cis Isomer: 111.9 (1a), −6.0 (1e), −1.3 (CF_3), 73.4 (4a), 40.3 (2,6a), 54.8 (2,6e), 45.6 (3,5a), 59.0 (3,5e), $J_{2,6a\text{-}e}$ = 286, $J_{3,5a\text{-}e}$ = 272, $J_{1a\text{-}4a}$ = 48, $J_{Fb\text{-}4a}$ = 26.

IR spectrum (mixed isomers): 1793 cm^{-1} (C=N). Mass spectra: (M^+) 445 (3%), (M−F) 426 (2%), (M−CF_3) 376 (3%), (M−C_4F_9) 226 (15%), CF_3^+ 69 (100%). Found, %: C 24.57, F 72.40. $C_9F_{17}N$. Calculated, %: C 24.27, F 72.58.

CONCLUSIONS

1. Perfluorinated tertiary amines with a variety of structures undergo dealkylation on heating with SbF_5 with the formation of the corresponding azomethines.

2. Amines containing the N−CF_3 grouping are cleaved under milder conditions.

LITERATURE CITED

1. H. Bürger, Köplin, and G. Pavelke, J. Fluorine Chem., 22, No. 2, 175 (1983).
2. A. G. Vinogradov, A. F. Gontar', and I. L. Knunyants, Zh. Vses. Khim. Ova., 10, No. 2, 234 (1965).
3. V. A. Petrov, G. G. Belen'kii, and L. S. German, Izv. Akad. Nauk SSSR, Ser. Khim., 1934 (1985).
4. A. Mitsch. Ronald, J. Am. Chem. Soc., 87, 328 (1965).
5. K. N. Makarov, N. S. Mirzabekyants, V. F. Snegirev, et al., Perfluorinated Hydrocarbons in Biology and Medicine [in Russian], Sci. Center Biol. Stud., Akad. Sci. USSR, Pushchino (1980), p. 21.
6. L. L. Gervits, V. F. Snegirev, K. N. Makarov, et al., Izv. Akad. Nauk SSSR, Ser. Khim., 2867 (1987).

REACTIONS OF HEXAFLUOROACETONE BENZENESULFONYL- AND TRIFLUOROACETYLIMINES WITH ARYLAMINES*

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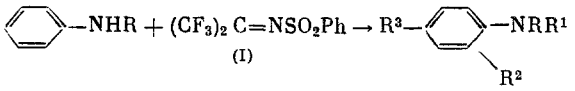
UDC 542.91:547.446.5'161'415.3:547.551

N,N-Dimethylaniline reacts under mild conditions with hexafluoroacetone benzenesulfonylimine (I) to give 4-(α-benzenesulfonylaminohexafluoroisopropyl)-N,N-dimethylaniline [2]. We here report a systematic study of the reactions of primary, secondary, and tertiary arylamines with (I) and hexafluoroacetone trifluoroacetylimine (II). As expected, the imine (I) reacts vigorously with aniline at 20°C with the formation of N-(α-benzenesulfonylaminohexafluoroisopropyl)aniline (III). With N-ethylaniline, (I) at 20°C gives the products of C^2- (IV) and C^4-alkylation (V), isolated chromatographically in low yields:



(III)–(V)

R=R²=R³=H, R¹=C(CF₃)NHSO₂Ph (III); R=Et, R¹=R³=H, R²=C(CF₃)NHSO₂Ph (IV);

R=Et, R¹ = R² = H, R³ = C(CF₃)NHSO₂Ph (V).

Indoline reacts with (I) on boiling in chloroform to give a complex mixture of products, from which, after partial chromatographic purification and treatment with MnO_2 in benzene, there was obtained 7-(α-benzenesulfonylaminohexafluoroisopropyl)indole (VI). The low yield

*For previous communication, see [1].

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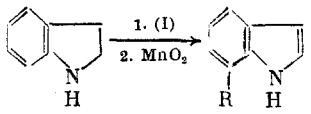
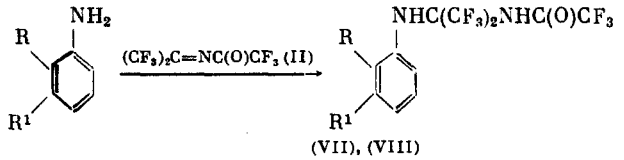
of (VI) (17%) did not allow the preferred orientation of alkylation of the indole by (I) to be established unambiguously, but the result obtained is in accordance with the previously reported regioselective C^7-alkylation of indoline by hexafluoroacetone [3]:



(VI)

$R = C(CF_3)_2NHSO_2Ph.$

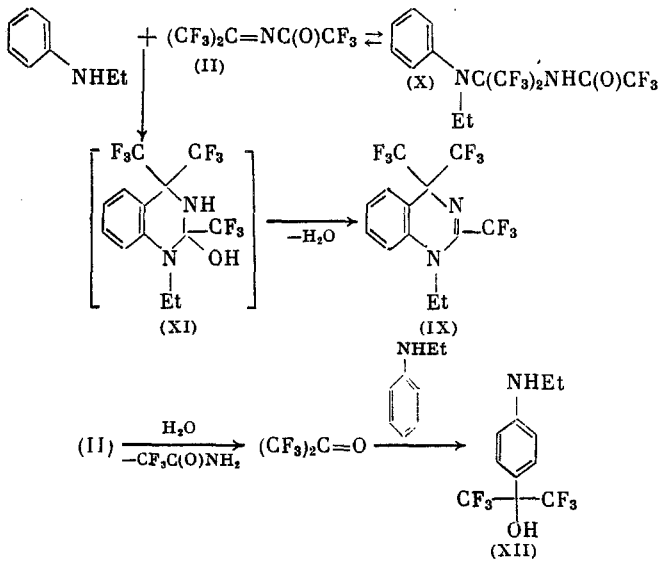
Compound (II) reacts vigorously with aniline and α-naphthylamine to give quantitative yields of the stable N-alkylation products (VII) and (VIII):



(VII), (VIII)

$R = R^1 = H$ (VII); R, R^1 =  (VIII).

The reaction of (II) with secondary arylamines has been examined in detail in the case of N-ethylaniline. Reaction of the reagents in this system [50% excess of (II)] at 20°C is complete in chloroform in 2 months, unexpectedly giving 2,4,4-tris(trifluoromethyl)-1-ethyl-1,4-dihydroquinazoline (IX) in 87% yield. The mechanism of this reaction, which was examined by ^1H and ^{19}F NMR spectroscopy, is as follows:



On mixing the reagents, the unstable N-alkylation product (X) is formed initially, which gradually disappears as the reagents react to give (IX), possible via the intermediate (XI) (which was not detected spectroscopically). The water liberated in this reaction causes hydrolysis of the imine (II) to occur as a side reaction (as shown by the accumulation of trifluoroacetamide and hexafluoroacetone hydrate) and the formation of 4-(α-hydroxyhexafluoroisopropyl)aniline (XII) [4]. When equimolar amounts of the starting materials are taken, the ratio of products (IX) and (XII) is ~3:2.

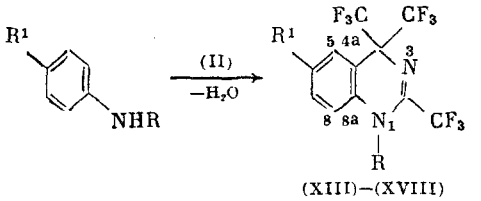
Increasing the temperature to 80°C and using a 10% excess of (II) shortens the reaction time to 2 h, (IX) being isolated in 56% yield. The use of a 1.5- to 3-fold excess of (II) at 60-80°C did not give any significantly greater yields of (IX).

It follows from the reaction sequence shown above that the rate of heterocyclization in this instance is determined by the stability of the N-alkylation product, which should decrease with increasing steric effects and the nitrogen atom. In fact, N-methylaniline reacts with (II) to give an N-alkylation product which does not undergo transformation at a signifi-

TABLE 1. Constants and Elemental Analyses for (III)-(IX) and (XIII)-(XX)

Compound	Yield, %	Mp, °C	R_f (system)	Empirical formula (M^+)	Found/Calculated, %		
					C	H	N
(III)	62	103–105	0,37 (B)	$C_{15}H_{12}F_6N_2O_2S$	44,97 / 45,20	2,85 / 3,04	7,17 / 7,03
(IV)	22	125 (with decomposition)	0,48 (A)	$C_{17}H_{16}F_6N_2O_2S$	47,81 / 47,89	3.67 / 3,78	6,45 / 6,57
(V)	26	152 (with decomposition)	0,31 (A)	$C_{17}H_{16}F_6N_2O_2S$	47.80 / 47,89	3,30 / 3,78	6,69 / 6,57
(VI)	17	162–164	0,46 (C)	$C_{17}H_{12}F_6N_2O_2S$	48,36 / 48,38	2,84 / 2,89	6,64 / 6.40
(VII)	100	53–55	0.60 (B)	$C_{11}H_7F_9N_2O$	36,81 / 37,30	1,72 / 1,99	7,78 / 7,91
(VIII)	100	74–75	0,44 (F)	$C_{15}H_9F_9N_2O$	44,48 / 44,57	2.05 / 2,24	6.91 / 6,93
(IX)	87	81	0,47 (D)	$C_{13}H_9F_9N_2$ (364)	42,74 / 42,87	2,53 / 2,49	8.03 / 7,69
(XIII)	31	89	0,89 (F)	$C_{12}H_7F_9N_2$	40,83 / 41.15	1.99 / 2,01	–
(XIV)	36	66	0,83 (F)	$C_{14}H_{11}F_9N_2$	44.26 / 44,45	2,58 / 2,93	7,38 / 7.41
(XV)	52	79–81	0,78 (E)	$C_{17}H_9F_9N_2$	49,38 / 49,53	2,24 / 2,20	6.56 / 6.79
(XVI)	49	35	0,74 (F)	$C_{15}H_{13}F_9N_2O$	41.11 / 40,74	2,54 / 2,44	6,93 / 6.79
(XVII)	66	80	0.50 (F)	$C_{15}H_{13}F_9N_2$	46,02 / 45,93	3.46 / 3,33	7.31 / 7,14
(XVIII)	81	83	0,86 (F)	$C_{14}H_{10}ClF_9N_2$	41,11 / 40,74	2,54 / 2,44	6,93 / 6,79
(XIX)	83	81–83	0,58 (B)	$C_{13}H_{11}F_9N_2O$	41,15 / 40,84	2,84 / 2,90	7.56 / 7,33
(XX)	71	87–90	0,82 (B)	$C_{15}H_{15}F_9N_2O$	43,49 / 43,88	3.56 / 3,68	6,67 / 6,85

cant rate at 20°C, and is converted into the dihydroquinazoline (XIII) only on heating (60°C, 10 h). N-Isopropylaniline, on the other hand, gives the heterocyclization product (XIV) at 20°C, the reaction being complete in 72 h (yield 36%). Diphenylamine is also converted into the heterocycle (XV) at 20°C:



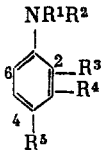
(XIII)–(XVIII)

R = Me, R^1 = H (XIII); R = *i*-Pr, R^1 = H (XIV); R = Ph, R^1 = H (XV); R = *i*-Pr, R^1 = OMe (XVI); R = *i*-Pr, R^1 = Me (XVII); R = *i*-Pr, R^1 = Cl (XVIII).

The effect of the substituent in the para-position to the amino group in N-alkylanilines on their reaction with (II) was examined in the case of N-isopropylanilines. With N-isopropyl-p-anisidine and N-isopropyl-p-toluidine, the dihydroquinazolines (XVI) and (XVII) were formed at 20°C in yields of 49 and 66%, respectively. The best heterocyclization was achieved with N-isopropyl-4-chloroaniline at 50°C [81% yield of (XVIII)].

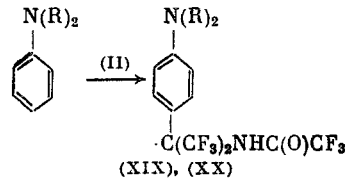
N,N-Dimethyl- and N,N-diethylanilines are alkylated quantitatively at C^4 to give 4-(α-trifluoroacetylaminohexafluoroisopropyl)-N,N-dialkylanilines (XIX) and (XX):

TABLE 2. Chemical Shifts (δ, ppm) in the ^{13}C and ^{19}F NMR Spectra of Common Fragments in (III)-(V), (VII)-(IX), (XIX), and (XX) in Acetone



Compound	^{13}C NMR spectrum*							^{19}F NMR spectrum
	C^1	C^2	C^6	C^3	C^5	C^4	CF_3	CCF_3	
(III)	143,1	118,4		128,0		123,4	121,4	66,4	−4,4 s
(IV)	147,3	109,2	114,5	129,7	127,6	112,1	122,0	69,8	−11,9 s
(V)	149,0	110,0		128,2		112,9	121,9	69,1	−9,2 s
(VII)	140,0	119,0		127,8		121,5	120,9	74,9	−6,2 s, −2,9 s (2 : 1)
(VIII)									−4,8 s, −1,9 s (2 : 1)
(IX)	135,2	108,8	114,5	130,8	127,0	125,0	122,7	65,3	−11,1 s, −4,3 d (1 : 2)
(X)†	142,1	132,1		129,8		128,7	123,1	79,1	−8,1 s, −2,1 s (2 : 1)
(XIX)	154,2	112,5		128,3		113,9	123,8	69,3	−9,4 s, −3,1 s (2 : 1)
(XX)	149,2	111,9		129,1		112,9	123,8	69,3	−9,4 s, −3,1 s (2 : 1) s

*Signals also seen for substituents R^1-R^5, δC=O 154.95 (VII); 154.72 (X).
†In CCl_4.



(XIX), (XX)

R = Me (XIX); Et (XX).

All the compounds obtained were crystalline solids which were stable under normal conditions, their properties and elemental analyses being given in Table 1.

The structures of the anilines (III)-(V), (VII), (VIII), (XIX), and (XX) were established by ^{13}C and ^{19}F NMR spectroscopy (Table 2). The site of substitution followed from examination of the chemical shifts in the ^{13}C NMR spectra [4]. The PMR spectrum of the α-naphthylamine (VIII) corresponded to a strongly-bonded semispin system, which together with the ^{19}F NMR data confirmed the structure assigned.

1-Substituted 2,4,4-tris(trifluoromethyl)-1,4-dihydroquinazolines have been most fully examined in the case of the N-ethyl compound (IX). The ^{13}C, ^{19}F, and ^{1}H NMR spectra shown in Tables 2 and 3, together with the mass spectrometric (Table 1) and IR spectral data (see Experimental section) establish unambiguously the structure of (IX). The ^{1}H and ^{19}F NMR spectra of the dihydroquinazolines (XIII)-(XVIII) are shown in Table 3. The structure of the unstable compound (X) was established by its ^{13}C and ^{19}F NMR spectra (Table 2). In the PMR spectrum of (X), the signals for the five protons of the aromatic ring were seen as a singlet at 7.37 ppm.

EXPERIMENTAL

The ^{1}H, ^{19}F, and ^{13}C NMR spectra of (IX) and (XIII)-(XVIII) were obtained on a Bruker WP-200 SY spectrometer, operating frequencies 200.13, 188.31, and 50.31 MHz, respectively, and the PMR spectrum of (VI) on a Bruker WP-360. Chemical shifts were measured relative to TMS as internal standard (^{1}H, ^{13}C) and CF_3COOH (external standard) (^{19}F). The mass spectrum was recorded on an AEI MS-30, and the IR spectrum on a UR-20 spectrometer in KBr disks. The R_f values of the products are given for Silufol UV-254 plates. Preparative chromatography

TABLE 3. Chemical Shifts (δ, ppm) in the ^1H and ^{19}F NMR Spectra of (IX) and (XIII)-(XVIII) in CCl_4

Compound	^1H NMR spectrum							^{19}F NMR spectrum
	C^5	C^6	C^7	C^8	CH	CH_2	CH_3	CF_3
(IX)	7,65 d.d.hept*	7,30 d.d.d	7,50 d.d.d	7,17 d.d	–	4,08 q	1,38 t	−11,1 s, −4,3 d* (1 : 2)
(XIII)	7,63 d.d.hept*	7,28 d.d.d	7,50 d.d.d	7,08 d.d	–	–	3,50 s	−11,1 s, −4,5 d* (1 : 2)
(XIV)	7,60 d.d.hept*		7,48–7,18		4,58 hept	–	1,63 d	−12,7 s, −4,8 d* (1 : 2)
(XV)								−12,6 s, −4,6 d* (1 : 2)
(XVI) †	6,99 d.hept*	–	6,86 d.d	7,19 d	4,43 hept	–	3,76 s, 1,51 d (1 : 2)	−12,0 s, −10,0 d (1 : 2)
(XVII)	7,30 d.hept*	–	7,23–7,08		4,43 hept	–	2,33 s, 1,50 d	−12,5 s, −4,7 d* (1 : 2)
(XVIII)	7,63 d.hept*	–	7,42 d.d	7,31 d	4,42 hept	–	1,67 d	−12,6 s, −4,9 d* (1 : 2)

*$^5J_{H-F} \approx 0.7$-0.9 Hz.

†The spectrum of (XVI) was obtained in DMSO-d_6.

was carried out on columns of silica gel 40/100 μm; in the case of (VI) separation was effected on 20 × 20 cm plates with an unbound layer of silica gel 5/40 μm (layer thickness 2 mm). The following solvent systems were used for chromatography: CCl_4–acetone, 10:1 (A), 6:1 (B), 4:1 (C), CCl_4 (D), benzene–hexane, 1:1 (E), and benzene (F). The reaction of N-ethylaniline with the imine (II) was carried out by mixing equimolar amounts of the reactants in CCl_4 (C 0.02 M) and placing the mixture in a sealed ampul, the progress of the reaction being followed daily by ^1H and ^{19}F NMR spectroscopy. The products were identified by comparison of their spectra with those of standard samples.

N-(α-Benzenesulfonylaminohexafluoroisopropyl)aniline (III). To 1.0 g of aniline in 10 ml of CCl_4 was added at 0°C 3.3 g of the imine (I) in 10 ml of CCl_4, and the mixture kept for 30 min at 20°C. The solid which separated was filtered off and recrystallized from CCl_4, to give 2.6 g of (III).

2-(α-Benzenesulfonylaminohexafluoroisopropyl)-N-ethylaniline (IV) and 4-(α-Benzenesulfonylaminohexafluoroisopropyl)-N-ethylaniline (V). To 1.1 g of N-ethylaniline in 10 ml of dry chloroform was added at 0°C 2.6 g of imine (I) in 10 ml of chloroform, and the mixture kept for 24 h at 20°C. It was then evaporated and chromatographed in system A. Recrystallization gave 0.8 g of (IV) (CCl_4–hexane) and 0.95 g of (V) (CCl_4).

7-(α-Benzenesulfonylaminohexafluoroisopropyl)indole (VI). To 4.7 g of the imine (I) in 20 ml of dry chloroform was added dropwise with stirring a solution of 1.7 g of indoline in 5 ml of chloroform, and the mixture boiled for 5 min and evaporated. The residue was dissolved in 10 ml of CCl_4, filtered, and the filtrate chromatographed in system (A), the fraction with R_f 0.46 (C) being collected. The crystalline solid was dissolved in 20 ml of dry benzene, 4.2 g of active MnO_2 [5] added, the mixture stirred for 30 min at 20°C, filtered, the residue washed with benzene, and the filtrate evaporated. Chromatography on SiO_2 plates (eluent acetone) gave 1.0 g of (VI). PMR spectrum (DMSO-d_6, δ, ppm): 10.0, 9.75 br.s (1H, NH), 9.91 br.s (1H, NH), 7.83 d.d (2H, H^2, H^6), 7.72 d.d (1H, H^4), 7.64 d.d (1H, $H^{4'}$), 7.55 d.d (2H, $H^{3'}$, $H^{5'}$), 7.41 d.d (1H, H^2), 7.20 br.d.d (1H, H^6), 7.08 d.d (1H, H^5), 6.54 d.d (1H, H^3).

N-(α-Trifluoroacetylaminohexafluoroisopropyl)aniline (VII). To 1.0 g of aniline in 10 ml of dry chloroform was added at −20°C 3.5 g of the imine (II). After the mixture had warmed spontaneously to 20°C, the solution was evaporated to give 3.8 g of (VII).

N-(α-Trifluoroacetylaminohexafluoroisopropyl)-α-naphthylamine (VIII). As described for (VII), from 0.34 g of α-naphthylamine and 0.77 g of (II) there was obtained 0.96 g of (VIII).

2,4,4-Tris(trifluoromethyl)-1-ethyl-1,4-dihydroquinazoline (IX). a. To 1 g of N-ethylaniline in 10 ml of dry chloroform was added at 0°C 3.3 g of the imine (II), and the mixture kept for 2 months at 20°C. The mixture was then evaporated and chromatographed in system (A) to give 2.6 g of (IX), which may be further recrystallized from hexane. IR spectrum (ν, cm^{-1}): 1670 (C=N).

b. To 1.5 g of N-ethylaniline in 10 ml of dry chloroform was added at 0°C 3.7 g of the imine (II), and the mixture heated for 2 h at 80°C in a sealed ampul. Isolation was carried out as in the preceding preparation, to give 2.5 g of (IX).

c. To 2.7 g of N-ethylaniline in 10 ml of dry chloroform was added at 0°C 16 g of the imine (II), and the mixture heated for 8 h at 60°C in a sealed ampul. Isolation was carried out as above, to give 5.0 g of (IX).

2,4,4-Tris(trifluoromethyl)-1-methyl-1,4-dihydroquinazoline (XIII). To 4.1 g of N-methylaniline in 10 ml of dry chloroform was added at 0°C 10.4 g of the imine (II), and the mixture heated for 10 h at 60°C in a sealed ampul. The mixture was evaporated and chromatographed in system (F) to give 4.5 g of (XIII).

2,4,4-Tris(trifluoromethyl)-1-isopropyl-1,4-dihydroquinazoline (XIV). To 5.5 g of N-isopropylaniline in 10 ml of dry chloroform was added at 0°C 10.9 g of the imine (II), and the mixture kept for 72 h at 20°C. It was then filtered, the filtrate evaporated, and worked up as for (XIII), recrystallization being from methanol, to give 5.5 g of (XIV).

2,4,4-Tris(trifluoromethyl)-1-phenyl-1,4-dihydroquinazoline (XV). To 0.67 g of diphenylamine in 10 ml of CCl_4 was added at 0°C 1.14 g of the imine (II), and the mixture kept at 20°C for 10 days. A further 1.0 g of (II) in 2 ml of CCl_4 was then added, the mixture kept for a further 5 days, and evaporated. The residue was chromatographed in system (D) to give 0.85 g of (XV).

6-Methoxy-2,4,4-tris(trifluoromethyl)-1-isopropyl-1,4-dihydroquinazoline (XVI). To 0.62 g of N-isopropyl-4-methoxyaniline in 4 ml of dry chloroform was added at 0°C 1.3 g of the imine (II), and the mixture kept for 48 h at 20°C. It was then evaporated and chromatographed in system (D) to give 0.8 g of (XVI).

6-Methyl-2,4,4-tris(trifluoromethyl)-1-isopropyl-1,4-dihydroquinazoline (XVII). To 1.5 g of N-isopropyl-4-methylaniline in 5 ml of dry chloroform was added at 0°C 3.3 g of the imine (II), and the mixture kept at 20°C for 16 h, and evaporated. The residue was chromatographed in system (D) to give 2.6 g of (XVII).

2,4,4-Tris(trifluoromethyl)-6-chloro-N-isopropylaniline (XVIII). To 0.51 g of N-isopropyl-4-chloroaniline in 4 ml of dry chloroform was added 1.0 g of the imine (II) in 1 ml of chloroform, and the mixture heated for 10 h at 50°C in a sealed ampul. The mixture was then evaporated and chromatographed in system (D) to give 1 g of (XVIII).

4-(α-Trifluoroacetylaminohexafluoroisopropyl)-N,N-dimethylaniline (XIX). To 1.5 g of N,N-dimethylaniline in 15 ml of dry chloroform was added at −40°C 3.6 g of the imine (II), and the mixture kept for 1 h at 20°C. It was then evaporated, and the residue extracted with pentane and the pentane removed to give 4.0 g of (XIX).

4-(α-Trifluoroacetylaminohexafluoroisopropyl)-N,N-diethylaniline (XX). As for (XIX), from 1.6 g of N,N-diethylaniline and 3.2 g of (II), after recrystallization from pentane, there was obtained 3 g of (XX).

CONCLUSIONS

1. Nonsterically hindered primary arylamines react with hexafluoroacetone benzenesulfonyl- and trifluoroacetylimines to give stable gem-diamino compounds.

2. The presence of substituents at the nitrogen of the arylamine destabilizes these gem-diamino compounds, with the formation of C^2- and C^4-alkylation products. With hexafluoroacetone trifluoroacetylimine, C^2-alkylation is accompanied by heterocyclization to give 1-substituted 2,4,4-tris(trifluoroacetyl)-1,4-dihydroquinazolines.

3. N,N-Dialkylanilines are regioselectively alkylated at C^4.

LITERATURE CITED

1. N. D. Chkanikov, V. L. Vershinin, A. F. Kolomiets, and A. V. Fokin, Izv. Akad. Nauk SSSR, Ser. Khim., 952 (1986).
2. G. F. Il'in, A. F. Kolomiets, and G. A. Sokol'skii, Zh. Vses. Khim. Ova., 25, 109 (1980).
3. N. D. Chkanikov, A. E. Zelenin, M. V. Galakhov, et al., Zh. Org. Khim., 21, 1358 (1985).
4. A. E. Zelenin, N. D. Chkanikov, M. V. Galakhov, et al., Izv. Akad. Nauk SSSR, Ser. Khim., 931 (1985).
5. J. Attenborow, A. F. B. Cameron, J. H. Chapman, et al., J. Chem. Soc., 1094 (1952).