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CHEMISTRY OF FLUORINATED QUINONES

I. THE DIELS-ALDER REACTIONS OF FLUORANIL

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SUMMARY

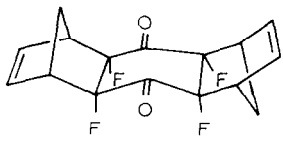
The Diels-Alder reaction of fluoranil with cyclopentadiene, 1,3-butadiene, and 1-acetoxy-1,3-butadiene gave 1,4, 5, 8-bis(methylene)-4a, 8a, 9a, 10a-tetrafluoro-1, 4, 4a, 5, 8, 8a, 9a, 10a-octahydroanthraquinone (I), 2, 3, 4a, 8a-tetrafluoro-4a, 5, 8, 8a-tetrahydro-1,4-naphthoquinone (III), and 5-acetoxy-2, 3, 4a, 8a-tetrafluoro-4a, 5, 8, 8a-tetrahydro-1,4-naphthoquinone (VI), respectively. Hydrogenation of I gave the expected saturated diketone(II). Hydrogenation of III afforded, with elimination of the two tertiary fluorines, 2,3-difluoro-5, 6, 7, 8-tetrahydro-1, 4-dihydroxynaphthalene (IV). In hydrogenation of VI, acetic acid and two moles of hydrogen fluoride were eliminated to give 2,3-difluoro-1, 4-dihydroxynaphthalene(VII). Both dihydroxy compounds IV and VII yielded on oxidation with ferric chloride the corresponding quinones, 2, 3-difluoro-5, 6, 7, 8-tetrahydro-1, 4-naphthoquinone (V) and 2, 3-difluoro-1, 4-naphthoquinone (VIII), respectively. Equivalent amounts of compounds IV and V gave a red-brown semiquinone IX, and a mixture of VI and VIII gave a dark-violet semiquinone X.

INTRODUCTION

Electronegative substituents are known to enhance the reactivity of dienophiles in Diels-Alder reactions. In this respect, fluoranil (tetrafluoro-1,4-benzoquinone) seemed to us especially attractive since its double bonds are flanked not only by carbonyl groups but also by strongly electronegative fluorine atoms. So far, only the reaction of fluoranil with 1,3-butadiene was described[1]. We treated fluoranil with several dienes and found that it reacts in the expected way although not as rapidly as we anticipated. The reactions did not take place at room temperature but required heating at 100-120° for several hours depending on the reactivity of the diene.

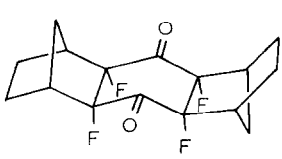
RESULTS AND DISCUSSION

The reaction of fluoranil with cyclopentadiene gave, regardless of the ratio of the reactants, a 1:2 adduct of the anticipated structure I : 1,4,5,8-bis(methylene)-4a,8a,9a,10a-tetrafluoro-1,4,4a,5,8,8a,9a,10a-octahydroanthraquinone. The fluorine NMR spectrum showed signals of two non-equivalent fluorines, and proton NMR gave signals of two non-equivalent vinylic protons, two tertiary protons, and multiplets of the methylene apex protons.

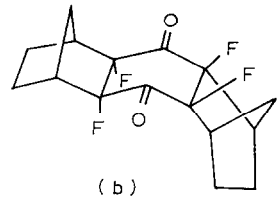


(a) I (b)

Hydrogenation of I gave a completely saturated diketone II, 1,4,5,8-bis(methylene)-4a,8a,9a,10a-tetrafluoro-1,2,3,4,4a,5,6,7,8,8a,9a,10a-dodecahydroanthraquinone.



(a) II

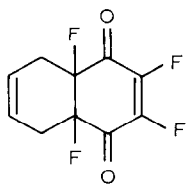


(b)

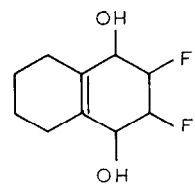
Six stereoisomeric structures can be drawn for compounds I and II. However, four can be ruled out by routine NMR analysis, leaving two possibilities, exo-syn-endo (Ia,IIa) and exo-anti-endo (Ib,IIb) structures. We hope to determine the actual correct structures of I and II through nuclear Overhauser effect experiments.

The reaction of fluoranil with 1,3-butadiene, even when a large excess of the diene was used, gave a 1:1 adduct having structure III. This compound was prepared by Yakobson et al. and subjected to reduction with zinc and acetic acid followed by chromium trioxide oxidation to give 2,3-difluoro-1,4-naphthoquinone[1].

We hydrogenated the adduct III with hydrogen over a palladium-on-carbon catalyst, and isolated 2,3-difluoro-5,6,7,8-tetrahydro-1,4-dihydroxy-naphthalene (IV). The structure of IV is supported by the absence of carbonyl adsorption and presence of hydroxyl absorption in the infrared spectrum, and by both fluorine and proton NMR spectra: the fluorine spectrum shows one signal, a singlet, and the proton spectrum two signals as expected for the ring methylenes, and a broad signal for phenolic hydroxyl.



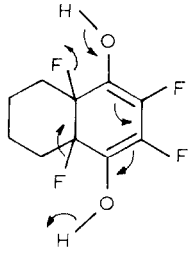
III



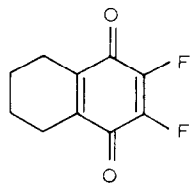
IV

We have made an attempt to find the mechanism of the formation of IV, for the very easy elimination of fluorine atoms during the hydrogena-

tion of III under very mild conditions contrasts with the thermal stability of compound III itself, which stands temperatures up to 160° without decomposition. When the hydrogenation of III was interrupted after the absorption of one mole of hydrogen, the product contained approximately 50% of the starting material III, 18% of 2,3-difluoro-5,6,7,8-tetrahydro-1,4-dihydroxynaphthalene IV, 17% of 2,3-difluoro-1,4-dihydroxynaphthalene VII, and 15% of 2,3-difluoro-1,4-naphthoquinone VIII. When the hydrogenation was stopped after the absorption of two moles of hydrogen, the product was a mixture of about 46% of the starting material III, 38% of the tetrahydro compound IV, 10% of 2,3-difluoro-1,4-dihydroxynaphthalene VII, and about 6% of 2,3-difluoro-1,4-naphthoquinone VIII. The conspicuously easy elimination of fluorine during the hydrogenation suggests the possibility of participation of hydroxylic hydrogens in a way shown in formula IIIa. If this is the case, then it is reasonable to expect also 2,3-difluoro-5,8-dihydronaphthoquinone to be formed during hydrogenation. We did not succeed in isolating this compound, however, NMR analysis of the crude hydrogenation product showed, in addition to compounds III, IV, VII and VIII, peaks which might be due to this dihydronaphthoquinone. Some participation of hydrogen is supported also by the fact that palladium on charcoal which was used as a catalyst for hydrogenation does not itself promote elimination of fluorine at a comparable rate. However, a more accurate study of the mechanism is difficult since reduction-oxidation reactions are frequently involved in partly hydrogenated naphthalene derivatives.



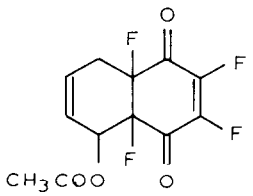
IIIa



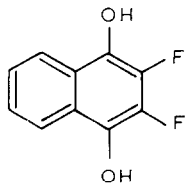
V

The compound IV showed color changes characteristic of oxidation-sensitive compounds, and could be easily oxidized with ferric chloride to the corresponding quinone, 2,3-difluoro-5,6,7,8-tetrahydro-1,4-naphthoquinone (V). This structure is supported by absence of hydroxyl peak and presence of carbonyl peak in the infrared spectrum, one singlet in the fluorine NMR spectrum, and two different methylene multiplets and absence of phenolic proton in the proton NMR .

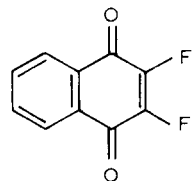
Addition of fluoranil to 1-acetoxy-1,3-butadiene gave also only 1:1 adduct even when an excess of the diene was used. Structure VI for this adduct is supported by both IR and NMR spectra. The infrared spectrum showed the presence of acetate plus two other carbonyl bands. The fluorine spectrum indicated four nonequivalent fluorines, two vinylic and two tertiary. The proton spectrum showed a three-proton singlet corresponding to acetate methyl and separate multiplets for the non-equivalent methylene protons and the methine proton. A complex multiplet corresponding to two vinylic protons was also seen.



VI



VII



VIII

Hydrogenation of compound VI gave again surprising results. Elimination of acetic acid and two moles of hydrogen fluoride yielded 2,3-difluoro-1,4-dihydroxynaphthalene (VII). The IR spectrum showed the presence of hydroxyl and absence of carbonyl absorption; fluorine NMR showed one singlet, and proton NMR AA'XX' aromatic and phenolic protons. Like compound IV, the compound VII changed its color in solution from colorless through brown to violet, and was readily oxidized with ferric chloride to 2,3-difluoro-1,4-naphthoquinone (VIII). This structure is confirmed by

absence of hydroxyl and presence of carbonyl absorption in IR spectrum, one singlet in fluorine NMR, and AA'XX' aromatic protons in proton NMR .

The dark color of compounds IV and VII is evidently due to a partial oxidation of the colorless "hydroquinones" to yellow quinones and to the combination of these two compounds to dark-colored 1:1 adducts, "quinhydrones" or "semiquinones". Indeed, when equimolecular amounts of compounds IV and V in carbon tetrachloride solutions were mixed, dark red-brown crystals of IX deposited on cooling. Similar treatment of compounds VII and VIII gave a dark-violet precipitate of the compound X. Both semiquinones evidently dissociate into their components when dissolved in organic solvents.

The easy Diels-Alder reaction of fluoranil with dienes, surprising behavior of some of the adducts during catalytic hydrogenation, spontaneous formation of aromatic and semiaromatic systems, reactivity of the vinylic fluorines toward nucleophiles, and potential reactions of quinone-hydroquinone systems thus formed makes these reactions very attractive for further studies, and experiments along these lines are in progress in our laboratories.

EXPERIMENTAL

Melting points points are not corrected. Samples for analyses were dried at 0.01-0.1 mm Hg at temperatures 50-80° below their melting points. Infrared spectra were taken in carbon tetrachloride solutions on a Beckman IR 5A or IR 20X spectrophotometer. NMR spectra were measured in carbon tetrachloride solutions on a JEOL PS 100 spectrometer using TMS and HFB (hexafluorobenzene) as internal standards.

1,3-Butadiene was commercial product of the Matheson Company. 1-Acetoxy-1,3-butadiene was prepared from crotonaldehyde, acetic anhydride and sodium acetate according to the literature[2]. It was distilled at

53-54° at 32 mm Hg. Cyclopentadiene was obtained by thermal depolymerization of its dimer. B.p. 42-45°. Fluoranil was prepared by oxidation of hexafluorobenzene with nitric acid according to the literature[3], and purified by sublimation at 110° at 20 mm Hg.

Catalytic hydrogenations were carried out in methanolic solutions using 10% palladium on charcoal, at atmospheric pressure and room temperature. The uptake of hydrogen was very fast and most hydrogenations were finished within 30-90 minutes.

Physical constants, analytical data, IR spectra, and proton and fluorine NMR spectra are summarized in Table 1.

1,4,5,8-Bis(methylene)-4a,8a,9a,10a-tetrafluoro-1,4,4a,5,8,8a,9a,10a-octahydroanthraquinone (I)

In a 15 ml thick-walled vial, 0.3 g (0.0017 mole) of fluoranil was dissolved in 2.5 ml of boiling benzene, the solution was cooled, and 0.4 g(0.0074 mole) of cyclopentadiene was added. The bright yellow color turned dark orange. The vial was sealed and heated in a water bath at 98° for 1.5 hours. The dark color changed to light yellow shortly after heating.

The solution was evaporated to dryness *in vacuo* at room temperature, and the residue (0.5 g, 96%) was recrystallized from carbon tetrachloride giving 0.4 g (75%) of white crystals of I, m.p. 151.5-152°.

1,4,5,8-Bis(methylene)-4a,8a,9a,10a-tetrafluoro-1,2,3,4,4a,5,6,7,8,8a,9a,10a-dodecahydroanthraquinone (II)

Catalytic hydrogenation of 0.6 g (0.0019 mole) of I absorbed after 90 minutes 86% of the theoretical volume of hydrogen for two double bonds and gave 0.4 g (65%) of II, m.p. 151-151.5° (CCl_4); mixed m.p. with I 138-139°.

2,3,4a,8a-Tetrafluoro-4a,5,8,8a-tetrahydro-1,4-naphthoquinone (III)

In a 15 ml ampoule, 1.2 g (0.0067 mole) of fluoranil was partly

Table 1

Compound	Formula	Yield,%	M.P.°C	Analysis,%[a] C	H	F
I	$C_{16}H_{12}F_4O_2$ 312.27	75	151.5-152	60.83 (61.54)	3.36 (3.88)	25.11 (24.34)
II	$C_{16}H_{16}F_4O_2$ 316.29	65	151-151.5	60.66 (60.76)	5.13 (5.10)	25.13 (24.03)
III	$C_{10}H_6F_4O_2$ 234.16	70	56.5-57.5	51.10 (51.25)	2.83 (2.58)	32.46 (32.46)
IV	$C_{10}H_{10}F_2O_2$ 200.19	42	122-124.5	59.92 (60.0)	4.38 (5.04)	
V	$C_{10}H_8F_2O_2$ 198.17	67	125-126	59.92 (60.60)	4.38 (4.07)	
VI	$C_{12}H_8F_4O_4$ 292.20	61	69.5-70	49.18 (49.32)	3.26 (2.76)	26.17 (26.0)
VII	$C_{10}H_6F_2O_2$ 196.16	75	162.5-165	60.77 (61.23)	3.77 (3.08)	18.14 (19.37)
VIII	$C_{10}H_4F_2O_2$ 194.14	65	192-192.5	61.29 (61.87)	2.69 (2.08)	18.72 (19.57)
IX	IV + V		152.5-153	59.96 (60.3)	4.80 (4.56)	
X	VII + VIII		157-158.5	60.83 (61.6)	3.47 (2.58)	

[a]Calculated values in parentheses.

[b]Downfield shifts relative to HFB are given positive values.

IR max, cm^{-1}	NMR	
	^{1}H	^{19}F[b]
1742,1168,1075	1.4-2.4 (complex multiplets,2) 3.34 (broad singlet,1)[c] 3.42 (broad singlet,1) 5.91 (singlet,1) 6.43 (singlet,1)	 2.3 (broad doublet,1) 10.3 (broad singlet,1)
2960,1725,1135 1070,870	1.0-2.5 (complex multiplets,6) 2.84 (multiplet,1) 2.92 (multiplet,1)	 -8.3 (broad doublet,1) 3.1 (broad triplet,1)
1727,1664,1359 1335,1105,1054 960,885	2.79 (distorted AB quartet,2) 5.68 (singlet,1)	-2.7 (very broad singlet,1) 27.0 (triplet,1)
3570,2910,1680, 1500,1475,1270, 1220,1025	1.78 (broad singlet,2) 2.60 (broad singlet,2) 4.6 (broad singlet,1)	-6.0 (singlet)
2930,1705,1680 1625,1340,1275 1235,1160,920	1.75 (multiplet,1) 2.45 (multiplet,1)	19.4 (singlet)
1780,1738,1680, 1370,1350,1217, 1035,935	1.92 (singlet,3) 2.56 (triplet,1) 3.22 (doublet of doublets,1) 5.28 (doublet of triplets,1) 5.7-6.1 (complex multiplets,2)	-18.3 (triplet of doublets,1) 12.4 (broad singlet) 25.7 (doublet of triplets,1) 26.6 (doublet of doublets,1)
3300,1650,1610, 1475,1420,1320, 1242,1035	7.46 (multiplet[d],2) 8.08 (multiplet[d],2) 5.0 (broad singlet,2)	-3.9 (singlet)
1700,1210,965 720	7.80 (multiplet[d],2) 8.16 (multiplet[d],2)	23.5 (singlet)

[c] Most of the "singlet" peaks reported are actually collections of large numbers of unresolved lines, resulting from complex spin-spin splitting.

[d] AA'XX' splitting pattern.

dissolved in 4 ml of boiling benzene. The mixture was cooled in Dry Ice, and 0.6 g (0.011 mole) of 1,3-butadiene was condensed in the ampoule. The ampoule was sealed and heated slowly to 98°, and then for 100 minutes at 120±5°. After cooling, the ampoule was opened releasing a slight pressure of excess butadiene, and the liquid was evaporated *in vacuo* at room temperature. The light brown oil (1.4 g, 90%) crystallized in the refrigerator. Sublimation at 9 mm Hg and 70-75° gave 0.1 g (8%) of unreacted fluoranil, and at 75-110°, 1.1 g (70%) of III. B.p. 63-64° at 0.005 mm Hg, m.p. 56.5-57.5° (pentane) (literature[1] m.p. 53.5-55°).

2,3-Difluoro-1,4-dihydroxy-5,6,7,8-tetrahydronaphthalene (IV)

The butadiene-fluoranil adduct III (0.55 g., 0.00235 mole) was dissolved in 10 ml of methanol and hydrogenated over 0.2 g of 10% palladium on activated charcoal. After 90 minutes when the rate of hydrogen absorption slowed down considerably and 2.2 moles of hydrogen has been consumed, the catalyst was filtered off with suction and the colorless filtrate was evaporated to dryness *in vacuo* at room temperature to give 0.5g of a brown crystalline residue smelling strongly of hydrogen fluoride (pH 2-3).

In an attempt to purify the residue by crystallization from hot water the crystals that deposited on cooling darkened rapidly on standing, evidently because of partial oxidation by air. The solution was treated with an excess of ferric chloride, the yellow precipitate was extracted with benzene, and the benzene extract was evaporated *in vacuo* to give 0.3 g of a dark brown residue. The NMR spectra showed the residue to be a mixture of approximately 27% of IV, 20% of V, and 53% of VIII. The mixture (0.3 g) was hydrogenated over 0.1 g of palladium on charcoal for 24 hours until no more hydrogen was taken up. The colorless solution after filtration of the catalyst was evaporated to dryness *in vacuo*, and the greenish grey crystals (0.2 g) (42%) were recrystallized from 4 ml

of carbon tetrachloride. The white-yellow crystals turned grey to brown on the filter paper, and it was impossible to squeeze all the solvent from the crystals. Two more crystallizations from carbon tetrachloride raised the m.p. to 122-124.5°.

2,3-Difluoro-5,6,7,8-tetrahydro-1,4-naphthoquinone (V)

Oxidation of an aqueous solution of 0.15 g (0.00075 mole) of IV with an excess of ferric chloride gave a yellow precipitate. Extraction of the mixture with benzene and evaporation of the extract in vacuo at room temperature gave 0.1 g (67%) of bright yellow needles of V. Vacuum sublimation at 10 mm Hg at 75-105° followed by crystallization from carbon tetrachloride gave pure V, m.p. 125-126°.

5-Acetoxy-2,3,4a,8a-tetrafluoro-4a,5,8,8a-tetrahydro-1,4-naphthoquinone (VI)

A solution of 0.3 g (0.0017 mole) of fluoranil and 0.4g(0.0036 mole) of 1-acetoxy-1,3-butadiene in 3 ml of benzene was sealed in an ampoule and heated in a boiling water bath for 1.5 hours. Evaporation of the reaction mixture in vacuo at 50° gave 0.6 g of an oil which crystallized after scratching. The crystalline mass was spread over a porous plate and recrystallized from a small amount of carbon tetrachloride to give 0.3 g(61%) of VI, m.p. 69.5-70°. Measurements of the reaction rate of 0.03 g of fluoranil and 0.05 g of 1-acetoxy-1,3-butadiene in 0.5 ml of benzene at 99° gave the following data (from NMR spectra): After 0.5, 1, 1.5, 2, 2.5, and 3.0 hours, 20, 45, 63, 83, 90, and 95% of fluoranil reacted, respectively.

2,3-Difluoro-1,4-dihydroxynaphthalene (VII)

Hydrogenation of 0.27g (0.00093 mole) of VI in 10 ml of methanol for 70 minutes consumed the theoretical volume required for two double bonds. The filtrate after the removal of the catalyst was colorless and smelled of acetic acid. Evaporation in vacuo at 30-40° gave 0.25 g

of light brown crystals. When dissolved in hot carbon tetrachloride or benzene the compound formed a bright yellow solution. This gelatinized on cooling to form a thixotropic gel. When filtered with suction the yellow gel turned to brown crystals (0.15 g,75%), and it was difficult to squeeze the solvent out from the crystalline mass on the filter. The brown crystals dissolved in benzene or carbon tetrachloride with yellow color, and left dark violet residue after evaporation of the solvent. M.p. after two recrystallizations from carbon tetrachloride was 162.5-165°.

2,3-Difluoro-1,4-naphthoquinone (VIII)

A solution of 0.15g(0.00076 mole)of VI in 10 ml of boiling water was treated with an excess of an aqueous solution of ferric chloride until no more precipitate was formed. The yellowish precipitate was extracted with benzene, and the yellow solution was freeze-dried at room temperature at 8 mm Hg to give 0.1 g (65%) of VIII, m.p. 192-192.5° (CCl_4) (after sublimation at 100° and 8 mm Hg). Literature[1] m.p. 189.5-190.5°.

Semiquinone IX

A solution of 20 mg of IV in 2 ml of hot carbon tetrachloride was added to a solution of 20 mg of V dissolved in 1 ml of the same solvent. The bright yellow solution deposited dark red-brown crystals on cooling. M.p. 152.5-153°.

Semiquinone X

A solution of 22 mg of VII in 1.5 ml of hot carbon tetrachloride was added to a solution of 21 mg of VIII in 1 ml of carbon tetrachloride. The yellow solution gave dark violet crystals on cooling. M.p. 157-158.5°.

ACKNOWLEDGEMENTS

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