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The synthesis of fluorinated α-pyrans *via* fluorinated vinylcopper reagents

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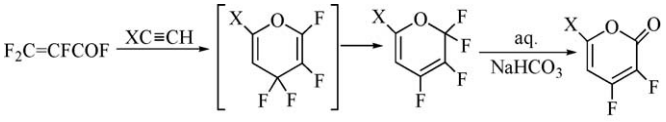
ABSTRACT

Fluorinated vinylcopper reagents were prepared *in situ via* reaction of fluorinated vinylbromides or iodides with cadmium or zinc powder followed by metathesis with Cu(I)Br. Hexafluoro-2-butyne was then added to the solution of the F-vinylcopper reagent which resulted in a stereospecific *syn* addition of the F-vinylcopper reagent to the alkyne to provide *in situ* the corresponding dienylcopper reagent. Subsequent acylation of the dienylcopper reagent gave a dienylketone, which spontaneously cyclized to the 2H-pyran. This methodology provides a useful one flask route to fluorinated 2H-pyrans.

1. Introduction

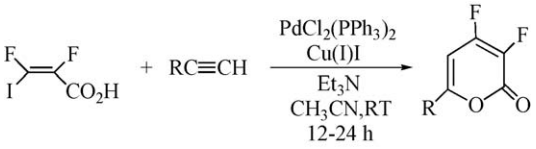
Organofluorine compounds have attracted the interest of pharmaceutical and agrochemists, since replacement of hydrogen atoms by fluorine atoms or fluoroalkyl groups can lead to major changes in lipophilicity and polarity factors which often leads to enhanced biological activity [1–5]. Pyrone derivatives are found in many natural products that display important biological activities. However, there has been little information reported on the fluorinated analogs of these interesting heterocycles. England and co-workers reported the seminal synthetic route to fluorine-containing 2-pyrones *via* the Diels–Alder reaction of perfluoroacryloyl fluorides with monosubstituted acetylenes, followed by isomerization of the adducts and hydrolysis in aqueous sodium bicarbonate [6] as illustrated in Eq. (1). Unfortunately, most of the fluorinated 2-pyrone



(1)

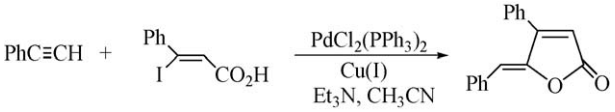
derivatives prepared by this methodology were obtained in poor yields.

Recently, we reported a more efficient and general synthetic route to this class of compounds utilizing the (2*E*)-2,3-difluoro-3-iodoacrylic acid synthon [7]. Under the co-catalysis of $PdCl_2(PPh_3)_2$ and Cu(I)I (2*E*)-2,3-difluoro-3-iodoacrylic acid reacted with 1-alkynes such as phenylacetylene, to form 3,4-difluoro-6-phenyl-2H-pyran-2-one, as illustrated in Eq. (2). A variety of alkynes were employed under similar conditions, such as aryl, alkyl, and pyridyl alkynes, and provided good to excellent isolated yields



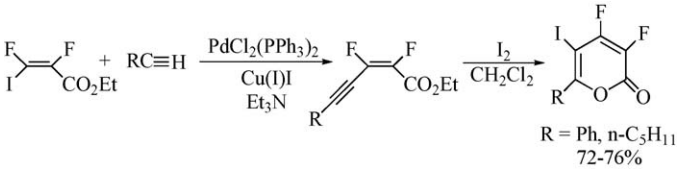
(2)

(43–71%). Non-fluorine-containing *cis*-β-haloacrylic acids, provided γ-(*Z*)-alkylidinebutenolides [8] under similar conditions Eq. (3). Our work gave only the



(3)

2-pyrones. As an extension of this work, we were able to prepare 3,4-difluoro-5-iodo-substituted-2-pyrones *via* Larock electrophilic cyclization of fluorine-containing enynes [7], as illustrated in Eq. (4). The iodo-substituted pyrones can



(4)

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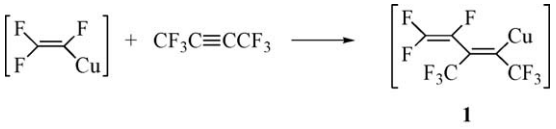
be further elaborated to provide more functionalized fluorinated 2-pyrones.

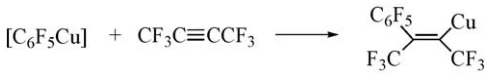
2. Results and discussion

In contrast to the limited work on fluorinated 2-pyrones, the formation of fluorinated α-pyrans has been achieved *via* the reaction of fluoroolefins with carbon nucleophiles derived from diethylmalonate, ethyl acetoacetate and acetylacetone [9–11]. Our recent work with F-vinyl and F-aryl copper reagents demonstrated that these reagents readily added to hexafluoro-2-butyne (*via syn* addition) to stereospecifically provide F-dienylcopper or F-arylvinylcopper reagents [12–14], as illustrated in [Eqs. (5) and (6)].



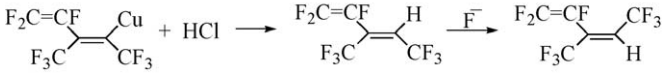
(5)

1



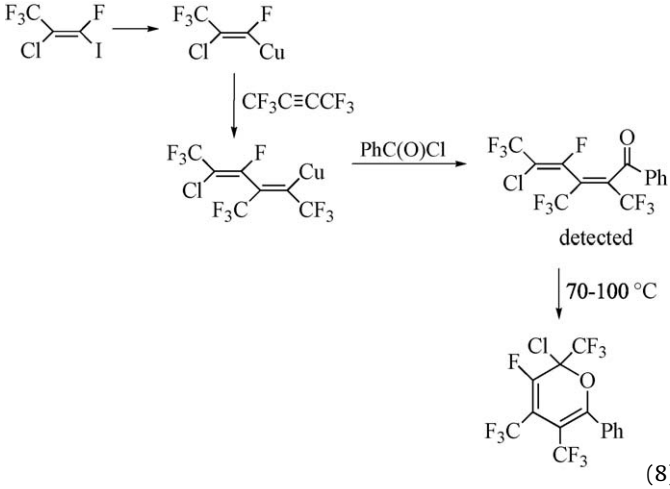
(6)

In a previous report, we demonstrated that F-vinylcopper reagents are easily acylated to provide the corresponding unsaturated ketones [15]. Consequently, acylation of the dienylcopper reagents, **1**, should provide the corresponding dienylketone. If the carbonyl oxygen is sufficiently nucleophilic to attack the vinyl carbon of the dienone, cyclization would yield the corresponding 2H-pyran derivative. Scheme 1 illustrates the overall concept. This approach would yield a one flask preparation of the 2H-pyrans, since all the reagents are added sequentially. Thus, when **1** was reacted with acyl halides, the dienylketone was formed, which spontaneously cyclized to the pyran derivative [16]. Table 1 summarizes the reactions studied *via* this overall process. In some cases protonation of the dienylcopper reagent occurred [17] to give the reduced diene. Authentic samples of these reduced products were prepared for comparison [18,19] Eq. (7).

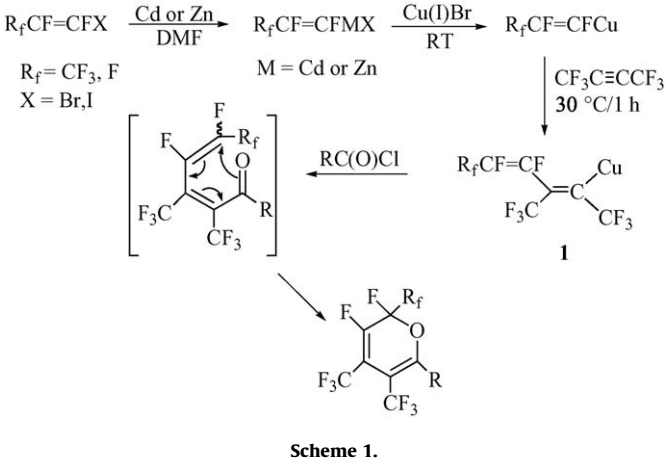


(7)

Increased steric hinderance at the vinyl carbon attacked by the carbonyl oxygen allowed us to observe (in solution) the dienylketone intermediate. Thus, when (*Z*)-$CF_3CCl{=}CFCu$ was added to hexafluoro-2-butyne, followed by acylation with benzoyl chloride, the dienylketone could be detected by ^{19}F NMR analysis of the reaction mixture Eq. (8).

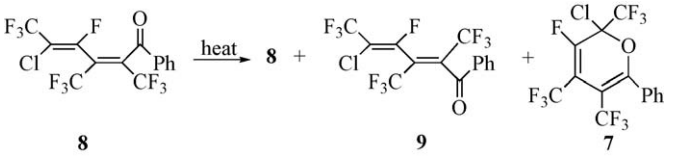


(8)



Scheme 1.

Subsequent heating of the dienylketone gave the corresponding pyran, as well as both isomers of the dienylketone Eq. (9). These results are summarized in Table 2.The reaction of $CF_3C{\equiv}CCO_2CH_3$ with (Z)-$CF_3CF{=}CFCu$ was attempted. However, ^{19}F NMR indicated that the reaction was not regiospecific, and this reaction was not investigated further.



8 **9** **7**

(9)

3. Experimental

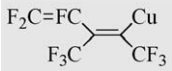
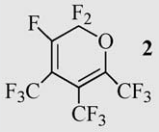
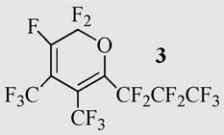
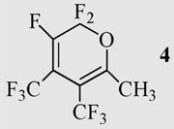
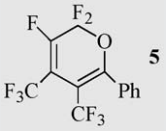
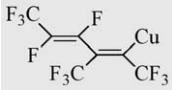
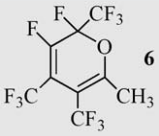
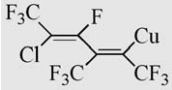
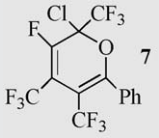
3.1. General experimental procedures

The ^{19}F NMR spectra were recorded on a JEOL FX90Q Spectrometer. Chemical shifts have been reported relative in ppm upfield from $CFCl_3$ and were generally determined in $CDCl_3$ solvent. ^{19}F NMR yields were determined by integration relative to internal benzotrifluoride. Routine ^{1}H NMR spectra were determined on a JEOL FX90Q Spectrometer. Chemical shifts are reported in ppm downfield from internal TMS. Infrared absorbance spectra were recorded on a Beckman Accu Lab 8 Spectrophotometer as liquid films between sodium chloride plates. All IR values have been reported in units of reciprocal centimeters. Low-resolution mass spectra (LRMS) were obtained with a Hewlett-Packard 5985 GC/MS system at 70 eV. DMF was distilled from P_2O_5 under partial vacuum. GLPC analyses were carried out on a Hewlett-Packard 5840A instrument using OV-101, SE-30 or Carbowax columns.

3.2. General procedure for the preparation of fluorinated-2H-pyrans

A 250 ml three-necked flask was equipped with a condenser, magnetic stirring bar, a septum port, a thermometer, and a glass tee leading to a source of dry nitrogen. Activated cadmium or zinc powder [20,21] and DMF were added to the flask. A portion (~1/4) of the fluorinated vinyl halide was added *via* syringe to the mixture and stirred until the reaction started, as evidenced by a sharp rise in temperature in some cases, where there was a long induction period, the reaction was initiated with a crystal of iodine or a small amount (40–50 μl) of PhC(O)Cl. After initiation, the remainder of the vinyl halide was gradually added so that the temperature was maintained at ~50 °C. After all the vinyl halide had been added, the reaction mixture was allowed to cool to room temperature (~1 h),

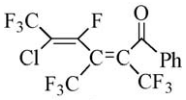
Table 1
2H-pyrans formed by the reaction of fluorinated dienylcopper reagents with acid halides.

Dienylcopper	Acid halide	2H-pyrans	Yield%[a]
	CF_3 C(O)Cl	 **2**	56
	CF_3 CF_2CF_2C(O)Cl	 **3**	42
	CH_3 C(O)Cl	 **4**	60
	PhC(O)Cl	 **5**	76
	CH_3C(O)Cl	 **6**	44
	PhC(O)Cl	 **7**	(50)

[a] Isolated yields; ^{19}F NMR yield in parentheses.

then pressure filtered under N_2 through a fritted glass filter to remove unreacted metal powder. Anhydrous Cu(I)Br was then added to the stirred filtered solution *via* a glass side-arm tube. Conversion of the vinylzinc or cadmium reagent to the vinylcopper reagent was complete within ~15 min as evidenced by ^{19}F NMR. The flask was fitted with a cold finger condenser cooled with a Dry Ice/isopropanol slush. Hexafluoro-2-butyne was then added drop wise *via* the cold finger condenser (maintaining the reaction temperature at ~40 °C). After completion of the butyne addition, stirring was continued for 1–2 h to complete the reaction (^{19}F NMR analysis confirmed complete conversion). Excess butyne was removed under vacuum (0.2 mm Hg), and the solution repressurized to atmospheric pressure with dry N_2. The acid chloride was added *via* syringe, the mixture stirred overnight at RT, then vacuum distilled to near dryness. The distillate was washed twice with ~5 volumes of water, the organic layer concentrated and dried over $MgSO_4$, gravity filtered, then fractionally distilled.

Table 2
Thermal isomerization of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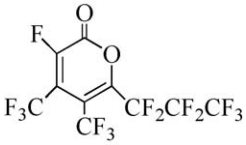
Time at 100 °C (h)	8%	9%	7%
0	100	0	0
(Flash distilled)	41	39	20
1.8	15	33	52
4.0	3	47	50

3.3. Preparation of 2,2,3-trifluoro-4,5,6-tris (trifluoromethyl)-2H-pyran, 2

Following the general procedure, trifluorovinylcopper was prepared from F_2C=CFBr (27.8 g, 173 mmol), Zn (11.30 g, 173 mmol) and Cu(I)Br (27.8 g, l94 mmol) in DMF (150 ml). Then hexafluoro-2-butyne (21.8 g, 173 mmol) was added to provide the dienylcopper reagent; ^{19}F NMR (DMF): δ −53.4 (qd, $^5J_{FF}$ = 12 Hz, $^4J_{FF}$ = 4 Hz), −58.2 (q, $^5J_{FF}$ = 12 Hz), −102.8 (dd, $^2J_{FF}$ = 73 Hz, $^3J_{FF}$ = 27 Hz), −115.8 (dd, $^3J_{FF}$ = 118 Hz, $^2J_{FF}$ = 73 Hz), −160.0 (partially overlapped dd, $^3J_{FF}$ = 118 Hz, $^3J_{FF}$ = 27 Hz). Then CF_3C(O)Cl (28 g, 212 mmol) was added to the dienylcopper reagent *via* the cold finger condenser. Work-up gave 32.7 g (56% based on CF_2=CFBr) of **2**, bp 97–97.5 °C (750 mm Hg), GLPC purity = 96%. ^{19}F NMR: δ −55.4 (qq, $^5J_{FF}$ = 12.1 Hz, $^5J_{FF}$ = 12.1 Hz), −58.2 (dqm, $^4J_{FF}$ = 24.2 Hz, $^5J_{FF}$ = 12.1 Hz), −66.9 (q, $^5J_{FF}$ = 12.1 Hz), −69.5 (brd, $^3J_{FF}$ = 15.1 Hz), −119.5 (qtm, $^4J_{FF}$ = 24.2 Hz, $^3J_{FF}$ = 15.1 Hz). GCMS: *m/z* (relative intensity): 340 (5.0, M^+), 321 (100, M-F). IR: 1625 (s), 1419 (s), 1358 (s), 1332 (s), 1215 (vs), 1121 (s).

3.4. Preparation of 2,2,3-trifluoro-4,5-bis(trifluoromethyl)-6-heptafluorobutyl)-2H-pyran, 3

Following the general procedure, the trifluorovinylcopper reagent was prepared from F_2C=CFBr (6.1 g, 38 mmol), Zn (2.98 g, 45.6 mmol), and Cu(I)Br (6.96 g, 48.5 mmol) in DMF (31 ml). Addition of $CF_3C{\equiv}CCF_3$ (8.5 g, 53 mmol) was followed by addition of $BF_3{\cdot}OEt_2$ (3.9 ml, 4.5 g, 31.7 mmol) (to convert any F^- to BF_4^- [22]). A portion of the dienylcopper reagent (28 ml) was reacted with $CF_3CF_2CF_2C$(O)Cl (2.8 ml, 4.34 g, 18.7 mmol). Work-up gave, after two distillations, 3.5 g (42% based on $CF_3CF_2CF_2COCl$) of **3**, bp 70–71 °C (67 mmHg). ^{19}F NMR: δ −54.1 (m), −58.2 (dqt, $^4J_{FF}$ = 23.8 Hz, $^5J_{FF}$ = 12 Hz, $^5J_{FF}$ = 1 Hz), −72.7 (d, $^3J_{FF}$ = 14 Hz), −81.4 (t, $^4J_{FF}$ = 9.8 Hz, −113.1 (qqm, $^5J_{FF}$ = 18 Hz, $^5J_{FF}$ = 12 Hz), −118.6 (qt, $^4J_{FF}$ = 23.8 Hz, $^3J_{FF}$ = 14.0 Hz), −123.7 (qm, $^6J_{FF}$ = 8.7 Hz). GCMS, *m/z* (relative intensity): 440 (9.0, M^+), 271 (93.2, M-$CF_2CF_2CF_3$), 243 (100, M-COC_3F_7). A major by-product (17% by GLPC) was assigned the structure, presumably formed by hydrolysis of 3



GCMS, m/z (relative intensity): 418 (6.6, M^+), 271 (77.2, M-COC_2F_5), 193 (100, C_5F_7).

3.5. Preparation of 2,2,3-trifluoro-4,5-bis(trifluoromethyl)-6-methyl-2H-pyran, 4

The dienylcopper reagent was prepared from F_2C=CFBr (11.5 g, 71.2 mmol), Zn (7.39 g, 113 mmol), Cu(I)Br (13.2 g, 91.8 mmol) and $CF_3C{\equiv}CCF_3$ (11.9 g, 73.4 mmol) in DMF (75 ml) as described in Section 3.2. Then $BF_3{\cdot}OEt_2$ (8.1 g, 56.9 mmol) was added to the dienylcopper solution, followed by CH_3C(O)Cl (5.6 g, 71 mmol).

The reaction mixture was stirred for 1.5 h at RT, then flash distilled; the distillate washed with cold water, extracted with 1.5 ml CH_2Cl_2 and the organic layer dried over $MgSO_4$. Fractional distillation gave 12.1 g (60%, based on $F_2C{=}CFBr$) of **4**, bp 59 °C/62 mmHg, GLPC purity = 97% [23]. ^{19}F NMR: δ −55.2 (q, $^5J_{FF}$ = 13.4 Hz), −58.7 (dq, $^4J_{FF}$ = 28.2 Hz, $^5J_{FF}$ = 13.4 Hz), −66.6 (d, $^3J_{FF}$ = 16.4 Hz), −130.3 (m, $^4J_{FF}$ = 28.2 Hz, $^3J_{FF}$ = 16.4 Hz). ^1H NMR: δ 2.32 (qq, $^5J_{FH}$ = 2.6 Hz, $^6J_{FH}$ = 1.1 Hz). GCMS, *m/z* (relative intensity): 286 (39.3, M^+), 267 (44.4, M-F), 236 (100, M-CF_2), 217 (26.6, M-CF_3).

3.6. Preparation of 2,2,3-trifluoro-4,5-bis(trifluoromethyl)-6-phenyl-2H-pyran, 5

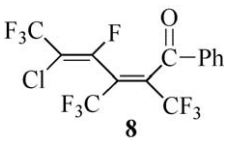
The dienylcopper reagents was prepared from $F_2C{=}CFBr$ (11.5 g, 71.2 mmol), Zn (9.11 g, 139 mmol), Cu(I)Br (10.90 g, 76.0 mmol), and $CF_3C{\equiv}CCF_3$ (12.1 g, 75.2 mmol) in DMF (65 ml) as described in Section 3.2. Then, $BF_3{\bullet}OEt_2$ (8.1 g, 56.9 mmol) was added to the dienylcopper reagent, followed by PhC(O)Cl (10.5 g, 74.9 mmol). The reaction mixture was stirred overnight at RT, then flash distilled; the distillate was washed with 200 ml cold water, extracted with 1.5 ml CH_2Cl_2, the lower layer separated and dried over $MgSO_4$. Fractional distillation gave 18.0 g (76%) based on $F_2C{=}CFBr$, of **5**, bp 70–73 °C/1 mm Hg; GLPC purity = 99%. ^{19}F NMR: δ −51.4 (q, $^5J_{FF}$ = 12 Hz), −57.5 (dq, $^4J_{FF}$ = 23 Hz, $^5J_{FF}$ = 12 Hz), −65.8 (d, $^2J_{FF}$ = 15 Hz), −129.4 (m). GCMS, *m/z* (relative intensity): 348 (100, M^+), 298 (92.5, M-CF_2), 105 (29.2, $Ph(O^+)$), 77 (36.8 (Ph^+).

3.7. Preparation of 2,3-difluoro-3,4,5-tris(trifluoromethyl)-6-methyl-2H-pyran, 6

Following the general procedure (*Z*)-$CF_3CF{=}CFCu$ was prepared from (*Z*)-$CF_3CF{=}CFI$ (15.5 g, 60.0 mmol), Cd (8.32 g, 74 mmol) and Cu(I)Br (11.85 g, 82.6 mmol) in DMF (60 ml) Then, $CF_3C{\equiv}CCF_3$ (12.9 g, 79.5 mmol) was added to provide the dienylcopper reagent. Then, $CH_3C(O)Cl$ (4.71 g, 60 mmol) was added to the reaction mixture *via* syringe. Work-up gave 8.9 g (44%, based on (*Z*)-$CF_3CF{=}CFI$) of **6**, bp 60–61 °C (47 mmHg). ^{19}F NMR: δ −55.0 (brq. $^5J_{FF}$ = 13.1 Hz, $^5J_{FH}$ = 2.6 Hz), −58.2 (dqd, $^4J_{FF}$ = 26.3 Hz, $^5J_{FF}$ = 13.1 Hz, $^5J_{FF}$ = 3.9 Hz), −80.6 (dd, $^4J_{FF}$ = 13.6 Hz, $^3J_{FF}$ = 5.8 Hz), −109.6 (dqm, $^3J_{FF}$ = 11.3 Hz, $^5J_{FF}$ = 3.9 Hz), −125.5 (dqq, $^4J_{FF}$ = 26.3 Hz, $^4J_{FF}$ = 13.6 Hz, $^3J_{FF}$ = 11.3 Hz). ^1H NMR: δ 2.33 (qq, $^5J_{FH}$ = 2.6 Hz, $^6J_{FH}$ = 1.1 Hz. GCMS, *m/z* (relative intensity): 336 (22.5, M^+), 267 (100, M-CF_3). (*E,Z*)-$CF_3CF{=}CFC(CF_3){=}C(CF_3)H$ was formed as a by-product (26% yield by ^{19}F NMR integration (before work-up); isolated yield 2.9 g (16%), bp 27 °C (46 mmHg). The ^{19}F NMR was identical to an authentic sample of (*E,Z*)-$CF_3CF{=}CFC(CF_3){=}C(CF_3)H$.

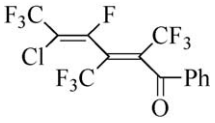
3.8. Preparation of 2-chloro-3-fluoro-4,5-bis(trifluoromethyl)-6-phenyl-2H-pyran, 7

Following the general procedure (*Z*)-$CF_3C(Cl){=}CFCu$ was prepared from (*Z*)-$CF_3CCl{=}CFI$ (1.10. g, 4.0 mmol), Cd (1.00 g, 8.9 mmol), Cu(I)Br (1.13 g, 7.9 mmol), CF_3 $C{\equiv}CCF_3$ (2.0 g, 12 mmol) in 5.4 ml DMF. Then $C_6H_5C(O)Cl$ (0.06 ml) was added to an aliquot (0.5 ml) of the dienylcopper reagent in DMF (5.4 ml). ^{19}F NMR analysis of the reaction mixture was in agreement



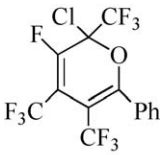
8

with the formation of the dienone (**8**), formed in 81% ^{19}F NMR yield (by integration *vs.* $C_6H_5CF_3$). ^{19}F NMR of (**8**): δ −58.1 (q, $^5J_{FF}$ = 11 Hz),−58.6 (CF_3, q, $^5J_{FF}$ = 11 Hz), −63.6 (d, $^4J_{FF}$ = 24 Hz), −87.4 (q, $^4J_{FF}$ = 24 Hz). GCMS, *m/z* (relative intensity): 416 (0.7, $^{37}ClM^+$), 414 (2.2, $^{35}ClM^+$), 379 (38.3, M-Cl), 105 (100, $PhCO^+$). The reaction mixture was flash distilled under vacuum into a liquid nitrogen cooled receiver. Analysis of the flash distillate by GCMS and ^{19}F NMR spectroscopy indicated two new compounds (in addition to (**8**). ^{19}F NMR and GCMS were consistent with the formation of



9

and



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^{19}F NMR of (**9**): δ −59.6 (CF_3,s), −59.8 (CF_3, s), −63.2 (d, $^4J_{FF}$ = 25 Hz), −87.5 (bd, q, $^4J_{FF}$ = 25 Hz. GCMS, *m/z* (relative intensity): 416 (0.6, $^{37}ClM^+$), 414 (1.7, $^{35}ClM^+$), 379 (11.5 M-Cl), 105 (100, $PhCO^+$), 77 (43.3, Ph^+). ^{19}F NMR of (**7**): δ −51.5 (q, $^5J_{FF}$ = 12 Hz),−57.2 (dq, $^4J_{FF}$ = 23 Hz, $^5J_{FF}$ = 12 Hz), −75.6 (d, $^4J_{FF}$ = 15 Hz), −122.4 (qq, $^4J_{FF}$ = 23 Hz, $^4J_{FF}$ = 15 Hz). GCMS, *m/z* (relative intensity): 416 (2.6, $^{37}ClM^+$), 414 (7.1, $^{35}ClM^+$), 379 (100, M-Cl), 139 (58.0, $C_2F_2C_6H_5$), 105 (46.0, $PhCO^+$), 77 (41.6, Ph^+), 69 (32.0, CF_3).

When an NMR tube containing an aliquot of the flash distillate was heated in an oil bath at 100 °C the dienone **8** was converted mainly to **9** and **10**. These results are tabulated in Table 2.

3.9. Preparation of (E,Z)-$CF_3CF{=}CFC(CF_3){=}C(CF_3)H$, 10

The (*E,E*)-($(CF_3CF{=}CFC(CF_3){=}C(CF_3)Cu$ was prepared from (*Z*)-$CF_3CF{=}CFI$ (6.45 g, 25.0 mmol), Cd (3.10 g, 27.6 mmol), Cu(I)Br (4.02 g, 28.0 mmol), and $CF_3C{\equiv}CCF_3$ (6.0 g, 37 mmol) in DMF (21 ml) *via* the procedure described in Section 3.2. Addition of aqueous HCl (2.0 ml of 12 M HCl), with cooling, followed by flash distillation under vacuum provided a distillate with two layers. The distillate was washed with 2 × 45 ml H_2O to remove DMF. The product was dried over 4 Å molecular sieves, then distilled to give 3.93 g (53%) of **10**, bp 57–58 °C (GLPC purity = 97%). ^{19}F NMR: δ −59.9 (pentet m, $^5J_{FF}$ = 9.8 Hz, $^3J_{FH}$ = 7.7 Hz, $^5J_{FF}$ = 2.4 Hz), −60.8 (qdd, $^5J_{FF}$ = 9.8 Hz, $^5J_{FF}$ = 8.0 Hz, $^4J_{FF}$ = 7.0 Hz), −68.8 (dd, $^4J_{FF}$ = 21.7 Hz, $^3J_{FF}$ = 9.3 Hz), −141.3 (dqqqd, $^3J_{FF}$ = 130 Hz, $^4J_{FF}$ = 21.7 Hz, $^4J_{FF}$ = 7.0 Hz, $^5J_{FF}$ = 2.4 Hz, $^4J_{FH}$ = 2.4 Hz), −160.0 (dqq, $^3J_{FF}$ = 130 Hz, $^3J_{FF}$ = 9.3 Hz, $^5J_{FF}$ = 8.0 Hz). ^1H NMR: δ 6.49 (qm, $^3J_{FH}$ = 7.3 Hz). GCMS, *m/z* (relative intensity), 294 (37.4, M^+), 275 (72.1, M-F), 225 (92.4, M-CF_3), 175 (100, M-CF_2CF_3).

3.10. Preparation of (Z)-$F_2C{=}CFC(CF_3){=}C(CF_3)H$, 11

The reagent, $F_2C{=}CFZnBr$, was prepared from $F_2C{=}CFBr$ (5.7 g, 35.6 mmol) and Zn (2.0 g, 30.6 mmol) in DMF (12 ml) according to the reported procedure [20]. Any unreacted $F_2C{=}CFBr$ was removed under vacuum. After repressurizing with N_2, Cu(I)Br (3.17 g, 22.1 mmol) was added to the zinc reagent mixture. Then, CF_3 $C{\equiv}CCF_3$ (5.6 g, 34 mmol) was added drop wise *via* a cold finger condenser (Dry Ice/isopropyl alcohol slush). The reaction mixture was stirred for 1 h at 30 °C; then excess alkyne removed under vacuum. After repressurization with N_2, the reaction mixture was cooled in an ice bath and 12 M HCl (1.5 ml) and H_2O (1.0 ml) were added and stirring continued for 20 min, at 10 °C, The product was

removed under vacuum; the distillate washed with H_2O to remove any DMF, and the clear, colorless lower layer analyzed by GLPC, purity = 97%, yield 3.13 g (72% based on $F_2C{=}CFZnX$) of **11**, bp 47–48 °C (746 mmHg). ^{19}F NMR: δ −58.4 (qdm, $^5J_{FF}$ = 11.4 Hz, $^3J_{FH}$ = 8.1 Hz), −60.5 (dqd, $^5J_{FF}$ = 11.5 Hz, $^5J_{FF}$ = 11.4 Hz, $^4J_{FF}$ = 6.8 Hz), −93.3 (dd, $^2J_{FF}$ = 53.0 Hz, $^3J_{FF}$ = 34.2 Hz), −108.5 (ddq, $^3J_{FF}$ = 113.3 Hz, $^2J_{FF}$ = 53.0 Hz, $^5J_{FF}$ = 11.5 Hz), −173.3 (ddm, $^3J_{FF}$ = 113.3 Hz, $^3J_{FF}$ = 34.2 Hz); ^1H NMR: δ 6.27 (q, $^3J_{FH}$ = 8.1 Hz). GCMS, *m*/*z* (relative intensity): 244 (28.7, M^+), 225 (34.9, M-F), 175 (100, M-CF_3).

4. Conclusion

F-vinylcopper reagents stereospecifically add (in a *syn* manner) to hexafluoro-2-butyne to provide an F-dienylcopper reagent. Subsequent acylation of the dienylcopper reagent produced a dienylketone, which spontaneously cyclized to the corresponding 2-H-pyran. All reactions are carried out in one flask and this methodology provides a new useful route to polyfluorinated 2-H pyrans.

Acknowledgements

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[16] Chambers, ref. 11, reported a reaction which could be interpreted *via* the same mechanistic scheme.
[17] The source of proton for production of the reduced dienes is not entirely clear; it could be carboxylic acid impurities in the acid chloride reagent–but distillation of CH_3COCl under anhydrous conditions from N,N-dimethylaniline did not eliminate reduced diene formation. It could also be due to HCl impurities in the acid halide, or in the case of CH_3COCl abstraction from the methyl group of the acid halide.
[18] The formation of isomerized reduced diene is most likely due to fluoride ion isomerization of the reduced diene from the original dienyl copper reagent. We have previously observed similar fluoride ion isomerization of a cis–$C(CF_3){=}C(CF_3)$– olefinic site in related diene systems [19].
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[22] In the absence of $BF_3{\bullet}OEt_2$, the major product after the addition of $CF_3CF_2CF_2COCl$, was $CF_3CF_2CF_2COF$, which was unreactive towards the copper reagent.
[23] ^{19}F NMR analysis of the reaction mixture indicated 15–20% **11**.