Reactions of polyfluorinated 2,5-cyclohexadienones at the carbonyl group

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Perfluoro-4-phenoxy-2,5-cyclohexadienone reacts with phenyl- and pentafluorophenylhydrazines to give products of nucleophilic substitution of the fluorine atom at the double bond, 3-arylazotetrafluorophenols. In the presence of aluminum chloride, the reactions proceed at the carbonyl groups of polyfluorinated cyclohexadienones to form the corresponding polyfluorinated azobenzenes. Perfluoro-4-phenoxy-2,5-cyclohexadienone reacts with butyllithium and butylmagnesium bromides to give the product of addition at the carbonyl group.

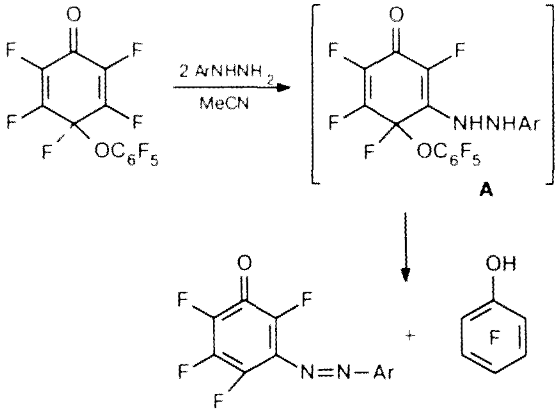
Key words: polyfluorinated cyclohexadienones, arylhydrazines, azobenzenes; organometallic compounds.

Polyfluorinated 2,4- and 2,5-cyclohexadienones are convenient synthons for preparing various fluorine-containing aromatic compounds. They react with *N*- and *O*-nucleophiles to give products of substitution of the F atom at positions 3 and 5 of the dienone ring,[1–3] whose reduction results in the formation of *meta*-substituted fluorine-containing phenols[2] and polyphenyl esters[3] as well as 3-substituted α-naphthols and 4-substituted β-naphthols.

It is noteworthy that nucleophilic reactions of nonfluorinated cyclohexadienones involve both the double bond and the carbonyl group.[4] Reactions at the carbonyl group are most characteristic of hydrazine[5] and organometallic compounds.[4,6]

In this work, the reactions of these reagents with several fluorine-containing cyclohexadienones have been studied.

Perfluoro-4-phenoxy-2,5-cyclohexadienone reacts with phenyl- and pentafluorophenylhydrazines to form mixtures of the corresponding 3-arylazotetrafluorophenols **1a,b** and pentafluorophenol in a 1 : 1 ratio.

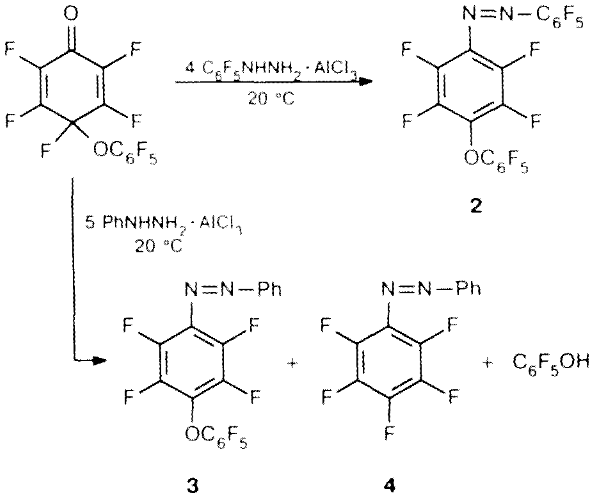


1a: Ar = C_6F_5
1b: Ar = Ph

Arylazotetrafluorophenols **1a,b** are obtained probably by disproportionation of the intermediate products in the nucleophilic substitution of the F atom at the double bond (**A**). An azophenol with a similar structure (**1**) was prepared by the oxidation of the product of the addition of phenylhydrazine to the double bond of 2,4-dimethyl-4-hydroxy-2,5-cyclohexadienone.[7]

The analysis of the published data shows that reactions of arylhydrazines with cyclohexadienones involving the carbonyl group are catalyzed by acids.[7,8] Therefore, we studied the reactions between polyfluorinated cyclohexadienones and complexes of phenyl- and pentafluorophenylhydrazine with $AlCl_3$.

Perfluoro-4-phenoxyazobenzene (**2**) is formed in a high yield in the reaction of perfluoro-4-phenoxy-2,5-cyclohexadienone with excess $C_6F_5NHNH_2 \cdot AlCl_3$ complex in ether. Under similar conditions, the reaction



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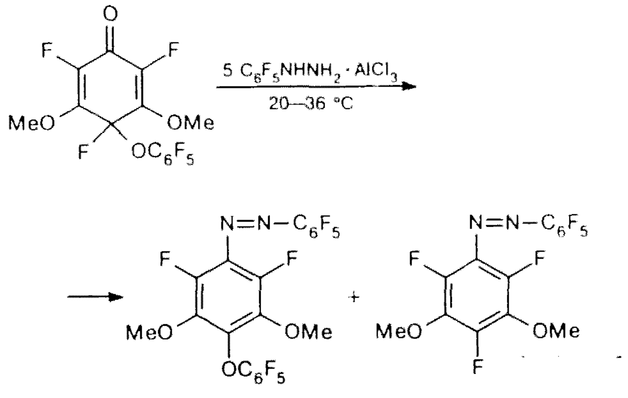
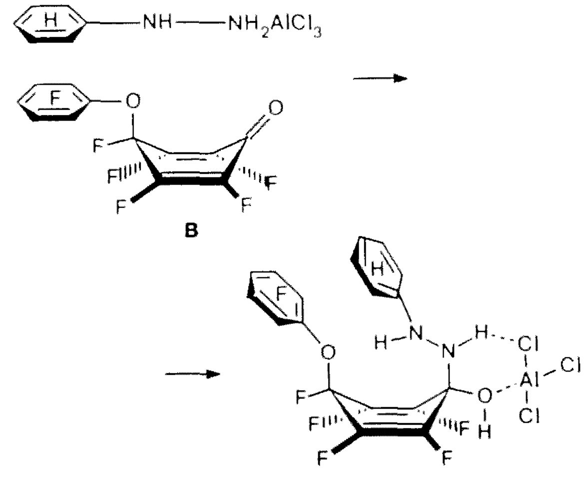
of this dienone with excess $PhNHNH_2 \cdot AlCl_3$ complex results in the formation of a mixture of 4-pentafluorophenoxy-2,3,5,6-tetrafluoroazobenzene (**3**), 2,3,4,5,6-pentafluoroazobenzene (**4**), and pentafluorophenol in a close ratio. No formation of compounds **1a,b** is observed. Azobenzene (**4**) has been previously obtained by the decomposition of pentafluorophenylazide in the presence of aniline.[9]

The reaction of 3,5-dimethoxy-4-pentafluorophenoxy-2,4,6-trifluoro-2,5-cyclohexadienone with excess $C_6F_5NHNH_2 \cdot AlCl_3$ complex in ether results in the formation of 3,5-dimethoxy-4-pentafluorophenoxyheptafluoroazobenzene (**5**) in a high yield along with a small amount of 3,5-dimethoxyoctafluoroazobenzene (**6**).



5 **6**

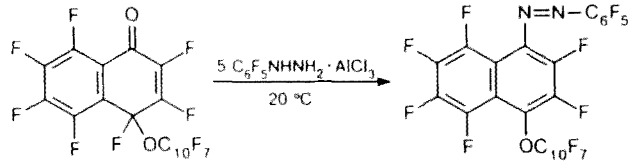
When azobenzenes are formed, either a F^- or $C_6H_5^-$ anion can be the group leaving from the geminal node of the studied cyclohexadienones. The F^- anion is predominately eliminated in reactions of $C_6F_5NHNH_2$, while the probabilities of both processes are approximately equal in the case of $PhNHNH_2$. This difference can be explained by the fact that "sandwich"-type intermediates are formed in the case of $PhNHNH_2$ (**B**, **C**) stabilized by π-interaction between the Ph and C_6F_5 substituents (the formation of π-complexes between fluorinated and nonfluorinated aromatic compounds is known[10]). This finally results in splitting off of the $C_6F_5O^-$ anion from the geminal node of dienone. For $C_6F_5NHNH_2$, this interaction of aromatic rings is destabilizing, and hence, the detachment of the F^- anion is observed to a greater extent.



B

C

The reaction of perfluoro-1-oxo-4-(1′-naphthoxy)-1,4-dihydronaphthalene with excess $C_6F_5NHNH_2 \cdot AlCl_3$ complex in ether results in the formation of perfluoro-4-(1′-naphthoxy)-1-(phenylazo)naphthalene (**7**).



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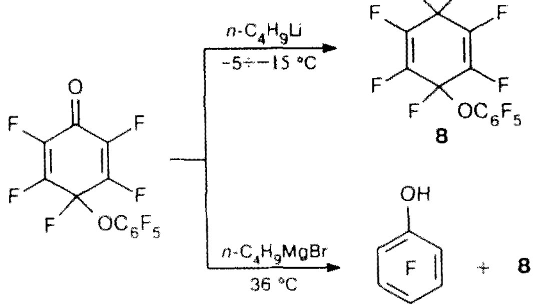
1-Butyl-4-pentafluorophenoxypentafluorocyclohexa-2,5-dien-1-ol (3) as a mixture of two isomers with similar chemical shifts in a ratio of $\sim$2 : 1 (from the ^{19}F and ^{1}H data) was obtained from perfluoro-4-phenoxy-2,5-cyclohexadienone under the action of *n*-BuLi in hexane.



The main isomer with an insignificant admixture of the second isomer was isolated by chromatography in a yield about 50 %. The IR spectrum of this product does not contain the band νCO (1705 cm^{-1}) characteristic of the initial dienone.[11]

The attempts to isolate the second isomer were unsuccessful likely due to its lower stability under chromatography conditions. Judging from the same sets of signals in the ^{19}F and ^{1}H NMR spectra, the obtained compounds are most likely *cis*- and *trans*-isomers.

Product **8** was also obtained in a low yield in the reaction of perfluoro-4-phenoxy-2,5-cyclohexadienone with threefold excess *n*-BuMgBr. However, the main direction of the reaction is the reduction to pentafluorophenol (according to the ^{19}F NMR data, a ratio C_6F_5OH : **8** in the reaction mixture is $\sim$2.3).

Thus, we have shown that, despite the existence of nucleophilically mobile fluorine atoms at the double bond in the cyclohexadienone fragment, 2,5-cyclohexadienones can react with nucleophilic reagents by the type of 1,2-addition to the carbonyl group.

Experimental

^{1}H and ^{19}F NMR spectra (C_6F_6 as internal standard, ppm) were obtained on a Bruker WP-200Y instrument, IR spectra were recorded on a Specord M-80 instrument for a 1 % solution in CCl_4, and UV spectra were recorded on a Specord UV-VIS instrument for solutions in EtOH (*c* $1 \cdot 10^{-4}$ mol L^{-1}). Mass spectra (EA, 70 eV) were recorded on a high-resolution GC/MC Finnigan MAT 8200 spectrometer.

Perfluoro-3-phenylazophenol (1a). Phenylhydrazine (0.24 g) was added to a solution of perfluoro-4-phenoxy-2,5-cyclohexadienone (0.22 g) in 20 mL of MeCN, and the mixture was kept for 1.5 days at ~20 °C. The solvent was evaporated, and the mixture of phenols isolated by chromatography on SiO_2 (CCl_4 as eluent) of the residue contained, according to the data of the ^{19}F NMR spectrum, azophenol **1a** and pentafluorophenol in a ratio 1 : 1. Azophenol **1a** (0.16 g, 74 %) with m.p. 155—158 °C (from CCl_4) was isolated by sublimation *in vacuo* (20 Torr). ^{19}F NMR (10 % solution in MeCN, ppm, C_6F_6 as internal standard): −2.5 (F-5), 0.2 (F_m), 5.5 (F-4), 11.6 (F_p), 12.7 (F_o), 14.7 (F-6), 16.0 (F-2). UV, λ_{max}/nm (log ε): 315 (4.29), 458 (3.51). Found: M^+ 359.99330. $C_{12}HF_9N_2O$. Calculated: M 359.99451.

3-Phenylazotetrafluorophenol (1b). Similarly, azophenol **1b** (0.11 g, 75 %) with m.p. 130—133 °C was obtained from perfluoro-4-phenoxy-2,5-cyclohexadienone (0.2 g) and $PhNHNH_2$ (0.12 g). ^{19}F NMR (a 10 % solution in MeCN): −2.7 (F-5), 4.0 (F-4), 10.9 (F-6), 14.3 (F-2). UV, λ_{max}/nm (log ε): 227 (4.06), 316 (4.15), 436 (2.93). Found: M^+ 270.04260. $C_{12}H_6F_4N_2O$. Calculated: M 270.04162.

Perfluoro-4-phenoxyazobenzene (2). Finely pulverized $AlCl_3$ (0.37 g) was added to a solution of pentafluorophenylhydrazine (0.5 g) in 20 mL of ether. The mixture was stirred for 15 min, and perfluoro-4-phenoxy-2,5-cyclohexadienone (0.2 g) was added dropwise. The mixture was stirred for 3.5 days at ~20 °C and treated with 20 % HCl (50 mL). The ether solution was separated, and an aqueous solution was extracted with ether (2×50 mL). The combined ether extracts were dried over $CaCl_2$ and evaporated *in vacuo* (20 Torr). The residue (0.37 g) was chromatographed on a column with SiO_2 (CCl_4 as eluent). Azobenzene **2** (0.25 g, 87 %), m.p. 151—154 °C (sublimed) was isolated. ^{19}F NMR (10 % solution in CCl_4): 0.4, 0.7 (F_m, F_m'), 3.6 (F_p'), 4.9 (F-3,5), 5.9 (F_o'), 13.0 (F_p), 13.7 (F_o, F-2,6). UV, λ_{max}/nm (log ε): 318 (4.31), 475 (3.01). Found: M^+ 525.9794. $C_{18}F_{14}N_2O$. Calculated: M 525.9787.

Reaction of perfluoro-4-phenoxy-2,5-cyclohexadienone with the $PhNHNH_2 \cdot AlCl_3$ complex. Finely pulverized $AlCl_3$ (0.67 g) was added to a solution of phenylhydrazine (0.54 g) in 10 mL of anhydrous ether. The mixture was stirred for 5 min, and perfluoro-4-phenoxy-2,5-cyclohexadienone (0.37 g) was added dropwise. The mixture was stirred for 26 h at ~20 °C and treated with 20 % HCl (50 mL). The ether solution was separated, and the aqueous solution was extracted with ether (2×50 mL). The combined ether extracts were dried over $CaCl_2$ and evaporated *in vacuo* (20 Torr). A brown solid product (0.39 g) containing, according to the ^{19}F NMR spectrum, mainly azobenzenes **3**, **4**, and C_6F_5OH in a close ratio was obtained. The mixture was chromatographed on a column with SiO_2 (hexane as eluent). Azobenzenes **4** (0.09 g, 33 %) and **3** (0.14 g, 32 %) were isolated. *4-Pentafluorophenoxy-2,3,5,6-tetrafluoroazobenzene* (**3**), m.p. 103—106 °C (hexane). ^{19}F NMR (10 % solution in CCl_4, ppm, C_6F_6 as internal standard): 4.9 (F_m), 7.5 (F_p), 8.9 (F_o), 10.5 (F-3,5), 16.4 (F-2,6). UV, λ_{max}/nm (log ε): 228 (4.09), 318 (4.31), 458 (2.93). Found: M^+ 436.0264. $C_{18}H_5F_9N_2O$. Calculated: M 436.0258.

Reaction of 3,5-dimethoxy-4-pentafluorophenoxy-2,4,6-trifluoro-2,5-cyclohexadienone with the $C_6F_5NHNH_2 \cdot AlCl_3$ complex. Finely pulverized $AlCl_3$ (0.34 g) was added to a solution of $C_6F_5NHNH_2$ (0.5 g) in 30 mL of ether. The mixture was stirred for 10 min, and 3,5-dimethoxy-4-pentafluorophenoxy-2,5-cyclohexadienone (0.2 g) was added. The mixture was stirred for 2.5 h at ~20 °C and for 7 h with boiling and treated with 20 % HCl (50 mL). The ether solution was separated, and the aqueous solution was extracted with ether (2×50 mL). The combined ether extracts were dried over $CaCl_2$ and evaporated *in vacuo* (20 Torr). 3,5-Dimethoxy-octafluoroazobenzene **6** (0.03 g, 15 %) and 3,5-dimethoxy-4-pentafluorophenoxy-heptafluoroazobenzene **5** (0.16 g, 57 %) were isolated from the residue (0.35 g) by chromatography on a column with SiO_2 (CCl_4 as eluent).

Azobenzene **6**, according to the ^{19}F NMR data, is a mixture of *cis*- and *trans*-isomers in a ratio of ~1 : 5. ^{19}F NMR spectrum of azobenzene (**6a**) (solution in CCl_4): −0.2 (F_m), 10.4 (F_p), 12.3 (F_o), 18.8 (F-2,6), 24.3 (F-4). ^{19}F NMR spectrum of azobenzene (**6b**): 2.0 (F_m), 8.6 (F_p), 14.5 (F_o), 18.4 (F-2,6), 20.5 (F-4). Found: M^+ 386.02970. $C_{14}H_6F_8N_2O_2$. Calculated: M 386.03014.

Azobenzene **5**, m.p. 114—116 °C (hexane). ^{19}F NMR spectrum (10 % solution in CCl_4): −1.0 (F_m'), 0.0 (F_m), 0.3 (F_p'), 4.7 (F_o), 10.8 (F_p), 12.5 (F_o), 19.4 (F-2,6). UV, λ_{max}/nm (log ε): 325 (4.28), 439 (3.08). Found: M^+ 550.01850. $C_{20}H_6F_{12}N_2O_3$. Calculated: M 550.01866.

Perfluoro-4-(1′-naphthoxy)-1-(phenylazo)naphthalene (7). Finely pulverized $AlCl_3$ (0.25 g) was added to a solution of pentafluorophenylhydrazine (0.36 g) in Et_2O (20 mL). The mixture was stirred for 10 min, and perfluoro-1-oxo-4-(1′-naphthoxy)-1,4-dihydronaphthalene (0.2 g) was added. The mixture was stirred for 2.5 days at ~20 °C and treated with 20 % HCl (50 mL). The ether solution was separated, and the aqueous solution was extracted with ether (2×50 mL). The combined ether extracts were dried over $CaCl_2$ and evaporated *in vacuo* (20 Torr). Azonaphthalene **7** (0.18 g, 69 %) with m.p. 136—139 °C (hexene) was isolated by chromatography of the residue (0.27 g) on a column with SiO_2 (CCl_4 as eluent). ^{19}F NMR (10 solution in Me_2CO): 0.7 (F_m), 8.0 (F-3, F-6, F-7), 8.5 (F-6), 9.6 (F-7),13.3 (F_p, F-2′ or F-3), 13.8 (F_o), 15.9 (F-3 or F-2′), 17.1 (F-5′, $J_{5',4'}$ = 62 Hz), 18.1 (F-2), 18.4 (F-5 or F-8), 18.9 (F-4′, $J_{4',5'}$ = 62 Hz), 19.7 (F-8 or F-5), 25.7 (F-8′). UV (heptane), λ_{max}/nm (log ε): 218 (5.00), 276 (4.33), 292 sh (4.27), 322 sh (4.08), 356 (3.92), 440 (3.34). Found: M^+ 697.96830. $C_{26}F_{18}N_2O$. Calculated: M 697.97230.

1-Butyl-4-pentafluorophenoxypentafluorocyclohexa-2,5-dien-1-ol (8). A 1.15 *M* solution of *n*-BuLi in *n*-C_6H_{14} (4.75 mL) was added dropwise to an emulsion of perfluoro-4-phenoxy-2,5-cyclohexadienone (2 g) in hexane (5 mL) at −10 °C with stirring in an argon flow. The mixture was stirred for 20 min at −5 to −15 °C, then cooling was stopped, and at 0 °C ice water (20 mL) and a 6 % solution of HCl (50 mL) cooled to 0 °C were added. The organic layer was separated, and the aqueous layer was extracted with hexane (25 mL). The combined organic solutions were dried over $MgSO_4$ and evaporated *in vacuo* (20 Torr). A light-yellow oil (1.95 g) containing, according to the ^{19}F NMR spectrum, about 25 % initial dienone and 75 % isomers **8** in a 1 : 2 ratio was obtained. A light-brown liquid (1.13 g) containing, according to the ^{1}H and ^{19}F NMR spectra, the main isomer with a slight admixture of the second isomer was isolated by chromatography on a column with SiO_2 ($CHCl_3$ as eluent). Dienol **8** as a viscous light-yellow oily liquid was obtained by distillation of the product *in vacuo* (100 °C, 0.1 Torr). UV, λ_{max}/nm (log ε): 207 (3.89), 225 (3.37), 260 (2.69). Found (%): C, 45.28;

H, 2.32; F, 45.64; M 424. $C_{16}H_{10}F_{10}O_2$. Calculated (%): C, 45.28; H, 2.36; F, 44.81; M 424.

Reaction of perfluoro-4-phenoxy-2,5-cyclohexadien-1-one with *n*-butylmagnesium bromide. A solution of perfluoro-4-phenoxy-2,5-cyclohexadienone (0.4 g) in ether (4 mL) was added dropwise to a solution of *n*-BuMgBr obtained from butyl bromide (0.5 g) and magnesium (0.08 g) in ether (15 mL), and the mixture was boiled for 6 h. Then 10 % HCl (30 mL) was added, the ether solution was separated, and the aqueous solution was extracted with ether (20 mL). The combined ether extracts were dried over anhydrous $CaCl_2$ and evaporated *in vacuo* (20 Torr). Viscous oil (0.4 g) containing, according to the ^{19}F NMR spectral data, 51 % C_6F_5OH and 22 % dienol **8** was obtained. ^1H NMR, ppm: 0.88 (3 H), 1.09 (2 H), 1.34 (2 H), 2.00 (2 H), 5.66 (1 H, OH). ^{19}F NMR ($CDCl_3$), C_6F_6 as internal standard, ppm: −0.7 (F-3,5), −0.4 (F_m), 4.6 (F_p), 11.0 (F_o), 14.7 (F-2,6), 48.5 (F-4). Ratio of intensities 2 : 2 : 1 : 2 : 2 : 1. IR, ν/cm^{-1}: 3593, 3570 (OH); 2960, 2925, 2870, 2855, (CH); 1723 (CF=CF).

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