Tetrahedron Letters No. 51, pp 5169 - 5172, 1972. Pergamon Press. Printed in Great Britain.

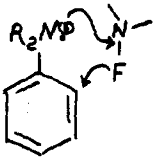
INTERACTION OF PERFLUOROPIPERIDINE WITH PHENOLS. MECHANISMS OF ORTHO- AND PARA-FLUORINATION

V.R.Polishchuk and L.S.German
Institute of Organoelement Compounds,
USSR Academy of Sciences,
Moscow, USSR

(Received in UK 23 October 1972; accepted for publication 15 November 1972)

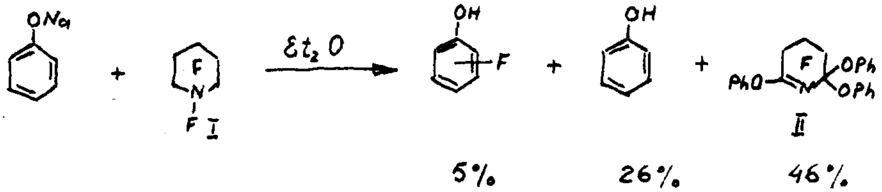
The direct introduction of fluorine into organic molecules by means of some commonly used flurinating agents has been recently shown to include oxidation of the substrate as a key stage. Thus, Tatlow et al. discuss two possible pathways of fluorination under the action of fluorides of transition metals in their maxivalence state: detachment of an electron from the molecule of the substrate (i.e. generation of the cation-radical) or detachment of the hydrogen atom (i.e. generation of the radical) /1/. Electrochemical fluorination of aromatic compounds is also supposed to include the generation of cation-radicals; orientation of the substitution is shown to be typical for the electrophilic process /2/. Generation of cation-radicals is confirmed by the ESR method during the fluorination of benzene by XeF_2 /3a/. The generation of cation-radicals was later shown to be a side-process, whereas the main reaction is supposed to proceed via the closed transition state /3b/.

In case aromatics containing strong electron-donating substituents ($-NR_2$, $-O^-$) if subjected to the action of such fluorinating agents as perchloryl fluoride /4/, trifluoromethyl hypofluorite /5/ and perfluoropiperidine /6/, the substitution is also electrophilic in character, its orientation being shown to be ortho-para. It is interesting to note that in some cases there takes place predominant /4c,5/ or exclusive /4b/ formation of sterically disadvantageous ortho-isomers. As has been shown by us /6/, N,N-dialkyl anilines may be fluorinated by perfluoropiperidine (I) into the ortho-position exclusively. In the reaction with N,N-dimethyl-aniline the generation of its cation-radical is confirmed by the ESR method. In explanation of the ortho-orientation of the fluorination, we suggested a "cage" mechanism involving the electron transfer from the nitrogen atom of the dialkylamino-group to the antibonding orbital of the N-F bond of the molecule (I):



In the present paper the interaction of (I) with phenols is discussed.

Dry sodium phenolate (PhONa) reacts with (I) giving a mixture of ortho- and para-fluorophenols in a ratio of 3.5:1. The low yield of fluorophenols can be explained by the fact that a considerable part of the starting phenolate is used for the formation of 2,6,6-triphenoxy-1-azaperfluorocyclohexene (II), m.p. 58-9°C, ^{19}F NMR [x]: three broadening peaks $\delta = 42.5$; 51.2 and 54.8 p.p.m. with the intensity ratio of 1:1:1. IR-spectrum, 1702 cm^{-1}; $M^{+} = 467$ (mass spectrum). Found, %: F, 24.91; N, 3.00. Calculated, %: F, 24.40; N, 3.25.



(1)

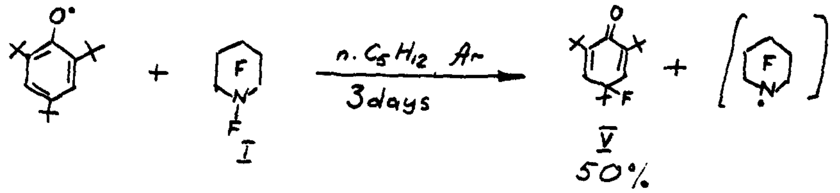
The predominant formation of ortho-fluorophenol allowed us to suppose the "cage" mechanism to take place in this case as well, the formation of para-isomer proceeding in a different way, probably, with the participation of the phenoxy radical.

To verify such a possibility, the interaction of (I) with 2,4,6-tris (tert.-butyl)phenol (III) gas been studied, the latter compound being advantageous in its ability of forming a stable phenoxy radical (IV). We found(IV)

---

[x] In all the ^{19}F NMR spectra chemical shifts are measured with regard to the external CF_3COOH. All the NMR and IR-spectra are recorded in CCl_4; UV-spectra are recorded in cyclohexane.

to react slowly with (I) forming 2,4,6-tris(tert.-butyl)para-quinofluoride (V), m.p. 76-7°C (EtOH-H_2O), ^{19}F NMR: triplet δ = 84 p.p.m., J_{F-H} = 10.7 Hz ^{1}H NMR: singlets δ = 0.92 and 1.18; doublet δ = 6.52. The intensity ratio is 9:18:2. IR-spectrum: 1652, 1676 cm^{-1}. UV-spectrum: λ_{max} = 238 mμ; $\mathcal{E}$ = 7620. Found, %: F, 6.38. Calculated, %: F, 6.79.



(2)

Here and hereafter + denotes $(CH_3)_3C$

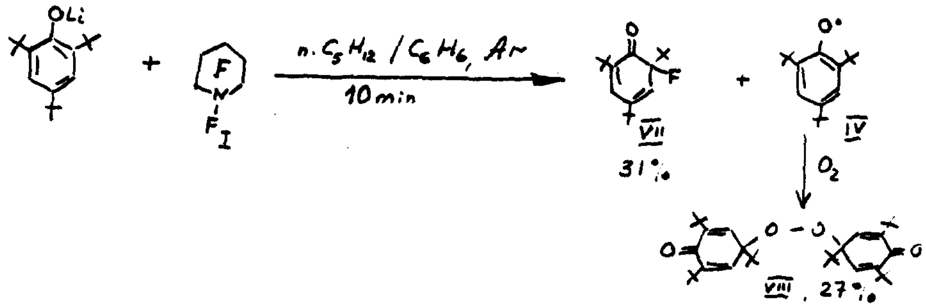
The reaction includes detachment of the fluorine atom from the N-F group of the molecule (I). This is conformed by the formation of N-phenylperfluoropiperidine (VI) [x] when the reaction is carried out in benzene at 100°C (sealed tube). At room temperature (I) is practically insoluble in C_6H_6, but at 100°C these compounds are fully mixed and do not interact.

In contrast to radical (IV), lithium phenolate obtained by mixing equivalent quantities of (III) and butyllithium, instantaneously reacts with (I) at room temperature, giving 2,4,6-tris -(tert.-butyl)ortho-quinofluoride(VII), m.p. 97-8°C. ^{19}F NMR:broadened doublet δ = 92.8 p.p.m.; ^{1}H NMR: δ_{2-CH_3} = 0.86; J_{2-CH_3-F} = 1.1 Hz; δ_{4-CH_3} and δ_{6-CH_3} = 1.08 and 1.14; δ_{3-H} = = 5.71; J_{3-H-F} = 11.8 Hz; δ_{5-H} = 6.54 $J_{3-H - 5-H}$ = 2.7 Hz. IR-spectrum: 1658,1692 cm^{-1}. M^+ = 280 (mass spectrum). UV-spectrum: λ_{max} = 217 mμ; $\mathcal{E}$ = 3380. The reaction by-product is radical (IV), characterized as peroxide (VIII), m.p. 146°C (Lit. m.p. 147-8°C /7/).

Rapid fluorination of Li-phenolate is a direct proof of the reaction proceeding in accordance with the "cage" mechanism which does not involve the formation of the aroxy radical: radical (IV) trained out of the "cage" has no time for entering into the fluorination reaction.

---

x) (VI) is separated by means of preparative GLC (25% QF-I on Chromosorb W, 155°C).Its structure is confirmed by NMR and mass spectra.



(3)

An analogous mechanism may, evidently, take place during the oxidation of phenol (III) with oxygen in an alkaline medium /8/. In this reaction, 2,4,6-tris(tert.-butyl)ortho-quinohydroperoxide is formed together with the para-isomer. At the same time radical (IV) is known to be attacked by oxygen into the para-position exclusively /7/.

Such one-electron mechanism may be true for certain reactions of electrophilic substitution in aromatics containing strong electron-donating substituents, since in such compounds orthosubstitution is often predominant. Chlorination of N,N-dimethyl aniline with chlorine and other chlorinating agents /9/, nitration of anisole /10/ and acetanilide /11/ in acetic anhydride can be cited as examples of such reactions.

ACKNOWLEDGEMENTS

The authors should like to express their gratitude to Academician I.L.Knunyants for the discussion of the results presented in this paper,to E.I.Mysov for the recording and interpretation of the mass spectra,to A.A.Volod'kin and V.V.Yershov through whose courtesy the authors could work with 2,4,6-tris(tert.-butyl)phenol.

REFERENCES

1. J.Burdon, J.W.Parsons,J.C.Tatlow, Tetrahedron, 28, 43 (1972).
2. I.N.Rozhkov, A.V.Bukhtiarov, N.D.Kuleshova, I.L.Knunyants, DAN SSSR, 193, 1322 (1970).
3a.M.J.Shaw, H.H.Hyman, R.Filler, J.Am.Chem.Soc.,91,1563(1969).
3b.M.J.Shaw,H.H.Heyman,R.Filler.J.Org.Chem. 36, 2917 (1971).
4a.D.Taub,Chem. & Ind.(Rev.), 1962, 558.
4b.J.S.Kende, P.McGregor, J.Am.Chem.Soc., 83, 4197(1961).
4c.A.N.Detsena,V.A.Koptyug, Zh.Org.Kh., 7, 2575 (1971).
5. D.H.R.Burton,A.K.Ganguly,R.H.Hesse, S.M.Loo,M.M.Rechet, Chem.Comm.,1968,806
6. V.R.Polishchuk,B.Ya.Medvedev,N.N.Bubnov,L.S.German,I.L.Knunyants(in the press)
7. E.Miller, K.Lee, Ber.87, 922 (1954).
8. H.R.Gersman, A.F.Bickel,J.Chem. Soc., 1959,2711
9. T.H.Chao, L.P.Cipriani, J.Org.Chem.,26, 1079 (1961)
10. J.G.Hoggett, R.B.Moodie, K.Schofield,Chem.Comm.,1969,605
11. S.R.Hartshern, R.B.Moodie, K.Schofiled, J.Chem.Soc.(B), 1971, 2454