (a) In the $NaNH_2$, HMPA-THF medium (run 1) distillation gave **3**: b.p. 80–81°/12 mm, $n_D^{20} = 1.5055$; NMR (CCl_4): 1.03, t, 6H (CH_3); 3.15, q, 4H (CH_2); 6.60–7.10, m, 4H (aromatic). All the characteristics of **3** (b.p., n_D, NMR and IR spectra) were identical with those of an authentic compound (obtained by the action of EtBr (3 moles) upon 2-fluoroaniline (1 mole) in the presence of $NaHCO_3$ (3 moles) in DMF). Analytical VPC of the crude product showed the presence of **4** as impurity (identified by VPC with the authentic sample obtained as **3** from 3-fluoroaniline). (b) In the complex base, THF medium (run 2) distillation gave (**3** + **4**) b.p. 82–88°/12 mm; identified by analytical VPC with an authentic sample and by NMR (CCl_4) (spectrum of **3**: vs run 1; spectrum of **4**: 1.12, t, 6H (CH_3); 3.26, q, 4H (CH_2); 6.0–6.40 and 6.70–7.20, 2 m, 4H (aromatic). The proportions of **3** and **4** are determinated in VPC.

Condensation of piperidine ($R = (CH_2)_5$). (a) In the $NaNH_2$, HMPA-THF medium (run 3) **3** was obtained by distillation: b.p. 108–110°/12 mm, $n_D^{18} = 1.5332$; NMR (CCl_4): 1.40–1.95, m, 6H (CH_2) in β, β' and γ of nitrogen); 2.75–3.25, m, 4H (CH_2 in α and α' of nitrogen); 6.58–7.12, m, 4H (aromatic). (b) In the complex base, THF medium (run 4) **3** + **4** was obtained by distillation: b.p. 108–112°/12 mm; identified by VPC with the pure isomers (**3** was obtained pure in run 3; **4** was isolated from the reaction of piperidine with 3-difluorobenzene under the conditions used in Table 1) and by NMR (CCl_4) (spectrum of **3**: vs run 3; spectrum of **4**: 1.45–1.90, m, 6H (CH_2 in β, β' and γ of nitrogen); 2.90–3.32, m, 4H (CH_2 in α and α' of nitrogen); 6.20–6.68 and 6.82–7.30, 2 m, 4H (aromatic).

Monocondensation of **2** *with* p-*difluorobenzene* **5** (Table 1)

Condensation of diethylamine ($R = C_2H_5$). (a) In the $NaNH_2$, HMPA-THF medium (run 5) distillation gave **6**: b.p. 92–93°/14 mm, lit.[6] b.p. 42°/0.2 mm, $n_D^{19} = 1.5164$, NMR (CCl_4): 1.06, t, 3H (CH_3); 3.18, q, 4H (CH_2); 6.35–7.05, m, 4H (aromatic). All the characteristics of **6** (b.p. n_D, NMR and IR spectra) were identical with those of an authentic compound (obtained as **3** from 4-fluoroaniline). Analytical VPC of the crude product showed the presence of **4** as impurity. (b) In the complex base, THF medium (run 6) distillation gave **6**, identical with the compound obtained in run 5 (b.p., n_D, superimposable IR and NMR). VPC of the crude product showed the presence of **4** as impurity.

Condensation of piperidine ($R = (CH_2)_5$). (a) In the presence of $NaNH_2$ (run 7) **6** was obtained by distillation, b.p. 110–112°/16 mm, lit.[6] b.p. 70°/3 mm; $n_D^{20} = 1.5348$; NMR (CCl_4) 1.30–1.90, m, 6H (CH_2 in β, β' and γ of nitrogen); 2.75–3.18, m, 4H

(CH_2 in α and α' of nitrogen); 6.55–7.10, m, 4H (aromatic). (b) In the presence of complex base-(run 8) **6** was obtained by distillation; identical with the compound obtained in run 7 (b.p. n_D, superimposable IR and NMR) VPC of the crude product showed the presence of **4** as impurity.

Evolution of o- *and* p-*aminofluorobenzenes* (Table 2);
Case of 2-N,N-*diethylaminofluorobenzene* **3** (R = C_2H_5)

(1) *Reaction with diethylamine* (R' = C_2H_5). (a) In the presence of $NaNH_2$ (run 9) distillation gave (**8** + **9**) b.p. 95–110°/0.05 mm; identified by VPC with authentic derivatives (obtained by the reaction of EtBr (6 moles) with *o*- and *p*-diaminobenzenes (1 mole) respectively, in the presence of NaH CO_3 (6 moles) in DMF) and by NMR (CCl_4) (spectrum of **8**: 0.98, t, 12H (CH_3); 3.18, q, 8H (CH_2); 6.75–7.90 (strong resonance at 6.80), m, 4H (aromatic); spectrum of **9**: 1.10, t, 12H (CH_3): 3.27, q, 8H (CH_2); 5.85–6.15 and 6.70–7.10, 2 m, 4H (aromatic). The proportions of **8** and **9** are determinated in VPC. (b) In the presence of complex base (run 10) distillation gave **9**. b.p. 105/0.1 mm, $n_D^{21.5}$ = 1.5473; lit.[7] b.p. 147–148°/9 mm, $n_D^{11.6}$ = 1.5537. NMR (CCl_4) vs run 9. All the characteristics of **9** (b.p., n_D, NMR and IR spectra) were identical with those of an authentic compound.

(2) *Reaction with piperidine* (R' = $(CH_2)_5$). (a) In the presence of $NaNH_2$ (run 11) distillation gave **8**: b.p. 115–117°/0.1 mm, n_D^{23} = 1.5390; NMR (CCl_4): 0.98, t, 6H (CH_3); 1.35–1.92, m, 6H (CH_2 in β, β' and γ of nitrogen). 2.75–3.45, m, including q at 3.18, 8H (CH_2 in α and α' of nitrogen, and $CH_2(CH_2–CH_3)$); 6.75–7.0 (strong resonance at 6.80); 4H (aromatic). Analytical VPC of the crude product showed the presence of **9** (identified with the pure isomer obtained in another run). (b) In the presence of complex base (run 12) distillation gave **9**: b.p. 123–125°/0.05 mm, $n_D^{23.5}$ = 1.5635; NMR (CCl_4): 1.10, t, 6H (CH_3); 1.38–1.90, m, 6H (CH_2 in β, β' and γ of nitrogen) 2.85–3.55, m, including q at 3.27, 8H (CH_2 in α and α' of nitrogen, and $CH_2(CH_2–CH_3)$); 5.90–6.30 and 6.70–7.15, 2 m, 4H (aromatic).

Case of 2-*piperidono fluorobenzene* **3** (R = $(CH_2)_5$

(1) *Reaction with piperidine* (R' = $(CH_2)_5$). (a) In the presence of $NaNH_2$ (run 13) **8** was obtained by distillation, m.p. 65°, NMR (CCl_4): 1.38–1.95, m, 12H (CH_2 in β, β' and γ of nitrogen); 2.78–3.28, m) 8H (CH_2 in α and α' of nitrogen); 6.78–6.98 (strong resonance at 6.82), 4H (aromatic). Analytical VPC of the crude product showed the presence of **9** (identified with the pure isomer isolated in another run). (b) In the presence of complex base (run 14) **9** was obtained by distillation, b.p. 140–142°/0.5 mm, m.p. 42–43°; lit.[8] m.p. 41–43°. NMR (CCl_4): 1.38–1.90, m, 12H (CH_2 in β, β' and γ of nitrogen), 2.85–3.30, m, 8H (CH_2 in α and α' of nitrogen); 6.15–6.45 and 6.75–7.15, 2 m, 4H (aromatic).

(2) *Reaction with diethylamine* (R' = C_2H_5). (a) In the presence of $NaNH_2$ (run 15) **8** + **9** was obtained by distillation, b.p. 112–122°/0.05 mm; identified by VPC with the pure isomers isolated in runs 11 and 12 respectively, and by NMR (CCl_4) (spectrum of **8**, vs run 11; spectrum of **9**, vs run 12). The proportions of **8** and **9** were determinated in VPC. (b) In the presence of complex base (run 16) **9** was obtained by distillation, identical with the compound isolated in run 12 (b.p., n_D, superimposable IR and NMR).

Case of 4-N,N-*diethylamino fluorobenzene* **6** (R = C_2H_5)

(1) *Reaction with diethylamine* (R' = C_2H_5). (a) In the presence of $NaNH_2$ (run 17) **9** + **10** was obtained by distillation, b.p. 150–155°/12 mm; identified by VPC with the authentic compounds (**10** was prepared as **9** from 4-diaminobenzene). The proportions of **9** and **10** were determinated in VPC. (b) In the presence of complex base (run 18) distillation gave **9** + **10** (vs run 17).

(2) *Reaction with piperidine* (R' = $(CH_2)_5$). (a) In the presence of $NaNH_2$ (run 19) distillation gave **10**; b.p. 132–133°/0.1 mm; $n_D^{23.5}$ = 1.5590; NMR (CCl_4): 1.05, t, 6H (CH_3); 1.35–1.90, m, 6H (CH_2 in β, β' and γ of nitrogen) 2.75–3.40, m, including q at 3.18, 8H (CH_2 in α and α' of nitrogen, and $CH_2(CH_2–CH_3)$); 6.45–6.80 (strong resonance at 6.57 and 6.62), m, 4H (aromatic. (b) In the presence of complex base (run 20) distillation gave **9** + **10**: b.p. 110–115°/0.01 mm, identified by NMR (CCl_4) (spectrum of **9**: vs run 12; spectrum of **10**: vs run 19). The proportions of **9** and **10** were determinated by NMR on the aromatic part of the spectrum.

Case of 4-*piperidino fluorobenzene* **6** (R = $(CH_2)_5$)

(1) *Reaction with piperidine* (R' = $(CH_2)_5$). (a) In the presence of $NaNH_2$ (run 21) distillation gave **10**: m.p. 108–109°; lit.[9] m.p. 108–109°; NMR (CCl_4): 1.35–1.85, m, 12H (CH_2 in β, β' and γ of nitrogen); 2.75–3.10, m, 8H (CH_2 in α and α' of nitrogen); 6.50–6.70 (strong resonance at 6.62) m, 4H (aromatic). (b) In the presence of complex base (run 22) **9** + **10** was obtained by distillation. B.p. 140–150°/0.5 mm, identified by NMR (CCl_4) (spectrum of **9**: vs run 14; spectrum of **10**: vs run 21). The proportions of **9** and **10** were determinated by NMR on the aromatic part of the spectrum.

(2) *Reaction with diethylamine* (R' = C_2H_5). (a) In the presence of $NaNH_2$ (run 23) **9** + **10** was obtained by distillation (vs run 20). (b) In the presence of complex base (run 24) distillation gave **9** + **10** (vs run 20).

Dicondensation of **2** *with* o-*diflourobenzene* **1** (Table 3)

Condensation of diethylamine (R = C_2H_5). (a) In the $NaNH_2$, HMPA–THF medium (run 25) **8** + **9** was obtained by distillation (vs run 9, Table 2). (b) In the complex base, THF medium (run 26) distillation gave **9**, identical with the compound obtained in run 10 (b.p., n_D, superimposable NMR and IR).

Condensation of piperidine (R = $(CH_2)_5$). (a) In the $NaNH_2$, HMPA–THF medium (run 27) distillation gave **8**, identical with the compound obtained in run 13 (m.p., superimposable NMR and IR). VPC of the crude product showed the presence of **9** (identified as in run 13). (b) In the complex base, THF medium (run 28) distillation gave **9**, identical with the compound obtained in run 14 (m.p., superimposable NMR and IR).

Dicondensation of **2** *with* p-*difluorobenzene* **5** (Table 3)

Condensation of diethylamine (R = C_2H_5). (a) In the presence of $NaNH_2$ (run 29) **9** + **10** was obtained by distillation (vs run 17). (b) In the presence of complex base (run 30) distillation gave **9** + **10** (vs run 17).

Condensation of piperidine (R = $(CH_2)_5$). (a) In the presence of $NaNH_2$ (run 31) distillation gave **10**, identical with the compound obtained in run 21 (m.p., superimposable NMR and IR). (b) In the presence of complex base (run 32) distillation gave **9** + **10** (vs run 22).

REFERENCES

[1]Taken, with Ref. 3, from the Thèse de Doctorat d'Etat of M. F. Moreau, University of Nancy (1975).

[2]Previous Paper [a]P. Caubere and L. Lalloz, *Bull. Soc. Chim. Fr.* 1983 (1974); [b]P. Caubere and L. Lalloz, *Ibid.* 1989 (1974); [c]P. Caubere and L. Lalloz, *Ibid.* 1996 (1974); [d]P. Caubere and L. Lalloz, *J. Org. Chem.* **40**, 2853 (1975); [e]P. Caubere and L. Lalloz, *Ibid.* 2859 (1975).

[3]P. Caubere and M. F. Hochu, *Bull. Soc. Chim. Fr.* 2854 (1969).

[4]J. D. Roberts, D. A. Semenow, H. E. Simmons and L. A. Carlsmith, *J. Am. Chem. Soc.* **78**, 601, 611 (1956).

[5]G. B. de Graaf, H. J. den Hertog and W. C. Melger, *Tetrahedron Letters* 963 (1965).

[6]C. Sellers and H. Suschitzky, *J. Chem. Soc.* 6186 (1965).

[7]F. Krollpfeiffer, *Ann. Chem.* **430**, 215 (1922).

[8]F. Effenberger, G. Prossel, E. Auer and P. Fisher, *Chem. Ber.* **103**, 1456 (1970).

[9]N. J. Leonard and R. R. Sauers, *J. Org. Chem.* **21**, 1187 (1956).