Reactions of Perfluoro-2-methyl-2-pentene and Octafluoroisobutylene with Arylamines

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Treatment of perfluoro-2-methyl-2-pentene with four moles of arylamine provided 1-aryl-2,4-bis(arylimino)-3-(1-arylimino-2,2,3,3,3-pentafluoropropyl)azetidine, 3-(*N,N'*-diarylamidino)-4-arylamino-2-(pentafluoroethyl)-quinoline and 2,4-bis(arylamino)-3-(1-arylimino-2,2,3,3,3-pentafluoropropyl)quinoline, depending on the basicity of the arylamine and on the solvent used. Octafluoroisobutylene also yielded similar azetidine and quinoline derivatives.

As has been previously reported,[1] perfluoro-2-methyl-2-pentene (**1**) is much more reactive with *O*-nucleophiles than another isomer of hexafluoropropene dimer, perfluoro-4-methyl-2-pentene. Reactions of **1** with alcohols and phenol very easily produced addition and substitution products. Now we wish to report on reactions of **1** with primary arylamines, which proceeded with similar facility, but with much more complexity.

Results and Discussion

Reaction of Perfluoro-2-methyl-2-pentene with Arylamines. Haszeldine and his co-workers[2] very recently reported that two moles of arylamine react with **1** affording a quinoline derivative, **3**. They presumed that the reaction occurs with the formation of a ketenimine, **2**, followed by intramolecular cyclization. We had independently found this quinoline ring formation using about two moles of aniline, toluidines and chloroanilines in *N,N*-dimethylformamide.[3] The results of this quinoline formation are summarized in Table 1.

However, we further found that as much as four moles of arylamine react with **1** to give azetidine and quinoline derivatives, **5**—**7**, depending on the basicity of the arylamine and on the solvent used.

For example, when a large excess of aniline was allowed to react with **1** in the presence of triethylamine in diethyl ether, yellow crystals of 1-phenyl-2,4-bis(phenylimino)-3-(1-phenylimino-2,2,3,3,3-pentafluoropropyl)azetidine, **5** (Ar=Ph), was obtained in a fair yield (52%). The structure of this compound was established on the basis of the spectral data. In the IR spectrum, a strong, wide absorption band at 1660 cm^{-1} was observed, which should be due to the C=N groups adjacent to the azetidine ring. A sharp band at 1765 cm^{-1} was ascribed to a similar group apart from the ring. In the PMR, one singlet signal at τ 4.90 and several signals in the region of τ 1.7—4.6 were assigned to one >CH proton and fifteen aromatic protons, respectively. In the MS, the parent peak and the fragment peaks appeared appropriately (Experimental section). These spectral data, in contrast with those of the quinoline derivatives, strongly supported the azetidine structure.

Naturally, this compound was susceptible to reactions with acids and alkalies, *e.g.*, acetic and hydrochloric acids, and aqueous alkali hydroxide solutions, and these reactions produce several decomposition products.

Interestingly, when this azetidine compound was treated with ethanolic hydrochloric acid at room temperature, it isomerized into a quinoline derivative, **6** (Ar=Ph; X=H) in a 34% yield.

The structure of **6** was evident also from its spectral analysis. The IR spectrum revealed the presence of N–H groups by the two absorption bands at 3400 and 3350 cm^{-1}. In the mass spectrum, a peak at *m/e* 440 (M^+—NHPh) was observed, which confirmed the structure of **6**, but not that of another isomeric quinoline derivative, **7**.

When *p*-toluidine was used instead of aniline under the same conditions, the quinoline derivative **3** (Ar=*p*-MeC_6H_4; X=6-Me) was obtained as a main product (38%).

Table 1. Physical data of quinoline and azetidine derivatives

Compound No	Ar	X	Yield %	Mp °C	F-Anal % (Calcd)	IR (KBr) cm^{-1}	^{19}F NMR ($CHCl_3$) δ[a]	^{1}H NMR ($CDCl_3$) τ
3	Ph	H	53	99.5—100	37.8 (37.4)	3450 (N-H), 1100—1240 (C-F)	−24.3 (CF_3), +29.0, +0.3 (CF_2CF_3)	1.8—3.3 (Ar)
	o-MeC_6H_4	8-Me	77	99.5—100	34.9 (35.0)	3420 (N-H), 1050—1250 (C-F)	−23.8 (CF_3), +28.7, +0.6 (CF_2CF_3)	2.4—3.7 (Ar), 7.28, 7.58 (CH_3)
	p-MeC_6H_4	6-Me	63	94.5—95	34.7 (35.0)	3400 (N-H), 1100—1250 (C-F)	−24.1 (CF_3), +29.6, +0.4 (CF_2CF_3)	2.04—3.4 (Ar), 7.78 (CH_3)
	o-ClC_6H_4	8-Cl	17	124—125	31.1 (32.0)	3420 (N-H), 1100—1240 (C-F)	−23.4 (CF_3), +28.7, +1.0 (CF_2CF_3)	2.1—3.7 (Ar)
	m-ClC_6H_4	7-Cl	21	103—104	31.9 (32.0)	3450 (N-H), 1100—1240 (C-F)	−23.7 (CF_3), +29.8, +1.2 (CF_2CF_3)	1.8—3.5 (Ar)
	p-ClC_6H_4	6-Cl	37	120—121	32.0 (32.0)	3455 (N-H), 1100—1240 (C-F)	−23.2 (CF_3), +29.7, +1.2 (CF_2CF_3)	1.8—3.5 (Ar)
5	Ph	—	52	128—129.5	17.7 (17.8)	1765, 1660 (C=N), 1060—1260 (C-F)	+31.2, +2.3 (CF_2CF_3)	4.9 (>CH), 1.8—4.6 (Ar)
	p-ClC_6H_4	—	34	145—146	13.4 (14.2)	1780, 1680 (C=N), 1080—1280 (C-F)	+33.2, +1.8 (CF_2CF_3)	5.00 (>CH), 1.8—4.6 (Ar)
	p-FC_6H_4	—	34	129—130	28.8 (28.3)	1767, 1680 (C=N), 1100—1260 (C-F)	+33.0, +2.0 (CF_2CF_3)	4.83 (>CH), 1.8—4.5 (Ar)
6	Ph	H	5 (34)[b]	132—132.5	17.7 (17.8)	3400, 3350 (N=H), 1628 (C=N), 1100—1250 (C-F)	+30.7, +1.7 (CF_2CF_3)	1.9—3.6 (Ar, NH)
	m-ClC_6H_4	7-Cl	16	169.5—170	14.5 (14.2)	3415, 3375 (N-H), 1655 (C=N), 1050—1260 (C-F)	+30.2, +1.7 (CF_2CF_3)	1.9—3.7 (Ar, NH)
7	*m*-ClC_6H_4	7-Cl	18	129.5—130	14.0 (14.2)	3460, 3415 (N-H), 1640 (C=N), 1050—1270 (C-F)	+32.4, +1.7 (CF_2CF_3)	2.1—3.4 (Ar), 4.35 (NH)
9	*p*-MeC_6H_4	—	18	124.5—125	13.6 (13.5)	1775, 1675 (C=N), 1100—1300 (C-F)	−14.5 d (CF_3), J_{H-F}=6.2 Hz	5.05 q (>CH)
10	*p*-MeC_6H_4	6-Me	12	131—131.5	13.6 (13.5)	3405, 3500 (N-H), ~1300 (C-F)	−24.8 s	2.2—3.4 (Ar, NH), 3.67 (NH), 7.65, 7.72 (CH_3)

a) Given in δ ppm from ext. CF_3CO_2H. b) Yield obtained by isomerization of **3** (Ar=Ph).

When *p*-fluoro- and *p*-chloroaniline were used, the azetidine derivatives (**5**) were obtained as in the case of aniline (Table 1).

m-Chloroaniline, however, gave two quinoline derivatives, **6** and **7** (Ar=*m*-ClC_6H_4; X=Cl), in yields of 16 and 18%, respectively. In this case, these isomeric quinoline derivatives were separated from each other by means of a column chromatography. A fraction which was assumed to contain azetidine derivative was obtained, but no confirmation of compound **5** (Ar=*m*-ClC_6H_4) could be made.

Assignments for the two quinoline derivatives, **6** and **7**, were rather easy. In their IR spectra, both compounds showed absorption at about 1650 cm^{-1}, characteristic of a C=N group. However, the C=N absorption of **6** was situated in that of the amidino group, so it was much stronger than that of **7**. The mass spectra gave more unambiguous evidence. Besides the parent peak at M^+ 668, the amidinoquinoline **6** showed a strong peak at *m/e* 542 ($M^+-NHC_6H_4Cl$), whereas arylaminopentafluoropropylquinoline **7** gave a peak at *m/e* 549 ($M^+-C_2F_5$). The former peak of *m/e* 542 was absent in the spectrum of **7**, and *vice versa*.

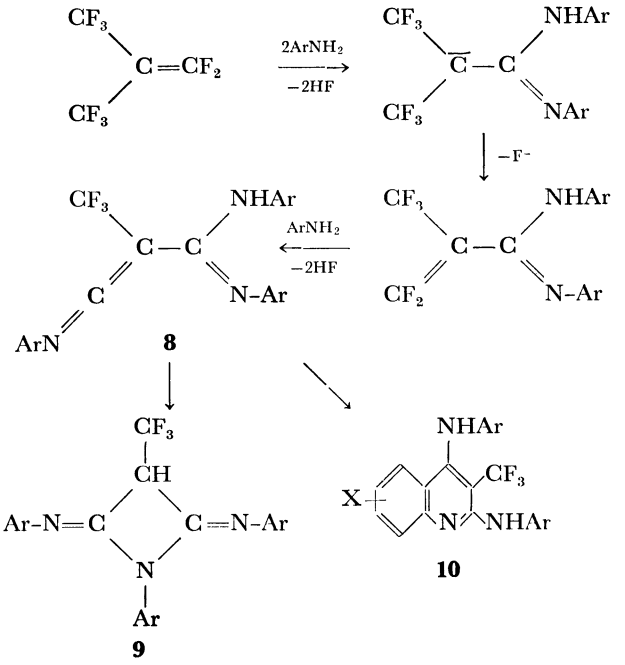
The reaction mechanisms assumed for the formation of the azetidine and quinoline derivatives are shown in the scheme. Four moles of aniline nucleophilically attacked **1**, replacing fluorine atoms successively to give the ketenimine intermediate **4**. When the positive carbon atom of the ketenimine attacked the nitrogen atom of ArNH, the azetidine ring was formed to give **5**. On the other hand, when the positive carbon atom attacked the *ortho* position of the aromatic ring of arylimino group, either Ar* or Ar**, a quinoline ring was formed to give **6** or **7**.

In general, the amino group should be kinetically more readily attacked by the ketenimine group to give azetidine, **5**. The azetidine derivatives thus formed are thermodynamically less stable than the quinoline derivative, so that **5** will isomerize into **6** by means of an acid or a base. This was confirmed experimentally as mentioned above. Presumably, the electron donative methyl group of toluidine prompted the intramolecular attack of the ketenimine group of **2** on the toluidino ring, and further retarded the reaction of **2** with other toluidino molecules.

When *p*-halogenoanilines were used, the *ortho* position to the amino group, *i.e.*, the *meta* position to the halogen, should be electron deficient, which means they are rarely attacked by the ketenimine group. Thus no quinoline derivatives, neither **6** nor **7**, could be obtained from *p*-chloro or *p*-fluoroaniline.

On the other hand, the amino group of *m*-halogenoaniline is less basic than that of the *p*-isomer, so that it will retard the formation of the azetidine ring. Conversely, the *ortho* position to the amino group, *i.e.*, *para* position to the halogen, may be attacked more easily by the ketenimine group than that of *p*-halogenoaniline. Thus, only quinoline derivatives **6** and **7** from *m*-chloroaniline could be obtained, though in poor yields.

Reaction of Octafluoroisobutylene with Arylamine. As has been mentioned previously, perfluoro-2-methyl-2-pentene (**1**) reacts easily with primary aromatic amines



to give azetidine and quinoline derivatives. This high reactivity and the mode of the reaction should have resulted from the existence of a *gem*-bis(trifluoromethyl) methylene group, $=C(CF_3)_2$. This prompted us to examine the similar reaction with octafluoroisobutylene, the simplest olefin of this type. We carried out the reaction of octafluoroisobutylene with an excess of *p*-toluidine in diethyl ether in the presence of triethylamine, and in *N,N*-dimethylformamide.

In diethyl ether in the presence of triethylamine, three moles of *p*-toluidine reacted, giving the azetidine derivative **9** (Ar=*p*-MeC_6H_4) in a 18% yield.

In *N,N*-dimethylformamide, also three moles of toluidine reacted, and as expected, a quinoline derivative **10** (Ar=*p*-MeC_6H_4; X=6-Me) was obtained in a 12% yield. In each case, large quantities of by-products were formed. The by-products could not be identified, but they were assumed to be other imidoyl fluoride derivatives.[4]

The structures of these azetidine and quinoline derivatives were evident from the spectral data. In particular, in the ^{19}F and ^1H NMR spectra of **9**, there appeared a doublet due to CF_3 and a quartet due to CH. This means that a $CH(CF_3)$ group is present in the molecule, and this fact strongly supports the azetidine structure.

The reaction mechanism is understood in a similar way, as in the case of **1**. Arylamine should have attacked the terminal difluoromethylene groups successively, thereby forming an amidinoketenimine intermediate, **8**. When the positive carbon of the ketenimine attacked the nitrogen atom in the arylamino group, the azetidine derivative was formed. On the other hand, if the *ortho* position of the arylimino group was attacked, the quinoline derivative was produced.

Experimental

*2-Pentafluoroethyl-3-trifluoromethyl-4-anilinoquinoline (**3**(Ar=Ph; X=H)).* A solution of aniline (2.23 g, 0.022 mol)

in *N,N*-dimethylformamide (5 ml) was added into an ice-cooled mixture of perfluoro-2-methyl-2-pentene (**1**) (3.0 g, 0.01 mol) and *N,N*-dimethylformamide (15 ml) in a pressure vessel. After sealing, the mixture was heated with stirring at 70 °C for 2.5 h, and the reaction mixture was poured into water (100 ml). The resulting precipitate was separated by filtration to give a crude product (3.3 g, mp 84—89 °C). Recrystallization from hexane yielded a pure quinoline derivative **3** (2.2 g), mp 99—100 °C, in a 53% yield.

Found: C, 53.51; H, 2.48; N, 7.03; F, 37.8%. Calcd for $C_{18}H_{10}N_2F_8$: C, 53.20; H, 2.48; N, 6.90; F, 37.4%. MS: 406 (M^+), 337 (M^+-CF_3), 218 ($M^+-CF_3-C_2F_5$).

In the above procedure, toluidines and chloroanilines were used instead of aniline. The formed quinoline derivatives (**3**) are tabulated in Table 1.

*1-Phenyl-2,4-bis(phenylimino)-3-(1-phenylimino-2,2,3,3,3-pentafluoropropyl)azetidine (**5** (Ar=Ph)).* Into a solution of aniline (8.2 g, 0.088 mol) and triethylamine (14.2 g, 0.154 mol) in diethyl ether (30 ml), a solution of perfluoro-2-methyl-2-pentene (6.0 g, 0.02 mol) in diethyl ether (15 ml) was added dropwise, while keeping the temperature at 35—40 °C. After the addition, the mixture was stirred at room temperature for 1 h. The reaction mixture was washed with dilute hydrochloric acid to remove excess triethylamine, and with water, and then dried over magnesium sulfate. On removing the ether, yellow crystals were produced, which were collected to give the crude product (7.1 g, 67%), mp 102—118 °C. Recrystallization from hexane yielded pure **5** (Ar=Ph), mp 128—129.5 °C (5.5 g, 52%).

Found: C, 67.62; H, 3.87; N, 10.55; F, 17.7%. Calcd for $C_{30}H_{21}N_4F_5$: C, 67.66; H, 3.97; N, 10.52; F, 17.8%. MS: *m/e* 532 (M^+), 338 (M^+–Ph–N=C=N–Ph), 219 (PhN=C–CH=C=NPh), 194 (PhN=C=NPh).

p-Fluoro- and *p*-chloroanilines were used instead of aniline in the above reaction and similar azetidine derivatives were obtained (Table 1).

*2-Pentafluoroethyl-3-(N,N'-diphenylamidino)-4-anilinoquinoline (**6** (Ar=Ph; X=H)).* The azetidine compound **5** (Ar=Ph) (0.5 g) was dissolved in ethanol (15 ml), and a small amount of conc. hydrochloric acid (5 drops) was added. The mixture was stirred at room temperature for 3 h and poured into water (200 ml). The resulting oily material containing crystals was taken into diethyl ether, and the ethereal solution was washed with water, and dried over magnesium sulfate. The ether was removed and the residue (0.7 g) was crystallized from petroleum ether, giving **6** (Ar=Ph; X=H) (0.17 g, 34%), mp 132—132.5 °C.

Found: C, 67.71; H, 3.76; N, 10.59; F, 17.7%. Calcd for $C_{30}H_{21}N_4F_5$: C, 67.66; H, 3.97; N, 10.52; F, 17.8%.

*2-Pentafluoroethyl-3-[N,N'-bis(m-chlorophenyl)amidino]-4-(m-chloroanilino)-7-chloroquinoline (**6** (Ar=m-ClC_6H_4; X=7-Cl)) and 2,4-bis(m-chloroanilino)-3-(1-m-chlorophenylimino-2,2,3,3,3-pentafluoropropyl)-7-chloroquinoline (**7** (Ar=m-C_6H_4; X=7-Cl)).* Into a solution of *m*-chloroaniline (5.6 g) and triethylamine (7.1 g) in diethyl ether (15 ml), a solution of perfluoro-2-methyl-2-pentene (3.0 g) in diethyl ether (15 ml) was added dropwise at ~40 °C. After 1 h of stirring at room temperature, the reaction mixture was washed with dilute hydrochloric acid and water, then dried over magnesium sulfate. The ether was removed, leaving a semi-solid mass (7.0 g). This crude product was subjected to silica-gel column chromatography, using a mixture of benzene and hexane as the eluent. Of the two main yellow bands observed, the first band was eluted. Evaporation of the eluate provided crystals (1.21 g, 18%), which were recrystallized from hexane yielding pure **7** (Ar=*m*-ClC_6H_4, H=7-Cl), mp 129.5—130 °C.

Found: C, 54.09; H, 2.50; N, 9.08; F, 14.0%. Calcd for $C_{30}H_{17}N_4Cl_4F_5$: C, 53.76; H, 2.56; N, 8.36; F, 14.2%. MS: 668 (M^+), 549 ($M^+-C_2F_5$), 111 (ClC_6H_4).

Elution of the second main band, followed by evaporation of the solvent, provided more of the product (1.07 g, 16%). Recrystallization from hexane gave pure **6** (Ar=*m*-ClC_6H_4; X=7-Cl), mp 169.5—170 °C.

Found: C, 54.25; H, 2.58; N, 8.65; F, 14.5%. Calcd for $C_{30}H_{17}N_4Cl_4F_5$: C, 53.76; H, 2.56; N, 8.36; F, 14.2%. MS: *m/e* 668 (M^+), 542 ($M^+-NHC_6H_4Cl$), 126 (NHC_6H_4Cl).

*1-(p-Tolyl)-2,4-bis(p-tolylimino)-3-(trifluoromethyl)azetidine (**9** (Ar=p-MeC_6H_4)).* *p*-Toluidine (7.07 g, 0.066 mol), triethylamine (11.1 g, 0.11 mol) and diethyl ether (25 ml) were placed in a glass pressure tube equipped with a mechanical stirrer. This reaction vessel was cooled to *ca.* −50 °C into which liquefied octafluoroisobutylene (4.0 g, 0.02 mol) was introduced. The mixture was stirred for 1 h at −20 to −5 °C, for 30 min at 0 °C, then for 1 h at room temperature. After the unreacted octafluoroisobutylene was driven off by an aspirator, the reaction mixture was washed with dilute hydrochloric acid and water, and was dried over magnesium sulfate. Diethyl ether was evaporated and the remaining oily material (7.1 g) was recrystallized from petroleum ether. The azetidine derivative **9** (1.5 g, 18%), mp 122—123 °C, was thus obtained, and was recrystallized further to give the pure product, mp 124.5—125 °C.

Found: C, 71.74; H, 5.44; N, 10.27; F, 13.6%. Calcd for $C_{25}H_{22}N_3F_3$: C, 71.24; H, 5.26; N, 9.97; F, 13.5%. MS: *m/e* 421 (M^+), 352 (M^+-CF_3), 222 (Ar–N=C=N–Ar), 199 (M^+–Ar–N=C=N–Ar).

*6-Methyl-2,4-bis(p-toluidino)-3-(trifluoromethyl)quinoline (**10** (Ar=p-MeC_6H_4; X=6-Me)).* *p*-Toluidine (3.54 g, 0.033 mol), *N,N*-dimethylformamide (15 ml) and octafluoroisobutylene (2.0 g, 0.01 mol) were placed in a reaction vessel as described above. The mixture was stirred for 30 min at room temperature, then for 2.5 h at 65—70 °C. A considerable amount of unidentified yellow crystals (2.33 g, mp 205—211 °C) were produced. This solid was removed by filtration and the filtrate was poured into water. The solid material thus obtained (0.50 g, 12%) was recrystallized from hexane to give pure **10**, mp 131—131.5 °C.

Found: C, 71.28; H, 5.49; N, 10.15; F, 13.6%. Calcd for $C_{25}H_{22}N_3F_3$: C, 71.24; H, 5.26; N, 9.97; F, 13.5%. MS: *m/e* 421 (M^+), 380 ($M^+-2HF-H$), 91 ($C_6H_5CH_2^+$).

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