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FLUORINE-CONTAINING SEVEN-MEMBERED BENZOHETEROCYCLES DERIVED FROM HEXAFLUOROPROPENE OLIGOMERS

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SUMMARY

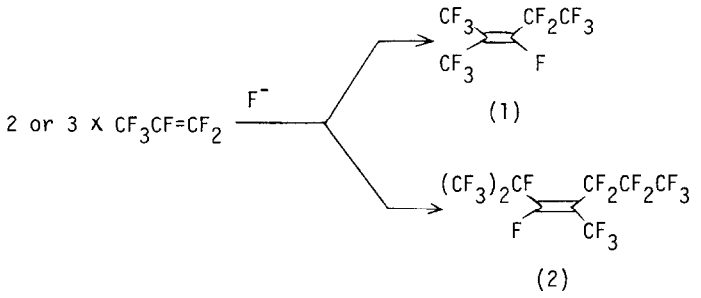
4-Fluoro-2-(F-ethyl)-3-(F-methyl)-1,5-benzoxazepine was prepared by reaction of F-2-methyl-2-pentene with 2-aminophenol in the presence of triethylamine in diethyl ether. The reaction of F-2,4-dimethyl-3-heptene with 2-aminophenol in dimethylformamide gave 7-(F-1-methylethyl)-8-(F-ethyl)-9,14-benzoxazepino[4,3-b]1,6-benzoxazepine. Several *ortho*-bifunctional benzenes reacted similarly with F-2-methyl-2-pentene and F-2,4-dimethyl-3-heptene to give the corresponding seven-membered benzoheterocycles.

INTRODUCTION

The systematic study of the reactivities of perfluoroolefins to nucleophiles, which represent extension of the syntheses of fluorinated heterocyclic compounds expected to be bioactive pharmaceuticals and agrochemicals [1], has generated considerable interest. In our lab's previous papers, we have reported the preparation of some five- and six-membered benzoheterocycles by the reactions of *ortho*-bifunctional benzenes with F-propene [2], its oxide [3,4], and F-2-methylpropene [5].

F-propene is also known to oligomerize readily in the presence of a base or a fluoride ion giving a mixture of the dimers and trimers [6-9], and several of their nucleophilic reactions are reported in the literature [10-14].

Our continuing studies of fluorinated heterocycles from perfluoro-olefins, led to search for new types of ring compounds. This paper will report the preparation of seven-membered benzoheterocycles from F-2-methyl-2-pentene (1) and F-2,4-dimethyl-3-heptene (2) which are a dimer and trimer of F-propene, respectively.



RESULTS AND DISCUSSION

Reaction of F-2-methyl-2-pentene (1) with 2-aminophenols

In a recent preliminary account [15], we outlined the formation of seven-membered benzoheterocycles from reaction of (1) with 2-aminophenol. Among the various aprotic polar solvents examined in continuing studies, the diethyl ether-triethylamine system was found to be most effective. Nevertheless, the yield of 4-fluoro-2-(F-ethyl)-3-(F-methyl)-1,5-benzoxazepine (6)(X=H) reached only 48 %.

The structure of (6, X=H) was elucidated by study of the ^{1}H and ^{19}F nmr and mass spectra. The ^{1}H nmr spectrum showed only one peak due to aromatic protons at δ 7.40-6.90. In the ^{19}F nmr spectrum, four peaks appeared at δ -50.7, -20.4, 3.7 and 37.3 ppm* in the ratio 1:3:3:2, respectively. The signal at δ -50.7(q) was assigned to the N=CF fluoride atom, split by the CF_3 group on the carbon-carbon double bond (J_{F-CF_3} = 15 Hz). The signal at δ -20.4 was assigned to the C=C-CF_3 fluorine atoms, split by all other fluorine nuclei in the molecule ($J_{CF_3-CF_2}$=17 Hz, $J_{CF_3-CF_2CF_3}$ = 3 Hz). The mass spectrum showed the molecular ion and other fragment ions, such as m/e 202, which is characteristic of imidoyl fluorides.

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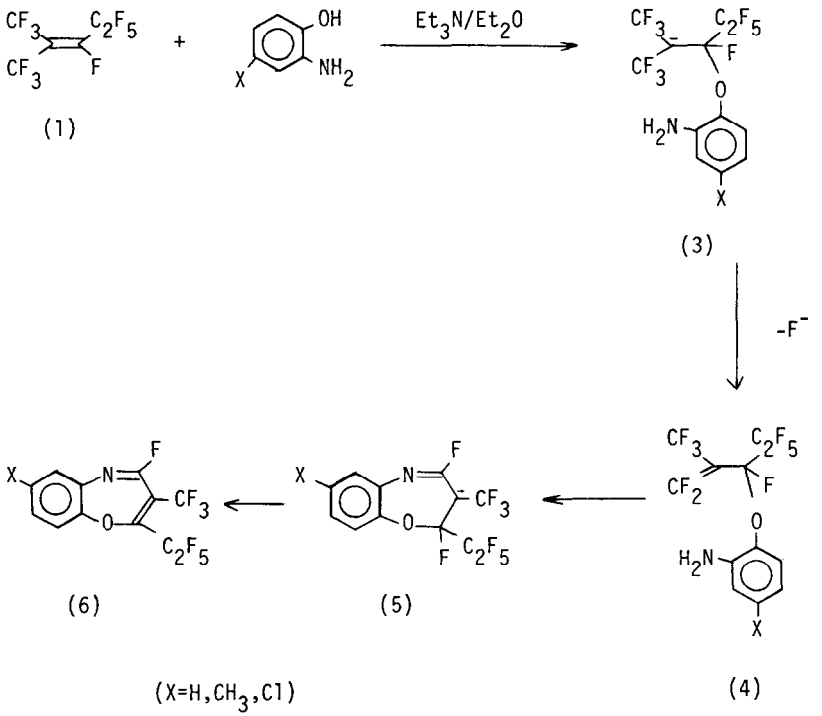
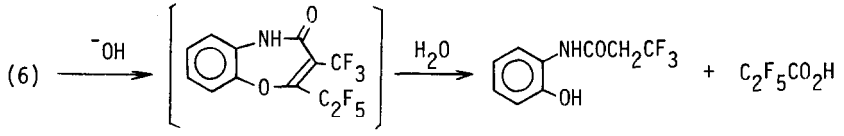
* All ^{19}F nmr chemical shifts throughout this article are given in δ ppm from external trifluoroacetic acid.



Scheme 1

Chemical evidence supporting the structure was obtained by hydrolysis of (6). Thus, on treating (6) with an aqueous sodium hydroxide solution, 2-(3,3,3-trifluoropropionylamino)phenol,mp 145.0-146.5 °C, was formed quantitatively.



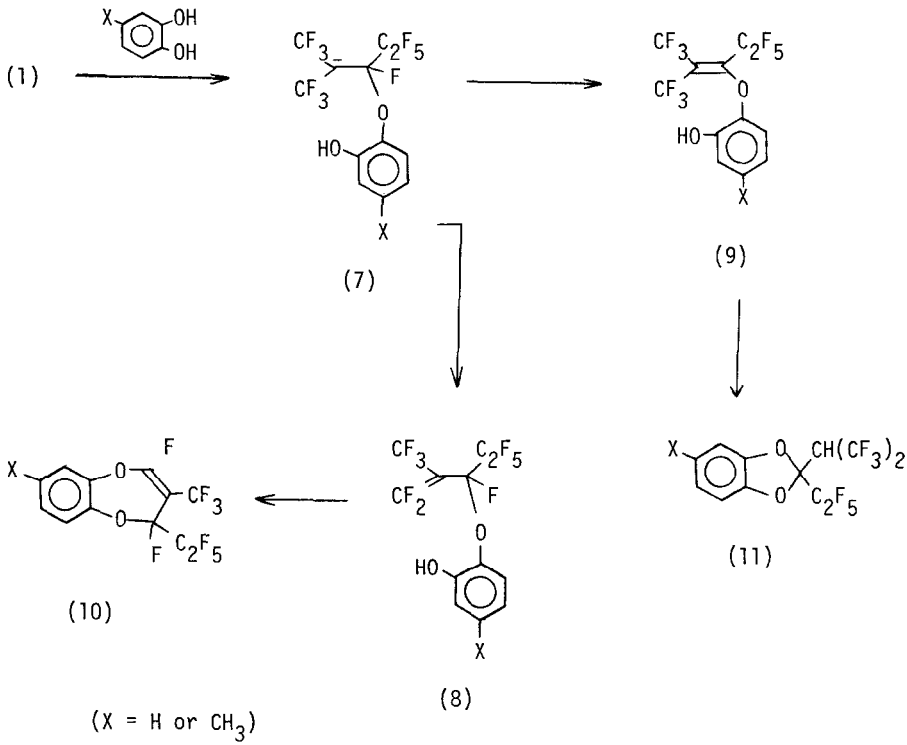
Formation of (6) should proceed according to Scheme 1. Thus, first step would be the nucleophilic attack by phenoxide ion leading to the carbanion (3), as in the case of the reaction between (1) and phenol in the presence of triethylamine [13]. Elimination of fluoride ion from carbanion (3) would lead to (4), a reactive terminal perfluoroolefin, which would undergo nucleophilic attack by the amino group in the molecule leading to (6)(X=H) via carbanion (5).

2-Amino-4-substituted phenols, containing an electron-donating methyl or electron-atracting chloro group on the benzene ring, also gave 7-methyl- or 7-chloro-1,5-benzoxazepine derivatives (6, X=CH_3 and Cl) in similar yields.

Reaction of (1) with catechol

When disodium catecholate was used as the nucleophile in the reaction with (1), 1,5-benzodioxepin and benzodioxole derivatives were produced in varying ratios depending on the solvent.

For example, when disodium catecholate in diethyl ether was allowed to react with (1), 2,4-difluoro-4-(F-ethyl)-3-(F-methyl)-4H-1,5-benzodioxepin (10) (X=H) and 2-(F-ethyl)-2-(1-F-methyl-2,2,2-trifluoroethyl)benzodioxole (11) (X=H) were obtained in yields of 44 and 20 %, respectively.



Scheme 2

The structure of (10) (X=H) was established by spectral data. The ^{19}F nmr spectrum showed peaks at δ -29.7, -21.6, 2.1, 30.4, 44.3 and 47.5 ppm in the ratio 1:3:3:1:1:1. The signal at δ -29.7 due to C=CF-O was an

overlapping quartet of doublets split by the OCF nucleus (J_{F-OCF}= 10.7 Hz) and the CF_3 on the carbon-carbon double bond (J_{F-CF_3} = 19.1 Hz). The resonance at δ -21.6 due to C=C-CF_3, was split by the fluorine on the OCF group (J_{CF_3-OCF} = 16.8 Hz) and the magnetically unequivalent fluorine atoms of CF_2CF_3($J_{CF_3-CF_A}$ = 10.1 Hz, $J_{CF_3-CF_B}$ = 17.9 Hz). The signal at δ 2.1 was assigned to CF_2CF_3 ($J_{CF_2CF_3-OCF}$= 8.0 Hz), and that at δ 30.3 to the OCF ($J_{OCF-CF_AF_B}$= 10.4 Hz), without coupling to the CF_A fluorine atom in either case. The peaks at δ 44.3 and 47.5 were assigned to the CF_AF_B fluorine atoms ($J_{F_A-F_B}$ = 286 Hz). In the ^{1}H nmr spectrum, the only peak was the aromatic signal at δ 7.32 ppm. The infrared spectrum showed an absorption band due to the carbon-carbon double bond at 1675 cm^{-1}. In the mass spectrum, the molecular ion (M^+ 370) and fragment peaks appeared appropriately.

Spectral data also supported the structure of (11)(X=H). In the ^{19}F nmr spectrum, three signals appeared at δ -15.5 (d of t), 2.6 (s) and 47.3 (sep) in the ratio 6:3:2. The resonance at δ -15.5 due to the $CH(CF_3)_2$ group was split by the CF_2CF_3 ($J_{CF_3-CF_2CF_3}$ = 6.5 Hz). The ^{1}H nmr spectrum showed two signals at δ 7.03 (Ar-H) and 3.97 (sep., J_{H-CF_3} = 7.7 Hz). In the mass spectrum, the molecular ion (M^+ 390), and fragment peaks appeared at appropriate positions.

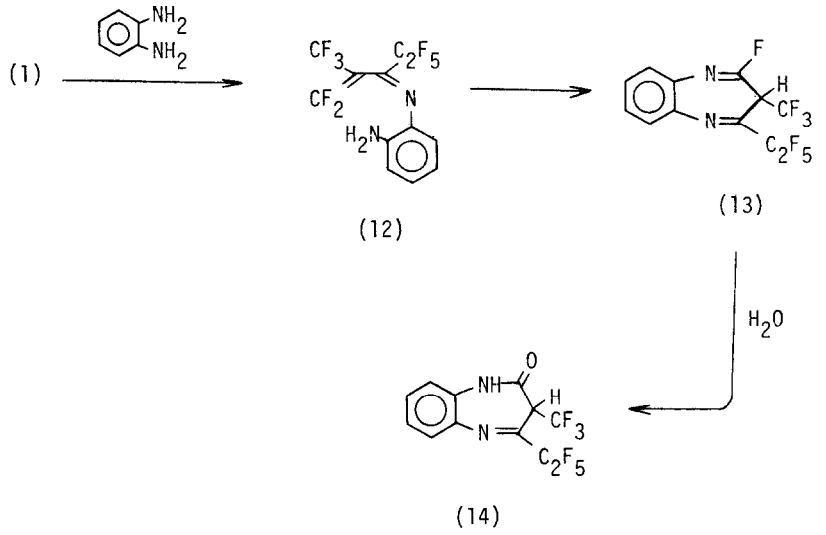
When the Et_3N-MeCN system was used in the above reaction, compound (11)(X=H) was obtained as the main product in a yield of 62 %. The reaction was assumed to proceed as shown in Scheme 2.

From comparison of the structures, the intermediate (9), an internal olefin, should be thermodynamically preferable to (8), a terminal olefin.

Reaction of (1) with o-phenylenediamine

The reaction of (1) with o-phenylenediamine was examined next, and 4-(F-ethyl)-3-(F-methyl)-1H-1,5-benzodiazepin-2(3H)-one (14) was obtained as the only isolated product, though in a very poor yield (6 %). Extraction of the tarry residues with a variety of solvents did not lead to the isolation of other products. In this reaction, cyclization should occur only from the syn form (12), and this would seriously limit its extent (Scheme 3). The fluoroimidoyl compound (13) would be very susceptible to hydrolysis and was actually not able to be isolated. The instability of the fluoroimidoyl group of (13), compared with that of (6),

can be ascribed to the fact that the C=N bond in the former compound is independent, whereas it is conjugated with the C=C bond in the latter.

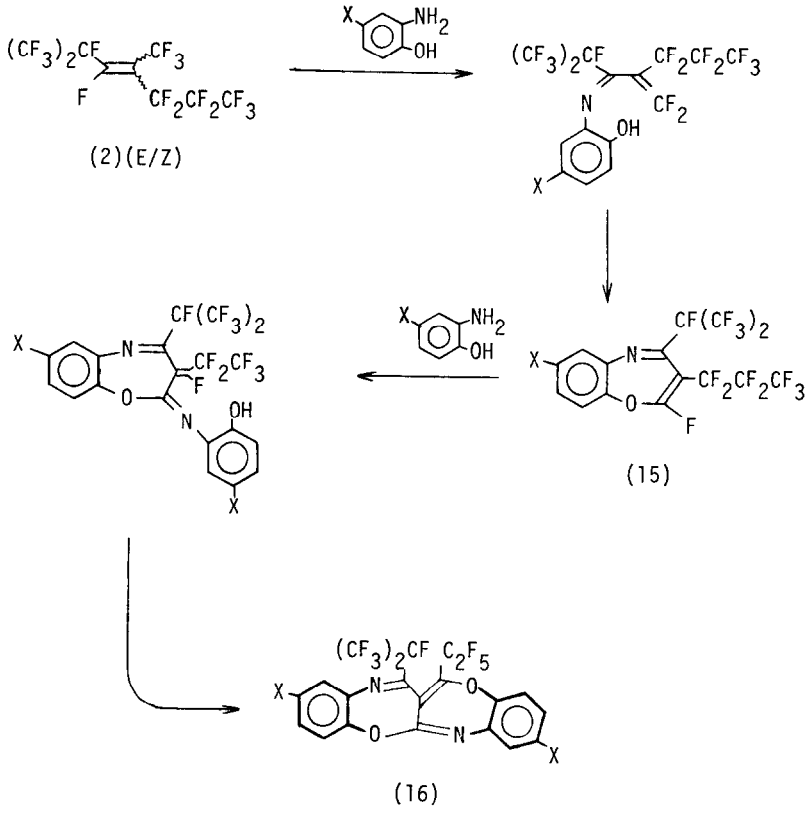


Scheme 3

Reaction of F-2,4-dimethyl-3-heptene (2) with 2-aminophenol

It is interesting to compare the behavior of F-2,4-dimethyl-3-heptene (2), one of the trimers of F-propene, with that of (1), one of the dimers. In an attempt to obtain new types of heterocycles, the reaction of (2) was carried out with 2-aminophenol in dimethylformamide. The only product of this reaction was 7-(F-1-methylethyl)-8-(F-ethyl)-9,14-benzoxazepino[4,3-b]1,6-benzoxazepine (16) (X=H), which was isolated in 74 % yield.

The reaction pathway was considered as shown in Scheme 4. The structure of the benzoxazepinobenzoxazepine (16) (X=H) was evident from its ^{19}F nmr and mass spectra. The ^{19}F nmr spectrum showed peaks at δ -4.5, 3.5, 36.5 and 98.5 in the ratio 6:3:2:1, respectively. The signals at δ -4.5 (d) and 98.5 (sep) due to the fluorine nuclei of the $(CF_3)_2CF$ group are split by each other (J_{CF_3-CF} = 6.8 Hz). In the ^1H nmr spectrum, only one peak due to the aromatic protons appeared at δ 7.83-6.83. The mass spectrum gave the molecular ion, M^+ 548, and other fragment peaks, such as m/e 287 ($C_{10}H_4NOF_7$), 150 (C_3F_6), 143 (C_4F_5), 119 (C_2F_5) and 69 (CF_3). In other words, there is a o-C_6H_4 N O C_3F_7i, but no o-C_6H_4 N O C_2F_5 fragment, thus supporting the structure (16) (X=H).



Scheme 4

Reaction of (2) with o-phenylenediamine

When o-phenylenediamine was allowed to react with (2) in dimethylformamide, 1H-1,7a-dihydro-7-(F-ethyl)-8-(F-1-methylethyl)-9,14-benzodiazepino[2,3-b]1,6-benzodiazepine (18) (X=H) and 2-(F-1-methylethyl)-3-(F-propylidene)-1,5-benzodiazepine (17) (X=H) were produced in yields of 54 and 30 %, respectively.

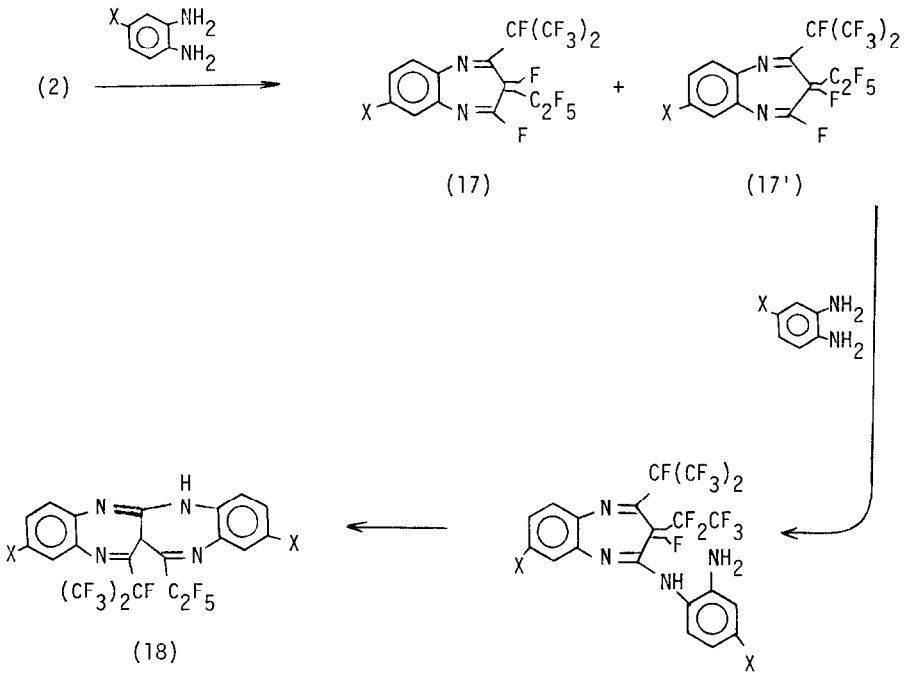
The structures of the two compounds (17) and (18) were also established on the basis of spectral data. The ^{19}F nmr spectrum of (17) (X=H) showed peaks at δ -47.3, -1.5, 5.4, 31.5, 37.7 and 108 in the ratios 1:6:3:1:2:1. The signal at δ -47.3 was assigned to N=CF and that at δ 31.5 was assigned to C=CF. The peaks at δ -1.5 and 108 due to $CF(CF_3)_2$ fluorine nuclei were multiplets. The ^{19}F nmr spectrum of (18)(X=H) showed peaks at δ -4.4, -3.4, 3.4, 35.0 and 99.5 in the ratio 3:3:3:2:1. The signals at δ

TABLE 1.

Properties of Products

Compound	bp (°C/mmHg) [mp °C]	Yield (%)	NMR ^{19}F	NMR ^{1}H	Anal.(%) Found (Calcd) C	H	N
(6) (X=H) (nc)	98-100/15	48	-50.7(N=CF), -20.4(CF_3), 3.7($\underline{CF}_3CF_2$), 37.3($CF_3\underline{CF}_2$)	6.9-7.4	41.26 (41.28)	1.25 (1.15)	4.04 (4.01)
(6) (X=CH_3) (nc)	[76.0-77.0]	41	-50.5(N=CF), -20.6(CF_3) 3.6($\underline{CF}_3CF_2$), 37.5($CF_3\underline{CF}_2$)	6.8-7.2 2.37	43.04 (42.99)	1.81 (1.67)	3.70 (3.86)
(6) (X=Cl) (nc)	[97.0-98.5]	44	-52.0(N=CF), -20.6(CF_3) 3.7($\underline{CF}_3CF_2$), 37.4($CF_3\underline{CF}_2$)	6.9-7.4	37.77 (37.57)	0.87 (0.79)	3.64 (3.65)
(10) (X=H) (nc)	94-97/18	44	-29.7(=CF), -21.6(CF_3), 2.1($\underline{CF}_3CF_2$), 30.3(CF), 44.3, 47.5($CF_3\underline{CF}_2$)	7.32	38.84	1.14	
(10) (X=CH_3) (nc)	98-100/11	35	-29.0(=CF), -21.0(CF_3), 2.1($\underline{CF}_3CF_2$), 29.6(CF), 44.0, 46.0($CF_3\underline{CF}_2$)	7.0-7.3 2.42	40.51 (40.64)	1.68 (1.57)	
(14) (nc)	[119.0-120.0]	6	-15.5(CF_3), 4.3($\underline{CF}_3CF_2$), 37.6($CF_3\underline{CF}_2$)	7.1-7.6	40.87 (41.64)	1.78 (1.75)	8.09 (8.09)
(16) (X=H) (nc)	92-94/0.1	74	-4.5(CF_3), 3.5($\underline{CF}_3CF_2$), 36.5($CF_3\underline{CF}_2$), 98.5(CF)	6.8-7.8	46.03 (46.00)	1.40 (1.47)	5.21 (5.11)
(16) (X=CH_3) (nc)	[88.0-88.5]	70	-4.5(CF_3), 3.8($\underline{CF}_3CF_2$), 36.0($CF_3\underline{CF}_2$), 98.1(CF)	6.7-7.6 2.36,2.41	48.68 (47.93)	2.13 (2.10)	4.90 (4.86)
(16) (X=Cl) (nc)	102-105/0.1	20	-4.4(CF_3), 4.0($\underline{CF}_3CF_2$), 36.5($CF_3\underline{CF}_2$), 98.7(CF)	6.9-7.9	41.02 (40.87)	1.21 (0.98)	4.52 (4.54)
(17) (X=H) (nc)	86-88/10	30	-47.3(N=CF), -1.5(CF_3), 5.4($\underline{CF}_3CF_2$), 31.5(=CF), 37.7($CF_3\underline{CF}_2$), 108.0(CF)	7.3-7.8	37.57 (37.68)	1.02 (0.84)	5.81 (5.86)

(17) ($X=CH_3$) (nc)	97-99/2	33	-46.6(N=CF), -1.6(CF_3), 5.5($C\underline{F}_3CF_2$), 7.1-7.6	39.21	1.16	5.59
			32.2(=CF), 37.9($CF_3C\underline{F}_2$), 108.1(CF) 2.45	(39.05)	(1.23)	(5.69)
(17) (X=Cl) (nc)	[148.5-150.5]	44	-48.7(N=CF), -1.6(CF), 5.3($C\underline{F}_3CF_2$), 7.1-7.8	35.16	0.79	5.33
			30.2(=CF), 37.9($CF_3C\underline{F}_2$), 108.4(CF)	(35.15)	(0/59)	(5.46)
(18) (X=H) (nc)	[157.5-159.0]	54	-4.4,-3.4(CF_3), 3.4($C\underline{F}_3CF_2$) 6.9-7.6	46.21	1.88	10.16
			35.0($CF_3C\underline{F}_2$), 99.5(CF) 8.25,6.25	(46.17)	(1.85)	(10.26)
(18) ($X=CH_3$) (nc)	[134.0-135.5]	48	-4.0,-3.3(CF_3), 3.4($C\underline{F}_3CF_2$), 6.9-7.5	48.12	2.49	9.81
			34.8($CF_3C\underline{F}_2$), 99.5(CF) 2.33,6.20	(47.93)	(2.46)	(9.75)
			8.14			
(18) (X=Cl) (nc)	[168.5-169.5]	17	-4.5,-3.5(CF_3), 5.5($C\underline{F}_3CF_2$), 7.1-7.6	41.27	1.44	9.20
			34.8($CF_3C\underline{F}_2$), 99.0(CF) 6.23,8.33	(40.87)	(1.63)	(9.08)
(20) (nc)	92-94/15	34	-21.3(=CF), -5.6,-4.5(CF_3), 7.1-7.4	34.62	0.76	
			2.3($C\underline{F}_3CF_2$), 25.9(CF)	(34.64)	(0.78)	
			45.3($CF_3C\underline{F}_2$), 99.1(CF)			
(21) (nc)	93-95/15	8	-23.6(=CF), -5.5(CF_3), 2.2($C\underline{F}_3CF_2$), 7.1-7.4	34.71	0.75	
			42.2(CF), 46.3($CF_3C\underline{F}_2$), 96.0(CF)	(34.64)	(0.78)	



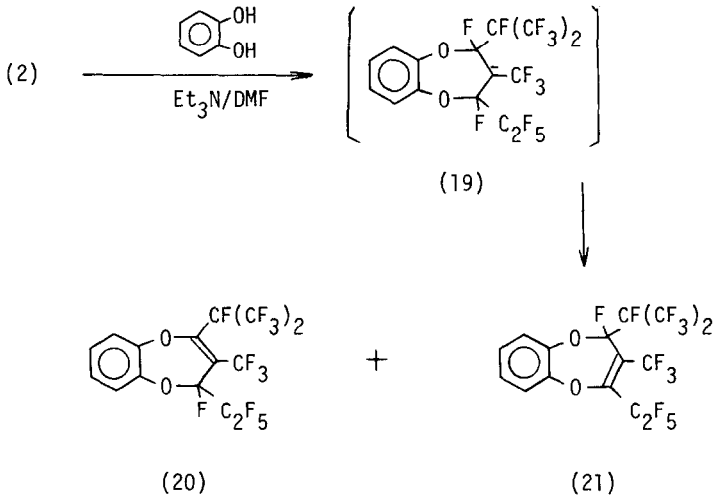
Scheme 5

-4.4 and -3.4 due to $CF(C\underline{F}_3)_2$ were the magnetically unequivalent CF_3 groups and that at δ 99.5 due to $C\underline{F}(CF_3)_2$ was an overlapping triplet of quartets of quartets split by $C\underline{F}_2CF_3$ and $CF(C\underline{F}_3)_2$ nuclei (J_{CF-CF_2} = 9.2 Hz). The signal at δ 35.0 due to $C\underline{F}_2CF_3$ nuclei was an overlapping doublet of quartets split by $C\underline{F}(CF_3)_2$ and $CF(C\underline{F}_3)_2$ nuclei ($J_{CF_2-CF_3}$ = 5.8 Hz). In the mass spectra, the molecular ion, M^+ 478 (17), 546 (18), and other appropriate fragment peaks appeared.

The first step in this reaction pathway, which is shown in scheme 5, should give the two isomeric forms (17) and (17'), of which (17') can proceed to the following cyclization, whereas (17) can not.

Reaction of (2) with catechol

Two fluorine atoms of (2) were replaced readily by catechol in dimethylformamide in the presence of triethylamine. Thus the reaction afforded 4-fluoro-4-(F-ethyl)-2-(F-1-methylethyl)-3-(F-methyl)-4H-1,5-benzodioxepin (20) (34 %), together with 4-fluoro-2-(F-ethyl)-4-(F-1-methylethyl)-3-(F-methyl)-4H-1,5-benzodioxepin (21) (8 %).



(20) (21)

Scheme 6

Various spectral data supported the structures of (20) and (21). The ^{19}F nmr spectrum of (20) showed peaks at δ -21.3, -5.6, -4.5, 2.3, 25.9, 45.3 and 99.1 in the ratio 3:3:3:3:1:2:1. The signal at δ -21.3 due to CF_3 was an overlapping doublet of doublets of triplets split by $C\underline{F}(CF_3)_2$, $C\underline{F}CF_2CF_3$ and $CFC\underline{F}_2CF_3$ nuclei ($J_{CF_3\text{-}CF}$ = 46.9 Hz, $J_{CF_3\text{-}C\underline{F}CF_2CF_3}$ = 27.3 Hz, $J_{CF\text{-}CFC\underline{F}_2CF_3}$ = 13.2 Hz). The signals at δ -5.6 and -4.5 were due to the magnetically unequivalent CF_3 groups on $CF(CF_3)_2$ ($J_{CF_3\text{-}CF_3}$ = 5.6 Hz, $J_{CF_3\text{-}CF}$ = 15.1 Hz) and that at δ 25.9 due to $C\underline{F}CF_2CF_3$ was an overlapping quartet of triplets split by $CFC\underline{F}_2CF_3$ and CF_3 nuclei ($J_{CF\text{-}C\underline{F}_2CF_3}$ = 7.3 Hz). In the ^{19}F nmr spectrum of (21), the signals were at δ -23.6 (CF_3,t, $J_{CF_3\text{-}C\underline{F}_2CF_3}$ = 6.6 Hz), -5.5 ($CF(CF_3)_2$,d, $J_{CF_3\text{-}CF}$ = 6.6 Hz), 2.2 ($CF_2C\underline{F}_3$,s), 42.2 (O-CF,d, $J_{OCF\text{-}CF}$ = 4.7 Hz), 46.3 ($C\underline{F}_2CF_3$,q) and 96.0 (CF,d of sep), in the ratio 3:6:3:1:2:1.

The reaction should proceed as shown in scheme 6. Release of fluoride ion from the carbanion (19) would give two isomers, (20) and (21). However, the former should be preferable to the latter, because the bulkier F-isopropyl group would tend to the sp^2 rather than the sp^3 carbon configuration.

Reviewing these results as a whole, it is interesting that perfluoroolefins (1) and (2) can be smoothly converted to new fluorinated seven-membered benzoheterocycles with *ortho*-bifunctional aromatics. This behavior as a convenient route to new types of heterocycles suggests that a wide variation of heterocycles can be prepared starting from perfluoroolefins derived from F-propene.

EXPERIMENTAL

General procedures will be described.

4-Fluoro-2-(F-ethyl)-3-(F-methyl)-1,5-benzoxazepines (6) (nc)

Into a mixture of 2-aminophenol (1.09 g, 10 mmol), F-2-methyl-2-pentene (1)(3.60 g, 12 mmol) and dry diethyl ether (30 ml), triethylamine (3.03 g, 30 mmol) was added dropwise, while keeping the temperature at -15∽-10°C. After stirring for 1h at that temperature, the reaction mixture was poured into water and the ethereal layer was seperated, washed with water, and dried over magnesium sulfate. After removing the solvent, the residual oily material was dissolved in n-hexane. This solution was subjected to column chromatography on silica gel, affording pure (6) (X=H) as an oil (1.68 g, 48 %). This compound was distilled although partial decomposition occured (bp 60-62°C/2 mmHg).

When 2-amino-4-methyl- and 2-amino-4-chlorophenols were used instead of 2-aminophenol in the above reaction, the corresponding products (6) ($X=CH_3$ and Cl), were obtained.

Hydrolysis of (6) (X=H)

(6) (X=H, 0.3 g, 0.86 mmol) and H_2O (1 ml) in dimethylformamide (2 ml) were stirred at room temperature. After 4h, the reaction mixture was poured into water, and the precipitates were collected by filtration. Recrystalization from chloroform gave 2-(3,3,3-trifluoropropionylamino)-phenol (nc), quantitatively.

^{19}F nmr($CDCl_3$) : δ -14.3 (CF_3, t, $J_{CF_3-CH_2}$ = 10.9 Hz)

^1H nmr : δ 3.60 (CH_2, q), 6.97, 7.90 (Ar-H), 8.87 (OH), 9.17 (NH)

Mass : M^+ 219 ; Anal. (%). Calcd for $C_9H_8NO_2F_3$; C, 49.32; H, 3.68; N, 6.39. Found ; C, 49.23; H, 3.61; N, 6.39.

2,4-Difluoro-4-(F-ethyl)-3-(F-methyl)-4H-1,5-benzodioxepins (10) (nc) and 2-(F-ethyl)-2-(1-F-methyl-2,2,2-trifluoroethyl)benzodioxoles (11) (nc)

A mixture of catechol (1.1 g, 10 mmol), sodium hydride (0.55 g, 23 mmol) and diethyl ether (25 ml) was stirred for 1.5h at room temperature. Into this mixture, (1)(3.30 g, 11 mmol) was added slowly at -10 ~ -7 °C. After 1.5h of stirring at that temperature, the reaction mixture was worked up as usual. Distillation of the oily product in vacuo gave (10) (X=H, 1.62 g, 44 %), bp 94-97 °C/18 mmHg, and (11) (X=H, 20 %)(nc). Further purification was performed by preparative glc (Silicone DC 550).

4-(F-Ethyl)-3-(F-methyl)-1H-1,5-benzodiazepin-2(3H)-one (14) (nc)

A mixture of o-phenylenediamine (1.08 g, 10 mmol), (1)(3.60 g, 12 mmol) and dimethylformamide (20 ml) was stirred at room temperature for 19h. The reaction mixture was worked up as before. The crude oily product was subjected to column chromatography and separated solid material was recrystallized from n-hexane giving pure (14)(0.21 g, 6 %), mp 119-120 °C.

7-(F-1-Methylethyl)-8-(F-ethyl)-9,14-benzoxazepino[4,3-b]1,6-benzoxazepines (16) (nc)

A mixture of 2-aminophenol (2.18 g, 20 mmol), (2)(4.50 g, 10 mmol) and dry dimethylformamide (20 ml) was stirred for 20h at room temperature. The reaction mixture was poured into water, and the products were extracted with diethyl ether. After removing the solvent, the residual oily material was dissolved in chloroform and the solution was subjected to column chromatography on silica, yielding pure (16)(X=H) as an oil which was decomposed readily on distillation (74 %).

2-Amino-4-methyl- and 2-amino-4-chlorophenols were used in the above reaction, and the products (16)(X=CH_3 and Cl) were isolated similarly.

2-Fluoro-4-(F-1-methylethyl)-3-(F-propylidene)-1,5-benzodiazepines (17)(nc) and 1H-1,7a-dihydro-7-(F-ethyl)-8-(F-1-methylethyl)-9,14-benzodiazepino[2,3-b]1,6-benzodiazepines (18)(nc)

o-Phenylenediamine (2.16 g, 20 mmol) was used in the above reaction, and worked up similarly. Separation by silica-gel column chromatography using chloroform as eluent gave 2-fluoro-4-(F-methylethyl)-3-(F-propylidene)-1,5-benzodiazepine (17) (X=H, 30 %) and 1H-1,7a-dihydro-7-((F-ethyl)-8-(F-1-methylethyl)-9,14-benzodiazepino[2,3-b]1,6-benzodiazepine (18) (X=H, 54 %), mp 157.5-159 °C.

In the same procedure, 2-amino-4-methyl- and 2-amino-4-chloroanilines were used yielding the products (17) and (18) ($X=CH_3$ and Cl) tabulated in Table.

4-Fluoro-4-(F-ethyl)-2-(F-1-methylethyl)-3-(F-methyl)-4H-1,5-benzodioxepin (20)(nc) and 4-fluoro-2-(F-ethyl)-4-(F-1-methylethyl)-3-(F-methyl)-4H-1,5-benzodioxepin (21)(nc)

A mixture of (2) (4.50 g, 10 mmol), catechol (1.10 g, 10 mmol), dimethylformamide (20 ml) and triethylamine (2.02 g, 20 mmol) was allowed to react for 20h at room temperature and worked up as previously described. The products were separated by column chromatography on silica gel giving (20) (34 %) and (21) (8 %).

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