Chemical consequences of fluorine substitution. Part 4.[†] Diels–Alder reactions of fluorinated *p*-benzoquinones with Dane's diene. Synthesis of fluorinated D-homosteroids

Michael Essers and Günter Haufe*

Organisch-Chemisches Institut, Westfälische Wilhelms-Universität Münster, Corrensstr. 40, D-48149 Münster, Germany. E-mail: haufe@uni-muenster.de.; Fax: +49-251-83-39772

Received (in Cambridge, UK) 15th August 2002, Accepted 19th September 2002 First published as an Advance Article on the web 24th October 2002



Four fluorinated *p*-benzoquinones (2) have been reacted with Dane's diene (1) in Diels–Alder reactions and the formed fluorinated D-homosteroids were characterized. The number of products, their stereochemistry and stability depends on the fluorine substitution pattern of the corresponding fluorinated *p*-benzoquinones. If the *p*-benzo-quinone (2) contains an unfluorinated double bond, this bond reacts faster with diene 1 yielding *endo*-products selectively. In contrast, [4+2]cycloadditions with 2,6-difluoro (2c) and 2,3,5,6-tetrafluorobenzoquinone (2d) gave the products with *exo*-orientation of the carbonyl part preferably.

Introduction

Published on 24 October 2002 on http://pubs.rsc.org | doi:10.1039/B208001J

Downloaded by Queens University - Kingston on 12/05/2013 09:06:02.

There is increasing interest in organofluorine compounds due to the strong influence of the fluorine substituent on the chemical, physical and physiological properties of these compounds.^{1,2} For example, in 1970 the share of fluorinated agrochemicals was 3%. Thirty years later, in 2000, 55% of the agrochemicals contained at least one carbon fluorine bond.³ In the same time period, the share of fluorinated pharmaceuticals on the world market rose from 2% to 18%.³ Diels–Alder reactions of fluorinated olefins are an attractive approach towards a range of selectively fluorinated cyclohexenes, many of which have potential biological activity. There are two contributions to the effect of a single fluorine at a double bond, the strong electron withdrawing effect (–I-effect) and the mesomeric p- π -interaction (+M-effect).^{4,5} Generally, the latter effect is dominating.⁵⁻⁷

Regarding simple vinyl fluorides, just the reactions of some fluorostyrenes with the highly reactive diphenylisobenzofuran⁶ and with some fluorinated dienes⁸ are known. Several more reactions of this type, which solely take place with strongly activated dienophiles such as 2-fluoroacroleins,⁹ α , β -unsaturated α -fluoroketones,^{5,10} α , β -unsaturated α -fluorocketones,¹¹ fluorinated vinylsulfones¹² or a fluorinated electron-poor vinyl sulfoxide¹³ have been published.¹⁴

A second fluorine substituent attached to the double bond seems to increase the reactivity of the corresponding alkenes in Diels–Alder reactions. Several reactions of perfluoroalkenyl ketones with various dienes,¹⁵ of cyclopentadiene with enol derivatives of difluoroacetaldehyde,¹⁶ of furan with perfluoropropene or a corresponding sulfonyl fluoride,¹⁷ and of trifluoroethylene with several substituted furans¹⁸ have been published recently. Furthermore, Diels–Alder reactions of tetrafluoro-*p*benzoquinone (**2d**) with buta-1,3-diene,^{19,20} 1-acetoxybuta-1,3diene,²⁰ and cyclopentadiene^{20,21} are known.

As part of our efforts directed toward the synthesis of fluorinated steroids, a substance class representing well known pharmaceuticals,²² the synthesis of fluorinated chrysenediones (3) *via* Diels–Alder reaction of various fluorinated *p*-benzo-



quinones (2) with Dane's diene (1) (Scheme 1)²³ was investigated, especially regarding the effect of the fluorine substitution pattern of the *p*-benzoquinones (2) on the outcome of the cycloadditions. The results of this study are reported in the present paper.

Results and discussion

Syntheses of the reactants

Dane's diene²⁴ (1) was synthesised according to the literature procedure.25 In our hands, the Grignard reaction of vinylmagnesium bromide with 6-methoxy-α-tetralone[‡] always yielded mixtures of the expected allylic alcohol 1,2,3,4-tetrahydro-6methoxy-1-vinyl-1-naphthol (4) and Dane's diene (1) in ratios varying from 4 : 1 to 1 : 2 (4 : 1, ¹H NMR). A similar partial dehydration was already reported for the reaction of 6methoxy-α-tetralone with ethynylmagnesium bromide.²⁶ The diene 1 is described to possess low stability 26-28 and our investigations are in accordance with these reports. Due to this instability, some literature procedures used a solution of 1 in benzene for subsequent reactions.^{26,29} As the dehydration of 4 can result in polymerisation,²⁶ in our study the mixture of 4 and 1 was used as, under the conditions of thermal Diels-Alder reactions, the tertiary allylic alcohol 4 could be expected to dehvdrate.

For the syntheses of fluorinated *p*-benzoquinones, some drastic conditions are described in the literature, *e.g.* reaction of

J. Chem. Soc., Perkin Trans. 1, 2002, 2719–2728 2719

[†] For Part 3 cf. G Haufe, O. G. J. Meyer, C. Mück-Lichtenfeld, Coll. Czech. Chem. Commun. 2002, in the press.

[‡] The IUPAC name for α -tetralone is 3,4-dihydro-1(2*H*)-naphthone.

Table 1 Yields and reaction times for the Elbs oxidation of the fluorophenols (5) to the fluorohydroquinones (6), and CAN oxidation of the fluorohydroquinones (6) to the fluoro-*p*-benzoquinones (2)

Entry	Fluorophenol	Reisolated 5 (%)	Time/h	Fluorohydroquinone	Yield ^{<i>a</i>} (%)	Fluoro-p-benzoquinone	Yield ^a (%)
1	5a	23	14	6a	47 (41) ^b	2a	94 (78) ^b
2	5b	41	14	6b	37	2b	93
3	5b	39	37	6b	33		
4	5c	45	14	6c	$26(22)^{c}$	2c	98
5				6d		2d	99
^a Yields	obtained in the liter	rature are given in bra	ckets. ^b Ref. 3	⁶ 9. ^{<i>c</i>} Ref. 40.			

a fluorinated aniline with a mixture of sulfuric acid and nitric acid³⁰ or substitution of appropriate chloro- derivatives with potassium fluoride at 350 °C.³¹ Furthermore, partly difficult to handle reagents like hydrogen fluoride or xenon difluoride have been employed.³² Several of the reactions mentioned also exhibit low selectivity.

Initially, an alternative approach to the fluoro-p-benzoquinones (2) was envisaged, whereby unfluorinated or monofluorinated hydroquinones are directly fluorinated with electrophilic fluorinating agents. Such agents have attracted much interest in recent years ^{33,34} and emphasis in the literature has been on fluorinations in the α -position to the carbonyl group and on fluorination of aromatic compounds.35,36 For our investigations we chose the cheap and readily available Selectfluor[™] [1-chloromethyl-4-fluoro-1,4-diazabicyclo[2.2.2]octan-1,4-diylium bis(tetrafluoroborate)]. However, reacting fluorohydroquinone (6a) with 1.2 to 2.0 equivalents of Selectfluor™ in dry acetonitrile or dry methanol in a closed vessel at temperatures between 20 °C and 100 °C afforded, apart from fluoro-p-benzoquinone (2a) (95%), only a maximum of 5% of 2,5-difluoro-p-benzoquinone (19 F NMR). Thus, oxidation of the hydroquinone 6a is obviously faster compared to the desired fluorination. Accordingly, an attempted electrophilic fluorination of hydroquinone using Selectfluor™ furnished almost pure p-benzoquinone. The oxidative properties of electrophilic fluorinating agents have already been reported.³⁷ In order to avoid oxidation to the corresponding benzoquinones, the reaction of 1,4-dimethoxybenzene with Selectfluor™ (2.2 equivalents, acetonitrile, 75 °C, 1 h) was investigated. Unfortunately, a complex product mixture was observed.

In contrast to this, Feiring and Sheppard presented a method which converts *o*-fluorophenol (**5a**) into fluorohydroquinone (**6a**) in 41% yield (crude product) *via* an Elbs oxidation.^{38,39} The subsequent oxidation with ceric ammonium nitrate (CAN) yielded fluoro-*p*-benzoquinone (**2a**) (78%) ³⁹ (Scheme 2, Table 1).



An Elbs oxidation as mentioned above was also used by King and Cohen for the oxidation of 2,6-difluorophenol (**5c**) to 2,6difluorohydroquinone (**6c**) (22%).⁴⁰ Generalizing the two-step reaction sequence of Elbs and CAN oxidation was envisaged as a means of easily accessing differently substituted fluoro-*p*benzoquinones for use in the subsequent [4+2]cycloadditions.

The results of application of this strategy for the synthesis of fluoro-p-benzoquinone (2a), 2,3-difluoro-p-benzoquinone (2b), 2,6-difluoro-p-benzoquinone (2c), and tetrafluoro-p-benzoquinone (2d, fluoranil), are shown in Scheme 2 and Table 1, starting from the corresponding fluorophenols 5, where for the synthesis of 2d commercially available tetrafluorohydroquinone (6d) was employed. The literature procedures³⁹ were slightly modified in order to improve the yields: omitting the yielddiminishing recrystallisation,³⁹ after chromatography the products of the Elbs oxidation did not result in diminished purity of the hydroquinones (6), which were obtained in an analytically pure form, except for fluorohydroquinone (6a) (94% (GC)). According to gas chromatographic analysis, the corresponding unreacted fluorophenols (5) were reisolated cleanly. Prolonged reaction time led, at least in the case of 5b, to slightly diminished yields (Table 1, entries 2 and 3). After the fast and easy CAN oxidation, the crude product was purified by column filtration instead of sublimation³⁹ giving the fluoro-pbenzoquinones 2a-d in an analytically pure form and in almost quantitative yields (Scheme 2, Table 1).

Diels-Alder reactions

Diels-Alder reaction with fluoro-p-benzoquinone

We began our study with the Diels–Alder reaction of fluoro-*p*benzoquinone (2a) with Dane's diene (1, mixture with 4).⁴¹ After heating the dienophile 2a with a slight excess of 1 in diethyl ether at 50 °C in a sealed tube, the formation of a brightyellow precipitate was observed which corresponded to the regioisomeric mixtures 7a/b and 8a/b (Scheme 3). The solubilities of 7a/b and 8a/b differ significantly in different solvents. Compounds 7a/b are only sparingly soluble in chloroform, whereas 8a/b are poorly soluble in acetone. These differing characteristics were exploited for separation in order to furnish the double bond isomers 7a/b and 8a/b as regioisomeric mixtures with respect to the position of the fluorine substituent.

Due to the Diels–Alder adducts being just partly stable under gas chromatographic conditions, quantitative information on regio- and diastereomeric ratios in the crude products cannot be obtained by this method. Such information could not be obtained by means of NMR, either, as owing to the great differences in solubility of **7a/b** and **8a/b**, no sufficiently concentrated solution for ¹⁹F NMR analysis could be obtained. However, no products were detected, which would hint at participation of the fluorinated double bond of **2a** in cycloaddition, resulting in "*ortho*"-**9** or "*meta*"-adduct ⁴² **10** (Scheme 3).

The regioisomeric mixture **7a/b**, bearing an olefinic proton in the C-ring, was furnished after crystallisation from acetone (13%). In this solid, the regioisomeric ratio was 91 : 9 (**7a** : **7b**, ¹H NMR). Thus, fluoro-*p*-benzoquinone (**2a**) reacted preferentially to the chrysenediones with the fluorine substituent in position 3 (Scheme 3). Compounds **8a/b** (11%), which evolve from the primary cycloadducts **7a/b** via double bond migration, bearing the higher substituted double bond, were obtained in a regioisomeric ratio of 92 : 8 (**8a** : **8b**, ¹H NMR). Such isomerisations have already been observed under acid catalysis





Scheme 3

Et₂O 50 °C, 1 h

in similar, unfluorinated compounds.^{26–28,43} The structures of **7a/b** and **8a/b** were confirmed by two-dimensional NMR experiments (¹H, ¹H- and ¹H, ¹³C). For preparative purposes, the conversion of reactants can presumably be enhanced by prolonged reaction times as the mother liquor still contained 32% **2a** and 11% fluorohydroquinone (**6a**) (GC). Furthermore, a greater excess of Dane's diene (1) could be helpful, too, as **1** might, especially in slowly proceeding Diels–Alder reactions where the fast "trapping" of the diene does not take place, decompose to some extent. The formation of fluorohydroquinone (**6a**) can be explained by a redox reaction in the course of which **2a** may be reduced to **6a** by **1**.

Additionally, the Diels-Alder reaction described above was conducted in toluene at 100 °C (65 min). Nevertheless, fluoro-pbenzoquinone (2a, 41%) and fluorohydroquinone (6a, 8%) were found in the crude product mixture as judged by gas chromatography. The higher reaction temperature promoted the double bond migration: Chrysenediones 8a/b (26%) were isolated in a regioisomeric ratio of 76 : 24 (8a : 8b, ¹⁹F NMR). Compounds 7a/b had a regiosisomeric ratio of 63 : 37. Thus, regioselectivity decreases with increasing reaction temperature. Under the reaction conditions just described, some addition of fluoro-p-benzoquinone (2a) via the fluorinated double bond cannot be ruled out as by mass spectrometry (GC-MS coupling) a peak with m/z = 292 was observed in the crude product mixture, which may have evolved from HF-elimination from "ortho"-adduct 9 or "meta"-adduct 10 (Scheme 3). Such an elimination is unlikely in the case of 7a/b and 8a/b and was not observed for these compounds.

Assignment of the position of the fluorine substituent in the fluorinated cycloadducts (Scheme 3) shall be demonstrated on the regioisomeric compounds **8a/b**: In **8a**, the fluorine atom couples to carbons 4a (${}^{3}J_{C,F} = 3.9$ Hz) and 4b (${}^{4}J_{C,F} = 1.8$ Hz), but not to carbon 12a. Consequently, the fluorine substituent must be in position 3 in **8a**. In the ${}^{13}C$ NMR spectrum of **8b**, no coupling of fluorine to carbon 4a is observed; instead the signal arising from carbon 12a is split (${}^{3}J_{C,F} = 3.3$ Hz).

The relative configuration (*endolexo*) of **7a/b** could not be assigned due to multiplets in the ¹H NMR spectrum for protons 4a and 4b from which no coupling constants could be deducted.

As chrysenediones **7a/b** as well as **8a/b** crystallise as fine needles, no crystals suitable for X-ray analysis could be obtained yet. Nevertheless, it is reasonable to assign *endo*-configuration for **7a/b**, as solely *endo*-adducts were observed in related studies with other *p*-benzoquinones,^{26,43b,44-47} the "*endo*-rule"⁴⁸ not being violated. Consequently, the π -electrons of the reactants approach each other in a manner enabling the best possible orbital overlap, *i.e.*, they lie directly on top of one another in the transition state *endo*-**11**, leading to the *endo*-adduct as shown for **7** in Scheme 4. Secondary orbital interactions might



also play a role.⁴⁹ Also for the reaction of fluorobenzoquinone (**2a**) with cyclopentadiene, the formation of the *endo*-adduct has been proven.⁵⁰

The [4+2]cycloaddition of **2a** with Dane's diene (1) showed the significantly lowered reactivity of monofluorinated compared to unfluorinated double bonds once more.⁵⁻⁷







Scheme 5

Diels-Alder reaction with 2,3-difluoro-p-benzoquinone

Subsequently the Diels-Alder reaction of 1 with 2,3-difluoro-pbenzoquinone (2b) was investigated. Dienophile 2b was reacted with 2.5 equivalents of Dane's diene (1) in diethyl ether (45 min at 50 °C). A yellow solid was formed in 76% crude product yield comprising of two isomers, presumably 12 and 13 (Scheme 5), in a 73 : 27 ratio (¹⁹F NMR).⁵⁸ On attempted separation by column chromatography, a drastic colour change to red occurred and hexahydrochrysene-1,4-diol 14 was obtained as a red solid (60%) (Scheme 5). As the primary adducts described above were not expected to be endolexo-isomers of 12 (cf. formation of 15, vide infra and ref. 50), we assume the regioisomers 12 and 13 were formed, whereat 12 tautomerized to the D-ring hydroquinone 14 on silica gel. This consideration is supported by the ¹⁹F NMR spectrum of the yellow crude product before subjection to column chromatography: The signals of two compounds in the ratio 73 : 27, each bearing two fluorine atoms, were observed. In the major isomer (-136.4 ppm, d, ${}^{3}J_{\rm EF} = 5.7$ Hz; -139.2 ppm, dd, ${}^{4}J_{\rm EH} = 5.7$, ${}^{3}J_{\rm EF} = 5.7$ Hz) as well as in the minor isomer (-136.7 ppm, d, ${}^{3}J_{F,F} = 5.7$ Hz; -137.9 ppm dd, ${}^{4}J_{F,H} = 5.7$, ${}^{3}J_{F,F} = 5.7$ Hz), due to the ${}^{4}J_{F,H}$ -coupling both fluorine atoms are obviously not bound to an aromatic ring, but taking a vinylic position (Fig. 1). Also the small vicinal



Fig. 1 Comparison of the chemical shifts and coupling constants of compounds 12, 13 and 14 with the "model compounds" 2b and 6b.

coupling constant ${}^{3}J_{\rm F,F}$ of 5.7 Hz, which in the case of the aromatic secondary product **14** is 21.0 Hz, rules out an aromatic D-ring for the primary products **12** and **13**. Additionally, the comparison with the chemical shifts of 19 F NMR-signals of 2,3-difluoro-*p*-benzoquinone (**2b**), $\delta = -144.6$, and 2,3-difluorohydroquinone (**6b**), $\delta = -160.3$, confirm these assignments (Fig. 1).

Finally, the identical coupling constants for isomers **12/13** (Fig. 1) strongly support the assumption of formation of

double bond isomers (also *cf.* **7/8**). For *endolexo*-isomers significantly different coupling constants are expected (*cf. endol exo*-**18**, *vide infra*).

Isolation of 14, but not of the sequential product of 13, is probably due to the purification method: compound 14 (or the corresponding tautomer) was probably not eluted by the eluents (pentane-diethyl ether mixtures) used. Very different solubility of similar double bond isomers was alrerady observed for 7 and 8.

As aromatisation of the D-ring was not observed for the Diels-Alder adducts of 1 with fluoro-*p*-benzoquinone (2a), despite migration of a double bond, this phenomenon can probably be accounted to the stronger influence of two fluorine substituents on the acidity of the tertiary protons.

Thus, also in the [4+2]-cycloaddition of 2,3-difluoro-*p*-benzoquinone (**2b**) with Dane's diene (**1**), the unfluorinated double bond reacted preferably.

Diels-Alder reaction with 2,6-difluoro-p-benzoquinone

Subsequently, the corresponding reaction of 2,6-difluoro-pbenzoquinone (2c) was envisaged in order to force one of the two monofluorinated double bonds of this dienophile into the desired cycloaddition. Initially, diene 1 was heated with an equimolar amount of 2,6-difluoro-p-benzoquinone (2c) in dry toluene at 110 °C (2 h). In the ¹⁹F NMR spectrum of the crude product mixture two main signals (-109.4 ppm, d, ${}^{3}J_{\rm FH}$ = 10.0 Hz and -134.4 ppm, d, ${}^{3}J_{F,H} = 7.6$ Hz) were observed in a 1:1 ratio, which represent two compounds and do not result from the primary adducts 15a or 15b (Scheme 6). The first signal is assigned to benzoquinone 17a (vide infra and Scheme 6). This assumption is further supported by comparison with the ¹⁹F NMR spectrum of the related chrysenedione 7a (-109.1 ppm d, ${}^{3}J_{F,H} = 11.2$ Hz) and the mass spectrum, which shows the expected molecular ion peak m/z =308 as the base peak. The formation of 17a can be rationalized by a tandem Diels-Alder reaction-HF-elimination, followed by an oxidative aromatisation (Scheme 6).

The dienophile 2,6-difluoro-*p*-benzoquinone (**2c**) might serve as an oxidant for this process. This is confirmed by the abovementioned second ¹⁹F NMR signal of the crude product mixture at $\delta = -134.4$ (in CDCl₃), which, taking recording of the spectra in different solvents into account, correlates well with the signal at $\delta = -133.1$ (in acetone-d₆) of 2,6-difluorohydroquinone (**6c**). On attempted chromatographic separation of the crude product mixture, some decomposition occurred and only product mixtures were obtained containing considerable amounts of **6c**.

In order to avoid the HF-elimination, which is favoured by the enolizable ketone functionality in **15a/b**, the abovementioned reaction was repeated under very mild conditions (rt, diethyl ether, 12.5 h). According to ¹⁹F NMR spectroscopy, the crude product isolated in quantitative yield contained 95%



3,4a-difluoro-8-methoxy-4a,4b,5,6,12,12a-hexahydrochrysene-1,4-dione (**15a/b**, Scheme 6); also the ¹H NMR spectrum indicated minor impurities only. The observed regioisomeric ratio *ortho* (**15a**) : *meta* (**15b**) was 93 : 7. The regioisomeric outcome of this reaction was assigned unambiguously *via* the coupling constants in the ¹H and ¹⁹F NMR spectra as shown exemplarily for **15a** (Fig. 2).



Fig. 2 Couplings from the ¹H- and ¹⁹F NMR spectra of compound **15a** as proof for the assigned regiochemistry.

The assignment of an *exo*-configuration for adduct **15a** is reasonable due to the ${}^{3}J_{\text{F-4a,H-4b}}$ -coupling of 19.1 Hz. For the *endo*-isomer a significantly smaller H,F-coupling constant should be found (*cf.* Fig. 3 and discussion for compounds *exo*-



Fig. 3 Assignment of the configuration of the diastereomeric 2,3,4a,12a-tetrafluoro-8-methoxy-4a,4b,5,6,12,12a-hexahydrochrysene-1,4-diones 18.

and *endo*-18). For the regioisomer 15b, the position of the fluorine substituents is easily confirmed by the fact that the fluorine atom in position 12a (Scheme 6) shows three ${}^{3}J_{\rm EH}$ -couplings consistent solely with this position.

İmmediately after attempted separation of the regioisomeric mixture **15a/b** by column chromatography, a regioisomeric mixture of **17a/b** (Scheme 6) started to precipitate (17%, **17a/ 17b** 86 : 14 (GC)), which astonishingly was almost insoluble in all common organic solvents. ¹⁹F NMR spectroscopic and mass spectrometric data of **17a** are consistent with those of the presumed naphthoquinone **17a**, which was observed in the above-mentioned reaction in toluene at 110 °C. Difluorochrysenediones **15a,b** could only be isolated again as partially decomposed material.

An analogous Diels–Alder reaction of Dane's diene (1) with 2,6-dimethyl-*p*-benzoquinone was reported earlier by Valenta and coworkers: for the thermal reaction in refluxing benzene they observed complete *ortho*-selectivity.^{46,47}

A tandem Diels–Alder reaction–elimination process with subsequent aromatisation was already observed by Carreño *et al.* for a similar system. On converting a sulfinyl-*p*-benzoquinone with Dane's diene (1), these authors found a tandem-Diels–Alder reaction–sulfoxide-elimination, followed by aromatisation on subjection of the crude product to column chromatography.^{44,45}

Diels-Alder reaction with tetrafluoro-p-benzoquinone

Due to the labile nature of the primary cycloadducts **15***a/b*, we next considered the thermal Diels–Alder reaction of tetrafluoro-*p*-benzoquinone (**2d**) with Dane's diene (**1**). The thermal reaction of **2d** with buta-1,3-diene,^{19,20} 1-acetoxybuta-1,3diene,²⁰ and cyclopentadiene^{20,21} has already been successfully investigated. Consequently, equimolar amounts of compounds **2d** and **1** were heated in toluene at 110 °C. Subsequent column chromatography afforded the diastereomeric tetrafluorochrysenediones *exolendo*-**18** (55%) in 89 : 11 ratio (Scheme 7). Furthermore, tetrafluorohydroquinone (**6d**) was isolated (33%).

Additionally, the reaction was conducted in a polar medium (diethyl ether–dichloromethane 4 : 7) at 75 °C in a sealed tube. The yield was slightly lower (49%) compared to the reaction in toluene and a nearly unchanged diastereomeric ratio of 86 : 14 (*exolendo*) was found for **18**. Furthermore, an attempt was made to perform the cycloadditon with 1.3 equivalents of boron trifluoride at -20 °C in analogy to a procedure⁴⁷ using 2,6-dimethyl-*p*-benzoquinone instead of **2d**. Unfortunately, only complete decomposition of diene **1** was observed.

The structure of *endo*-18 was additionally confirmed by two-dimensional NMR experiments (${}^{1}H$, ${}^{1}H$ - and ${}^{1}H$, ${}^{13}C$). The configuration of *exolendo*-18 was assigned *via* the vicinal coupling constant ${}^{3}J_{H-4b,F-4a}$, which should differ considerably for *exo*-18 and *endo*-18 due to the different dihedral angles.⁵¹ After optimisation of the two structures on AM1 level (closed shell), the dihedral angles depicted in Fig. 3 were calculated.

Due to the angles calculated and taking the Karplus equation⁵¹ into account, a small coupling constant ${}^{3}J_{H-4b,F-4a}$ (Fig. 3) for *endo*-18 and a significantly greater one in case of *exo*-18 can be expected. The ¹H NMR spectrum for *exo*-18 shows a coupling constant ${}^{3}J_{H-4b,F-4a}$ of 14.3 Hz, while for *endo*-18 no resolved ${}^{3}J_{H,F}$ -coupling could be found in the ¹⁹F NMR spectrum and therefore ${}^{3}J_{H+4b,F-4a}$ is obviously less than *ca.* 4 Hz. The ¹H NMR spectrum for *endo*-18 displays a multiplet for H-4b, from which no H,F-coupling could be extracted. As the



 ${}^{3}J_{\text{H,F}}$ -coupling is the only criterion so far to assign the configuration, we tried to obtain single crystals of **18** suitable for X-ray analysis, but so far only very fine needles have been grown. Interestingly, *exo*-**18** is stable under gas chromatographic conditions, while *endo*-**18** probably suffers a retro-Diels–Alder reaction as a signal is observed which shows a retention time very similar to that of Dane's diene (**1**).

According to AM-1 calculations, *exo-18* ($\Delta H_f = -211.5$ kcal mol⁻¹) is 2.1 kcal mol⁻¹ more stable than endo-18 ($\Delta H_{\rm f}$ = -209.4 kcal mol⁻¹). Thus, in the Diels-Alder reaction of tetrafluoro-p-benzoquinone (2d) with diene 1 at 75 and 110 °C, the thermodynamically more stable product has been formed preferentially. This means that the dienophiles 2c and 2d show a reverse diastereoselectivity compared to the unfluorinated p-benzoquinones^{26,43b,44-47} investigated to date and to fluoro-pbenzoquinone (2a) and 2,3-difluoro-p-benzoquinone (2b). All these dienophiles reacted in an endo-selective fashion as expected (vide supra and refs. 48,50). Exo-selectivity has already been reported for Diels-Alder reactions of other monofluorinated or cis-1,2-difluorinated vinylic compounds.^{5,7,10,11d,11e,13,18,52} Due to quantum chemical calculations done for related fluorinated dienophiles, kinetic effects of fluorine substituents should be responsible for the reverse diastereoselectivity rather than higher thermodynamic stability of the exo-products.5,6b

Compared to **15a/b**, the cycloadduct resulting from 2,6difluoro-*p*-benzoquinone (**2c**) and Dane's diene (**1**), it should be pointed out that HF-eliminination was successfully prevented for compounds **18a/b** under identical reaction conditions due to the lack of an enolizable ketone functionality.

Conclusion

We presented a general, concise and practical method for the synthesis of fluorinated *p*-benzoquinones. The differently fluorinated *p*-benzoquinones have been reacted with Dane's diene (1) in Diels-Alder reactions and the observed cycloadducts were characterised. An unfluorinated double bond in the benzoquinone leads, as deduced from literature precedents,26,43b,44-48,50 to selective formation of the endocycloadducts, which evolve from [4+2]addition of the unfluorinated double bond of the benzoquinone. Benzoquinones with fluorinated, less reactive double bonds, form the corresponding exo-adducts. The number of cycloadducts and their stability depends on the fluorine substitution pattern of the corresponding fluorinated benzoquinones. The primary Diels-Alder products, except 18, were observed to stabilise themselves tautomerisation, HF-elimination and/or oxidative via aromatisation.

Experimental

General

NMR spectra of solutions in CDCl₃ or acetone-d₆ were recorded at 300 or 400 MHz (¹H), at 75, 100, or 150 MHz (¹³C) and at 282 MHz (¹⁹F) and are reported in ppm downfield from TMS (¹H and ¹³C) or CFCl₃ (¹⁹F). The multiplicity of ¹³C NMR signals was determined by DEPT experiments. Coupling

constants J are given in Hz. Mass spectra were recorded by GC/MS coupling (EI, 70 eV) or by ESI-MS (Nanospray). Gas chromatographic analyses were performed using a column HP-5 (30 m, \emptyset 0.32 mm, film 0.25 µm, carrier gas N₂). Thinlayer chromatography was carried out on a coated plate 60 F₂₅₄. Column chromatography was carried out with silica gel 60 (0.063–0.2 mm). Elemental analyses: Microanalytical laboratory, Organic Chemistry Institute, University of Münster. All reactions involving air-sensitive agents were conducted under an argon atmosphere applying Schlenk-techniques. All reagents purchased from suppliers were used without further purification. Solvents for chromatography were distilled prior to use.

General procedure A: oxidation of phenols to the corresponding 1,4-hydroquinones (Elbs oxidation)^{38,39}

To the fluorophenol (100 mmol) dissolved in 6% aqueous NaOH (400 cm³) was added solid potassium persulfate (27.0 g, 100 mmol) with stirring, in several portions, over 10 min, resulting in a dark solution. This was stirred overnight at rt, then concentrated to ca. one third of its original volume under reduced pressure. The solution was cooled to 0 °C, neutralised with concentrated HCl and extracted once with diethyl ether (200 cm³). This organic phase was dried (MgSO₄) and concentrated under reduced pressure to reisolate unreacted substrate. The aqueous solution was acidified with concentrated HCl (100 cm³), refluxed for 1 h, then concentrated to ca. 50 cm³ under reduced pressure. Addition of acetone (200 cm³) precipitated the inorganic salts, which were removed by filtration. The filtrate was taken to dryness on the rotary evaporator and the dark residue, dissolved in acetone, was coated on silica gel (12 g). The dry material was subjected to column chromatography (pentane-diethyl ether 2 : 1 (6b, 6c) or cyclohexaneethyl acetate 3:1 (6a)).

General procedure B: oxidation of 1,4-hydroquinones to the corresponding *p*-benzoquinones with ceric ammonium nitrate (CAN oxidation)³⁹

The fluorohydroquinone (23.0 mmol) was added to a solution of ceric ammonium nitrate (26.6 g, 48.5 mmol) in water (150 cm³) and stirred for 1 h at rt. The reddish solution was extracted with diethyl ether (3×100 cm³) and the combined organic phases dried (MgSO₄). The filtrate was passed through a silica gel column (2×9 cm) and eluted (diethyl ether). After concentration of the obtained filtrate on the rotary evaporator, the corresponding benzoquinone was furnished as brightyellow to bright-orange crystals which were stored protected from light.

6-Methoxy-1,2,3,4-tetrahydro-1-vinyl-1-naphthol (4) and 3,4dihydro-6-methoxy-1-vinylnaphthalene (Dane's diene, 1)

6-Methoxy-1,2,3,4-tetrahydro-1-vinyl-1-naphthol (4) was prepared according to the literature method.²⁵ In our hands, the Grignard reaction of vinyl magnesium bromide (97 cm³ of a 1 M solution in THF) with 6-methoxy- α -tetralone (9.0 g, 51.1 mmol) in dry THF (60 cm³) yielded a mixture (13.66 g, 99.8%) of the expected allylic alcohol (4) and Dane's diene (1) (ratios of 4 and 1 varying from 4 : 1 to 1 : 2 (¹H NMR)). This mixture, which decomposes with attempted column chromatography on silica gel or distillation,²⁶⁻²⁸ was used as is for the subsequent cycloadditions. Spectroscopic data of 1 and 4 agree with published ones.²⁵

o-Fluorohydroquinone (6a)

Following the general procedure A, *o*-fluorophenol (**5a**) (10.08 g, 90.0 mmol) was reacted. Compound **5a** (2.30 g, 23%) was reisolated and *o*-fluorohydroquinone (**6a**) was obtained as beige crystals (5.40 g, 47%, 94% purity (GC)). Recrystallisation from chloroform yielded analytically pure **6a** (2.54 g, 27%); mp 121–122 °C (lit.,³⁹ 122–123 °C); ¹H NMR (acetone-d₆) δ 6.50 (ddd, ⁵*J*_{H,F} 1.4, ⁴*J*_{H,H} 2.9, ³*J*_{H,H} 8.7, 1 H, 5-H), 6.59 (dd, ⁴*J*_{H,H} 2.9, ³*J*_{H,F} 12.4, 1 H, 3-H), 6.81 (dd, ⁴*J*_{H,F} 9.9, ³*J*_{H,H} 8.7, 1 H, 6-H), 7.78 (s, 1 H, OH), 7.99 (s, 1 H, OH); ¹³C NMR (acetone-d₆) δ 103.9 (dd, ²*J*_{C,F} 20.3, C-3), 111.2 (dd, ⁴*J*_{C,F} 3.8, C-5), 118.4 (dd, ³*J*_{C,F} 3.8, C-6), 137.9 (d, ²*J*_{C,F} 12.7, C-1), 151.0 (d, ²*J*_{C,F} 8.9, C-4), 151.9 (d, ¹*J*_{C,F} 239.1, C-2); ¹⁹F NMR (acetone-d₆) δ –135.6 (pseudo t, ⁴*J*_{E,H} 9.9, ³*J*_{E,H} 12.4 Hz); *m*/*z* [as bis(TMS-ether)] 272 (100%, M⁺), 257 (37, M⁺ – CH₃), 242 (75, 257 – CH₃), 213 (14), 199 (2, M⁺ – TMS), 197 (3), 185 (3), 183 (2, 199 – O), 165 (7, 183 – F + H), 137 (9), 77 (13), 73 (61, TMS⁺), 45 (9). ¹H and ¹⁹F NMR data agree with published data.³⁹

2,3-Difluorohydroquinone (6b)

Following the general procedure A, 2,3-difluorophenol (**5b**) (2.061 g, 15.8 mmol) was reacted. Phenol **5b** (0.814 g, 41%) was reisolated and 2,3-difluorohydroquinone (**6b**) (0.843 g, 37%) was obtained as colourless crystals (Found: C, 49.38; H, 2.80%. C₆H₄F₂O₂ (146.1) requires C, 49.33; H, 2.76%); mp 124–126 °C (pentane–diethyl ether); ¹H NMR (acetone-d₆) δ 6.56–6.63 (m, 2 H, 5-H, 6-H), 8.19 (br s, 2 H, OH); ¹³C NMR (acetone-d₆) δ 111.9 (d, 2 C, C-5, C-6), 139.1 (pseudo t, ²J_{C,F} = ³J_{C,F} 5.1, 2 C, C-1, C-4), 141.6 (dd, ²J_{C,F} 12.7, ¹J_{C,F} 242.9, 2 C, C-2, C-3); ¹⁹F NMR (acetone-d₆) δ –160.3 (s); *m*/*z* 146 (100%, M⁺), 126 (5, M⁺ - F - H), 117 (3, M⁺ - COH), 98 (26, 117 - F), 70 (24), 69 (8), 62 (3, C₂F₂⁺), 53 (3), 39 (6, C₃H₃⁺]. Found (HRMS): M⁺, 146.0209. C₆H₄F₂O₂ (146.1) requires 146.0179.

2,6-Difluorohydroquinone (6c)

Following the general procedure A, 2,6-difluorophenol (**5c**) (4.00 g, 30.75 mmol) was reacted. Phenol **5c** (1.78 g, 45%) was reisolated and 2,6-difluorohydroquinone (**6c**) (1.16 g, 26%) was obtained as colourless crystals (Found: C, 49.32; H, 2.78%. $C_6H_4F_2O_2$ (146.1) requires C, 49.33; H, 2.76%); mp 151–152 °C (dichloromethane) (lit.,⁴⁰ 150.5–152 °C); ¹H NMR (acetone-d₆) δ 6.41–6.53 (m, 2 H, 5-H, 6-H), 8.02 (s, 1 H, OH), 8.41 (s, 1 H, OH); ¹³C NMR (acetone-d₆) δ 99.6 (dd, ² $J_{C,F}$ 25.4, 2 C, C-3, C-5), 126.9 (t, ² $J_{C,F}$ 16.5, 1 C, C-1), 150.3 (t, ³ $J_{C,F}$ 12.7, 1 C, C-4), 153.3 (dd, ³ $J_{C,F}$ 7.6, ¹ $J_{C,F}$ 240.3, 2 C, C-2, C-6); ¹⁹F NMR (acetone-d₆) δ –133.1 (d, ³ $J_{H,F}$ 7.6); *m*/*z* 146 (100%, M⁺), 126 (1, M⁺ - F - H), 125 (4), 117 (5, M⁺ - COH), 98 (25, 117 - F), 73 (10), 70 (33), 69 (8), 63 (3, C_2F_2H ⁺), 53 (6), 39 (9, C_3H_3⁺].¹H NMR data can be found in ref. 40 which agree with those obtained in this study.

2-Fluoro-p-benzoquinone (2a)

Following the general procedure B, 2-fluorohydroquinone (**6a**) (2.50 g, 19.5 mmol) was reacted and 2-fluoro-*p*-benzoquinone (**2a**) (2.32 g, 94%) was obtained; mp 77–78 °C (diethyl ether) (lit.,³⁹ 78–79 °C); ¹H NMR (acetone-d₆) δ 6.58 (dd, ³J_{H,F} 10.7, ⁴J_{H,H} 2.2, 1 H, 3-H), 6.83–6.96 (m, 2 H, 5-H, 6-H); ¹³C NMR (acetone-d₆) δ 115.4 (dd, ²J_{C,F} 7.6, C-3), 135.1 (dd, ³J_{C,F} 3.8, C-6), 137.2 (d, C-5), 159.7 (d, ¹J_{C,F} 293.6, C-2), 179.8 (d, ²J_{C,F} 24.2, C-1), 187.8 (d, ³J_{C,F} 15.3, C-4); ¹⁹F NMR (acetone-d₆) δ –114.4 (m); *m*/*z* 128 (18%, M⁺ + 2 H), 126 (100, M⁺), 108 (3, M⁺ - F + H), 100 (7, M⁺ - C₂H₂), 98 (40, M⁺ - CO), 82

(7), 80 (7, 100 – HF), 72 (99, 98 – C_2H_4), 70 (39), 54 (30), 53 (25, 72 – F), 44 (44, 72 – CO). ¹H and ¹⁹F NMR data can be found in ref. 39 which agree with those obtained in this study.

2,3-Difluoro-p-benzoquinone (2b)

Following the general procedure B, hydroquinone **6b** (613 mg, 4.20 mmol) was reacted and 2,3-difluoro-*p*-benzoquinone **2b** (560 mg, 93%) was obtained (Found: C, 49.70; H, 1.43%. $C_6H_2F_2O_2$ (144.1) requires C, 50.02; H, 1.40%); mp 79–81 °C (diethyl ether); ¹H NMR (acetone-d₆) δ 6.95 (ddd, ⁵*J*_{H,F} 2.2, ⁴*J*_{H,F} 6.4, ³*J*_{H,H} 4.8, 2 H, 5-H, 6-H); ¹³C NMR (acetone-d₆) δ 134.7 (d, 2 C, C-5, C-6), 145.2 (dd, ²*J*_{C,F} 6.4, ¹*J*_{C,F} 284.8, 2 C, C-2, C-3), 180.2 (dd, ²*J*_{C,F} 15.3, ³*J*_{C,F} 10.2, 2 C, C-1, C-4); ¹⁹F NMR (acetone-d₆) δ –144.6 (d, ⁴*J*_{F,H} 6.4); *m*/*z* 146 (15%, M⁺ + 2 H), 144 (100, M⁺), 118 (3, M⁺ – C₂H₂), 116 (20, M⁺ – CO), 98 (5), 97 (3, 116 – F), 90 (45), 88 (47), 71 (8, C₃FO⁺), 62 (26, C₂F₂⁻), 53 (11). Found (HRMS): M⁺, 144.0039. C₆H₂F₂O₂ (144.1) requires 144.0023.

2,6-Difluoro-p-benzoquinone (2c)

Following the general procedure B, 2,6-difluorohydroquinone (6c) (429 mg, 2.94 mmol) was reacted and the 2,6-difluoro-*p*benzoquinone 2c (416 mg, 98%) was obtained (Found: C, 49.66; H, 1.42%. C₆H₂F₂O₂ (144.1) requires C, 50.02; H, 1.40%); mp 81–82 °C (diethyl ether) (lit.,³⁰ 83–85 °C); ¹H NMR (acetone-d₆) δ 6.64 (dm, ³J_{H,F} 9.3, 2 H, 3-H, 5-H); ¹³C NMR (acetone-d₆) δ 115.5 (dd, ²J_{C,F} 10.2, 2 C, C-3, C-5), 159.8 (dd, ³J_{C,F} 10.2, ¹J_{C,F} 284.8, 2 C, C-2, C-6), 172.5 (t, ²J_{C,F} 28.0, C-1), 185.8 (t, ³J_{C,F} 15.3, C-4); ¹⁹F NMR (acetone-d₆) δ –118.7 (d, ³J_{F,H} 9.3); *m*/*z* 146 (9%, M⁺ + 2 H), 144 (100, M⁺), 126 (2, M⁺ - F + H), 116 (9, M⁺ - CO), 100 (2, M⁺ - C₂HF), 98 (5), 97 (3, 116 - F), 88 (23), 72 (51, C₃HFO⁺), 62 (1, C₂F²), 53 (11), 44 (34); ¹H and ¹⁹F NMR data can be found in ref. 30 which agree with those obtained in this study.

2,3,5,6-Tetrafluoro-p-benzoquinone (2d, fluoranil)

Following the general procedure B, 2,3,5,6-tetrafluorohydroquinone (6d) (3.38 g, 18.57 mmol) was reacted and 2,3,5,6tetrafluoro-*p*-benzoquinone 2d (3.33 g, 99%) was obtained as bright-yellow leaves; mp 172–174 °C (subl., lit.,⁵³ 173 °C); ¹³C NMR (acetone-d₆) δ 144.6 (dd, ²J_{C,F} 7.6, ¹J_{C,F} 284.8, 4 C, C-2, C-3, C-5, C-6), 188.9 (m, 2 C, C-1, C-4); ¹⁹F NMR (acetone-d₆) δ – 146.6 (s). ¹⁹F NMR data can be found in ref. 30 which agree with those obtained in this study.

Diels-Alder reaction of fluoro-*p*-benzoquinone (2a) with Dane's diene (1)

Dane's diene (1, mixture with 4)⁴¹ (481 mg, 2.58 mmol) in diethyl ether (17 cm³), fluoro-p-benzoquinone (2a) (264 mg, 2.10 mmol) and a trace of hydroquinone in a glass tube with a Young's tap were heated at 50 °C for 1 hour. During the reaction a bright-yellow precipitate was formed and the supernatant solution darkened. After cooling down to room temparature, the reaction mixture was left in the refrigerator for crystallisation overnight. After filtration, the residue (45% crude product yield) was washed with diethyl ether. Gas chromatographic analysis of the filtrate showed 2a (32%) and fluorohydroquinone (6a) (11%) to be present. The residue was extracted with acetone and the filtrate thus obtained concentrated under reduced pressure, furnishing a regioisomeric mixture of 7a,b as a bright-yellow solid, which crystallised as fine needles on slow evaporation of the solvent. The residue of the last filtration contained a regioisomeric mixture of 8a,b as a bright-yellow solid, which was also crystallised as fine needles. Spectroscopic data were obtained from the spectra of the two regioisomeric mixtures.

3- and 2-Fluoro-8-methoxy-4a,4b,5,6,12,12a-hexahydrochrysene-1,4-dione (7a and 7b). 82 mg (13%) of 17a and 17b (91 : 9, ¹H NMR) (Found: C, 72.43%; H, 5.11%. C₁₉H₁₇FO₃ (312.3) requires C, 73.06; H, 5.49%); Found (HRMS): M + Na⁺, 335.1098. C₁₉H₁₇FO₃ + Na⁺ requires 335.1060.

Compound 7a. ¹H NMR (acetone-d₆) δ 1.78–1.88 (m, 1 H, 5-H), 2.27 (ddt, ³ or ²J_{H,H} 12.9, ³ or ²J_{H,H} 12.2, ³J_{H,H} 5.2, 1 H, 5-H), 2.40–2.60 (m, 2 H, 12-H), 2.62–2.90 (m, 3 H, 6-H, H-4b), 3.29–3.41 (m, 1 H, 12a-H), 3.71–3.77 (m, 1 H, 4a-H), 3.76 (s, 3 H, OCH₃), 6.09–6.11 (m, 11-H), 6.44 (dd, ⁴J_{H,H} 1.1, ³J_{H,F} 12.2, 1 H, 2-H), 6.64 (d, ⁴J_{H,H} 2.6, 1 H, 7-H), 6.71 (dd, ⁴J_{H,H} 2.6, ³J_{H,H} 8.8, 1 H, 9-H), 7.51 (d, ⁴J_{H,H} 8.8, 1 H, 10-H); ¹³C NMR (acetone-d₆) δ 26.5 (t, C-5 or C-6), 27.2 (t, C-5 or C-6), 31.2 (t, C-12), 38.1 (dd, ⁴J_{C,F} 2.6, C-4b), 48.6 (d, C-12a), 50.0 (dd, ³J_{C,F} 3.8, C-4a), 54.9 (q, OCH₃), 113.1 (d, C-7 or C-9), 113.4 (d, C-7 or C-9), 114.6 (d, C-11), 117.2 (dd, ³J_{C,F} 8.9, C-2), 124.9 (d, C-10), 127.2 (s, C-10a), 129.4 (s, C-10b), 138.5 (s, C-6a), 159.2 (s, C-8), 191.9 (d, ³J_{C,F} 14.5, C-1), 198.8 (d, ²J_{C,F} 21.1, C-4);⁵⁴ ¹⁹F NMR (acetone-d₆) δ −111.7 (d, ³J_{E,H} 12.2); *m*/*z* 312 (100%, M⁺), 297 (12, M⁺ - CH₃), 295 (14), 291 (12), 290 (13), 284 (36, 312 - CO), 281 (9, M⁺ - OCH₃), 249 (14), 207 (14), 191 (24), 167 (24), 147 (32), 115 (13).⁵⁵

Compound 7b. ¹H NMR (acetone-d₆) δ 1.78–1.88 (m, 1 H, 5-H), 2.27 (ddt, ³ or ²J_{H,H} 12.9, ³ or ²J_{H,H} 12.2, ³J_{H,H} 5.2, 1 H, 5-H), 2.40–2.60 (m, 2 H, 12-H), 2.62–2.90 (m, 3 H, 6-H, H-4b), 3.29–3.41 (m, 1 H, 12a-H), 3.71–3.77 (m, 1 H, 4a-H), 3.76 (s, 3 H, OCH₃), 6.09–6.11 (m, 11-H), 6.50 (d, ³J_{H,F} 12.2, 1 H, 3-H), 6.64 (d, ⁴J_{H,H} 2.6, 1 H, 7-H), 6.71 (dd, ⁴J_{H,H} 2.6, ³J_{H,H} 8.8, 1 H, 9-H), 7.53 (d, ⁴J_{H,H} 9.1, 1 H, 10-H); ¹⁹F NMR (acetone-d₆) δ –115.6 (dd, ⁴J_{E,H} 5.7, ³J_{E,H} 12.2); *m*/*z* 312 (100%, M⁺), 297 (26, M⁺ – CH₃), 295 (23), 291 (13), 284 (4, 312 – CO), 263 (36), 249 (23), 220 (24), 207 (23), 167 (28), 109 (22), 88 (27).⁵⁵

3- and **2-Fluoro-8-methoxy-4a,5,6,11,12,12a-hexahydrochry-sene-1,4-dione (8a and 8b).** 72 mg (0.23 mmol, 11%) ⁵⁶ of **8a** and **8b** (92 : 8, ¹H NMR) (Found: C, 72.54%; H, 5.22%. $C_{19}H_{17}FO_3$ (312.3) requires C, 73.06; H, 5.49%); *m/z* (ESI) 313 (100%, M + H⁺), 285 (8, 313 - CO), 186 (92, $C_{13}H_{14}O^+$; retro-Diels–Alder after tautomerisation), 161 (28), 155 (27), 121 (13). Found (HRMS): M + Na⁺, 335.1084. $C_{19}H_{17}FO_3$ + Na⁺ requires 335.1060.

Compound 8a. ¹H NMR (CDCl₃) δ 1.95–2.14 (m, 2 H, 11-H), 2.15–2.38 (m, 2 H, 5-H), 2.40–2.65 (m, 2 H, 12-H), 2.66–2.94 (m, 2 H, 6-H), 3.08–3.17 (m, 12a-H), 3.64–3.70 (m, 4a-H), 3.76 (s, 3 H, OMe), 6.37 (dd, ⁴J_{H,H} 0.7, ³J_{H,F} 11.2, 1 H, 2-H), 6.68–6.74 (m, 2 H, 7-H, 9-H), 7.09–7.14 (m, 1 H, 10-H); ¹³C NMR (CDCl₃) δ 24.2 (t, C-12), 25.2 (t, C-11), 27.7 (t, C-5), 28.3 (t, C-6), 48.4 (d, C-12a), 52.4 (dd, ³J_{C,F} 3.9, C-4a), 55.3 (q, OCH₃), 111.1 (d, C-9), 113.5 (d, C-7), 118.7 (dd, ²J_{C,F} 7.7, C-2), 123.5 (d, C-10), 125.0 (d, ⁴J_{C,F} 1.8, C-4b), 127.9 (s, C-10a), 129.4 (s, C-10b), 137.6 (s, C-6a), 158.9 (s, C-8), 162.8 (d, ¹J_{C,F} 297.7, C-3), 191.1 (d, ²J_{C,F} 19.2, C-4), 198.9 (d, ³J_{C,F} 14.4, C-1); ¹⁹F NMR (CDCl₃) δ –109.1 (d, ³J_{F,H} 11.2).⁵⁵

Compound 8b. ¹H NMR (CDCl₃) δ 1.95–2.14 (m, 2 H, 11-H), 2.15–2.38 (m, 2 H, 5-H), 2.40–2.65 (m, 2 H, 12-H), 2.66–2.94 (m, 2 H, 6-H), 3.08–3.17 (m, 12a-H), 3.64–3.70 (m, 4a-H), 3.76 (s, 3 H, OMe), 6.41 (d, ${}^{3}J_{\rm H,F}$ 11.0, 1 H, 3-H), 6.68–6.74 (m, 2 H, 7-H, 9-H), 7.09–7.14 (m, 1 H, 10-H); 13 C NMR (CDCl₃) δ 24.0 (t, C-12), 24.8 (t, C-11), 27.7 (t, C-5), 28.3 (t, C-6), 46.5 (dd, ${}^{3}J_{\rm C,F}$ 3.3, C-12a), 54.0 (d, C-4a), 55.3 (q, OCH₃), 111.1 (d, C-9), 113.1 (d, C-7), 119.2 (dd, ${}^{2}J_{\rm C,F}$ 7.9, C-3), 123.4 (d, C-10), 128.0 (s, C-10a), 130.0 (s, C-10b), 137.6 (s, C-6a), 158.8 (s, C-8), 162.0 (d, ${}^{1}J_{\rm C,F}$ 296.4, C-2), 192.5 (d, ${}^{2}J_{\rm C,F}$ 18.3, C-1), 197.2 (d, ${}^{3}J_{\rm C,F}$ = 12.4, C-4);⁵⁷ ¹⁹F NMR (CDCl₃) δ –110.6 (dd, ${}^{4}J_{\rm FH}$ 3.8, ${}^{3}J_{\rm FH}$ 11.0).⁵⁵

2726 J. Chem. Soc., Perkin Trans. 1, 2002, 2719–2728

Diels–Alder reaction of 2,3-difluoro-*p*-benzoquinone (2b) with Dane's diene (1)

To Dane's diene (1) (215 mg, 1.16 mmol) in diethyl ether (8 cm³) was added 2,3-difluoro-*p*-benzoquinone (2b) (68 mg, 0.47 mmol). The solution turned red immediately and was stirred at 50 °C for 45 min in a glass tube with a Young's tap. The reaction was accompanied by precipitation of a yellow solid, which was filtered after cooling down to room temperature. The residue (118 mg) contained a share of 90% (¹⁹F NMR) of two products (73 : 27),⁵⁸ each of which contained two fluorine atoms per molecule.

main product. ¹⁹F NMR (CDCl₃) δ –136.4 (d, ³J_{EF} 5.7, 1 F), –139.2 (dd, ⁴J_{EH} 5.7, ³J_{EF} 5.7, 1 F).

minor product. ¹⁹F NMR (CDCl₃) δ –136.7 (d, ³*J*_{F,F} 5.7, 1 F), –137.9 (dd, ⁴*J*_{E,F} 5.7, ³*J*_{E,F} 5.7, 1 F).

2,3-Difluoro-8-methoxy-4b,5,6,12-tetrahydrochrysene-1,4-diol (14). was obtained as a red solid (93 mg, 60%) on attempted column-chromatographic separation (after coating crude product on silica gel; pentane-diethyl ether 10:1, 6:1) of the residue. (Found: C, 68.62; H, 4.59. C₁₉H₁₆F₂O₃ (330.3) requires C, 69.08; H, 4.88%); mp 151–152 °C (diethyl ether). ¹H NMR C, 09:06, 11, 4:06 / 0, 111 p 17-152 C (dictip) chief). If Territ (acetone-d₆) δ 1.55 (ddt, ${}^{3}J_{\text{Hax,Heq}}$ 5.5, ${}^{3}J_{\text{Hax,Hax}}$ 12.6, ${}^{3}J_{\text{Hax,Hax}} = {}^{2}J_{\text{H,H}}$ 12.2, 1 H, 5-H_{ax}), 2.80 (ddt, ${}^{3}J_{\text{Heq,Hax}}$ 6.2, ${}^{3}J_{\text{Heq,Hax}} = {}^{3}J_{\text{Heq,Heq}}$ 1.9, ${}^{2}J_{\text{H,H}}$ 12.2, 1 H, 5-H_{eq}), 2.88 (dd, ${}^{3}J_{\text{Heq,Hax}}$ 6.0, ${}^{2}J_{\text{H,H}}$ 17.3, 1 H, 6-H_{eq}), 3.14 (ddd, ${}^{3}J_{\text{Hax,Hax}}$ 12.6, ${}^{3}J_{\text{Hax,Heq}}$ 6.0, ${}^{2}J_{\text{H,H}}$ 17.3, 1 H, 6-H_{eq}), 3.43 (dm, ${}^{3}J_{\text{Hax,Hax}}$ 12.6, ${}^{3}J_{\text{Hax,Heq}}$ 6.0, ${}^{2}J_{\text{H,H}}$ 17.3, 1 H, 6-H_{ax}), 3.43 (dm, ${}^{3}J_{\text{Hax,Hax}}$ 3.7, 1 H, 12-H), 3.52 (2.6) (m + 1.1 H) (4.1 3.62 (m, 1 H, 4b-H), 3.77 (s, 3 H, 13-H), 6.01 (t, ${}^{3}J_{H,H}$ 3.7, 1 H, 11-H), 6.67 (d, ${}^{4}J_{H,H}$ 2.6, 1 H, 7-H), 6.73 (dd, ${}^{4}J_{H,H}$ 2.6, ${}^{3}J_{H,H}$ 8.6, 1 H, 7-H), 7.38 (d, ${}^{3}J_{H,H}$ 8.6, 10-H), 8.09 (s, 1 H, OH), 8.19 (s, 1 H, OH); ¹³C NMR (acetone-d₆) δ 25.3 (dt, ⁴J_{C,F} 2.5, C-12), 30.5 (t, C-5 or C-6), 32.2 (t, C-5 or C-6), 35.7 (dd, ${}^{4}J_{CF}$ 2.5, C-4b), 54.9 (q, C-13), 112.6, 113.5, 114.7 (each d, C-7, C-9, C-11), 118.2 (d, ³J_{CF} 2.5, C-4a or C-12a), 122.3 (d, ³J_{CF} 2.5, C-4a or C12a), 125.7 (d, C-10), 130.3 (s, C-10a), 135.3 (d, ${}^{2}J_{C,F}$ 11.4, C-1 or C-4), 135.8 (s, C-10b), 136.2 (d, ${}^{2}J_{C,F}$ 11.4, C-1 or C-4), 137.6 (s, C-6a), 139.6 (dd, ${}^{2}J_{C,F}$ 15.3, ${}^{1}J_{C,F}$ 239.1, C-2 or C-3), 140.1 (dd, ${}^{2}J_{C,F}$ 15.3, ${}^{1}J_{C,F}$ 239.1, C-2 or C-3), 159.4 (s, C-8); ${}^{19}F$ NMR (acetone-d₆) δ –163.9 (d, ${}^{3}J_{F,F}$ 21.0), –164.2 (d, ${}^{3}J_{EF}$ 21.0); m/z 330 (100%, M⁺), 326 (25), 315 (19, M⁺-CH₃), $302 (32, M^+-CO after tautomerisation), 299 (10, M^+ - OCH_3),$ 279 (15), 265 (15), 253 (22), 209 (18, M⁺ – COHC₂F₂COH – H), 207 (21), 185 (22, $C_{13}H_{14}O^+$ – H; retro Diels–Alder after tautomerisation), 158 (18, 185 – C_2H_3), 147 (22), 145 (23, $C_6H_2F_2O_2^+$ + H; retro Diels-Alder after tautomerisation), 121 (23), 102 (20), 66 (21), 40 (92). Found (HRMS): M⁺, 331.1149. $C_{19}H_{16}F_2O_3 + H^+$ (331.3) requires 331.1146.55

Diels–Alder reaction of 2,6-difluoro-*p*-benzoquinone (2c) with Dane's diene (1)

3,4a- and 2,12a-Difluoro-8-methoxy-4a,4b,5,6,12,12a-hexahydrochrysene-1,4-dione (15a and 15b). Dane's diene (1) (173 mg, 0.93 mmol) and 2,6-difluoro-*p*-benzoquinone (2c) (146 mg, 1.01 mmol) were dissolved in diethyl ether (6 cm³) and stirred for 12.5 h at rt. The solution turned bright-red immediately and the formation of a yellow precipitate was observed. The product mixture was concentrated under reduced pressure (water bath of rotary evaporator not exceeding 40 °C) and the regioisomeric mixture of cycloadducts (315 mg, quantitative) 15a and 15b (93 : 7, ¹⁹F NMR) was furnished as a green foam, showing a purity of 95% (¹⁹F NMR; also ¹H NMR just indicated minor impurities). 15a,b. *m*/*z* (ESI) 353 (28%, M + Na⁺), 331 (13, M + H⁺).

Compound 15a. ¹H NMR (CDCl₃) δ 1.86–1.96 (m, 2 H, 5-H), 2.55–2.93 (m, 5 H, 4b-H, 6-H, 12-H), 3.39 (dt, ³J_{H,F} 10.7, ³J_{H,H} 6.4, 1 H, 12a-H), 3.76 (s, 3 H, OMe), 6.02–6.07 (m, 1 H, 11-H), 6.47 (d, ³J_{H,F} 10.7, 1 H, 2-H), 6.57 (d, ⁴J_{H,H} 2.6, 1 H, 7-H), 6.71

Downloaded by Queens University - Kingston on 12/05/2013 09:06:02. Published on 24 October 2002 on http://pubs.rsc.org | doi:10.1039/B208001J (dd, ${}^{4}J_{H,H} 2.6$, ${}^{3}J_{H,H} 8.8$, 1 H, 9-H), 7.40 (d, ${}^{3}J_{H,H} 8.8$, 1 H, 10-H); ${}^{19}F$ NMR (CDCl₃) δ -111.2 (dd, ${}^{4}J_{F,F} 3.8$, ${}^{3}J_{F,H} 10.7$, 1 F, 3-F), -147.2 (dd, ${}^{4}J_{F,F} 3.8$, ${}^{3}J_{F,H} 19.1$, ${}^{3}J_{F,H} 10.7$, 1 F, 4a-F).

Compound 15b. ¹⁹F NMR (CDCl₃) δ –113.1 (dd, ⁴ $J_{\rm FF}$ 6.7, ³ $J_{\rm FH}$ 10.5, 1 F, 2-F), –152.9 (dddd, ⁴ $J_{\rm FF}$ 6.7, ³ $J_{\rm FH}$ 28.6, ³ $J_{\rm FH}$ 21.0, ³ $J_{\rm EH}$ 7.6, 1 F, 12a–F).

3- and 2-Fluoro-8-methoxy-5,6-dihydrochrysene-1,4-dione (17a and 17b). On attempted chromatographic separation (after coating the product mixture 15a,b on silica gel; cyclohexaneethyl acetate 4 : 1) of the crude product mixture 15a,b, these cycloadducts suffered from HF-elimination and oxidative aromatisation of the C-ring. Immediately after column chromatography, a regioisomeric mixture of 17a,b started to precipitate in the collected fractions as fine, dark-red leaves which were isolated by filtration (49 mg, 17%, 17a/17b 86 : 14, GC) and were virtually insoluble in all common organic solvents: only in dichloromethane and toluene were 17a,17b sufficiently soluble for spectrometric and spectroscopic characterisation. Compounds 15a,b could only be isolated as partially decomposed material.

Compounds 17a and 17b. (Found: C, 72.55; H, 4.44. $C_{19}H_{13}$ -FO₃· $\frac{1}{3}H_2O$ requires C, 72.61; H, 4.38%); ν_{max} /cm⁻¹ (KBr): 3450 (br s, crystal water), 3078 (w, v–C=C–H_{aromat}), 2933 (w, v–CH₂), 2837 (w, v–OCH₃), 1673 (m) or 1653 (s) (v–C=O), 1640/1625 (m, v–C=C and δ –OH_{crystal water}), 1563 (m), 1502 (m, ring vibration-aromat</sub>), 1460 (w, δ –CH₂/CH₃), 1336 (w), 1309 (w), 1281/1254 (m, v–C–O–Ph and v–C–F), 1171 (w), 1150 (w), 1040 (w), 978 (w), 820 (w), 620 (w).

Compound 17a. ¹H NMR (toluene-d₈) δ 2.41 (t, ³*J*_{H,H} 7.1, 2 H, 5-H or 6-H), 3.32 (t, ³*J*_{H,H} 7.1, 2 H, 5-H or 6-H), 3.32 (s, 3 H, 13-H), 5.88 (d, ³*J*_{H,F} 10.0, 1 H, 2-H), 6.52 (d, ⁴*J*_{H,H} 2.6, 1 H, 7-H), 6.64 (d, ⁴*J*_{H,H} 2.6, ³*J*_{H,H} 8.6, 1 H, 9-H), 7.21 (d, ³*J*_{H,H} 8.6, 1 H, 10-H), 7.43 (d, ³*J*_{H,H} 8.1, 1 H, 11-H or 12-H), 7.89 (d, ³*J*_{H,H} 8.1, 1 H, 11-H or 12-H), 7.89 (d, ³*J*_{H,H} 8.1, 1 H, 11-H or 12-H), 7.89 (d, ³*J*_{H,H} 8.1, 1 H, 11-H or 12-H); ¹³C NMR (toluene-d₈) δ 25.6 (t, C-5), 28.4 (t, C-6), 52.7 (q, C-13), 113.1 (d, C-7 or C-9), 113.3 (d, C-7 or C-9), 115.1 (dd, ²*J*_{C,F} 10.2, C-2), 126.4 (d, C-10 or C-12), 128.1 (d, C-10 or C-12), 161.0 (s, C-8), 161.3 (d, ¹*J*_{C,F} 287.4, C-3), 179.4 (d, ²*J*_{C,F} 22.9, C-4), 183.6 (d, ³*J*_{C,F} 18.1, C-1);^{59 19}F NMR (toluene-d₈) δ -109.4 (d, ³*J*_{F,H} 10.0); *m/z* 307 (100%, M⁺ - H), 292 (7, 307 - CH₃), 279 (9, 307 - CO), 264 (43, M⁺ - C₂HF), 249 (12, 264 - CH₃), 237 (13), 218 (15), 207 (27), 201 (10, M⁺ - CH₃OC₆H₃ - H), 189 (33), 187 (10, 201 - CH₂), 174 (5, M⁺ - CH₃OC₆H₃C₂H₄), 165 (28), 130 (7), 110 (7), 93 (13), 81 (5).⁶⁰

Compound 17b. Due to the very low solubility of **17a/b**, from the minor compound **17b** only a mass spectrum could be obtained, but owing to the almost identical fragmentation pattern compared to that of **17a**, the very similar retention time in GC, the elemental analysis of the product mixture **17a,b** and the presence of **15b** in the crude product, the structure of **17b** could be assigned. m/z 307 (100%, M⁺ – H), 292 (7, 307 – CH₃), 279 (4, 307 – CO), 278 (14), 265 (35, M⁺ – C₂HF + H), 260 (11), 248 (9), 237 (13), 217 (17), 207 (25), 201 (4, M⁺ – CH₃OC₆H₃ – H), 189 (31), 187 (11, 201 – CH₂), 174 (4, M⁺ – CH₃OC₆H₃C₂H₄), 165 (33), 130 (7), 118 (11), 110 (7), 94 (9), 81 (6).⁶⁰

2,3,4a,12a-Tetrafluoro-8-methoxy-4a,4b,5,6,12,12a-hexahydrochrysene-1,4-dione (18)

Dane's diene (1) (380 mg, 2.04 mmol) and a trace of hydroquinone in dry toluene (5 cm³) were added dropwise to a solution of tetrafluoro-*p*-benzoquinone (2d) (360 mg, 2.00 mmol) in toluene (2 cm³). Directly after addition the solution turned dark. The reaction mixture was heated at 110 °C for 2 h in a glass tube with a Young's tap. After removal of the solvent under reduced pressure, the black crude product was coated on 2.5 g of silica gel and subjected to column chromatography (cyclohexane–ethyl acetate 15 : 1, 8 : 1). A bright red solid (401 mg, 55%) of *exo-*18 and *endo-*18 (89 : 11, ¹⁹F NMR) was isolated (Found: C, 62.47; H, 4.29. $C_{19}H_{14}F_4O_3$ (366.3) requires C, 62.30; H, 3.85%); mp 161–163 °C (for a 87 : 13 mixture of *exo-*18 and *endo-*18).

Compound exo-18. ¹H NMR (CDCl₃) & 2.00-2.14 (m, 1 H, 5-H_{ax}), 2.32 (dq, ${}^{3}J_{H,H}$ 4.8, ${}^{2}J_{H,H}$ 12.2, 1 H, 5-H_{eq}), 2.75–3.03 (m, 4 H, 6-H, 12-H), 3.32 (tt, ${}^{4}J = {}^{3}J_{H,H}$ 2.9, ${}^{3}J_{H,F} = {}^{3}J_{H,H}$ 14.3, 1 H, 4b-H), 3.79 (s, 3 H, 13-H), 6.08-6.16 (m, 1 H, 11-H), 6.73 (d, ${}^{4}J_{H,H}$ 2.9, 1 H, 7-H), 6.76 (dd, ${}^{4}J_{H,H}$ 2.9, ${}^{3}J_{H,H}$ 8.8, 1 H, 9-H), 7.61 (d, ${}^{3}J_{H,H}$ 8.8, 1 H, 10-H); ${}^{13}C$ NMR (acetone-d₆) δ 23.3 (dt, ${}^{3}J_{C,F}$ 3.8, C-5), 30.3 (t, C-6), 32.8 (dt, ${}^{3}J_{C,F}$ 2.5, ${}^{2}J_{C,F}$ 25.4, C-12), 39.4 (ddd, ${}^{3}J_{C,F}$ 2.6, ${}^{2}J_{C,F}$ 22.9, C-4b), 55.2 (q, C-13), 93.8 (ddd, ${}^{3}J_{C,F}$ 5.1, ${}^{2}J_{C,F}$ 19.1, ${}^{1}J_{C,F}$ 200.9, C-4a or C-12a), 96.6 (ddd, ${}^{3}J_{C,F}$ 5.1, ²J_{C,F} 17.8, ¹J_{C,F} 194.6, C-4a or C-12a), 110.5 (d, C-11), 113.5 (d, C-7 or C-9), 113.6 (d, C-7 or C-9), 124.9 (s, C-10a), 125.4 (d, C-10), 132.9 (d, ${}^{3}J_{C,F}$ 7.6, C-10b), 138.8 (s, C-6a), 146.0-150.8 (m, C-2, C-3), 159.5 (s, C-8), 181.6-184.2 (m, 2 C, C-1, C-4); ¹⁹F NMR (acetone-d₆, proton decoupled) δ –135.8 (d, ${}^{3}J_{\text{FF}}$ 5.7, 1 F, 2-F or 3-F), -137.8 (pseudo q, ${}^{5}J_{\text{FF}}$ = ${}^{4}J_{\text{FF}}$ = ${}^{3}J_{\text{FF}}$ 5.7, 1 F, 2-F or 3-F), -160.1 (dd, ${}^{4}J_{\text{FF}}$ 5.7, ${}^{3}J_{\text{FF}}$ 12.2, 1 F, 4a-F or 12a-F), -170.0 (dd, ${}^{5}J_{\text{FF}}$ 5.7, ${}^{3}J_{\text{FF}}$ 12.2, 1 F, 4a-F or 12a-F); ¹⁹F NMR (acetone-d₆) δ -135.8 (d, ³J_{F,F} 5.7, 1 F, 2-F or 3-F), -137.8 (pseudo q, ${}^{5}J_{F,F} = {}^{4}J_{F,F} = {}^{3}J_{F,F} 5.7$, 1 F, 2-F or 3-F), -159.9 to -160.2 (m, 1 F, 4a-F or 12a-F), -169.8 to -170.2 (m, 1 F, 4a-F or 12a-F); m/z 366 (38%, M⁺), 346 (100, M⁺ -HF), 331 (18, 346 - CH₃), 327 (23, 346 - F), 326 (19, 346 -HF), 290 (20), 284 (19), 270 (22), 255 (20), 246 (25), 238 (27), 228 (35, M⁺ - COC₂F₂CO - HF), 213 (34), 201 (27), 189 (32), 186 (82, $C_{13}H_{14}O^+$; retro Diels-Alder), 171 (94, 186 - CH₃), $165(25), 159(52, 186 - C_2H_3), 155(22, 186 - OCH_3), 153(43),$ 145 (47), 128 (75), 115 (63), 51 (22, C₄H₃⁺), 45 (27).

Compound *endo*-18.⁶¹ (Found: C, 62.20; H, 4.26. $C_{19}H_{14}F_4O_3$ (366.3) requires C, 62.30; H, 3.85%); ¹H NMR (CDCl₃) δ 1.81–1.96 (m, 1 H, 5-H_{ax}), 2.24 (dq, ³J_{H,H} 4.3, ²J_{H,H} 12.9, 1 H, 5-H_{eq}), 2.74 (ddd, ³J_{H,F} 1.9, ³J_{H,H} 4.6, ²J_{H,H} 17.9, 1 H, 12-H), 2.83–2.90 (m, 2 H, 6-H), 3.04 (dd br s, ³J_{H,H} 4.6, ²J_{H,H} 17.9, 1 H, 12-H), 3.81 (s, 3 H, 13-H), 4.62–4.71 (m, 1 H, 4b-H), 6.25 (dt, ⁴J_{H,F} 1.9, ³J_{H,H} 4.6, 1 H, 11-H), 6.65 (d, ⁴J_{H,H} 2.6, 1 H, 7-H), 6.79 (dd, ⁴J_{H,H} = 2.6, ³J_{H,H} 8.8, 1 H, 9-H), 7.65 (d, ³J_{H,H} 8.8, 1 H, 10-H); ¹³C NMR (CDCl₃) δ 27.8 (t, C-6), 28.4 (d br t, ³J_{C,F} 1.4, C-12), 29.5 (t, C-5), 55.3 (q, C-13), 72.8 (dd, ²J_{C,F} 4.2, C-4b), 110.2 (d, C-11), 112.9 (d, C-7 or C-9), 113.3 (d, C-7 or C-9), 124.5 (s, C-10a), 124.8 (d, C-10), 136.7 (s, C-10b), 137.6 (s, C-6a), 159.5 (s, C-8),⁶² ¹⁹F NMR (CDCl₃) δ –129.5 (t, ⁴J_{F,F} = ³J_{F,F} 9.5, 1 F, 2-F or 3-F), -130.5 (t, ⁴J_{E,F} = ³J_{E,F} 9.5, 1 F, 2-F or 3-F), -159.5 (dd, ⁴J_{E,F} 9.5, ³J_{E,F} 3.8, 4a-F or 12a-F), -160.1 (dd, ⁴J_{E,F} 9.5, ³J_{E,F} 3.8, 4a-F or 12a-F), -160.1 (dd, ⁴J_{E,F} 9.5, ³J_{E,F} 3.8, 4a-F or 12a-F), -150.1 (dd, ⁴J_{E,F} 9.5, ³J_{E,F} 3.8, 4a-F or 12a-F), -150.1 (dd, ⁴J_{E,F} 9.5, ³J_{E,F} 3.8, 4a-F or 12a-F), -150.1 (dd, ⁴J_{E,F} 9.5, ³J_{E,F} 3.8, 4a-F or 12a-F), -150.1 (dd, ⁴J_{E,F} 9.5, ³J_{E,F} 3.8, 4a-F or 12a-F), -150.1 (dd, ⁴J_{E,F} 9.5, ³J_{E,F} 3.8, 4a-F or 12a-F), -150.1 (dd, ⁴J_{E,F} 9.5, ³J_{E,F} 3.8, 4a-F or 12a-F), -150.1 (dd, ⁴J_{E,F} 9.5, ³J_{E,F} 3.8, 4a-F or 12a-F), -150.1 (dd, ⁴J_{E,F} 9.5, ³J_{E,F} 3.8, 4a-F or 12a-F), -150.1 (dd, ⁴J_{E,F} 9.5, ³J_{E,F} 3.8, 4a-F or 12a-F), -150.1 (dd, ⁴J_{E,F} 9.5, ³J_{E,F} 3.8, 4a-F or 12a-F), -150.1 (dd, ⁴J_{E,F} 9.5, ³J_{E,F} 3.8, 4a-F or 12a-F), -150.1 (dd, ⁴J_{E,F} 9.5, ³J_{E,F} 3.8, 4a-F or 12a-F), -150.1 (dd, ⁴J_{E,F} 9.5, ³J_{E,F} 3.8, 4a-F or 12a-F), -150.1 (dd, ⁴J_{E,F} 9.5, ³J_{E,F} 3.8, 4a-F or 12a-F), -150.1 (dd, ⁴J_{E,F} 9.5, ³J_{E,F}

Furthermore, tetrafluorohydroquinone (**6d**) (120 mg, 33%) was isolated by column chromatography. ¹H NMR (acetone-d₆) δ 9.09 (br s, 2 H, OH); ¹³C NMR (acetone-d₆) δ 128.2 (tt, ³J_{C,F} 6.4, ²J_{C,F} 10.2, 2 C, C-1, C-4), 139.0 (dddd, ⁴J_{C,F} 5.1, ³J_{C,F} = ²J_{C,F} 10.2, ¹J_{C,F} 240.3, 4 C, C-2, C-3, C-5, C-6); ¹⁹F NMR (acetone-d₆) δ –164.7 (s); *m*/*z* 182 (100%, M⁺), 162 (5, M⁺ – HF), 106 (95, M⁺ – 4 F), 75 (32), 71 (43), 56 (22). ¹⁹F NMR data for this compound can be found in ref. 63 which agree with those obtained in this study.

Acknowledgements

This work was supported by the Deutsche Forschungsgemeinschaft. M. E. is grateful to the Graduiertenkolleg "Hochreaktive Mehrfachbindungssysteme" and the "Graduiertenförderung des Landes Nordrhein-Westfalen" for stipends.

References

- 1 (a) J. A. Wilkinson, Chem. Rev., 1992, 92, 505-519; (b) R. E. Banks, B. E. Smart, J. C. Tatlow, Organofluorine Chemistry: Principles and Commercial Applications, Plenum Press, New York, 1994; (c) T. Hiyama, Organofluorine Compounds. Chemistry and Applications, Springer, Berlin, 2000.
- 2 (a) Organofluorine Compounds in Medicinal Chemistry and Biomedical Applications, eds. R. Filler, K. Kobayashi, L. M. Yagupolskii, Elsevier, Amsterdam, 1993; (b) Biomedical Frontiers of Fluorine Chemistry, eds. I. Ojima, J. R. McCarthy, J. T. Welch, ACS Symposium Series, vol. 639, American Chemical Society, Washington, 1996; (c) J. T. Welch, S. Esarakrishnan, Fluorine in Bioorganic Chemistry; John Wiley & Sons, New York, 1991, pp. 187–219.
- 3 S. Ratton, 13th European Symposium on Fluorine Chemistry, Bordeaux, France, July 2001, Book of Abstracts, PL3.
- 4 R. D. Chambers and J. F. S. Vaughan, Top. Curr. Chem., 1997, 192, 1-38 and references cited therein.
- 5 M. Essers, C. Mück-Lichtenfeld and G. Haufe, J. Org. Chem., 2002, 67, 4715-4721 and references cited therein.
- 6 (a) T. Ernet and G. Haufe, Tetrahedron Lett., 1996, 37, 7251-7252; (b) T. Ernet, A. H. Maulitz, E.-U. Würthwein and G. Haufe, J. Chem. Soc., Perkin Trans. 1, 2001, 1929–1938.
- 7 M. Essers, B. Wibbeling and G. Haufe, Tetrahedron Lett., 2001, 42, 5429-5433
- 8 A. A. Bogachev, L. S. Kobrina, O. G. J. Meyer and G. Haufe, *J. Fluorine Chem.*, 1999, **97**, 135–143.
- 9 (a) J. Buddrus, F. Nerdek, P. Hentschel and D. Klamann, Tetrahedron Lett., 1966, 5379-5383; (b) I. H. Jeong, Y. S. Kim and K. Y. Cho, Bull. Korean Chem. Soc., 1990, 11, 178-179.
- 10 T. Ernet, PhD Thesis, University of Münster, 1997.
- 11 (a) Y. A. Kotikyan, B. L. Dyatkin and Y. A. Konstantinov, Izv. Akad. Nauk SSSR, Ser. Khim., 1971, 358-362; Bull. Acad. Sci. USSR (Engl. Transl.), 1971, 292-295; (b) T. Iwaoka, N. Katagari, M. Sato and C. Kaneko, *Chem. Pharm. Bull.*, 1992, **40**, 2319–2324; (c) E. Tanyama, K. Araki, N. Sotojima, T. Murata and T. Aoki, (Mitsubishi), Jap. Patent 0189902/1995 (Chem. Abstr., 1995, 123, 111593); (d) H. Ito, A. Saito and T. Taguchi, Tetrahedron: Asymmetry, 1998, 9, 1979–1987 and 1989–1994; (e) H. Ito, A. Saito, A. Kakuuchi and T. Taguchi, Tetrahedron, 1999, 55, 12741-12750.
- 12 P. J. Crowley, J. M. Percy and K. Stansfield, Tetrahedron Lett., 1996, 37, 8233-8240.
- 13 M. Sridhar, K. L. Krishna and J. M. Rao, Tetrahedron, 2000, 9, 3539-3545
- 14 (a) J. M. Percy, Top. Curr. Chem., 1997, 193, 131–195; (b) M. H. Rock, in Methods of Organic Chemistry, eds. B. Baasner, H. Hagemann and J. C. Tatlow, vol E/10b, Thieme, Stuttgart, 1999, pp. 513–515.
- 15 Ê Chanteau, M. Essers, R. Plantier-Royon, G. Haufe and R. Portella, Tetrahedron Lett., 2002, 43, 1677-1680.
- 16 (a) J. M. Percy and M. H. Rock, Tetrahedron Lett., 1992, 33, (6177–6180; (b) P. J. Crowley, J. M. Percy and K. Stansfield, Tetrahedron Lett., 1996, **37**, 8233–8240.
- 17 V. A. Al'bekov, A. F. Benda, A. F. Gontar, G. A. Sokol'skii and I. L. Knunyants, Izv. Akad. Nauk SSSR, Ser. Khim., 1988, 897-900 (Chem. Abstr., 1988, 109, 128739j).
- 18 R. D. Chambers, A. F. Gilbert and R. L. Powell, J. Fluorine Chem., 2000, 104, 233-237.
- 19 G. G. Yakobson, V. D. Shteingarts, N. G. Kostina, O. I. Osina and N. N. Vorozhtsov, Jr., Zh. Obshch. Khim., 1966, 36, 142-145 (Chem. Abstr., 1966, 64, 17509d).
- 20 M. Hudlicky and H. M. Bell, J. Fluorine Chem., 1975, 5, 189-201.
- 21 R. M. Wilson, J. Org. Chem., 1983, 48, 707-711.
- 22 E.g.: (a) R. Filler, J. Fluorine Chem., 1986, 33, 361-375; (b) R. L. Powell, in Methods of Organic Chemistry (Houben-Weyl), eds. B. Baasner, H. Hagemann and J. C. Tatlow, vol E/10a, Thieme, Stuttgart, 1999, pp. 59-86.
- 23 Throughout this article, the cycloadducts of the Diels-Alder reactions of *p*-benzoquinones and Dane's diene (1) are numbered according to the numbering for chrysenes.
- 24 E. Dane, O. Höss, A. W. Bindseil and J. Schmitt, Liebigs Ann. Chem., 1937, 532, 39-51.
- 25 C. Symmes Jr. and L. D. Quin, J. Org. Chem., 1979, 44, 1048-1056.
- 26 P. A. Robins and J. Walker, J. Chem. Soc., 1956, 3249-3260 and references cited therein.
- 27 G. Quinkert, M. Del Grosso, A. Döring, W. Döring, R. I. Schenkel, M. Bauch, G. T. Dambacher, J. W. Bats, G. Zimmermann and G. Dürner, Helv. Chim. Acta, 1995, 78, 1345-1391 and references cited therein.
- 28 (a) G. Quinkert, M. Del Grosso, A. Bucher, W. Döring, M. Bauch, J. W. Bats and G. Dürner, Tetrahedron Lett., 1992, 33, 3617-3620;
- 2728 J. Chem. Soc., Perkin Trans. 1, 2002, 2719–2728

(b) G. Quinkert, M. Del Grosso, A. Bucher, J. W. Bats and G. Dürner, Tetrahedron Lett., 1991, 32, 3357-3360.

- 29 Z. G. Hajos, D. R. Parrish and M. W. Goldberg, J. Org. Chem., 1965, 30, 1212–1222
- 30 M. Hudlicky and H. M. Bell, *J. Fluorine Chem.*, 1975, **6**, 201–212. 31 K. Wallenfels and W. Draber, *Chem. Ber.*, 1957, **90**, 2819–2832.
- 32 V. N. Kovtonyuk, L. S. Kobrina and G. G. Yakobson, J. Fluorine Chem., 1985, 28, 89-98.
- 33 G. S. Lal, G. P. Pez and R. G. Syvret, Chem. Rev., 1996, 5, 1737-1755.
- 34 E.g.: L. Hintermann and A. Togni, Angew. Chem., 2000, 112, 4530-4533 and references cited therein.
- 35 R. E. Banks, M. K. Besheesh, S. N. Mohialdin-Khaffaf and I. Sharif, J. Chem. Soc., Perkin Trans. 1, 1996, 2069-2076
- 36 A. J. Poss and G. A. Shia, Tetrahedron Lett., 1999, 40, 2673-2676.
- 37 R. E. Banks, N. J. Lawrence and A. L. Popplewell, Synlett, 1994, 831-832
- 38 (a) K. Elbs, J. Prakt. Chem., 1893, 48, 179–185; (b) W. Baker and N. C. Brown, J. Chem. Soc., 1948, 2303–2307; (c) E. J. Behrman, Org. React., 1988, 35, 421-511.
- 39 A. E. Feiring and W. A. Sheppard, J. Org. Chem., 1975, 40, 2543-2545
- 40 M. M. King and L. A. Cohen, J. Am. Chem. Soc., 1983, 105, 2752-2760
- 41 As in all subsequent reactions Dane's diene (1) was also used as a mixture with 4, for convenience it is simply denoted Dane's diene (1) throughout the following text.
- 42 (a) The terms "ortho" and "meta" are used here as usual for the nomenclature of chrysene-derivatives (cf., refs. 44,45,47). They were already used earlier in association with the Diels-Alder reaction: cf. K. Alder, M. Schuhmacher and O. Wolff, Liebigs Ann. Chem., 1949, 564, 79-96; (b) K. Alder, H. Vagt and W. Vogt, Liebigs Ann. Chem., 1949, 565, 135-148 and references cited therein.
- 43 (a) R. B. Woodward, F. Sondheimer, D. Taub, K. Heusler and W. M. McLamore, J. Am. Chem. Soc., 1952, 74, 4223-4251; (b) J. E. Cole, W. S. Johnson, P. A. Robins and J. Walker, J. Chem. Soc., 1962, 244-278.
- 44 M. C. Carreño, J. L. G. Ruano, C. Z. Remor, A. Urbano and Jean Fischer, *Tetrahedron Lett.*, 1997, **38**, 9077–9080. 45 M. C. Carreño, J. L. G. Ruano, C. Z. Remor and A. Urbano,
- Tetrahedron: Asymmetry, 2000, 11, 4279–4296.
- 46 R. A. Dickinson, R. Kubela, G. A. MacAlpine, Z. Stojanac and Z. Valenta, *Can. J. Chem.*, 1972, **50**, 2377–2380.
- 47 J. Das, R. Kubela, G. A. MacAlpine, Z. Stojanac and Z. Valenta, Can. J. Chem., 1979, 57, 3308-3319.
- 48 K. Alder and G. Stein, Angew. Chem., 1937, 50, 510-519.
- 49 (a) J. Sauer and R. Sustmann Angew. Chem., 1980, 92, 773-801; Angew. Chem. Int. Ed. Engl., 1980, 19, 779–807; (b) J. I. García, J. A. Mayoral and L. Salvatella, Acc. Chem. Res., 2000, 33, 658-664; (c) A. Arrieta, F. P. Cossío and B. Lecea, J. Org. Chem., 2001, 66, 6178-6180.
- 50 The reaction of fluorobenzoquinones 2a and 2b, respectively, with cyclopentadiene at rt, gave only the corresponding endo-adducts, whose configurations were confirmed by NOE-experiments: M. Essers, PhD Thesis, University of Münster, 2001.
- D. H. Williams, I. Fleming, Spectroscopic Methods in Organic 51 Chemistry, McGraw-Hill, London, New York, 1966, pp. 104-120.
- 52 C. De Tollenaere and L. Ghosez, Tetrahedron, 1997, 53, 17127-17138.
- 53 M. J. M. Campbell, B. Demetriou and R. Jones, J. Chem. Soc., Perkin Trans. 2, 1983, 917-922.
- 54 Compound 7a is poorly soluble in acetone-d₆, therefore the signal for C-3 could not be assigned from the available spectrum.
- 55 The NMR assignments for this compound were confirmed by ¹H, ¹H- and ¹H, ¹³C NMR-correlation spectroscopy.
- 56 Conducting the reaction in toluene at 100 °C for 65 min furnished chrysenediones 8a/b (76 : 24, ¹H NMR) in 26% yield.
- 57 C-4b could not be assigned from the available spectrum.
- 58 As this crude product mixture was just sparingly soluble in CDCl₃, the ratio observed by NMR possibly is not representative.
- 59 Due to the low solubility of this compound and/or superimposition with the signals arising from toluene-d₈, the resonances of the other carbons could not be assigned from the available spectrum.
- 60 Assignment of the regiochemistry was rationalized by the share of chrysenedione 15a in the crude product.
- 61 Compound endo-18 could be fully characterised after reaction of the diastereomeric mixture of 18 with diisobutylaluminium hydride, where solely exo-18 reacted and endo-18 remained unchanged: M. Essers, PhD Thesis, University of Münster, 2001. 62 Due to extensive ¹³C, ¹⁹F couplings leading to low signal intensities,
- the quarternary carbons of the D-ring could not be assigned from the available spectrum.
- 63 S. Ando and T. Matsuura, Magn. Reson. Chem., 1995, 33, 639-645.