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SHORT COMMUNICATIONS

Synthesis of Fluorine-Containing Poly(phenylamino)-1,4-naphthoquinones

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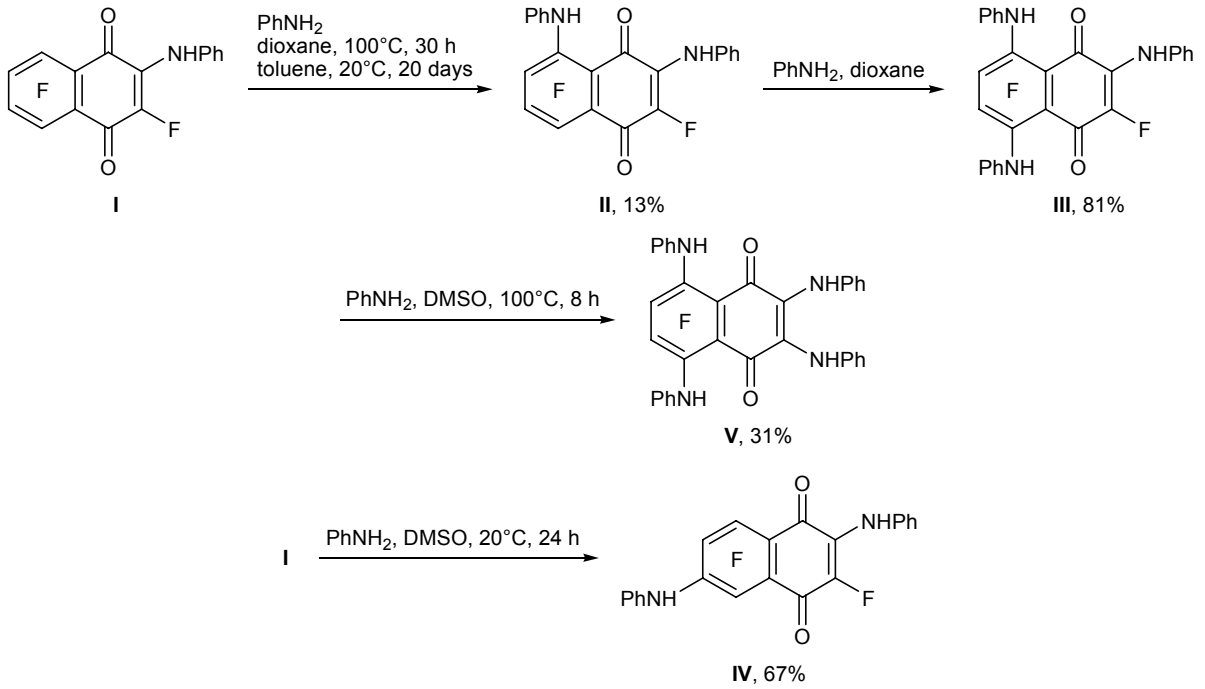
2-X-Substituted pentafluoro-1,4-naphthoquinones (X = BuNH, Et_2N, MeO) are readily converted into the corresponding di- and polysubstituted quinones via nucleophilic replacement of fluorine by the action of aliphatic amines R^1R^2NH (R^1R^2N = BuNH, EtNH, Et_2N) [1]. When X = BuNH or Et_2N, nucleophilic attack is directed at the aromatic ring to give products of replacement of one to three fluorine atoms in that ring. On the other hand, 2-methoxypentafluoro-1,4-naphthoquinone reacts with butylamine to give products of fluorine replacement in both aromatic and quinone rings. Thus the regioselectivity of these reactions depends on the nature of substituent in position *2* of the substrate. The solvent nature is also important: the ratio of β- and α-substituted products changes toward the latter as the solvent polarity decreases; obviously, the reason is stabilization of transition state for α-substitution via intramolecular hydrogen bonding [1]. In the present work we made an attempt to elucidate whether analogous relations are inherent to reactions of polyfluorinated 1,4-naphthoquinones with aromatic amines. For this purpose, we examined nucleophilic substitution of fluorine in 2-phenylaminopentafluoro-1,4-naphthoquinone (**I**) which is the primary product of the reaction of perfluoro-1,4-naphthoquinone with aniline [1]. As solvents we selected dioxane, toluene, and dimethyl sulfoxide (DMSO).

The reaction of quinone **I** with aniline at a molar ratio of 1:3 in dioxane at 100°C afforded in 3, 9, and 18 h mixtures containing, respectively, ~70, 25, and 17% of unreacted quinone **I**, ~10, 9, and 7% of 3,5,6,7-tetrafluoro-2,8-bis(phenylamino)-1,4-naphthoquinone (**II**), and ~7, 50, and 60% of 3,6,7-trifluoro-2,5,8-tris(phenylamino)-1,4-naphthoquinone (**III**). After 30 h, the fraction of quinone **III** attained 90%, and it was isolated in 81% yield. The fact that quinone **II** which is an obvious precursor of **III** does not accumulate in the reaction mixture during the process (its fraction does not exceed 10%) indicates that the former is more reactive toward aniline than quinone **I**. The reason is the lack of effective conjugation in molecule **II** between the nitrogen atom in the 8-phenylamino group (which is forced out from the benzene ring plane) and reaction center (C^5–F). Analogous explanation was proposed for change of *meta* orientation in the defluorination of pentafluoroaniline to *para* in going to *N*-phenylpentafluoroaniline [2].

Unlike previously reported [1] reaction of 2-X-pentafluoro-1,4-naphthoquinones (X = BuNH, Et_2N) with alkylamines in dioxane, nucleophilic substitution of fluorine atom in quinone **I** occurs mainly at the α-position of the benzene fragment. Therefore, stabilization of transition state in the substitution reaction with aniline (which is a stronger NH acid than alkylamines) may be contributed to an appreciable extent by coordination of hydrogen atom of the amino group to oxygen.

Quinone **II** was obtained in a poor yield when the reaction was carried out in toluene. The major product in DMSO was 3,5,7,8-tetrafluoro-2,6-bis(phenylamino)-1,4-naphthoquinone (**IV**). Presumably, in this case stabilization of transition state for α-substitution via intramolecular hydrogen bonding is weak due to higher polarity of DMSO as compared to dioxane (cf.



the data reported in [1] for double defluorination of quinone **I**).

The reaction of quinone **III** with aniline in DMSO resulted in replacement of the fluorine atom in the quinone ring with formation of 6,7-difluoro-2,3,5,8-tetrakis(phenylamino)-1,4-naphthoquinone (**V**, yield 31%, conversion 55%). In contrast, the reaction of 2,5,8-tris(butylamino)-3,6,7-trifluoro-1,4-naphthoquinone (**IIIa**) with butylamine gave 2,5,6,8-tetrakis(butylamino)-3,7-difluoro-1,4-naphthoquinone as a result of fluorine replacement in the aromatic ring [1]. Presumably, the observed change of the relative reactivity of the benzene and quinoid fragments is related to sharp weakening of electron-donating effect of the RNH substituent in going from quinone **IIIa** (R = Bu) to **II** (R = Ph), though replacement of fluorine at the quinoid double C=C bond is likely to be more sensitive to the neighboring substituent as compared to the replacement in the benzene ring.

The structure of newly synthesized compounds **II**–**V** was determined on the basis of their ^{19}F and ^{1}H NMR and high-resolution mass spectra. Signals in the ^{19}F NMR spectra were assigned by analogy with the corresponding fluorinated butylamino-1,4-naphthoquinones [1]. Quinones **II**–**IV** displayed in the ^{19}F NMR spectra multiplets in the region δ_F 27.2–28.3 ppm, which were assigned to the 3-F atom; the 3-F signal in the spectrum of initial quinone **I** is located at δ_F 28.1 ppm [3]. The ^{19}F NMR spectrum of **II** also contained three signals with equal intensities at δ_F 15.5, 17.4, and 32.5 ppm. The first of these (6-F) appeared as a triplet of multiplets with $J_{FF} \approx 18$ Hz due to similarity of two coupling constants $J_{F,o\text{-}F}$, while the second (d.d) and third signals (d.d.m due to neighborhood of amino group [1]) were characterized each by one coupling with $J_{F,o\text{-}F} = 19.4$ and 17.3 Hz and $J_{F,m\text{-}F} \approx 9$ Hz and were assigned to 5-F and 7-F, respectively. Signals with equal intensities at δ_F 23.4, 25.7, and 36.5 ppm in the ^{19}F NMR spectrum of quinone **IV** belong to 8-F, 7-F, and 5-F, respectively, taking into account doublet splittings with $J_{F,o\text{-}F} \approx 18$, $J_{F,p\text{-}F} \approx 10.5$ Hz and $J_{F,m\text{-}F} \approx 12$, $J_{F,p\text{-}F} \approx 10.5$ Hz for the first and third signals and with $J_{F,o\text{-}F} \approx J_{F,m\text{-}F} \approx 16$ Hz for the second signal. Two signals with equal intensities at δ_F 30.2 and 34.7 ppm in the spectrum of **III** were assigned to 7-F and 6-F, for their δ_F values are close to the chemical shifts calculated using PhNH increments ($\Delta\delta_F$ values corresponding to replacement of 8-F in quinone **I** by PhNH group). Symmetric quinone **V** showed only one signal in the ^{19}F NMR spectrum. In the ^{1}H NMR spectra of quinones **II**, **III**, and **V** NH protons in the α-positions resonated in the region δ 10.5–11.5 ppm, whereas signals from β-NH protons in quinones **II**–**V**, as well as in the quinoid fragment of **I** [3], appeared in a stronger field, at δ 7.0–7.5 ppm, as in the spectra of structurally similar fluorinated butylamino-1,4-naphthoquinones [1]. Signals from protons in the phenyl rings were located as a rule in the region δ 7.0–7.5 ppm. An exception was compound **V**.

Aromatic protons in the PhNH group in the quinoid fragment of **V** resonated in the region δ 6.3–7.0 ppm (as in aniline [4]), obviously due to rupture of conjugation between the nitrogen atom and quinoid ring as a result of steric interactions.

3,5,6,7-Tetrafluoro-2,8-bis(phenylamino)-1,4-naphthoquinone (II). A mixture of 0.051 g (0.19 mmol) of hexafluoro-1,4-naphthoquinone, 0.019 g (0.21 mmol) of aniline, and 1.5 ml of toluene was stirred for 4 h at room temperature. Aniline, 0.035 g (0.38 mmol), was added to the resulting solution of quinone **I** [3], and the mixture was stirred for 20 days at room temperature. The precipitate was separated by centrifugation, and quinone **II** was isolated therefrom by thin-layer chromatography (chloroform–hexane, 3:1). Yield 0.010 g (13%), dark violet crystals, mp 228–232°C. ^{1}H NMR spectrum (acetone-d_6), δ, ppm: 7.12–7.44 m (11H, H_{arom}, NH), 10.51 br.s (1H, NH). ^{19}F NMR spectrum, δ_F, ppm: 28.3 m (1F, 3-F), 17.4 d.d (1F, 5-F, $J_{5,6}$ = 19.4, $J_{5,7} \approx 9$ Hz), 15.5 t.m (1F, 6-F, $J_{5,6} \approx J_{6,7} \approx 18$ Hz), 32.5 d.d.m (1F, 7-F, $J_{6,7}$ = 17.3, $J_{5,7} \approx 9$ Hz). Found: *m*/*z* 412.0823 $[M]^+$. $C_{22}H_{12}F_4N_2O_2$. Calculated: *M* 412.0829.

3,6,7-Trifluoro-2,5,8-tris(phenylamino)-1,4-naphthoquinone (III). Aniline, 0.051 g (0.56 mmol), was added to a solution of quinone **I**, prepared as described above in 1.5 ml of dioxane, and the mixture was heated for 30 h at 100°C. The mixture was diluted with ~5 ml of water, and the precipitate was separated by centrifugation, washed with water (2×3 ml), dried in air, and recrystallized from ethanol. Yield 0.074 g (81%), dark blue crystals, mp 163–165°C. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 7.02–7.21 m (9H, H_{arom}), 7.25–7.39 m (7H, H_{arom}, NH), 11.24 br.s (1H, NH), 11.45 br.s (1H, NH). ^{19}F NMR spectrum, δ_F, ppm: 27.2 m (1F, 3-F), 34.7 d (1F, 6-F, $J_{6,7}$ = 14.2 Hz), 30.2 d (1F, 7-F, $J_{7,6}$ = 14.2 Hz). Found: *m*/*z* 485.1339 $[M]^+$. $C_{28}H_{18}F_3N_3O_2$. Calculated: *M* 485.1346.

3,5,7,8-Tetrafluoro-2,6-bis(phenylamino)-1,4-naphthoquinone (IV). Aniline, 0.017 g (0.19 mmol), was added to a solution of quinone **I** in 1.5 ml of DMSO, prepared as described above for the solution in toluene, and the mixture was stirred for 24 h at room temperature. The precipitate was separated by centrifugation, washed with water (2×4 ml) and chloroform (3×2 ml), and dried under reduced pressure (0.03 mm). Yield 0.052 g (67%), dark brown crystals, mp 310–313°C. ^{1}H NMR spectrum (acetone-d_6), δ, ppm: 7.08–7.44 m (12H, H_{arom}, NH). ^{19}F NMR spectrum, δ_F, ppm: 28.3 m (1F, 3-F), 36.5 d.d (1F, 5-F, $J_{5,7} \approx 12$, $J_{5,8} \approx$ 10.5 Hz), 25.7 t (1F, 7-F, $J_{5,7} \approx J_{7,8} \approx 16$ Hz), 23.4 d.d (1F, 8-F, $J_{7,8}$ = 17.9, $J_{5,8} \approx 10.5$ Hz). Found: *m*/*z* 412.0825 $[M]^+$. $C_{22}H_{12}F_4N_2O_2$. Calculated: *M* 412.0829.

6,7-Difluoro-2,3,5,8-tetrakis(phenylamino)-1,4-naphthoquinone (V). A mixture of 0.021 g (0.04 mmol) of quinone **III**, 0.008 g (0.09 mmol) of aniline, and 0.7 ml of DMSO was heated for 8 h at 100°C. Water, ~3 ml, was added, and the precipitate was separated by centrifugation, washed with water (3×3 ml), and dried under reduced pressure (0.03 mm). Compound **V** was isolated by thin-layer chromatography using chloroform–hexane (3:1) as eluent. Yield 0.0074 g (31%; 56% with account taken of the recovery of quinone **III**, 0.0095 g, 45%), blue crystals, mp 76–79°C. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 6.30–6.39 m (4H, *o*-H in 2,3-NHPh), 6.73 t.t (2H, *p*-H in 2,3-NHPh, *J* = 1.0, 7.4 Hz), 6.84–6.95 m (4H, *m*-H in 2,3-NHPh), 7.05–7.16 m (6H, *o*-H in 5,8-NHPh, NH or *p*-H), 7.26–7.37 m (6H, *m*-H in 5,8-NHPh, NH or *p*-H), 11.17 br.s (2H, NH in 5,8-NHPh). ^{19}F NMR spectrum, δ_F, ppm: 31.3 s (2F, 6-F, 7-F). Found: *m*/*z* 558.1858 $[M]^+$. $C_{34}H_{24}F_2N_4O_2$. Calculated: *M* 558.1862.

The ^{1}H and ^{19}F NMR spectra were recorded on a Bruker AV-300 spectrometer operating at 300.13 and 282.36 MHz, respectively, using the residual solvent signal ($CDCl_3$, δ 7.24 ppm; acetone-d_6, δ 2.07 ppm) or C_6F_6 (δ_F 0.0 ppm) as internal reference. The mass spectra were obtained on a Thermo Fisher Scientific DFS high-resolution mass spectrometer. Reagents and solvents were purified as described previously [1, 3]. Preparative thin-layer chromatography was performed using Sorbfil plates.

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