15. V. Gutman, The Chemistry of Coordination Compounds in Nonaqueous Solvents [Russian translation], Mir, Moscow (1971).

SYNTHESIS OF NITRONES OF THE POLYFLUOROAROMATIC SERIES

N. I. Petrenko, T. N. Gerasimova, and
E. P. Fokin

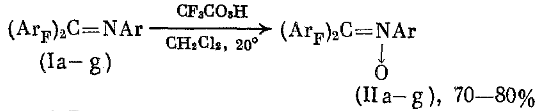
UDC 542.943:547.574.4

Nitrones are a reactive and intensively investigated class of compounds [1-4] however polyfluoroaromatic nitrones have not been obtained up to the present time with the exception of α,α-diphenyl-N-pentafluorophenylnitrone in [5].

In the present work the possibility has been investigated of obtaining polyfluoro-substituted α,α,N-triarylnitrones by the oxidation of anils of polyfluoroaromatic ketones which were synthesized by the method developed by us previously in [6, 7].

It is known that Schiff bases are oxidized by peracids forming nitrones as a result of electrophilic interaction of the reagent with the unshared pair on the nitrogen atom, or more frequently forming oxaziridines by orthogonal attack at the carbon atom of the azomethine bond. In those cases when such attack is sterically hindered the reaction forming nitrones predominates [8-10].

It was found by us that the anil of decafluorobenzophenone (Ia) was stable to the extended action of AcOOH in CH_2Cl_2 at ∿20°C. The interaction of the same anil (Ia) with CF_3CO_3H under these conditions led to the formation of α,α-bis(pentafluorophenyl)-N-phenylnitrone (IIa) in good yield. Similar results were obtained on oxidizing substituted anils of decafluorobenzophenone and also the anil of perfluoro-p-tolylketone (Ig).



$$\underset{\text{(Ia–g)}}{(Ar_F)_2C{=}NAr} \xrightarrow[CH_2Cl_2,\ 20^\circ]{CF_3CO_3H} \underset{\text{(IIa–g), 70–80\%}}{(Ar_F)_2C{=}\overset{}{\underset{\underset{O}{\downarrow}}{N}}Ar}$$

$Ar_F = C_6F_5$, $Ar = Ph$ (a); $Ar_F = C_6F_5$, $Ar = o\text{-}MeC_6H_4$ (b);
$Ar_F = C_6F_5$, $Ar = p\text{-}MeC_6H_4$ (c); $Ar_F = C_6F_5$, $Ar = o\text{-}FC_6H_4$ (d);
$Ar_F = C_6F_5$, $Ar = p\text{-}MeOC_6H_4$ (e); $Ar_F = Ar = C_6F_5$ (f);
$Ar_F = p\text{-}CF_3C_6F_4$, $Ar = Ph$ (g).

Compound (If), the nucleophilicity of the nitrogen in which is significantly reduced as a result of the acceptor influence of the pentafluorophenyl group, was oxidized more slowly than the remaining anils of type (I), however nitrone (IIf) was formed in high yield in this way. At the same time the anils of 2,3,4,5,6-pentafluorobenzophenone (IIIa, b) containing one pentafluorophenyl residue on the C=N bond interacts with CF_3CO_3H less unequivocally and gave the corresponding nitrones (IVa, b) in lowest yield

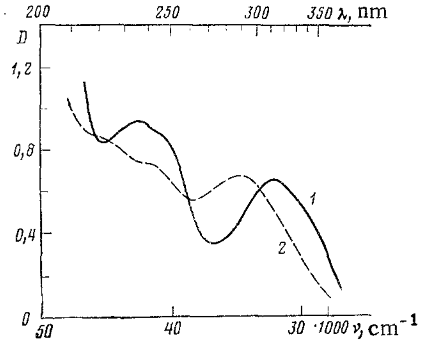


Fig. 1. UV spectra, concentration 0.5 ×10^{-4} mole/liter, cell path length 1 cm of 1) α,α,N-triphenylnitrone and 2) α,α-bis(pentafluorophenyl)-N-phenylnitrone (IIa).

Novosibirsk Institute of Organic Chemistry, Siberian Branch, Academy of Sciences of the USSR. Translated from Izvestiya Akademii Nauk SSSR, Seriya Khimicheskaya, No. 6, pp. 1378-1384, June, 1984. Original article submitted May 10, 1983.

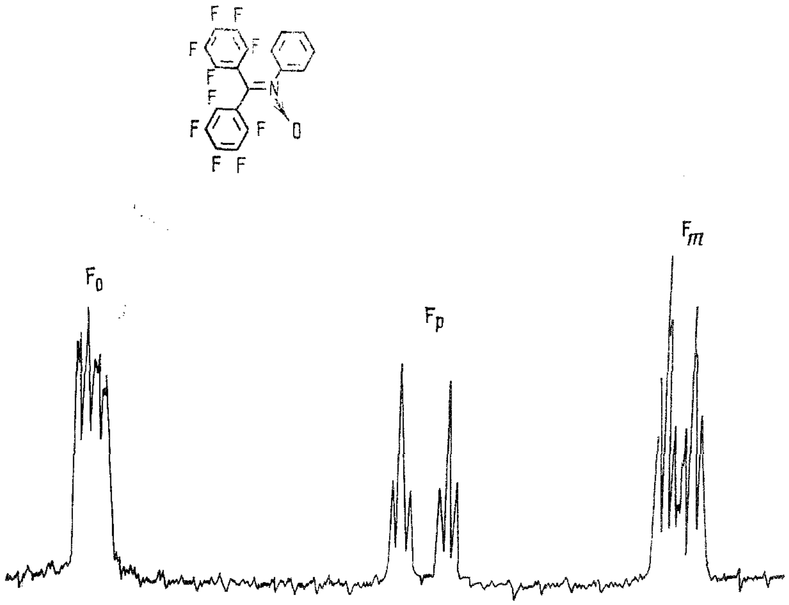
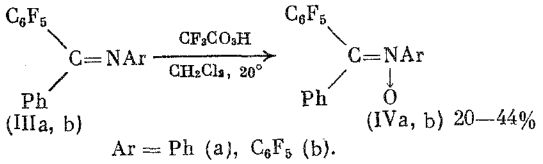


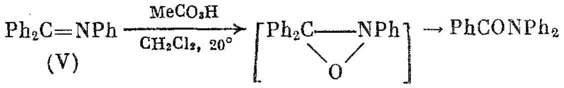
Fig. 2. ^{19}F NMR spectrum of α,α-bis(pentafluorophenyl)-N-phenylnitrone (IIa) in THF, scanning 5000 Hz.



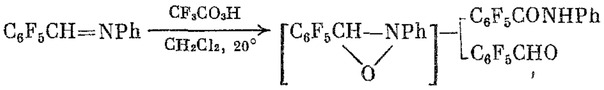
$$\underset{\text{(IIIa, b)}}{(C_6F_5)(Ph)C{=}NAr} \xrightarrow[CH_2Cl_2,\ 20°]{CF_3CO_3H} \underset{\text{(IVa, b) 20—44\%}}{(C_6F_5)(Ph)C{=}\overset{}{N}(\rightarrow O)Ar}$$

Ar = Ph (a), C_6F_5 (b).

All this forms a basis for the supposition that the main factor, in accordance with the data of [10], determining the direction of the reaction of anils of types (I) and (II) with CF_3CO_3H is the steric hindrance towards reaction at the carbon atom of the C=N bond. In reality the oxidation of benzophenone anil (V), the molecule of which is less sterically screened in comparison with the anils of the polyfluoroaromatic ketones, did not lead to the formation of α,α,N-triphenylnitrone although it proceded under milder conditions (AcOOH, 20°C). The N,N-diphenylbenzamide isolated from the reaction mixture is in all probability the rearrangement product of the thermally unstable 2,3,3-triphenyloxaziridine formed as an intermediate (cf. [8])



We also failed to detect α-pentafluorophenyl-N-phenylnitrone (VI), synthesized alternatively from pentafluorobenzaldehyde and phenylhydroxylamine, in the reaction mixture obtained on oxidation of N-(2,3,4,5,6-pentafluorobenzylidene)aniline with CF_3CO_3H. The anilide of pentafluorobenzoic acid and pentafluorobenzaldehyde were identified in the reaction mixture by ^{19}F NMR. These were evidently formed as a result of rearrangement and hydrolytic fission of 2-phenyl-3-pentafluorophenyloxaziridine



The formation of pentafluorobenzaldehyde by hydrolysis of the initial anil seems less probable since it was shown previously that the latter was stable in CF_3COOH in [7].

The structure of the obtained nitrones was confirmed by data of elemental analysis and by physicochemical methods. A peak was observed in the mass spectrum of compound (IIa) for the molecular ion at mass 453 and a peak at M − 16 was characteristic of an N-oxide [4]. The UV spectra of nitrones (II) and (IV) were similar to the spectrum of α,α,N-triphenylnitrone [11] and contained an intense (log ε >4) absorption band in the 280-312 nm region, charac-

TABLE 1. Preparation of Polyfluoro-Substituted α,α,N-Triarylnitrones (I) → (II)

Initial anil	Yield of (II), %	Mp, ℃ (from alcohol)	Found/calculated, %				Empirical formula	λ_{max}, nm* (lg ε)	δ ^{19}F ppm (ratio of intensities)
			C	H	F	N			
(Ia)	70	89–91	50,20/50,35	1,15/1,11	41,69/41,92	3,07/3,09	$C_{19}H_5F_{10}NO$	288 (4,05)	136,9; 137,8; 150,6; 152,6; 161,9; 163,0 (2 : 2 : 1 : 1 : 2 : 2)
(Ib)	80	109–110	51,29/51,40	1,47/1,51	40,58/40,66	2,88/3,00	$C_{20}H_7F_{10}NO$	283 (4,26)	135,3; 136,7; 142,9; 151,1; 160,8; 162,1 (3 : 1 : 1 : 1 : 2 : 2) †
(Ic)	87	137–139	51,66/51,40	1,69/1,51	40,63/40,66	2,75/3,00	$C_{20}H_7F_{10}NO$	286 (4,08)	137,1; 150,8; 152,6; 161,8; 163,0 (4 : 1 : 1 : 2 : 2)
(Id)	83	126–127	47,50/48,42	0,87/0,86	44,34/44,35	2,63/2,97	$C_{19}H_4F_{11}NO$	286 (4,09)	122,6; 131,4; 137,2; 139,3; 148,8; 151,0; 160,9; 161,9 (1 : 1 : 2 : 1 : 1 : 1 : 2 : 2) †
(Ie)	76	136–138	49,69/49,70	1,27/1,46	39,20/39,32	2,93/2,90	$C_{20}H_7F_{10}NO_2$	282 (4,09) 328 inflection (3.89)	137,3; 150,8; 152,7; 161,8; 163,0 (4 : 1 : 1 : 2 : 2)
(If)	80 ‡	146–148	41,68/42,01	–	52,59/52,47	2,68/2,58	$C_{19}F_{15}NO$	290 (4,07)	135,0; 137,8; 147,0; 148,0; 150,2; 160,1; 162,1 (2 : 2 : 2 : 1 : 2 : 4 : 2)
(Ig)	85	154–155	45,53/45,59	1,07/0,91	48,00/48,08	2,53/2,53	$C_{21}H_5F_{14}NO$	292 (4,21)	56,6; 135,0; 140,1 (3 : 2 : 2)

---

*Long wave absorption bands are cited.

†^{19}F NMR spectra were taken on a Bruker HX-90 (84.7 MHz) instrument in $CDCl_3$, Δδ for C_6F_6 and CCl_3F were taken as 163.0 ppm.

‡Reaction mixture was stirred for 24 h.

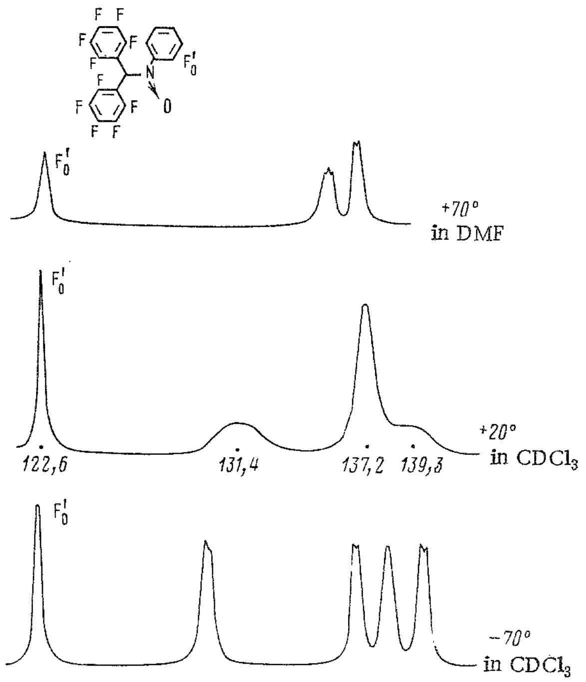


Fig. 3. ^{19}F NMR spectrum of α,α-bis-(pentafluorophenyl)-N-(o-fluorophenyl)-nitrone (IId) in the region 120-140 ppm, scanning 6000 Hz.

teristic of the nitrone group conjugated with an aromatic ring [12] (Fig. 1 and Table 1). In the spectra of nitrones (la-g), the molecules of which contain two polyfluorinated rings in the α position, these bands were shifted towards the shorter wavelength region by ∿15-25 nm in comparison with the unfluorinated analog.

The ^{19}F NMR spectrum of compounds (IVa) contained three signals with intensity ratios 2:1:2 characteristic of pentafluorophenyl groups. In the ^{19}F NMR spectrum of nitrone (IIa), which contains two C_6F_5 groups, six signals were observed of relative intensity 2:2:1:1:2:2 (Fig. 2). This makes it possible to consider different shielding of the fluorine atoms of the C_6F_5 groups situated cis and trans to the N-phenyl residue. Since the greatest difference of chemical shifts was observed for para fluorine atoms it may be proposed that the determining factor was the electronic interaction of the polar nitrone group with the pentafluorophenyl residues oriented relative to it in various ways. It must be noted that the signals of the ortho fluorine atoms were removed furthest from one another in the ^{19}F NMR spectra of anils of polyfluoroaromatic ketones, i.e., in the case in question the relative deshielding played a more significant role as a result of the difference in spatial influence of the unshared pair of the nitrogen and the N-aryl ring [6, 7].

The ^{19}F NMR spectrum of α,α-bis(pentafluorophenyl)-N-(o-fluorophenyl)nitrone (IId) contained four signals at low field (120-140 ppm) with relative intensity 1:1:2:1 (Fig. 3). The signal at 122.6 ppm belonged to the fluorine atom in the N-aryl ring and the remaining three to the four fluorine atoms in the ortho positions of the C_6F_5 groups. An increase of temperature to 70°C led to a strengthening of the signals at 131.4 and 139.3 ppm and a decrease to —70°C to the appearance in this region of four signals of equal intensity. Similar temperature changes in the ^{19}F NMR spectrum were also observed for α,α-bis(pentafluorophenyl)-N-(o-tolyl)nitrone (IIb) and are evidently explained by the magnetic nonequivalence of the ortho fluorine atoms of one of the pentafluorophenyl groups (at ∿20°C) or of the fluorine atoms in all ortho positions of these groups (at reduced temperature). This may be explained by increased hindrance to the rotation of the pentafluorophenyl rings in the molecules of nitrones (IIb, d) around the $C_{arom}—C_{sp^2}$ bond and by the presence of a nonbonding interaction of one of the ortho fluorine atoms of the C_6F_5 group with the oxygen atom. A similar interaction leading to strong deshielding of the ortho hydrogen atoms was proposed previously when interpreting the NMR spectra of α-arylnitrones in [13, 14].

EXPERIMENTAL

UV spectra were taken on a Specord UV-VIS instrument in EtOH, ^{19}F NMR spectra on a Varian A56/60A (56.4 MHz) instrument in THF, Δδ for C_6F_6 and CCl_3F were taken as 163.9 ppm. Molecular weight was determined on a MS-3301 high resolution mass spectrometer.

Synthesis of Initial Anils. Anils (Ia-e, g) and (IIIa) were obtained according to [6, 7]. N-(2,3,4,5,6-Pentafluorobenzylidene)aniline was synthesized according to [15]. Anils (Ie), (IIIb), (V) were synthesized by the method described in [7] increasing the reaction time to 7-10 h.

Pentafluoro-N-(2,3,4,5,6-pentafluorobenzhydrylidene)aniline (IIIb), yield 80%, mp 112-114°C (from EtOH). UV spectrum, λ_{max}, nm (log ε): 268 (4.26), 320 (3.50). ^{19}F NMR spectrum, (δ, ppm): 138.4; 151.0; 151.8; 160.9; 162.1; 163.9 (2:1:2:2:1:2). Found: C 52.19; H 1.09; F 43.20; N 3.28%. $C_{19}H_5F_{10}N$. Calculated: C 52.19; H 1.25; F 43.45; N 3.21%.

Perfluorobenzhydrylideneaniline (If), yield 70%, mp 117-118°C (from EtOH). UV spectrum, λ_{max}, nm (log ε): 246 (4.15), 325 (3.44). ^{19}F NMR spectrum, (δ, ppm): 139.9; 142.2; 148.6; 149.8; 151.6; 160.1; 161.0; 163.1 (2:2:1:1:2:3:2:2). Found: C 43.49; F 53.74; N 2.68%. $C_{19}F_{15}N$. Calculated: C 43.28; F 54.06; N 2.66%.

Benzophenone anil (V), yield 74%, mp 112-113°C (from EtOH) (cf. [16]).

Polyfluoro-Substituted α,α,N-Triarylnitrones. Trifluoroacetic anhydride (0.71 ml) and 90% H_2O_2 (0.2 ml) in CH_2Cl_2 (10 ml) dried over $CaCl_2$ were stirred for 0.5 h at 20°C. The solution of peracid was then added dropwise to a solution of the initial Schiff base (1 mmole) in CH_2Cl_2 (10 ml), the mixture was stirred for 1 h at 20°C, poured onto ice, and extracted with ether. The ether solution was washed with aqueous $NaHCO_3$ solution, dried over $MgSO_4$, evaporated, and the residue washed with alcohol. The yields and characteristics of the obtained nitrones (II) are shown in Table 1.

α-Pentafluorophenyl-α,N-diphenylnitrone (IVa) was synthesized and isolated similarly to that described above. Yield of product (IVa) was 44% mp 129-131°C (from EtOH). UV spectrum λ_{max}, nm (log ε)*: 304 (4.20). ^{19}F NMR spectrum (δ, ppm): 137.1; 151.8; 162.3 (2:1:2). Found: C 63.00; H 2.94; F 25.75; N 3.70%. $C_{19}H_{10}F_5NO$. Calculated: C 62.81; H 2.77; F 26.15; N 3.86%.

α-Phenyl-α,N-bis(pentafluorophenyl)nitrone (IVb) was isolated by TLC. Separation of the mixture was carried out on plates with a bound layer of SiO_2 of type LSL_{254} 5/40 μm in benzene. Yield of compound (IVb) was 20%†, mp 144-146°C (from EtOH). UV spectrum, λ_{max}, nm (log ε)*: 312 (4.20). ^{19}F NMR spectrum (δ, ppm): 137.5; 148.3; 149.9; 152.9; 160.9 (2:2:1:1:4). Found: C 50.35; H 1.01; F 42.15; N 3.30%. $C_{19}H_5F_{10}NO$. Calculated: C 50.35; H 1.11; F 41.92; N 3.09%.

Oxidation of N-(2,3,4,5,6-Pentafluorobenzylidene)aniline. A solution of CF_3CO_3H prepared from trifluoroacetic anhydride (0.71 ml) and 90% H_2O_2 (0.2 ml) in CH_2Cl_2 (10 ml) was added dropwise to a solution of the anil of pentafluorobenzaldehyde (0.27 g) and stirred for 1 h at 20°C. The reaction mixture was processed as described above. The obtained product contained pentafluorobenzaldehyde and pentafluorobenzoic acid anilide in a 1:1 ratio according to data of the ^{19}F NMR spectrum.

Oxidation of the Anil of Benzophenone. A solution of AcOOH prepared from acetic anhydride (0.33 ml) and 90% H_2O_2 (0.15 ml) in CH_2Cl_2 (5 ml) was added dropwise to a solution of benzophenone anil (0.2 g) in CH_2Cl_2 (8 ml) and stirred for 15 h at 20°C. The product, isolated in the usual manner, was washed with petroleum ether (bp 40-70°C) and N,N-diphenylbenzamide (0.1 g: 48%) was obtained which was identical to a sample described in the literature in melting point and IR spectrum [17].

Preparation of α-Pentafluorophenyl-N-phenylnitrone (VI). Pentafluorobenzaldehyde (1 mmole) and freshly prepared phenylhydroxylamine (1 mmole) in dimethylformamide (DMF) (5 ml) were stirred for 20 h at 20°C. The solution was poured into water, the solid filtered off, and washed with alcohol. Yield of (VI) was 90%, mp 130-133°C (from EtOH). UV spectrum, λ_{max}, nm (log ε)*: 298 (4.11). ^{19}F NMR spectrum (δ, ppm): 132.9; 154.5; 164.1 (2:1:2). Found: C 54.22; H 1.92; F 32.87; N 4.67%. $C_{13}H_6F_5NO$. Calculated: C 54.36; H 2.11; F 33.08; N 4.88%.

---

*Long-wave absorption band is given.

†Reaction mixture was stirred for 5 h.

CONCLUSIONS

1. Anils of polyfluorobenzophenones are oxidized by trifluoroperacetic acid in methylene chloride at 20°C forming polyfluoro-substituted α,α,N-triarylnitrones. A condition of this direction for the reaction is the presence on the carbon atom of the azomethine bond of a least one pentafluorophenyl group.

2. Oxidation of the anil of pentafluorobenzaldehyde with trifluoroperacetic acid led to the formation of pentafluorobenzoic acid anilide and pentafluorobenzaldehyde.

LITERATURE CITED

1. J. Hamer and A. Macaluso, Chem. Rev., 64, 473 (1964).
2. G. R. Delpierre and M. Lamehen, Quart. Rev., 19, 329 (1965).
3. G. G. Spence, E. C. Taylor, and O. Buchardt, Chem. Rev., 70, 231 (1970).
4. E. Breuer, in: S. Patai (editor), The Chemistry of Amino, Nitroso, and Nitro Compounds and Their Derivatives, Part 1, Interscience (1982), p. 459.
5. R. E. Banks, W. T. Flowers, R. N. Haszeldine, and P. E. Jackson, Chem. Communs., 201 (1965).
6. T. V. Fomenko, T. N. Gerasimova, and E. P. Fokin, Zh. Vses. Khim. O-va., 24, 92 (1979).
7. N. I. Danilenko, T. V. Fomenko, I. K. Korobeinicheva, T. N. Gerasimova, and E. P. Fokin, Izv. Akad. Nauk SSSR, Ser. Khim., 1606 (1980).
8. É. Shmits, Three-Membered Rings with Two Heteroatoms [in Russian], Mir, Moscow (1970), p. 17.
9. J. Ogata and J. Sawaki, J. Am. Chem. Soc., 95, 4692 (1973).
10. J. Bjorgo, D. R. Boyd, and D. C. Neill, J. Chem. Soc. Perkin Trans 1, 254 (1977).
11. Sadtler Standard Spectra, Ultraviolet Spectra, Sadtler Research Laboratories, Philadelphia, No. 9824.
12. T. Kubota, M. Yamakana, and J. Mori, Bull. Chem. Soc. Jpn., 36, 1552 (1963).
13. K. Kayano and H. Suzuki, Bull. Chem. Soc. Jpn., 42, 3306 (1969).
14. D. A. Kerr and D. A. Wilson, J. Chem. Soc. C, 1718 (1970).
15. A. K. Barbour, M. W. Buxton, P. L. Coe, R. Stephens, and J. C. Tatlow, J. Chem. Soc., 808 (1961).
16. Sadtler Standard Spectra. Infrared Grating Spectra. Sadtler Research Laboratories, Philadelphia, No. 37209P.
17. Sadtler Standard Spectra. Infrared Prism Spectra. Sadtler Research Laboratories, Philadelphia, No. 9754.