

Reactions involving fluoride ion Part 46. Reactions of dialkyl acetylenedicarboxylates

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Abstract

The vinyl anion (**2b**) is generated from dimethyl acetylenedicarboxylate by addition of fluoride ion, and this anion reacts with perfluorocyclopentene to give the novel diene (**5**). Reactions of (**5**) with nucleophiles are described. © 2001 Elsevier Science B.V. All rights reserved.

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1. Introduction

The chemistry described in this series of papers derives from fluorinated carbanions which are generated by addition of fluoride ion to unsaturated fluorinated compounds. In particular, we have reported that the carbanion (**2a**), generated by the addition of fluoride ion to diethyl acetylenedicarboxylate (**1a**), reacts with pentafluoropyridine, Scheme 1 [1,2].

Here, we describe an approach to the synthesis of unusual fluorinated dienes by reaction of the anion (**2b**), with perfluorocycloalkenes. From perfluorocyclopentene (**4**), two isomers (**5a**) and (**5b**), were obtained, one of which crystallised from the mixture on standing (Scheme 2). This was identified as the *Z* isomer (**5b**), by examination of the ¹⁹F NMR spectrum which showed a singlet and a multiplet, attributable to the two vinylic fluorine atoms. The presence of a singlet, and therefore, absence of ‘through space’ F–F coupling between these two atoms, indicates that this crystalline isomer has the *Z* structure. Furthermore, the multiplet arising from this isomer is less complicated than the corresponding multiplet in the non-crystalline isomer, and this also is consistent with the assignments (**5a**) and (**5b**).

The analogous reactions of anion (**2b**) with perfluoro-cyclobutene (**6**) and -cyclohexene (**7**) were less successful. Perfluorocyclobutene (**6**) competed successfully with the

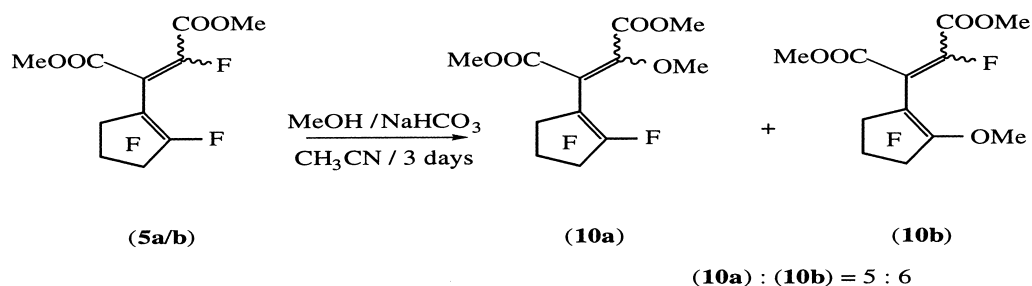
alkyne (**1b**) for fluoride ion because the main components in the reaction product are oligomers of perfluorocyclobutene (**8**) [3], together with small amounts of material with mass-spectra that are consistent with the adducts (**9a**) and (**9b**), Scheme 3. Conversely, perfluorocyclohexene (**7**) is much less reactive than (**5**) towards fluoride ion and it has a correspondingly low reactivity with the anion (**2b**). Consequently, only a very low conversion to product was observed. Neither reaction of anion (**2b**) with (**6**) or (**7**) were preparatively useful procedures. Electronically, the cycloalkenes (**4**), (**6**) and (**7**) are essentially equivalent and therefore, the differences in reactivity towards nucleophile (**2b**) may be attributed to increasing angle-strain in the series (**7**) < (**6**) < (**4**) which, of course, is alleviated on the addition of a nucleophile, to give a carbanion intermediate. This has also been noted previously, accounting for large differences in reactivity between fluorinated bicycloalkenes, and corresponding acyclic systems, towards nucleophiles [4], Scheme 4.

We have demonstrated that, the novel diene (**5a/b**) is reactive towards nucleophiles. Reaction with methoxide occurs at both vinylic positions, suggesting that in the developing allylic anions, which are the transition-states leading to (**10a**) and (**10b**), the polyfluorocycloalkyl groups situated at the carbon sites have a similar activating influence to that of an ester group, Scheme 5.

Substitution of both fluorine atoms at vinylic sites occurred with catechol after a prolonged period of reaction, surprisingly, giving the product (**11**). The ¹⁹F NMR spectrum of (**11**) shows the presence of two CF₂ groups, and the presence of two triplets of triplets in the ¹³C NMR spectrum

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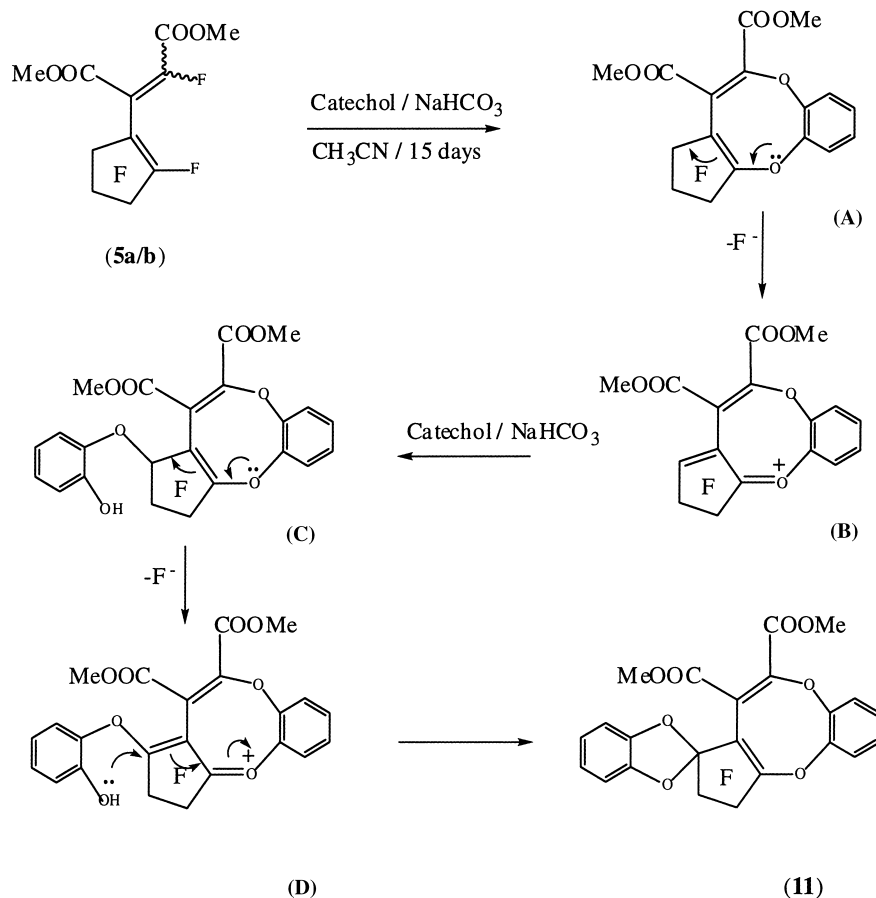


Scheme 5. Reaction of (5a/b) with methanol.

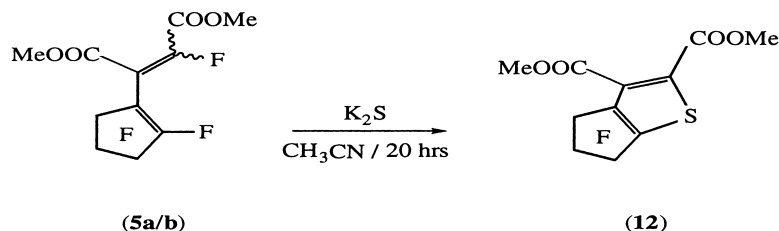
for formation of (11) is shown in Scheme 6, where, the first stage is probably the formation of intermediate (A), followed by loss of fluoride ion, giving (B), which would be very activated towards attack by catechol giving (C). A repeat of this process of expulsion of fluoride ion would lead to (D), followed by formation of (11). Clearly, variants of this mechanism may be written, where the rearranged cyclopentene system could occur via an S_N2' process, or via rearrangement induced by fluoride ion.

Reaction of the diene (5a/b) with potassium sulphide gave the thiophene derivative (12) quite readily, Scheme 7, and

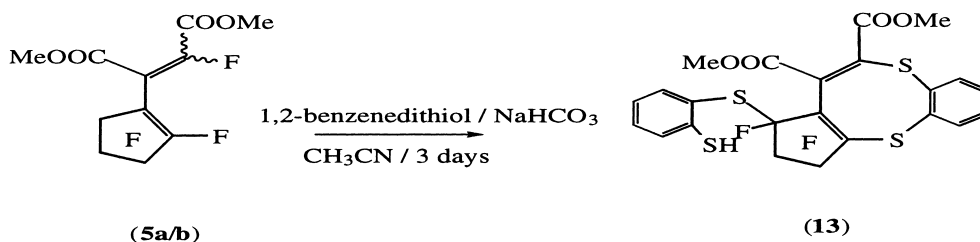
reaction of (5a/b) with benzene-1,2-dithiol gave the heterocycle (13), Scheme 8. The NMR data for (11) and (13) are similar except that in the spectrum of (13) there was an additional fluorine signal, with appropriate coupling in the ^{13}C spectrum. Moreover, coupling of a fluorine atom to an adjacent doubly-bonded carbon atom gave added support to this assignment. This is revealing, because one thiol group remains in this system, in contrast to the corresponding reaction with catechol, Scheme 6, where isolation of an intermediate corresponding to (13) was not observed. This adds support to the mechanism indicated in Scheme 6.



Scheme 6. Reaction of (5a/b) with catechol.



Scheme 7. Reaction of (5a/b) with potassium sulphide.



Scheme 8. Reaction of (5a/b) with 1,2-benzenedithiol.

2. Experimental

Unless indicated otherwise, ^1H and ^{19}F NMR spectra were recorded at room temperature on a Bruker AC 250 spectrometer operating at 250.13 or 235.34 MHz, respectively. Samples were dissolved in CDCl_3 , and tetramethylsilane and fluorotrichloromethane were used as internal references. Coupling constants are given in Hertz. GLC mass spectra were recorded on a VG 7070E spectrometer linked to a Hewlett Packard 5790A gas chromatograph fitted with a 25 m cross-linked methyl silicone capillary column. Mass spectra were generated by electron impact. Perfluorocyclobutene was obtained from Lancaster Chemical Co., perfluorocyclohexene, from Dr. P.L. Coe, University of Birmingham, and perfluorocyclopentene was made by a published procedure [5].

2.1. Reaction between perfluorocyclopentene (4) and dimethyl acetylenedicarboxylate (1b)

A Carius tube, fitted with a tap and charged with dry caesium fluoride (11.9 g, 78 mmol) and dry tetraglyme (40 ml), was attached to a vacuum line and cooled in liquid air. Perfluorocyclopentene (4), (47.6 g, 224 mmol) was transferred into the tube under vacuum before it was sealed and allowed to warm to room temperature. Under an atmosphere of dry nitrogen, the tap was replaced by a septum cap and through it, dimethyl acetylenedicarboxylate (10.2 g, 71.9 mmol) was injected over a period of some 200 min. This reaction mixture was allowed to stand overnight, after which unreacted perfluorocyclopentene (37.7 g, 178 mmol) was recovered. The remaining reaction product was combined with a second product, obtained from an identical

reaction, and poured into water. After washing, a lower layer was separated and the aqueous layer was extracted with diethylether. The extracts were combined with the lower layer from the initial water washing and dried (MgSO_4). Ether was removed by rotary evaporation and the residue was fractionated (Fischer Spaltrohr) under reduced pressure to yield a mixture of *E* and *Z* isomers, methyl-(2*E* and 2*Z*)-2-fluoro-3-(2,3,3,4,4,5,5-heptafluorocyclopent-1-enyl)-4-methoxy-penta-2,4-dienoate (5a) and (5b), 14.1 g, 40.7 mmol, yield 40%, (*E*:*Z* ratio ca. 3:2); b.p. 58–63°C, 0.04 mm Hg; Found: C 37.6; H 1.7; F 42.45; $\text{C}_{11}\text{H}_6\text{F}_8\text{O}_4$ requires C 37.3; H 1.7; F 42.9%. On standing, a crystalline solid was deposited, m.p. 48°C; *Z* isomer (5b); δ_{H} 4.0 (1H, br s, CH_3), 4.1 (1H, br s, CH_3); δ_{F} -93.1 (1F, s, =CF), -109.1 (2F, d, $^4J_{\text{FF}} = 10$, $\text{CF}_2\text{CF}_2\text{CF}_2\text{CF}=\text{}$), -119.8 (2F, d, $^3J_{\text{FF}} = 14$, $\text{CF}_2\text{CF}=\text{}$), -122.8 (1F, m, =CF ring), -129.8 (2F, s, $\text{CF}_2\text{CF}_2\text{CF}_2\text{CF}=\text{}$); δ_{C} 53.8 (s, 2 CH_3), 106.1 (tdd, $^2J_{\text{CF}} = 48.5$, $^2J_{\text{CF}} = 24.7$, $^3J_{\text{CF}} = 4.2$, $\text{CF}_2\text{C}=\text{ring}$), ca. 114 (tm, $^1J_{\text{CF}} = \text{ca. } 257$, 3 CF_2), 153.8 (d, $^1J_{\text{CF}} = 297.6$, =CF), 157.5 (dtm, $^1J_{\text{CF}} = \text{ca. } 310$, $^2J_{\text{CF}} = 45$, $\text{CF}_2\text{CF}=\text{ring}$), 158.6 (s, COOMe), 160.6 (s, COOMe); m/z 354 (M^+ 10%), 295 (100%). *E* isomer (5a) (not obtained pure); δ_{H} 4.0 (1H, br s, CH_3), 4.1 (1H, br s, CH_3); δ_{F} -101.8 (1F, m, =CF), -108.0 (2F, t, $^4J_{\text{FF}} = 12.6$, $\text{CF}_2\text{CF}_2\text{CF}_2\text{CF}=\text{}$), -115.6 (1F, m, =CF ring), -119.0 (2F, d, $^3J_{\text{FF}} = 15$, $\text{CF}_2\text{CF}=\text{}$), -130.3 (2F, s, $\text{CF}_2\text{CF}_2\text{CF}_2\text{CF}=\text{}$); m/z 354 (M^+ 10%), 295 (100%).

When similar reactions were carried out using perfluorocyclobutene, (6), a mixture of starting material, its oligomers and a small amount of material believed to be the adduct, (9a/b), { m/z 304 ($\text{C}_{10}\text{H}_6\text{F}_6\text{O}_4$ requires 304)}, was produced. When perfluorocyclohexene, (7), was the starting material, only a tiny yield (ca. 1%) of material, believed to be the 1:1 adduct, { m/z ($\text{C}_{12}\text{H}_6\text{F}_{12}\text{O}_4$ requires 404)}, was obtained.

2.2. Reactions of (5a/b)

2.2.1. Reaction with methanol in the presence of base

To a three necked flask, charged with a stirred mixture of the dienes (**5a/b**) (2.1 g, 6.0 mmol), methanol (1.5 g, 48.1 mmol) and acetonitrile (10 ml), was slowly added, at room temperature, sodium hydrogen carbonate (3.0 g, 35.5 mmol). After stirring for 3 days, the mixture was filtered and the volatile components were removed using a rotary evaporator. The residual oil was distilled from trap to trap in vacuo to give a colourless oil which was shown by gc to consist of two components in the ratio of 6:5. The major component crystallised out in part and was identified as methyl (*E/Z*)-3-(2,3,3,4,4,5,5-heptafluoropent-1-enyl)-2,4-dimethoxypenta-2,4-dienoate, (**10a**); Found: C 39.3; H 2.3; C₁₂H₉F₇O₅ requires C 39.3; H 2.5%; δ_H 3.9 (1H, s, COOCH₃), 4.0 (1H, s, COOCH₃), 4.2 (1H, s, OCH₃); δ_F -106.4 (3F, s, =CF and CF₂CF₂CF₂C(OCH₃)=), -114.9 (2F, s, CF₂C(OCH₃)=), -130.3 (2F, s, CF₂CF₂CF₂C(OCH₃)=); δ_C 53.6 (s, 2COOCH₃), 59.6 (s, CF₂C(OCH₃)=), 106.1 (m, CF₂C= ring), 110.1 (tp, ¹J_{CF} = 273, ²J_{CF} 24.6, CF₂CF₂CF₂C(OCH₃)=), 111.5 (d, ²F_{CF} 35, C= non-ring), 112.3 (tt, ¹J_{CF} 261, ²J_{CF} 25.6, CF₂C(OCH₃)= or CF₂C=), 115.3 (tt, ¹J_{CF} 257, ²J_{CF} 24.2, CF₂C(OCH₃)= or CF₂C=), 151.0 (d, ¹J_{CF} = 286, =CF non-ring), 154.2 (t, ²J_{CF} 19, CF₂=C(OCH₃)), 159.1 (d, ²J_{CF} 30.8, =CFCOOMe), 163.1 (d, ³J_{CF} 10.0, CF=CCOOMe); *m/z* (CI (NH₃)) 384, (M + NH₄)⁺ 100%. Methyl (*E/Z*)-2-fluoro-3-(3,3,4,4,5,5-hexafluoro-2-methoxycyclopent-1-enyl)-4-methoxypenta-2,4-dienoate, (**10b**) δ_H 3.9 (1H, s, COOCH₃), 4.0 (1H, s, COOCH₃), 4.2 (1H, s, OCH₃); δ_F -109.8 (2F, d, ⁴J_{FF} 10.1, CF₂CF₂CF₂CF=), -120.2 (2F, d, ³J_{FF} 14.1, CF₂CF=), -123.5 (1F, m, CF₂CF=), -131.4 (2F, s, CF₂CF₂CF=); *m/z* 366(M⁺ 7%), 59 (100%). Crude yield (mixture of isomers), ca. 90%.

2.2.2. Reaction with catechol in the presence of sodium hydrogen carbonate

To a three necked flask, charged with a stirred mixture of the dienes (**5a/b**) (1.15 g, 3.3 mmol), and sodium hydrogen carbonate (1.5 g, 17.5 mmol), catechol (0.8 g, 6.9 mmol) in acetonitrile (40 ml), was slowly added, at room temperature, sodium hydrogen carbonate. After stirring for fifteen days, the mixture was filtered and the volatile components were removed using a rotary evaporator. The residual yellow solid (1.3 g) was washed with cold ether to give a white solid which was sublimed under reduced pressure to give the methyl-1,1,2,2-tetrafluoro-5-(methoxycarbonyl)spiro[1,2,3-trihydrobenzo [b] cyclopenta [1,2-e] 1,4-dioxocin-3,2'-benzo [d] 1,3-dioxolene]-4-carboxylate, (**11**) (2.1 mmol, 64% yield); m.p. 152°C; Found: C 55.9; H 2.7; F 15.9. C₂₃H₁₄F₄O₈ requires C 55.9; H 2.8, F 15.4%; δ_H 3.4 (3H, s, COOCH₃), 3.8 (3H, s, COOCH₃), 6.9 (4H, s, ArH), 7.1 (1H, m, ArH), 7.2 (2H, m, ArH), 7.4 (1H, d, ArH); δ_F -118.4 (1F, s, CF₂CF₂), -130 (1F, s, CF₂CF₂); δ_C 52.9

(s, OCH₃), 53.2 (s, OCH₃), 111.3 (tt, ¹J_{CF} 270.6, ²J_{CF} 22.2, CF₂), 112.7 (tt, ¹J_{CF} 259.4, ²J_{CF} 25.5, CF₂), 161.4 (s, CO), 112.7 (s, CO), aromatic resonances at 109.1, 121.9, 122.9, 124.7, 126.0, 127.6 and other resonances at 114.6, 143.6, 146.5, 149.0 and 149.3; *m/z* 494 (M⁺ 14%).

2.2.3. Reaction with potassium sulphide

To a stirred solution of the dienes (**5a/b**) (6.2 g, 17.5 mmol) in dry acetonitrile (10 ml), was added freshly ground potassium sulphide (2.6 g, 23.5 mmol). After an initial exotherm, the mixture was stirred for a further 20 h. The solvent was removed by rotary evaporation under reduced pressure and chloroform was added to the residue. This mixture was filtered to remove inorganic material and solvent was removed by reduced pressure distillation, again using a rotary evaporator. The residue was distilled from trap to trap under vacuum to give a colourless oil (2.6 g) which eventually crystallised and was identified as methyl 4,4,5,5,6,6-hexafluoro-2-(methoxycarbonyl)-4,5,6-trihydrocyclopenta[1,2-b] thiophene-3-carboxylate, (**12**), (1.8 g, 5.1 mmol, 29% yield); m.p. 40°C; Found: C 37.7; H 1.6; F 33.3; C₁₁H₆F₆O₄S requires C 37.9; H 1.7, F 32.8%; δ_H 4.0 (1H, s, COOCH₃), 4.1 (1H, s, COOCH₃); δ_F -102.7 (1F, s, CF₂CF₂C=), -106.8 (1F, s, CF₂=), -124.8 (1F, s, CH₂CF₂C=); δ_C 53.4 (s, COOCH₃), 53.7 (s, COOCH₃), 108–118 (overlapping t, CF₂), 131.1 (s, SC=COOCH₃), 140.0 (m, C=C), 141.4 (m, C=C), 144.4 (s, C=CC=COOCH₃), 159.6 (s, COOCH₃), 160.7 (s, COOCH₃); *m/z* 348 (M⁺, 12%), 317 (100).

2.2.4. Reaction with 1,2-benzenedithiol in the presence of sodium hydrogen carbonate

To a three necked flask, charged with a stirred mixture of the dienes (**5a/b**) (1.2 g, 3.4 mmol), 1,2-benzenedithiol (1.1 g, 7.75 mmol) and acetonitrile (10 ml) was slowly added, at room temperature, sodium hydrogen carbonate (1.4 g, 17 mmol). After stirring for 3 days, the mixture was evaporated down under reduced pressure using a rotary evaporator. Chloroform was added to the residue and this gave a solution containing a white solid. Filtration gave a solution which was evaporated to yield a yellow solid (1.4 g). A sample of this material was washed with acetonitrile and recrystallised from ethanol to give methyl 1,1,2,2,3-pentafluoro-5-(methoxycarbonyl)-3-(2-sulphanylphenylthio)-1,2,3-trihydrobenzo [b]cyclopenta [1,2-e] 1,4-dithiocin-4-carboxylate, (**13**) (2.5 mmol (crude), 75% yield); m.p. 138°C; Found: C 48.8; H 2.9. C₂₃H₁₅F₅O₄S₄ requires C 47.8; H 2.6%; δ_H 3.8 (3H, s, COOCH₃), 3.9 (3H, s, COOCH₃), 5.5 (1H, s, SH), 7.1 (7H, m, ArH), 7.2 (1H, m, ArH); δ_F -111.3 (1F, dm, J_{FF} 258.4, CFF), -114.7 (1F, dm, J_{FF} 221.2, CFF), -121.1 (1F, br s, CFS), -125.4 (1F, dm, J_{FF} 258.2, CFF), -128.6 (1F, dm, J_{FF} 223.1, CFF); δ_C 53.8 (s, CH₃), 54.9 (s, CH₃), 112.2 (t, J_{CF} ca. 260, CF₂), 114.2 (t, J_{CF} ca. 270, CF₂), 134.6 (d, ²J_{CF} 26, =CCFS), 150.6 (d, ¹J_{CF}

ca. 290, =CCFS), 167.4 (s, CO), 169.0 (s, CO), unassigned others at 70.3, 118.3, 121.9, 126.7, 136.9 and some obscured by overlapping; m/z 578 (M^+ 0.6%), 211 (100%); Accurate mass, found: 577.9773; $C_{23}H_{15}F_5O_4S_4$ requires 577.977338.

Acknowledgements

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