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Regio- and stereoselective synthesis of fluorinated enynes and dienes via 1,1- or 1,2-halofluoroalkenes

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Summary Monofluorinated enynes and dienes were synthesized stereospecifically through palladium-catalyzed condensation of 1-halo-1-fluoroalkenes or 1-halo-2-fluoroalkenes with monosubstituted alkynes or alkenes, or with allyltributyltin. The various halofluoroalkenes were efficiently and selectively prepared either from fluorinated unsaturated acids or through 'XF' addition to alkynes.

fluoroenyne / fluorodiene / halofluoroalkene / palladium-catalysed condensation

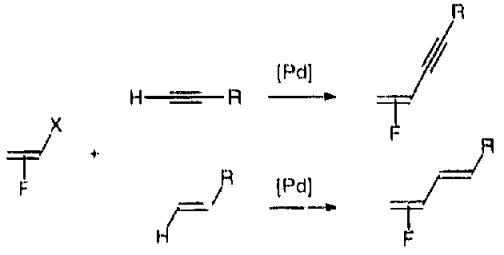
Résumé — Synthèse régio- et stéréosélective d'énynes et de dièns fluorés par l'intermédiaire de 1,1- ou 1,2-halogénofluoroalcènes. Des énynes et des dièns monofluorés ont été préparés par condensation stéréospécifique, catalysée au palladium, de 1-halogéno-1-fluoroalcènes ou de 1-halogéno-2-fluoroalcènes avec des alcynes vrais, des alcènes, ou de l'allyltributylétain. Les halogénofluoroalcènes ont été préparés sélectivement soit à partir d'acides fluorés insaturés, soit par addition de 'XF' à un alcyne.

fluoroényne / fluorodiène / halogénofluoroalcène / condensation catalysée au palladium

Introduction

Monofluorinated analogs of natural molecules often exhibit interesting biological activity, since the fluorine atom mimics a hydrogen atom by its bulk but confers a different chemical reactivity to the molecule [1]. Compounds in which the fluorine atom occupies a vinylic position are particularly interesting synthetic targets, requiring correct control of the position and stereochemistry of the fluorinated double bond. For instance, several analogs of insect pheromones bearing one [2–4] or more [5] fluorine atom in vinylic positions have been synthesized in the last years. A few accesses to monofluorinated enynes [3] and conjugated dienes [2, 6] have been developed. The use of fluorinated organometallics has allowed the synthesis of various species fluorinated at a vinylic position [7, 8]. Palladium-catalyzed condensation of organozinc compounds, fluorinated or not, with halofluoroalkenes has been used to synthesize di- or tetrafluorinated dienes [5, 9] and enynes [10].

The present work reports a method for the synthesis of monofluorinated enynes and conjugated dienes, based on direct palladium-catalyzed condensation of alkynes or alkenes on 1,1- or 1,2-halofluoroalkenes, according to scheme 1. A synthesis of fluorinated 1,4-diene is also described. Part of this work has appeared as preliminary communications, concerning the use of 1-bromo-1-fluoroalkenes [11] and 1-bromo-2-fluoroalkenes [12].



Scheme 1

Preparation of bromo- or iodofluoroalkenes

Synthesis of 1-bromo-1-fluoroalkenes

The most direct way to 1-bromo-1-fluoroalkenes is the Wittig-type reaction between a carbonyl compound, fluorotribromomethane and a phosphine, developed by Burton [13], but this method could not be made stereoselective.

* Correspondence and reprints

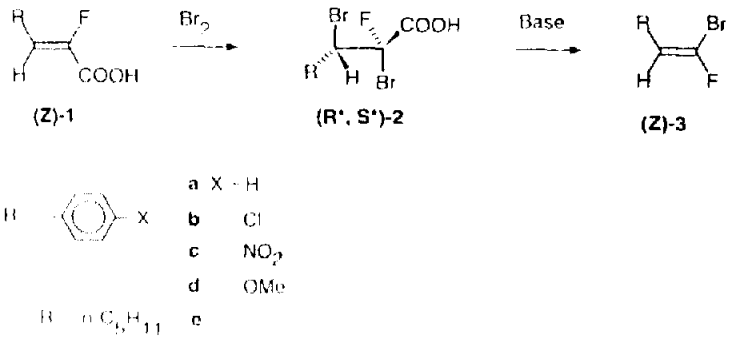
Few stereoselective accesses to 1-halo-1-fluoroalkenes have been reported. Recently 1-iodo-1-fluoroalkenes have been prepared via (fluorovinyl)stannanes [14, 15].

We obtained the (*Z*)-1-bromo-1-fluoroalkenes by bromine addition on unsaturated fluoroacids, followed by decarboxylative elimination (scheme 2). The starting fluoroacids (*Z*)-**1** were made available either through Darzens condensation of ethyl fluoroacetate with aldehydes [16], followed by saponification, or through in situ bromine-catalyzed isomerisation of the (*E*) isomer, conveniently obtained from Wittig-Horner reaction of ethyl (diethylphosphono)fluoroacetate with the appropriate aldehyde [17].

As can be seen from table I, bromination of aromatic (*Z*)-2-fluoroacids led quite selectively to (2*R**,3*S**)-2,3-dibromo-2-fluoroacids, except for (**Z**)-**1d**, bearing an electron-donating substituent on the benzene ring. The use of 4-(dimethylamino)pyridinium tribromide instead of bromine only slightly improved the selectivity. In the case of the aliphatic fluoroacid (**Z**)-**1e**, attempts to use bromine led to a mixture containing both addition and substitution products, whereas 4-(dimethylamino)pyridinium tribromide appeared as a satisfying brominating agent both for yield and stereoselectivity.

The (*E*) fluoroacids could not be stereoselectively brominated in the same way to (2*R**,3*R**)-2,3-dibromo-2-fluoroacids, due to their rapid bromine-catalyzed isomerization to the (*Z*) isomers. Bromination of (*E*)-2-fluoro-3-phenylprop-2-enoic acid followed under several reaction conditions. The use of bromine-induced rapid isomerization of the starting acid to the (*Z*) isomer (completed in 2 min at room temperature) followed by much slower addition of bromine, leading therefore exclusively to the (2*R**,3*S**)-2,3-dibromo-2-fluoro-3-phenylpropanoic acid. With pyridinium tribromide the isomerisation rate was of the same order as the bromination rate, so that both diastereomers were obtained in proportions varying with the reaction progress.

The following step is decarboxylative hydrogen bromide elimination on the 2,3-dibromo-2-fluoroacids. The corresponding reaction on unfluorinated substrates is known to be stereoselective with *anti* elimination of carbon dioxide and bromide, providing it is performed in a solvent of sufficiently low polarity such as acetone [18]. As expected, the same stereoselectivity was obtained: in acetone solution, (**2*R**,3*S**)-2** yielded exclusively (*Z*)-1-bromo-1-fluoroalkenes (**Z**)-**3**, and the (**2*R**,3*S**)-2** + (**2*R**,3*R**)-2** diastereomer mixture led to (**Z**)-**3** + (**E**)-**3** in approximately the same proportions. The base suitable for elimination was either sodium hydrogen carbonate for aromatic compounds bearing no electron-withdrawing groups, or tetrabutylammonium hydroxide for the other substrates.



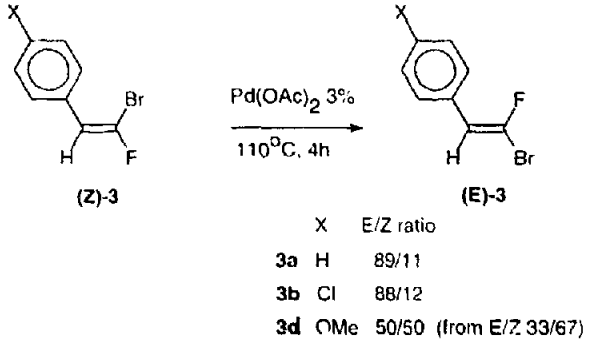
Scheme 2

Table I. Preparation of 1-bromo-1-fluoroalkenes RCH=CFBr from unsaturated fluoroacids **1**

Starting material	*R*	*Bromination*			*Decarboxylative elimination*		
		Brominating agent[a]	*Isolated yield of* **2**	(*R**,*S**)/(*R**,*S**) *ratio*	*Base*	*Isolated yield of* **3**	*Z*/*E* ratio
(**Z**)-**1a**	Ph	Br_2	84	100/0	$NaHCO_3$	82	100/0
(**E**)-**1a**	Ph	Br_2	100[b]	100/0			
(**E**)-**1a**	Ph	Br_2, PyH$^+$[c]	83[b,c]	12/88			
(**Z**)-**1b**	4-ClPh	Br_2	88	100/0			
(**Z**)-**1c**	4-NO_2-Ph	Br_2	82	100/0	Bu_4N^+ ^-OH	69	100/0
(**Z**)-**1d**	4-OMe-Ph	Br_2	93	67/33	Bu_4N^+ ^-OH	83	100/0
(**Z**)-**1d**	4-OMe-Ph	Br_2, Me_2N-PyH$^+$	85	74/26	$NaHCO_3$	70	67/33
(**Z**)-**1e**	nC_5H_{11}	Br_2, Me_2N-PyH$^+$	72	88/12	$NaHCO_3$	60	86/14

[a] Conditions used (unless otherwise indicated): 1.1 equiv. of brominating agent, refluxing CCl_4, 5 h. [b] Yield determined by NMR. [c] Pyridinium tribromide: 5 equiv., CH_2Cl_2, 25 °C, 2 days. [d] Other components: (**E**)-**1a** 11%, (**Z**)-**1a** 6%. With 4-dimethylaminopyridinium tribromide a very similar mixture was obtained. [e] Refluxing CH_2Cl_2, 18 h.

Since the method described above was not suitable for preparing (*E*)-1-bromo-1-fluoroalkenes, conditions for isomerization of (**Z**)-**3** to (**E**)-**3** were investigated. *Z*/*E* isomerization of alk-1-enylbenzenes has been shown to be catalyzed by palladium (II) [19]. Fairly pure (*E*)-1-bromo-1-fluoro-2-arylethylenes (**E**)-**3a** and (**E**)-**3b** could be prepared by heating the (*Z*) isomer in the presence of palladium (II) diacetate without solvent, as shown in scheme 3. A small amount of (*Z*) isomer remained present even at longer reaction times. The corresponding 4-methoxy-substituted compound (**E**)-**3d** could not be efficiently isomerized under those conditions.



Scheme 3

Synthesis of 1-bromo-2-fluoroalkenes and 1-iodo-2-fluoroalkenes

• *Addition of XF elements to alkynes (X = Br, I)*

Association of a positive halogen reagent with a fluoride source is an efficient way of adding XF elements to alkenes or alkynes. *Anti* addition of BrF to alkynes has been performed by using *N*-bromoacetamide in the presence of fluorohydric acid [20], or more efficiently *N*-bromosuccinimide (NBS) with pyridinium poly(hydrogen fluoride) [21]. Various other reagents have been reported in the case of alkenes, for instance triethylamine tris hydrofluoride as fluoride source [22]; 1,3-dibromo-5,5-dimethylhydantoin (DBH) was shown to be a more efficient brominating agent than NBS [23].

Bromofluorination of monosubstituted alkynes by DBH as positive bromine source, along with pyridinium poly(hydrogen fluoride) as fluoride source in sulfolane actually gave satisfying results. The reaction was totally regioselective, leading to the bromine atom on the unsubstituted side of the double bond. The (*E*) bromofluoroalkenes **4** were obtained with a good stereoselectivity (scheme 4, table II).

Table II. Preparation of 1-halo-2-fluoroalkenes RCF=CHX by addition of "XF" to alkynes

X	*R*	*Product*	*Isolated yield (%)*	*Z/E ratio*
Br	Ph	**4a**	93	92:8
Br	n-C_5H_{11}	**4b**	65	90:10
I	Ph	**5a**	72	95:5
I	n-C_5H_{11}	**5b**	83	98:2

The use of NBS instead of DBH led mainly to the dibromoalkene RCBr=CHBr. The same compound was formed as an important byproduct (ca 20%) when the reaction was performed in dichloromethane instead of sulfolane.

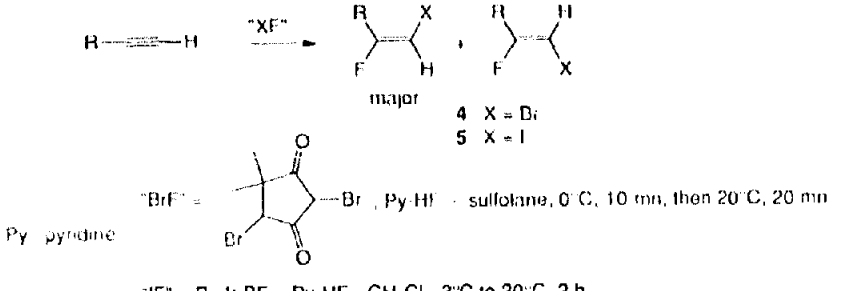
When the fluorinated enyne (**E**)-**13a** (described below) was treated with NBS and pyridinium poly(hydrogen fluoride) in sulfolane, the only product formed was the naphthalene derivative **6** (scheme 5), in a way analogous to reported cyclizations induced by positive iodine [24]. The scope and extent of this reaction was not further investigated.

Iodofluorination of alkynes has been effected by *N*-iodosuccinimide and pyridinium poly(hydrogen fluoride) [21], by methyliodine(III) difluoride [25] or by *N*-iodosuccinimide and polymer-supported hydrogen fluoride [26]. In the two latter cases *syn* stereoselectivity was reported. Bis(pyridine)iodonium (I) tetrafluoroborate has been shown to be an efficient positive iodine source towards alkynes [27] and to effect *anti* iodofluorination of alkenes [28]. Therefore association of this reagent with a fluoride source could be expected to allow iodofluorination of alkynes.

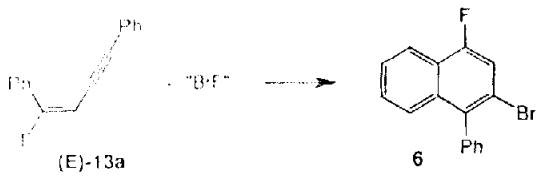
Synthesis of 1-iodo-2-fluoroalkenes **5** was efficiently performed by iodolipyridinium tetrafluoroborate with pyridinium poly(hydrogen fluoride) in dichloromethane. The reaction led nearly exclusively to the *E* isomer of **5**, corresponding to *anti* stereoselectivity. The results are summarized in scheme 4 and table II.

• *Bromination dehydrobromination of unsaturated fluoroesters*

Some disubstituted 1-bromo-2-fluoroalkenes were easily obtained from the unsaturated fluoroesters **7**: bromination of either *E* or *Z*-**7** followed by dehydrobromination



Scheme 4



Scheme 5

under mild conditions (DBU, 20 °C) afforded selectively *Z*-**9**, as shown in scheme 6. The 1-bromo-2-fluoroalkenes **9a** and **9b** were obtained from **7a** and **7b** with global isolated yields of 76% (*Z*/*E* ratio 95:5) and 61% (*Z*/*E* ratio 98:2) respectively.

The observed stereoselectivity results from the previously discussed selectivity of bromine addition, leading in all cases to the *R**,*S** dibrominated compound **8**, followed by *anti* dehydrobrominations. Preparations of monofluoroalkenes making a similar use of *anti* elimination reactions have been reported [28, 29].

Palladium-catalyzed condensations

The structures of the fluorinated 1,3-enynes and 1,3-dienes synthesized through palladium-catalyzed condensations are summarized in scheme 7.

Synthesis of fluorinated 1,3-enynes

Palladium-catalyzed condensation of either 1,1- or 1,2-halofluorinated alkenes with monosubstituted alkynes proceeded with good yields, under conditions similar to those described for other vinylic bromides or iodides [30]: palladium diacetate and triphenylphosphine as catalyst, in refluxing butylamine or triethylamine. The reaction was totally stereoselective, except in the case of the most hindered substrates **9**, which required harder reaction conditions. The results are summarized in table III.

It can be noticed that no Pd(0)-catalyzed isomerization of (**Z**)-**3** occurred under those conditions. Addition of CuI to the reaction mixture, often recommended in this type of reaction [31], did not improve our results, but catalyzed oxidative coupling of the alkyne when the reaction was not performed under inert atmosphere.

When attempted in butylamine, reaction of **3c** with an alkyne under the conditions described above did not lead to the expected enyne, but to the amide **15c**. Formation of **15c** from **3c**, and of its unsubstituted analog **15a** from **3a**, were checked to occur without the presence of an alkyne, and to require the presence of the palladium catalyst. This result can be explained by palladium-catalyzed substitution of bromine by butylamine [32], followed by hydrolysis of the resulting fluoroenamine (scheme 8); fluoroenamines are known to undergo fast hydrolysis to amides [33]. Use of triethylamine allowed to obtain the normal condensation reaction of **3c**.

Table III. Palladium-catalyzed condensation of halofluorinated alkenes with monosubstituted alkynes R–C≡CH. Reaction conditions: alkyne 1-2 equiv, $Pd(OAc)_2$ 2%, PPh_3 4%, *n*-$BuNH_2$ or NEt_3, reflux, 3 h.

Starting material	*R*	*Product*	*Isolated yield (%)*	*E/Z ratio*
(**Z**)-**3a**	Ph	**10a**	71	100:0
(**E**)-**3a**[a]	Ph	**10a**	81	10:90
(**Z**)-**3a**	*n*-C_5H_{11}	**11a**	63	100:0
(**Z**)-**3a**	CMe_2OH	**12a**	40	100:0
(**Z**)-**3b**	Ph	**10b**	75	100:0
(**Z**)-**3b**	*n*-C_5H_{11}	**11b**	73	100:0
(**Z**)-**3c**	Ph	**10c**	71	100:0
3d[b]	Ph	**10d**	93	67:33
(**E**)-**5a**	Ph	**13a**	83	100:0[c]
(**E**)-**5b**	Ph	**13b**	75	100:0[c]
(**Z**)-**9a**[c]	Ph	**14**[f]	68[d]	40:60

[a] Containing 10% *Z* isomer. [b] 67:33 *Z*/*E* mixture. [c] The minor *Z* isomer (from minor *E* isomer in the starting material) was no longer detected after purification of the product. [d] Other products: *E* and *Z* **1a**. [e] Containing 5% *E* isomer. [f] Phenylacetylene 3 equiv, $Pd(OAc)_2$ 4%, PPh_3 8%, reaction time 24 h.

Synthesis of fluorinated 1,3-dienes

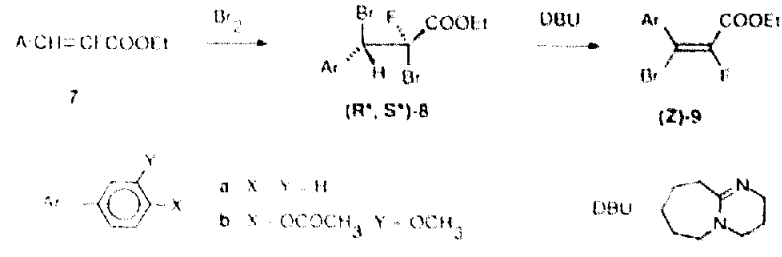
Reaction of 1,1- or 1,2-halofluoroalkenes with suitable ethylenic compounds under the same conditions as above led to fluorinated 1,3-dienes **16**–**19** (scheme 7), as shown in table IV.

In all cases the reaction was stereoselective concerning the unfluorinated double bond as usual in such reactions, only the hydrogen atom *trans* to the substituent was removed [34]. It was also stereoselective concerning the halogenated double bond which retained its initial stereochemistry, except for substrates **9** which led to an *E*/*Z* mixture.

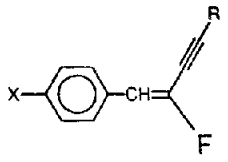
Preparations of the 2-fluorinated isomer of the 1-fluorinated diene **17** have been described recently [35].

Synthesis of fluorinated 1,4-dienes

Direct palladium-catalyzed coupling of vinylic halides with a carbon–hydrogen bond does not occur in the



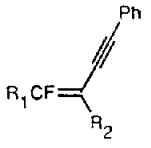
Scheme 6



R = Ph **10** a X = H; b Cl; c NO_2; d OMe

R = n-C_5H_{11} **11** a X = H; b Cl

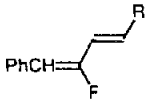
R = CMe_2OH **12** a X = H



R_1 = Ph, R_2 = H **13a**

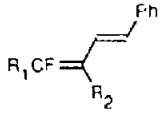
R_1 = n-C_5H_{11}, R_2 = H **13b**

R_1 = COOEt, R_2 = Ph **14**



R = 4-Me-Ph **16**

R = COOEt **17**



R_1 = Ph, R_2 = H **18a**

R_1 = n-C_5H_{11}, R_2 = H **18b**

R_1 = COOEt, R_2 = Ph **19**

Scheme 7

allylic position, therefore preparation of 1,4-dienes requires the use of an organometallic compound. Allylic tributyltin derivatives are known to undergo easy palladium-catalyzed condensation with vinylic halides [36]. Reaction of allyltributyltin with (**Z**)-**3a** in the presence of tetrakis(triphenylphosphine)palladium in refluxing tetrahydrofuran led to pure (*E*)-2-fluoro-1-phenylpenta-1,4-diene **20** in a 79% yield (scheme 9).

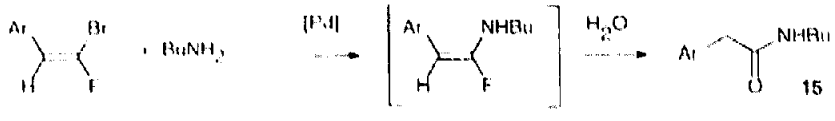
Conclusion

Preparations of 1,1- and 1,2-halofluoroalkenes have been described. Palladium-catalyzed condensation on these compounds appears as an efficient method for stereoselective synthesis of fluorinated enynes and dienes. Direct condensation with alkynes or alkenes without the intermediacy of an organometallic compound is often possible; except in the case of hindered halofluoroalkenes, it proceeds quite stereoselectively.

Experimental section

^{1}H NMR spectra were recorded on a Bruker AM 250 spectrometer, ^{13}C NMR spectra on a Bruker AM 250 or a Bruker AM 400 spectrometer. Chemical shifts (δ) are given in ppm downfield from tetramethylsilane as internal standard. For ^{13}C NMR spectra indications in parentheses (CH_3, CH_2, CH or C) refer to the number of H atoms borne by the considered carbon, as determined from the *J*-spectrum. When the peak intensity corresponds to more than one carbon it is also mentioned (eg, 2CH). In the tables these indications are not detailed for each carbon, but the assignments made are always consistent with the corresponding data.

Infrared spectra were recorded on a Perkin-Elmer 599 instrument. Mass spectra (MS) were obtained on a

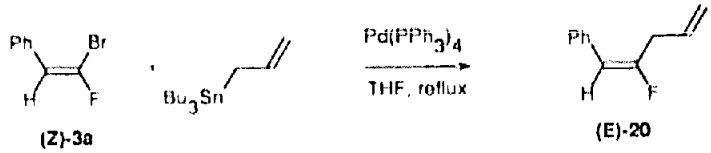


Scheme 8

Table IV. Palladium-catalyzed condensation of halofluorinated alkenes with ethylenic compounds R-CH=CH_2. Reaction conditions: alkene 1, 2 equiv, $Pd(OAc)_2$ 2%, PPh_3 4%, NEt_3, reflux, 2 h

Starting material	*R*	*Product*	*Isolated yield (%)*[a]	*Product stereochemistry*	*Separated yield (%)*[b]
(**Z**)-**3a**	4-Me-Ph	**16**	92	(*E*,*E*)/(*Z*,*E*) 95:5	73 (*E*,*E*); 3.9 (*Z*,*E*)
(**Z**)-**3a**	COOEt	**17**[c]	90	(*E*,*E*)/(*Z*,*E*) 95:5	71 (*E*,*E*)
(**E**)-**4a**[d]	Ph	**18a**	95	(*E*,*E*)/(*Z*,*E*) 86:14	42 (*E*,*E*); 4 (*Z*,*E*)
(**E**)-**5b**	Ph	**18b**	93	(*E*,*E*)	82
(**Z**)-**9a**[e]	Ph	**19**[f]	95	(*E*,*E*)/(*Z*,*E*) 74:26	

[a] Before stereoisomer separation. [b] Isolated yield for separated, purified stereoisomers from chromatography on silica gel. [c] $Pd(OAc)_2$ 4%, PPh_3 6%, reaction time 18 h. [d] Containing 8% *Z* isomer. [e] Containing 5% *E* isomer. [f] Styrene 3 equiv, $Pd(OAc)_2$ 5%, PPh_3 10%.



Scheme 9

Nermag R10-10C mass spectrometer. Elemental analyses were performed by the Service de Microanalyse de l'Université Pierre et Marie Curie. Melting points were measured using a Büchi 510 capillary apparatus and are uncorrected.

Solvents were distilled on appropriate reagents (diethyl ether and THF over sodium-benzophenone after drying on potassium hydroxide, dichloromethane and triethylamine over calcium hydride, pentane on phosphoric anhydride).

Bromination: 2,3-dibromo-2-fluoroacids **2**

• *General procedure for bromination by molecular bromine*

Bromine (1.75 mL, 33 mmol, 1.1 equiv) was added dropwise to a solution of 2-fluoroprop-2-enoic acids **1a**, **1b**, **1d** (30 mmol, 1 equiv) in tetrachloromethane (100 mL), or **1c** (30 mmol) in dichloromethane (100 mL). The reaction mixture was stirred at reflux temperature for 5 h. The cooled solution was washed with a solution of sodium hydrogenosulfite in order to eliminate unreacted bromine, then with water. The organic phase was dried ($MgSO_4$) and the solvent was evaporated under reduced pressure. The residue was purified by recrystallization in tetrachloromethane.

The ^1H and ^{13}C NMR data of compounds **2** are displayed in tables V and VI respectively.

• *(2R*,3S*)-2,3-Dibromo-2-fluoro-3-phenylpropanoic acid* **(R*,S*)-2a**

Yield 84%, Mp 143–144 °C.

IR (KBr): 3060, 2910, 2835, 1750, 1500, 1460, 1420, 1355, 1315, 1260, 1215, 1160, 1085, 1045, 1010, 930, 895, 850, 760, 750, 720, 700, 630, 620, 605, 565, 520 cm^{-1}.

MS (EI, 70 eV): *m/z* 247, 245 (M^+ – Br), 203, 202, 200, 166, 165, 146, 137, 129, 122, 121, 120, 118, 110, 103, 102, 101, 94, 89, 82, 81, 80, 79, 77, 76, 75, 74, 69, 63, 57.

• *(2R*,3S*)-2,3-Dibromo-2-fluoro-3-(4-chlorophenyl)propanoic acid* **(R*,S*)-2b**

Yield 88%, Mp 166–167 °C.

IR (KBr): 3020, 2945, 1750, 1730, 1590, 1490, 1415, 1260, 1210, 1110, 1090, 1045, 1015, 890, 825, 800, 775, 725, 600, 585 cm^{-1}.

MS (EI, 70 eV): *m/z* 364, 362, 360, 358 (M^+), 281, 279, 236, 234, 202, 200, 180, 120, 111, 99, 82, 75, 63, 57.

• *(2R*,3S*)-2,3-Dibromo-2-fluoro-3-(4-nitrophenyl)propanoic acid* **(R*,S*)-2c**

Yield 82%, Mp 211–212 °C.

MS (EI, 70 eV): *m/z* 292, 290 (M^+ – Br), 247, 245, 217, 216, 211, 189, 187, 165, 150, 136, 133, 120, 108, 101, 94, 81, 77, 75, 63, 57, 55.

MS (CI, NH_3): *m/z* 391, 389, 387 ($M + NH_4^+$).

• *2,3-Dibromo-2-fluoro-3-(4-methoxyphenyl)-propanoic acid* **(R*,S*)-2d** + **(R*,R*)-2d**

Yield 93%, 67:33 mixture of (*R*,S**)/(*R*,R**) from ^1H NMR.

IR (KBr): 3060, 3025, 1645, 1605, 1510, 1460, 1280, 1250, 1180, 1075, 905, 805, 730, 650 cm^{-1}.

MS (EI, 70 eV): *m/z* 314, 312, 310 (M^+ – CO_2), 305, 303, 230, 224, 215, 196, 179, 176, 161, 180, 170, 89, 81, 77, 63, 57.

• *(2R*,3S*)-2,3-Dibromo-2-fluorooctanoic acid* **(R*,S*)-2e**

Solid 4-(dimethylamino)pyridinium tribromide (2.72 g, 7.5 mmol, 1.2 equiv) was added to a solution of (*E*)-2-fluorooct-2-enoic acid (*E*)-**1e** (1.00 g, 6.25 mmol, 1 equiv) in dichloromethane (10 mL), and the mixture was stirred at reflux temperature for 18 h. The cooled solution was diluted with dichloromethane and washed with a solution of sodium hydrogenosulfite in order to eliminate unreacted 4-(dimethylamino)pyridinium tribromide. The organic phase was washed with a 20% aqueous hydrochloric acid solution, dried ($MgSO_4$), and the solvent was evaporated under reduced pressure to give **1e** (1.43 g, 72%) as a colorless oil (88:12 (*R*,S**)/(*R*,R**) mixture according to ^1H NMR).

Table V. ^1H NMR spectra (CD_3COCD_3, 250 MHz) of 2,3-dibromo-2-fluoroacids **2**, R–CHBr–CFBr–COOH.

Compound	*R*	*CH*		*R*
		δ	$^3J_{HF}$	
(*R*,S**)-**2a**	Ph	5.61	26.5	7.40 (m, 3H), 7.60 (m, 2H)
(*R*,S**)-**2b**	4-Cl-Ph	5.92	26.8	7.51 (d, 7.5 Hz, 2H), 7.68 (d, 7.5 Hz, 2H)
(*R*,S**)-**2c**	4-NO_2-Ph	6.52	25.0	7.98 (d, 8.9 Hz, 2H), 8.26 (d, 8.9 Hz, 2H)
(*R*,S**)-**2d**	4-OMe-Ph	5.57	26.5	3.85 (s, 3H), 6.92 (d, 8.7 Hz, 2H), 7.51 (d, 8.7 Hz, 2H)
(*R*,R**)-**2d**	4-OMe-Ph	5.51	25.0	3.80 (s, 3H), 6.85 (d, 8.5 Hz, 2H), 7.50 (d, 8.5 Hz, 2H)
(*R*,S**)-**2e**	*n*-C_6H_{13}	4.50[a]	25.1	0.90 (t, 6.0 Hz, 3H), 1.32 (m, 6H), 1.71 (m, 1H), 2.03 (m, 1H)

[a] Dd, J = 25.1 Hz, 11.3 Hz and 2.2 Hz.

Table VI. ^{13}C NMR spectra (CD_3COCD_3, 62.8 MHz) of 2,3-dibromo-2-fluoroacids **2**. R–$C^{(1)}$HBr–$C^{(2)}$FBr–$C^{(3)}$OOH. For R = aryl, the carbon atoms at positions 1, 2 (and 6), 3 (and 5), 4 of the phenyl ring are respectively referred to as $C^{(i)}$, $C^{(o)}$, $C^{(m)}$, $C^{(p)}$.

Compound	*R*	$C^{(1)}$	$C^{(2)}$	$C^{(3)}$	$C^{(i)}$	$C^{(o)}$	$C^{(m)}$, $C^{(m')}$	*Other*
(*R*,S**)-**2a**	Ph	169.2 (25)	95.5 (271)	52.3 (21)	131.3	129.9	128.5, 130.1	
(*R*,S**)-**2b**	4-Cl-Ph	165.8 (25)	96.8 (270)	52.6 (18)	132.0	135.3	129.1, 132.6	
(*R*,S**)-**2c**	4-NO_2-Ph	166.7 (23)	95.5 (273)	49.6 (22)	137.7	147.1	128.6, 136.3	
(*R*,S**)-**2d**	4-OMe-Ph	164.3 (26)	96.2 (269)	51.5 (28)	131.1	156.5	111.5, 130.1	55.2 (CH_3)
(*R*,S**)-**2e**	*n*-C_6H_{13}	167.5 (27)	97.6 (260)	57.6 (23)	14.9 (CH_3), 22.3 (CH_2), 26.9 (CH_2), 30.7 (CH_2), 31.8 (CH_2)			

[a] Doublet due to ^{13}C–^{19}F coupling. In parentheses, coupling constant in Hz. [b] Not assigned respectively. [c] Solvent $CDCl_3$.

IR (film): 2945, 2920, 2850, 1750, 1460, 1380, 1260, 1165, 1100, 1060, 875, 845, 725, 680, 600, 575 cm^{-1}.

MS (CI, NH_3): *m/z* 340, 338, 336 ($M + NH_4^+$), 262, 178, 159.

The same procedure, applied to (*E*)-2-fluoro-3-(4-methoxyphenyl)prop-2-enoic acid (***E*)-1d** (0.392 g, 2 mmol) led to 2,3-dibromo-2-fluoro-3-(4-methoxyphenyl)-propanoic acid **2d** (0.606 g, 85%) as a 74:26 (*R*,S**)/(*R*,R**) mixture.

Decarboxylative elimination: 1-bromo-1-fluoroalkenes **3**

The ^1H and ^{13}C NMR data of compounds **3** are displayed in tables VII and VIII respectively.

• *(Z)-1-Bromo-1-fluoro-2-phenylethene* **(Z)-3a**

A solution of dibromoacid (***R*,S****)-2a** (71.3 g, 0.22 mol) in acetone (600 mL) was stirred at reflux temperature with sodium hydrogen carbonate (54.8 g, 0.65 mol) for 5–7 h. Acetone was evaporated under reduced pressure. Water and diethyl ether were added to the residue, the mixture was extracted with ether. The organic phase was dried ($MgSO_4$) and the solvent was evaporated under reduced pressure. The residue (45 g) was purified by distillation under reduced pressure to give (**Z**)-**3a** (36.1 g, 82%), Bp_{22} 96 °C.

IR (film): 3045, 3020, 1655, 1645, 1573, 1442, 1275, 1105, 1090, 1070, 1030, 912, 860, 830, 750, 690, 635, 580, 500 cm^{-1}.

MS (EI, 70 eV): *m/z* 202, 200 (M^+), 121, 120, 101, 91, 77, 75, 74, 69.

• *(Z)-1-Bromo-1-fluoro-2-(4-chlorophenyl)ethene* **(Z)-3b**

A solution of dibromoacid (***R*,S****)-2b** (9.00 g, 25 mmol) and tetrabutylammonium hydroxide 40% in water (19.2 g, 30 mmol, 1.2 equiv) in acetone (140 mL) was stirred at reflux temperature for 18 h. Acetone was evaporated under reduced pressure. Water and diethyl ether were added to the residue, the mixture was extracted with ether. The organic phase was dried ($MgSO_4$) and the solvent was evaporated under reduced pressure. The residue (4.8 g) was purified by distillation under reduced pressure to give (**Z**)-**3b** (4.09 g, 69%), $Bp_{0.02}$ 58 °C.

IR (film): 3050, 3020, 1720, 1645, 1590, 1560, 1485, 1400, 1320, 1300, 1270, 1180, 1100, 1045, 1025, 1010, 850, 790, 700, 625 cm^{-1}.

MS (EI, 70 eV): *m/z* 236, 234 (M^+), 154, 135, 120, 112, 99, 89, 87, 75, 74, 73, 63, 62, 50.

• *(Z)-1-Bromo-1-fluoro-2-(4-nitrophenyl)ethene* **(Z)-3c**

Decarboxylative elimination was performed on dibromoacid (***R*,S****)-2c** (2.24 g, 6 mmol) according to the same procedure as the preparation of (**Z**)-**3b** from (***R*,S****)-2b**. The residue obtained after evaporation of the solvent was purified by recrystallization in ethanol to give (**Z**)-**3c** (1.23 g, 83%), Mp 34–35 °C.

IR (KBr): 3025, 2920, 2825, 1650, 1600, 1520, 1410, 1350, 1280, 1215, 1120, 1100, 1050, 1015, 885, 865, 800, 750, 690, 640, 585, 540, 500, 480 cm^{-1}.

MS (EI, 70 eV): *m/z* 247, 245 (M^+), 217, 215, 120, 108, 100, 94, 84, 74, 57.

• *1-Bromo-1-fluoro-2-(4-methoxyphenyl)ethene* **(E)-3d + (Z)-3d**

Decarboxylative elimination was performed on dibromoacid **2d** (8.40 g, 23.6 mmol) with (*R*,S**)/(*R*,R**) ratio of 67:33, according to the same procedure as the preparation of (**Z**)-**3a** from (***R*,S****)-2a**. The residue obtained after evaporation of the solvent was purified by distillation under reduced pressure to give **3d** (3.80 g, 70%), $Bp_{0.03}$ = 83 °C. According to ^1H NMR, **3d** was obtained as a 67:33 *Z*/*E* mixture.

Table VII. ^1H NMR spectra ($CDCl_3$, 250 MHz) of 1-bromo-1-fluoroalkenes **3**, R CH=CFBr.

Compound	*R*	*H*		*R*
		δ	$^3J_{HF}$	
(**Z**)-**3a**	Ph	6.65	15.0	7.32 (m, 3H), 7.91 (m,2H)
(**E**)-**3a**	Ph	5.95	32.5	7.35 (m, 3H), 7.50 (m,2H)
(**Z**)-**3b**	4-Cl-Ph	6.63	14.8	7.32 (s, 4H)
(**E**)-**3b**	4-Cl-Ph	5.95	32.5	7.37 (s, 4H)
(**Z**)-**3c**	4-NO_2-Ph	6.74	14.1	7.68 (d, 8.7 Hz, 2H), 8.24 (d, 8.7 Hz, 2H)
(**Z**)-**3d**	4-OMe-Ph	6.60	15.0	3.83 (s, 3H), 6.96 (d, 8.9 Hz, 2H), 7.51 (d, 8.9 Hz, 2H)
(**E**)-**3d**	4-OMe-Ph	5.91	32.0	3.80 (s, 3H), 6.89 (d, 8.9 Hz, 2H), 7.40 (d, 8.9 Hz, 2H)
(**Z**)-**3e**	*n*-C_5H_{11}	5.48[a]	12.8	0.92 (t, 6.2 Hz, 3H), 1.36 (m, 6H), 2.07 (qd, 7.5 and 2.2 Hz, 2H)

[a] dt, J = 12.8 Hz and 7.5 Hz.

Table VIII. ^{13}C NMR spectra ($CDCl_3$, 62.8 MHz) of 1-bromo-1-fluoroalkenes **3**, R CH=CFBr. For R aromatic, the carbon atoms at positions 1, 2 (and 6), 3 (and 5), 4 of the phenyl ring are respectively referred to as $C^{(1)}$, $C^{(2)}$, $C^{(3)}$, $C^{(4)}$.

Compound	*R*	$C^{(CFBr)}$	$C^{(CFBr)}$	$C^{(1)}$	$C^{(4)}$	$C^{(2)}$, $C^{(3)}$	*Other*
(**Z**)-**3a**	Ph	131.9 (315)	111.6 (22)	131.5 (9)	128.39	128.0[a], 128.11	
(**E**)-**3a**	Ph	133.8 (332)	113.0 (5.7)	131.9 (10)	128.10	128.1, 128.33	
(**Z**)-**3b**	4-Cl-Ph	134.9 (311)	110.7 (25)	130.6 (4.5)	133.6	128.6, 130.6	
(**E**)-**3b**	4-Cl-Ph	134.3 (331)	112.0 (6.3)	130.9 (4.7)	135.6	128.9, 129.7	
(**Z**)-**3c**	4-NO_2-Ph	137.5 (311)	110.5 (25)	138.2 (10)	147.5	123.7, 129.0[a]	
(**Z**)-**3d**	4-OMe-Ph	134.9 (311)	111.3 (22)	124.3 (6.5)	159.3[b]	114.1, 129.8	55.3 (CH_3)
(**Z**)-**3e**	*n*-C_5H_{11}	135.0 (315)	109.9 (13)	13.7 (CH_3), 22.3 (CH_2), 27.1 (CH_2), 28.2 (CH_2), 31.1 (CH_2)			

[a] Doublet due to C–F coupling. In parentheses: coupling constant in Hz. [b] Not assigned respectively. [c] Very close doublet corresponding to a coupling constant of 1–2 Hz, attributed to long-range coupling of $C^{(CF)}$ with fluorine.

• *1-Bromo-1-fluorohept-1-ene* (**E**)-**3c** + (**Z**)-**3c**

A solution of dibromoacid **2c** (0.960 g, 3 mmol) with a (*R**,*S**)/(*R**,*R**) ratio of 88:12, and tetrabutylammonium hydroxide 40% in water (3.09 g, 4.8 mmol, 1.6 equiv) in acetone (40 mL) was stirred at reflux temperature for 18 h. Acetone was evaporated under reduced pressure. Water and pentane were added to the residue, the mixture was extracted with pentane. The organic phase was dried ($MgSO_4$) and the solvent was evaporated under reduced pressure to give **3c** (0.310 g, 60%) as a colorless oil. According to ^{1}H NMR, **3c** was obtained as a 86:14 *Z*/*E* mixture.

IR (film): 2 950, 2 920, 2 850, 1 665, 1 465, 1 375, 1 255, 1 110, 1 035, 820, 785, 615, 580 cm^{-1}.

MS (EI, 70 eV): the two isomers were separated by GC/MS.

(**Z**)-**3c**: *m*/*z* 196, 194 (M^+), 139, 137, 113, 111, 95, 71, 70, 57, 55, 51.

(**E**)-**3c**: *m*/*z* 196, 194 (M^+), 139, 137, 113, 111, 95, 71, 70, 57, 55, 51.

Palladium-catalyzed isomerization of (**Z**)-**3** *to* (**E**)-**3**

• *(E)-1-Bromo-1-fluoro-2-phenylethene* (**E**)-**3a**

A mixture of (**Z**)-**3a** (0.402 g, 2 mmol) and palladium diacetate (13.5 mg, 0.06 mmol, 0.03 equiv) was stirred at 110 °C for 60 h. Water and pentane were added, the mixture was extracted with pentane. The organic phase was dried ($MgSO_4$) and the solvent was evaporated under reduced pressure to give **3a** (0.375 g, 93%) as a 89:11 *E*/*Z* mixture according to ^{1}H NMR.

The use of 0.1 equiv of palladium diacetate at 60 °C for 16 h led to comparable results: **3a** was obtained as a 88:12 *E*/*Z* mixture.

MS (EI, 70 eV): the two isomers were separated by GC/MS.

(**E**)-**3a**: *m*/*z* 202, 200 (M^+), 121, 120, 101, 91, 77, 75, 74, 69.

• *(E)-1-Bromo-1-fluoro-2-(4-chlorophenyl)ethene* (**E**)-**3b**

A mixture of (**Z**)-**3b** (0.470 g, 2 mmol) and palladium diacetate (18.0 mg, 0.08 mmol, 0.04 equiv) was stirred at 110 °C for 4 h. Work-up as above gave quantitatively **3b** as a 88:12 *E*/*Z* mixture.

MS (EI, 70 eV): the two isomers were separated by GC/MS.

(**E**)-**3b**: *m*/*z* 236, 234 (M^+), 154, 135, 120, 112, 99, 89, 87, 75, 74, 73, 63, 62, 50.

Addition of "XF" to alkynes

The ^{1}H and ^{13}C NMR data of compounds **4** and **5** are displayed in tables IX and X respectively.

• *(E)-2-Bromo-1-fluoro-1-phenylethene* (**E**)-**4a**

Pyridinium poly(hydrogen fluoride) (Aldrich, molar composition 30% pyridine, 70% HF; 22 mL) was added to a solution of phenylacetylene (2.00 g, 19.6 mmol) in sulfolane (8 mL). The solution was cooled to 0 °C, and a solution of 1,3-dibromo-5,5-dimethylhydantoin (2.86 g, 10 mmol, 1.02 equiv) in sulfolane (20 mL) was added with stirring. The mixture was stirred 1 h at room temperature. Water was added, the mixture was extracted with pentane. The organic phase was washed successively with a saturated aqueous solution of sodium hydrogen carbonate and with water, dried ($MgSO_4$) and the solvent was evaporated under reduced pressure. The residue was purified by distillation under reduced pressure to give **4a** (3.65 g, 93%) Bp_{18} 102 °C (Lit $Bp_{0.1}$ 48–50 °C [20]). According to ^{1}H NMR, **4a** was obtained as a 92:8 *E*/*Z* mixture.

MS (EI, 70 eV): the two isomers were separated by GC/MS.

(**E**)-**4a**: *m*/*z* 202, 200 (M^+), 121, 120, 102, 101, 95, 94, 75, 51.

(**Z**)-**4a**: *m*/*z* 202, 200 (M^+), 121, 120, 102, 101, 75, 74, 51.

• *(E)-1-Bromo-2-fluorohept-1-ene* (**E**)-**4b**

This compound was prepared according to the same procedure as **4a**, starting from hept-1-yne (3.00 g, 31.2 mmol). The residue obtained after evaporation of the solvent was purified by distillation under reduced pressure to give **4b** (3.96 g, 65%). Bp_{18} 65 °C. According to ^{1}H NMR, **4b** was obtained as a 90:10 *E*/*Z* mixture.

IR (film): 3 110, 2 960, 2 930, 2 870, 1 670, 1 470, 1 460, 1 435, 1 380, 1 285, 1 260, 1 145, 940, 910, 900, 875, 805, 750, 650, 525 cm^{-1}.

MS (EI, 70 eV): the two isomers were separated by GC/MS.

(**E**)-**4b**: *m*/*z* 196, 194 (M^+), 139, 137, 113, 111, 99, 95, 73, 57, 55.

(**Z**)-**4b**: *m*/*z* 196, 194 (M^+), 139, 137, 113, 111, 99, 95, 73, 57, 55.

• *2-Bromo-4-fluoro-1-phenylnaphthalene* **6**

Pyridinium poly(hydrogen fluoride) (2.5 mL) was added to a solution of enyne **13a** (0.850 g, 3.8 mmol) in sulfolane (6 mL). The solution was cooled to 0 °C, and a solution of *N*-bromosuccinimide (0.740 g, 4.18 mmol, 1.1 equiv) in sulfolane (12 mL) was added with stirring. The mixture was stirred 1 h at room temperature. After the same work-up as in preparation of **4**, evaporation of the solvent gave **6** (0.930 g, 81%) as a colorless oil.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.27 (m, 2H), 7.42–7.65 (m, 7H), 8.17 (d, $^3J_{HF}$ = 8.5 Hz, 1H).

Table IX. ^{1}H NMR spectra ($CDCl_3$, 250 MHz) of 1-bromo-2-fluoroalkenes **4** and **9** and 2-fluoro-1-iodoalkenes **5**, $R^{2)}CF{=}CXR^{1)}$.

Compound	$R^{1)}$	$R^{2)}$	*X*	$R^{2)}$	$R^{1)}$
(**E**)-**4a**	Ph	H	Br	6.23 (d, $^3J_{HF}$ 15.7 Hz, 1H)	7.43 (m, 3H), 7.80 (m, 2H)
(**Z**)-**4a**	Ph	H	Br	6.42 (d, $^3J_{HF}$ 28.0 Hz, 1H)	7.30 (m, 3H), 7.50 (m, 2H)
(**E**)-**5a**	Ph	H	I	6.20 (d, $^3J_{HF}$ 18.0 Hz, 1H)	7.54 (m, 3H), 7.86 (m, 2H)
(**E**)-**4b**	n-C_5H_{11}	H	Br	5.85 (d, $^3J_{HF}$ 13.6 Hz, 1H)	0.92 (t, 7.0 Hz, 3H), 1.35 (m, 4H), 1.57 (m, 2H), 2.12 (dt, 23.0 and 7.2 Hz, 2H)
(**Z**)-**4b**	n-C_5H_{11}	H	Br	5.31 (d, $^3J_{HF}$ 28.1 Hz)	0.90 (t, 7.0 Hz, 3H), 1.35 (m, 4H), 1.52 (m, 2H), 2.26 (dt, 17.4 and 7.7 Hz, 2H)
(**E**)-**5b**	n-C_5H_{11}	H	I	5.65 (d, $^3J_{HF}$ 17.5 Hz)	0.91 (t, 7.0Hz, 3H), 1.35 (m, 4H), 1.58 (m, 2H), 2.50 (dt, 22.5 and 5.0 Hz, 2H)
(**Z**)-**9a**	COOEt	Ph	Br	7.42 (m, 5H)	1.06 (t, 7.1 Hz, 3H), 4.12 (q, 7.1 Hz, 2H)
(**E**)-**9a**	COOEt	Ph	Br	7.56 (m, 5H)	1.45 (t, 7.1 Hz, 3H), 4.40 (q, 7.1 Hz, 2H)
(**Z**)-**9b**	COOEt	Ar*	Br	2.31 (s, 3H), 3.85 (s, 3H), 6.87 (m, 3H)	1.05 (t, 7.0 Hz, 3H), 4.08 (q, 7.0 Hz, 2H)

*Ar = 4-acetoxy-3-methoxyphenyl.

Table X. ^{13}C NMR spectra ($CDCl_3$, 100.5 MHz) of 1-bromo-2-fluoroalkenes **4** and **9** and 2-fluoro-1-iodoalkenes **5**, $R^{(2)}C^{(2)}F{=}C^{(1)}XR^{(1)}$.

Compound	$R^{(1)}$	$R^{(2)}$	X	$C^{(1)}$ [a]	$C^{(2)}$ [a]	$R^{(1)}$	$R^{(2)}$
(*E*)-4a	Ph	H	Br	87.8 (52)	158.0 (250)	127.9 (d, $^3J_{CF}$ = 6 Hz, 2CH), 128.2 (2CH), 130.1 (CH), 130.1 (d, $^2J_{CF}$ = 27 Hz, C)	
(*E*)-5a	Ph	H	I	53.7 (45)	156.7 (251)	128.2 (2CH), 128.6 (d, $^3J_{CF}$ = 5 Hz, 2CH), 130.2 (CH), 130.2 (d, $^2J_{CF}$ = 28 Hz, C)	
(*E*)-4b	*n*-C_5H_{11}	H	Br	87.4 (48)	163.1 (152)	13.9 (CH_3), 22.3 (CH_2), 25.0 (CH_2), 26.0 (CH_2), 28.8 (d, $^2J_{CF}$ = 23 Hz, CH_2)	
(*Z*)-4b	*n*-C_5H_{11}	H	Br	82.0 (20)	162.6 (161)	13.7 (CH_3), 22.1 (CH_2), 25.2 (CH_2), 30.7 (CH_2), 31.7 (d, $^2J_{CF}$ = 22 Hz, CH_2)	
(*E*)-5b	*n*-C_5H_{11}	H	I	58.6 (48)	160.3 (149)	13.2 (CH_3), 22.1 (CH_2), 25.1 (CH_2), 25.9 (CH_2), 28.5 (d, $^2J_{CF}$ = 23 Hz, CH_2)	
(*Z*)-9a	COOEt	Ph	Br	119.5 (28)	146.3 (260)	13.4 (CH_3), 61.8 (CH_2), 158.5 (d, $^2J_{CF}$ = 37 Hz, C)	128.1 (2CH), 128.9 (2CH), 129.6 (CH), 135.7 (C)
(*Z*)-9n	COOEt	Ar[b]	Br	118.4 (30)	145.9 (250)	13.4 (CH_3), 61.8 (CH_2), 158.4 (d, $^2J_{CF}$ = 40 Hz, C)	20.5 (CH_3), 55.9 (CH_3), 113.1 (CH), 121.6 (CH), 122.5 (CH), 134.1 (C), 140.7 (C), 150.7 (C)

[a] Doublet due to C–F coupling. In parentheses: coupling constant in Hz. [b] Ar = 4-acetoxy-3-methoxyphenyl.

MS (EI, 70 eV): *m/z* 302, 300 (M^+), 280, 246, 198, 120, 101, 77.

• *(E)-1-Fluoro-2-iodo-1-phenylethene* **(*E*)-5a**

Pyridinium polyhydrogenofluoride (8 mL) was added to a solution of phenylacetylene (0.500 g, 4.90 mmol) in dichloromethane (10 mL). The solution was cooled to 3 °C, and a solution of bis(pyridine)iodonium (I) tetrafluoroborate (2.20 g, 5.88 mmol, 1.2 equiv) in dichloromethane (12 mL) was added dropwise with stirring. The mixture was stirred 2 h at room temperature. The solvent was evaporated under reduced pressure. Water was added and the mixture was extracted with pentane. The organic phase was dried ($MgSO_4$) and the solvent was evaporated under reduced pressure. The residue was purified by chromatography on silica gel (pentane) to give **(*E*)-5a** (0.859 g, 71%) as a colorless oil.

MS (EI, 70 eV): *m/z* 248 (M^+), 229, 103, 102, 101, 76, 51, 50.

• *(E)-2-Fluoro-1-iodohept-1-ene* **(*E*)-5b**

This compound was prepared according to the same procedure as **5a**, starting from 1-heptyne (0.440 g, 4.4 mmol). Evaporation of the solvent gave **(*E*)-5b** (0.285 g, 84%).

MS (EI, 70 eV): *m/z* 242 (M^+), 186, 95.

Bromination–dehydrobromination of unsaturated fluoroesters

The ^1H and ^{13}C NMR data of compounds **9** are displayed in tables IX and X respectively.

• *Ethyl (2R*,3S*)-2,3-dibromo-2-fluoro-3-phenylpropanoate* **(*R*,S**)-8a**

This compound was prepared according to the same procedure as the bromoacids **2a,b**, starting from ethyl 2-fluoro-3-phenylprop-2-enoate **7a** (3.70 g, 19 mmol). Evaporation of the solvent gave **(*R*,S**)-8a** (6.32 g, 94%).

IR (KBr): 2975, 2920, 1765, 1700, 1490, 1450, 1370, 1280, 1250, 1205, 1040, 910, 890, 855, 695, 625, 610 cm^{-1}.

^1H NMR ($CDCl_3$, 400 MHz): δ 1.43 (t, *J* = 7.1 Hz, 3H), 4.48 (q, *J* = 7.1 Hz, 2H), 5.58 (d, *J* = 26.5 Hz, 1H), 7.44 (m, 3H), 7.58 (m, 2H).

^{13}C NMR ($CDCl_3$, 62.8 MHz): δ 13.5 (CH_3), 52.9 (CH_2), 57.6 (CH, d, $^2J_{CF}$ = 18 Hz), 96.0 (C, d, $^1J_{CF}$ = 275 Hz), 128.7 (2CH), 129.8 (CH), 130.1 (2CH), 135.0 (C), 163.5 (C, d, $^2J_{CF}$ = 23 Hz).

MS (EI, 70 eV): *m/z* 356, 354, 352 (M^+), 275, 273, 227, 225, 203, 202, 201, 194, 165, 150, 129, 122, 109, 101, 75, 57.

Anal. calc. for $C_{11}H_{11}Br_2FO_2$: C, 37.32; H, 3.13. Found: C, 37.85; H, 3.18.

• *Ethyl (2R*,3S*)-2,3-dibromo-2-fluoro-3-(4-acetoxy-3-methoxyphenyl)propanoate* **8b**

This compound was prepared according to the same procedure as **8n**, starting from ethyl 2-fluoro-3-(4-acetoxy-3-methoxyphenyl)prop-2-enoate **7b** (3.00 g, 10.6 mmol). The residue obtained after evaporation of the solvent was purified by recrystallization in pentane, giving **(*R*,S**)-8b** (3.32 g, 74%).

^1H NMR ($CDCl_3$, 400 MHz): δ 1.44 (t, *J* = 7.1 Hz, 3H), 2.35 (s, 3H), 3.89 (s, 3H), 4.45 (q, *J* = 7.1 Hz, 2H), 5.54 (d, *J* = 26.2 Hz, 1H), 7.0–7.2 (m, 3H).

^{13}C NMR ($CDCl_3$, 100.5 MHz): δ 13.5 (CH_3), 52.9 (CH_2), 57.6 (CH, d, $^2J_{CF}$ = 18 Hz), 96.0 (C, d, $^1J_{CF}$ = 275 Hz), 128.7 (2CH), 129.8 (CH), 130.1 (2CH), 135.0 (C), 163.5 (C, d, $^2J_{CF}$ = 23 Hz).

MS (EI, 70 eV): *m/z* 356, 354, 352 (M^+), 275, 273, 227, 225, 203, 202, 201, 194, 165, 150, 129, 122, 109, 101, 75, 57.

• *Ethyl (Z)-3-bromo-2-fluoro-3-(4-acetoxy-3-methoxyphenyl)prop-2-enoate* (**Z**)-**9a**

A solution of DIBAL (3.90 g, 26.4 mmol, 1.5 equiv) in THF (20 mL) was added dropwise at room temperature to a stirred solution of **8a** (6.10 g, 17.4 mmol) in THF (40 mL). The mixture was stirred for 20 min, ice was added, followed by a 1 M aqueous solution of sulfuric acid. The mixture was extracted with diethyl ether, the organic phase was dried ($MgSO_4$), the solvent was evaporated under reduced pressure. The residue was purified by distillation under reduced pressure to give **9a** (3.79 g, 80%). $Bp_{0.01}$ = 76 °C. According to ^1H NMR, **9a** was obtained as a 96:4 *Z*/*E* mixture.

IR (film): 2975, 1725, 1640, 1440, 1390, 1365, 1300, 1230, 1165, 1150, 1015, 920, 880, 760, 710, 690, 650 cm^{-1}.

MS (EI, 70 eV): the two isomers were separated by GC/MS.

(**Z**)-**9a**: *m*/*z*: 274, 272 (M^+), 202, 200, 165, 121, 120, 101, 100, 93, 89, 87, 81, 75, 74.

(**E**)-**9a**: *m*/*z*: 274, 272 (M^+), 202, 200, 165, 121, 120, 101, 100, 93, 89, 87, 81, 75, 74.

Anal calc for $C_{13}H_{12}BrFO_5$: C, 48.36; H, 3.69. Found: C, 48.56; H, 3.75.

• *Ethyl (Z)-3-bromo-2-fluoro-3-(4-acetoxy-3-methoxyphenyl)prop-2-enoate* **9b**

This compound was prepared according to the same procedure as **9a**, starting from dibromoester **8b** (0.500 g, 1.1 mmol). Evaporation of the solvent gave **9b** (0.419 g, 83%), as a colorless oil.

MS (EI, 70 eV): *m*/*z*: 362, 360 (M^+), 320, 318, 243, 207, 179, 163, 151, 124, 91, 75.

Palladium catalyzed couplings

• *General procedure for preparation of fluorinated enynes* **10**–**13**

A mixture of palladium diacetate (0.02 equiv), triphenylphosphine (0.01 equiv), halofluoroalkene (2.10 mmol), alkyne (1.2 equiv) and butylamine or triethylamine (0.5 mL/1 mmol halofluoroalkene) was stirred at reflux (conditions for **9b**). The consumption of halofluoroalkene was monitored by TLC. Water was added to the cooled mixture, the mixture was extracted with pentane, the organic phase was washed with a 10% hydrochloric acid solution, then with a saturated sodium hydrogen carbonate solution, and dried ($MgSO_4$). After evaporation of the solvent under reduced pressure the residue was purified in the appropriate way as described below.

The ^1H and ^{13}C NMR data of compounds **10**–**12** are displayed in tables XI and XII respectively.

• *(E)-1,4-Diphenyl-2-fluorobut-1-en-3-yne* (**E**)-**10a**

Starting from (**Z**)-**3a** (0.80 g, 4 mmol) and phenylacetylene (0.81 g, 8 mmol, 2 equiv), distillation under reduced pressure gave (**E**)-**10a** (0.631 g, 71%). $Bp_{0.3}$ 134 °C.

IR (film): 3020, 2200, 1640, 1490, 1445, 1370, 1120, 910, 860, 690, 650, 570, 520, 500 cm^{-1}.

MS (EI, 70 eV): *m*/*z* 222 (M^+), 220, 202, 170, 157, 126, 110, 98, 86, 74, 63.

Anal calc for $C_{16}H_{11}F$: C, 86.48; H, 4.95. Found: C, 86.03; H, 5.05.

• *(Z)-1,4-Diphenyl-2-fluorobut-1-en-3-yne* (**Z**)-**10a**

Starting from (**E**)-**3a** (2.01 g, 10 mmol) as a 90:10 *E*/*Z* mixture, and phenylacetylene (2.01 g, 20 mmol, 2 equiv), purification by flash chromatography on silica gel (pentane) gave (**Z**)-**10a** (1.79 g, 81%), as a colorless solid. Mp 57–58 °C.

IR (KBr): 3050, 3005, 2200, 1640, 1595, 1490, 1440, 1315, 1300, 1110, 1020, 1000, 915, 900, 850, 830, 690 cm^{-1}.

MS (EI, 70 eV): *m*/*z* 222 (M^+), 221, 220, 207, 202, 110, 97, 95, 87, 83, 71, 69, 57, 55.

Anal calc for $C_{16}H_{11}F$: C, 86.48; H, 4.95. Found: C, 86.13; H, 5.07.

• *(E)-4-Fluoro-1-phenylnon-1-en-3-yne* (**E**)-**11a**

Starting from (**Z**)-**3a** (2.01 g, 10 mmol) and hept-1-yne (0.96 g, 10 mmol, 1 equiv), distillation under reduced pressure gave (**E**)-**11a** (1.46 g, 67%). $Bp_{0.1}$ 106–107 °C.

IR (film): 3040, 3000, 2940, 2860, 2220, 1645, 1600, 1500, 1470, 1450, 1375, 1150, 1030, 1010, 915, 810, 690, 645, 500 cm^{-1}.

MS (EI, 70 eV): *m*/*z* 216 (M^+), 187, 173, 160, 159, 152, 146, 140, 133, 115, 91, 83.

Anal calc for $C_{15}H_{17}F$: C, 83.34; H, 7.87. Found: C, 83.02; H, 7.95.

Table XI. ^1H NMR spectra (CDCl$_3$, 250 MHz) of fluorinated enynes **10**–**12**: Ar, CH=, CF, C=C–R

Compound	Ar	R′	H″	Ar	R
(*E*)-**10a**	Ph	Ph	6.53 (d, 17)	7.41 (m, 4H); 7.50 (m, 2H)	7.46 (m, 5H)
(*Z*)-**10a**	Ph	Ph	6.20 (d, 36)	7.60 (m, 5H)	7.42 (m, 5H)
(*E*)-**11a**	Ph	n-C_5H_{11}	6.36 (d, 17)	7.34 (m, 3H); 7.46 (m, 2H)	0.80 (t, 7 Hz, 3H); 1.28 (m, 4H); 1.50 (m, 2H); 2.40 (m, 2H)
(*E*)-**12a**	Ph	Me_2COH	6.64 (d, 17)	7.40 (m, 3H); 7.64 (m, 2H)	1.62 (s, 6H)
(*E*)-**10b**	4-Cl-Ph	Ph	6.50 (d, 17)	7.41 (m, 2H); 7.60 (m, 2H)	7.48 (m, 5H)
(*E*)-**11b**	4-Cl-Ph	n-C_5H_{11}	6.45 (dd, 17, 1.6)	7.28 (d, 8.7 Hz, 2H); 7.34 (d, 8.7 Hz, 2H)	0.91 (t, 6.9 Hz, 3H); 1.38 (m, 4H); 1.68 (m, 2H); 2.48 (m, 2H)
(*E*)-**10c**	4-NO_2-Ph	Ph	6.70 (d, 17.5)	7.86 (d, 8.8 Hz, 2H); 8.34 (d, 8.8 Hz, 2H)	7.46 (m, 3H); 7.58 (m, 2H)
(*E*)-**10d**	4-OMe-Ph	Ph	6.46 (d, 17.5)	3.81 (s, 3H); 7.21 (m, 2H); 7.33 (m, 2H)	7.42 (m, 5H)
(*Z*)-**10d**	4-OMe-Ph	Ph	6.10 (d, 36)	3.87 (s, 3H); 7.32 (m, 2H); 7.86 (m, 2H)	7.48 (m, 5H)

[a] Doublet, heptet, multiplet, singlet, triplet, etc. [b] $J_{H,F}$ in Hz.

Table XII. ^{13}C NMR spectra ($CDCl_3$, 100.5 MHz) of fluorinated enynes **10**–**12**. Ar-$C^{(1)}H=C^{(2)}F-C^{(3)}\equiv C^{(4)}-R$.

Compound	Ar	R	$C^{(1)}$ [a]	$C^{(2)}$ [a]	$C^{(3)}$ [a]	$C^{(4)}$ [a]	Ar [b]	R
(*E*)-**10a**	Ph	Ph	117.5 (30)	141.0 (235)	81.2 (40)	97.3 (10)	132.2 (9.5), 128.2, 128.1, 128.47	121.2 (C), 128.52 (2CH), 129.5 (CH), 131.7 (2CH)
(*Z*)-**10a**	Ph	Ph	116.1 (15)	141.2 (245)	82.3 (10)	92.4 (10)	131.7 (7), 128.6, 128.1, 128.4	121.4 (C), 129.1 (CH), 129.2 (2CH), 131.6 (2CH)
(*E*)-**11a**	Ph	*n*-C_5H_{11}	115.7 (32)	141.3 (230)	73.0 (40)	100.0 (7.5)	132.4 (10), 127.79, 127.76, 128.3	13.9 (CH_3), 19.5 (CH_2), 22.1 (CH_2), 27.8 (CH_2), 31.0 (CH_2)
(*E*)-**12a**	Ph	Me_2COH	117.5 (32)	140.5 (230)	74.3 (32)	101.8 (10)	131.3 (10), 128.2, 127.9, 128.3	30.8 (2CH3), 65.5 (C)
(*E*)-**10b**	4-Cl-Ph	Ph	116.3 (33)	141.3 (230)	80.8 (10)	97.8 (10)	130.7 (10), 133.4, 129.2, 128.6	121.0 (C), 128.7 (2CH), 129.7 (CH), 131.7 (2CH)
(*E*)-**11b**	4-Cl-Ph	*n*-C_5H_{11}	114.7 (35)	141.7 (234)	72.8 (41)	100.6 (6.4)	131.9 (10), 133.4, 129.0, 128.5	13.9 (CH_3), 19.6 (CH_2), 22.2 (CH_2), 27.7 (CH_2), 31.1 (CH_2)
(*E*)-**10c**	4-NO_2-Ph	Ph	114.9 (38)	143.6 (239)	81.1 (11)	99.3 (10)	139.5 (7.5), 147.1, 128.5, 123.8	121.3 (C), 128.7 (2CH), 130.2 (CH), 131.8 (2CH)
(*E*)-**10d**	4-OMe-Ph	Ph	117.2 (38)	139.9 (228)	81.5 (13)	97.1 (10)	124.6 (7.5), 159.6, 114.0, 129.0; 55.3 (CH_3)	121.1 (C), 128.5 (2CH), 131.6 (2CH), 132.5 (CH)
(*Z*)-**10d**	4-OMe-Ph	Ph	115.8 (20)	140.3 (243)	82.7 (13)	93.0 (10)	125.6 (1), 159.1, 114.1, 129.2; 55.3 (CH_3)	121.6 (C), 128.5 (2CH), 130.4 (2CH), 131.6 (CH)

[a] Doublet due to C–F coupling. In parentheses: coupling constant in Hz. [b] Successively $C^{(1')}$ ($^4J_{CF}$ in Hz), $C^{(2')}$, $C^{(3')}$, $C^{(4')}$, $C^{(5')}$ can be distinguished from $C^{(6')}$ since it appears as a very close doublet corresponding to a coupling constant of 1–2 Hz, attributed to long-range coupling of $C^{(6')}$ with fluorine. [c] Assignment may be reversed.

• *(E)-3-Fluoro-2-methyl-6-phenylhex-1-en-3-yn-2-ol* (**E**)-**12a**

Starting from (**Z**)-**3a** (2.01 g, 10 mmol) and 2-methylbut-3-yn-2-ol (0.84 g, 10 mmol, 1 equiv), purification by flash chromatography on silica gel (pentane–ethyl acetate (85:15)) gave (**E**)-**12a** (1.14 g, 56%) as a viscous oil.

IR (film): 3400, 3075, 3000, 2940, 2240, 1645, 1600, 1500, 1450, 1375, 1245, 1170, 980, 940, 920, 870, 820, 760, 700, 650, 545, 500 cm^{-1}.

MS (EI, 70 eV): *m/z* 204 (M^+), 189, 187, 159, 147, 146, 145, 141, 133, 125, 120, 115, 107, 91, 87, 77.

Anal. calc. for $C_{13}H_{13}FO$: C, 76.47; H, 6.42. Found: C, 76.44; H, 6.69.

• *(E)-1-(4-Chlorophenyl)-3-fluoro-4-phenylbut-1-en-3-yne* (**E**)-**10b**

Starting from (**Z**)-**3b** (0.471 g, 2 mmol) and phenylacetylene (0.408 g, 4 mmol, 2 equiv), purification by column chromatography on silica gel (pentane) gave (**E**)-**10b** (0.485 g, 75%) as a viscous oil.

MS (EI, 70 eV): *m/z* 258, 256 (M^+), 221, 220, 200, 110, 74, 63.

Anal. calc. for $C_{16}H_{10}ClF$: C, 74.85; H, 3.89. Found: C, 74.70; H, 4.06.

• *(E)-1-(4-Chlorophenyl)-3-fluoronon-1-en-3-yne* (**E**)-**11b**

Starting from (**Z**)-**3b** (0.471 g, 2 mmol) and hept-1-yne (0.384 g, 4 mmol, 2 equiv), purification by column chromatography on silica gel (pentane) gave (**E**)-**11b** (0.365 g, 73%) as a viscous oil.

IR (film): 3060, 2960, 2940, 2870, 2220, 1905, 1650, 1600, 1570, 1500, 1475, 1465, 1430, 1415, 1315, 1220, 1160, 1100, 1040, 1020, 875, 820, 745 cm^{-1}.

MS (EI, 70 eV): *m/z* 252, 250 (M^+), 195, 193, 171, 170, 167, 165, 159, 158, 157, 133, 125, 81, 75, 71, 63, 62, 57, 56, 55, 51, 51, 50.

• *(E)-2-Fluoro-1-(4-nitrophenyl)-4-phenylbut-1-en-3-yne* (**E**)-**10c**

The coupling reaction of (**Z**)-**3c** (0.216 g, 1 mmol) and phenylacetylene (0.204 g, 2 mmol, 2 equiv) was run in triethylamine (3 mL). Purification by recrystallization in ethanol gave (**E**)-**10c** (0.190 g, 71%), Mp: 85–86 °C.

IR (KBr): 2960, 2920, 2850, 2200, 1635, 1590, 1515, 1490, 1415, 1345, 1260, 1215, 1110, 1095, 1025, 915, 875, 835, 800, 750, 685, 590 cm^{-1}.

MS (EI, 70 eV): *m/z* 267 (M^+), 221, 220, 219, 218, 200, 97, 88, 86, 85, 84, 83, 77, 71, 69, 57, 55.

Anal. calc. for $C_{16}H_{10}FNO_2$: C, 71.90; H, 3.74; N, 5.21. Found: C, 71.85; H, 3.87; N, 5.18.

• *2-Fluoro-1-(4-methoxyphenyl)-4-phenylbut-1-en-3-yne* **10d**

Starting from **3d** (0.216 g, 1.06 mmol) as a 67:33 *Z*/*E* mixture and phenylacetylene (0.111 g, 1.08 mmol, 1.3 equiv), purification by column chromatography on silica gel (pentane) gave **10d** (0.216 g, 85%) with a global *E*/*Z* composition of 67:33. Although *E* and *Z* isomers were incompletely separated from each other, each of them could be obtained pure.

(E)-2-Fluoro-1-(4-methoxyphenyl)-4-phenylbut-1-en-3-yne (*E*)-**10d**

IR (film): 3045, 3000, 2945, 2920, 2825, 2200, 1680, 1600, 1505, 1485, 1440, 1370, 1300, 1250, 1185, 1120, 1095, 1030, 910, 865, 825, 755, 685 cm^{-1}.

MS (EI, 70 eV): *m/z* = 252 (M^+), 237, 219, 209, 207, 189, 183, 110, 71, 43.

(Z)-1-Fluoro-1-(4-methoxyphenyl)-4-phenylbut-1-en-3-yne **(Z)-10d**

IR (film): 3040, 3000, 2945, 2925, 2820, 2205, 1680, 1600, 1505, 1485, 1440, 1375, 1300, 1255, 1185, 1120, 1090, 1030, 910, 860, 825, 755, 685 cm^{-1}.

MS (EI, 70 eV): *m/z* 252 (M^+), 237, 219, 209, 207, 189, 183, 126, 110, 101, 98, 87, 74, 63.

• *2-Fluoro-1-(4-methoxyphenyl)non-1-en-3-yne*

(E)-11d* + *(Z)-11d

Starting from **3d** (0.462 g, 2 mmol) as a 67:33 *Z/E* mixture and hept-1-yne (0.384 g, 4 mmol, 2 equiv), purification by column chromatography on silica gel (pentane) gave **11d** (0.373 g, 76%) with a global *E/Z* composition of 67:33. The *E* and *Z* isomers could not be separated from each other.

IR (film): 2950, 2920, 2850, 2220, 1640, 1605, 1570, 1505, 1460, 1440, 1300, 1250, 1175, 1150, 1035, 910, 865, 820, 755, 730, 685 cm^{-1}.

MS (EI, 70 eV): the two isomers were separated by GC/MS.

(E)-11d: *m/z* 246 (M^+), 203, 191, 190, 180, 176, 159, 146, 133, 121, 55.

(Z)-11d: *m/z* 246 (M^+), 203, 191, 190, 189, 176, 159, 146, 133, 121, 55.

• *(E)-1,4-Diphenyl-1-fluorobut-1-en-3-yne* ***(E)-13a***

Starting from (***E***)-**5a** (0.700 g, 2.82 mmol) and phenylacetylene (0.345 g, 3.38 mmol, 1.2 equiv), purification by column chromatography (pentane) gave (***E***)-**13a** (0.520 g, 83%) as a viscous oil.

IR (film): 3045, 3020, 2920, 2200, 1635, 1595, 1485, 1410, 1325, 1300, 1075, 1025, 1000, 910, 825, 755, 685, 620, 520 cm^{-1}.

^1H NMR ($CDCl_3$, 250 MHz): δ 5.80 (d, J = 17.4 Hz, 1H), 7.30 (m, 3H), 7.39–7.55 (m, 5H), 8.18 (m, 2H).

^{13}C NMR ($CDCl_3$, 62.8 MHz): δ 84.2 (C, d, $^2J_{CF}$ = 20 Hz), 89.8 (CH, d, $^2J_{CF}$ = 38 Hz), 96.0 (C), 122.4 (C), 126.2 (CH, d, $^3J_{CF}$ = 8 Hz), 126.6 (CH), 128.3 (2CH), 128.5 (2CH), 129.2 (CH), 130.2 (CH), 131.0 (C, d, $^4J_{CF}$ = 2.2 Hz), 131.4 (2CH), 165.0 (C, d, $^1J_{CF}$ = 219 Hz).

MS (EI, 70 eV): *m/z* 222 (M^+), 221, 220, 202, 170, 157, 120, 110, 98, 87, 75, 71, 63, 51.

Anal. calc. for $C_{16}H_{11}F$: C, 86.18; H, 4.95. Found: C, 86.16; H, 5.07.

• *(E)-1-Fluoro-1-phenylnon-1-en-3-yne* ***(E)-13b***

Starting from (***E***)-**5b** (0.265 g, 1.30 mmol) and phenylacetylene (0.208 g, 2.04 mmol, 1.5 equiv), purification by chromatography on silica gel (pentane) gave (***E***)-**13b** (0.220 g, 75%) as a viscous oil.

IR (film): 2960, 2925, 2870, 1660, 1600, 1490, 1480, 1280, 1240, 1165, 1090, 880, 760, 700, 570 cm^{-1}.

^1H NMR ($CDCl_3$, 250 MHz): δ 0.92 (t, J = 7.1 Hz, 4H), 1.38 (m, 4H), 1.63 (m, 2H), 2.54 (dt, J = 2.1 Hz and 7.5 Hz, 2H), 5.40 (d, J = 13.9 Hz, 1H), 7.30 (m, 4H), 7.50 (m, 3H).

^{13}C NMR ($CDCl_3$, 62.8 MHz): δ 13.9 (CH_3), 22.3 (CH_2), 27.9 (CH_2), 30.0 (d, $^4J_{CF}$ = 2.6 Hz, CH_2), 31.0 (CH_2), 83.3 (C, d, $^2J_{CF}$ = 22 Hz), 89.9 (CH, d, $^2J_{CF}$ = 42 Hz), 93.3 (C), 123.4 (C), 128.0 (CH), 128.3 (2CH), 131.2 (2CH), 172.4 (C, d, $^1J_{CF}$ = 264 Hz).

• *Ethyl 5,5-diphenyl-2-fluoropent-2-en-4-ynoate*

(Z)-14* + *(E)-14

A mixture of palladium diacetate (29.5 mg, 0.04 mmol, 0.04 equiv), triphenylphosphine (22 mg, 0.08 mmol, 0.08 equiv), bromofluoroester (***Z***)-**9a** (0.289 g, 1.05 mmol), phenylacetylene (0.323 g, 3.16 mmol, 3 equiv) and triethylamine (3 mL) was stirred at reflux temperature for 24 h. Water was added to the cooled mixture, the mixture was extracted with diethyl ether, the organic phase was washed with a 10% hydrochloric acid solution, then with a saturated sodium hydrogen carbonate solution, and dried ($MgSO_4$). The residue obtained after evaporation of the solvent under reduced pressure consisted mainly of (*E*) and (*Z*) **14**, along with (***Z***)-**9a**, (*E*) and (*Z*) **7a** as minor products. Purification by chromatography on silica gel (pentane/ethyl acetate (95:5)) gave **14** (0.210 g, 68%) as a 60:40 *Z/E* mixture.

^1H NMR ($CDCl_3$, 250 MHz):

(E)-14: δ 1.10 (t, J = 7.2 Hz, 3H), 4.12 (q, J = 7.2 Hz, 2H), 7.34–7.50 (m, 10H).

(Z)-14: δ 1.40 (t, J = 7.2 Hz, 3H), 4.35 (q, J = 7.2 Hz, 2H), 7.35–7.50 (m, 10H).

MS (EI, 70 eV): the two isomers were separated by GC/MS.

(E)-14: *m/z* 294 (M^+), 265, 220, 209, 200, 189, 110, 105, 77, 63, 51.

(Z)-14: *m/z* 294 (M^+), 265, 220, 209, 200, 189, 110, 105, 77, 63.

• *N-Butyl-2-phenylethanamide* **15a**

A mixture of palladium diacetate (16.8 mg, 0.075 mmol, 0.03 equiv), triphenylphosphine (39.3 mg, 0.15 mmol, 0.06 equiv), bromofluoroalkene (***Z***)-**3a** (0.500 g, 2.5 mmol), and butylamine (1 mL) was stirred at reflux temperature for 3 days. Water was added to the cooled mixture, the mixture was extracted with pentane, the organic phase was washed with a 10% hydrochloric acid solution, then with a saturated sodium hydrogen carbonate solution, and dried ($MgSO_4$). Evaporation of the solvent gave **15a** (0.43 g, 90%).

IR (film): 3260, 2950, 2860, 2210, 1640, 1550, 1435, 1420, 720, 680, 530 cm^{-1}.

^1H NMR ($CDCl_3$, 250 MHz): δ 0.86 (t, J = 7.0 Hz, 3H), 1.28 (m, 2H), 1.40 (m, 2H), 3.22 (m, 2H), 3.58 (s, 2H), 5.84 (broad s, 1H), 7.40 (m, 5H).

^{13}C NMR ($CDCl_3$, 100.5 MHz): δ 13.5 (CH_3), 19.7 (CH_2), 31.3 (CH_2), 39.1 (CH_2), 43.4 (CH_2), 126.8 (CH), 128.4 (2CH), 129.1 (2CH), 135.1 (C), 170.8 (C).

MS (EI, 70 eV): 191 (M^+), 100, 92, 91, 90, 89, 69, 67, 57.

• *(1E,3E)-2-Fluoro-4-(4-methylphenyl)-1-phenylbuta-1,3-diene* ***(E,E)-16*** *and (1Z,3E)-2-fluoro-4-(4-methylphenyl)-1-phenylbuta-1,3-diene* ***(Z,E)-16***

A mixture of palladium diacetate (22.4 mg, 0.1 mmol, 0.02 equiv), triphenylphosphine (52.5 mg, 0.2 mmol, 0.04 equiv), bromofluoroalkene (***Z***)-**3a** (1.00 g, 5 mmol), (4-methylphenyl)ethene (0.684 g, 5.8 mmol, 1.15 equiv) and triethylamine (6 mL) was stirred at reflux temperature for 5 h. After the same work-up as for the preparation of enynes **10**–**13**, purification by flash chromatography on silica gel (pentane) gave (***E,E***)-**16** (0.870 g, 73%) as a colorless oil. ^1H and ^{13}C NMR data: see tables XIII and XIV respectively.

IR (film): 3020, 2965, 2920, 1685, 1630, 1600, 1595, 1510, 1490, 1450, 1415, 1355, 1320, 1260, 1180, 1160, 1110, 1020, 975, 965, 930, 900, 840, 810, 750, 715, 700, 690, 620 cm^{-1}.

MS (EI, 70 eV): *m/z* 238 (M^+), 223, 222, 220, 202, 161, 159, 147, 146, 119, 95, 91, 77, 65, 57.

Anal. calc. for $C_{17}H_{15}F$: C, 85.71; H, 6.30. Found: C, 85.41; H, 6.35.

The minor isomer (***Z,E***)-**16** could be isolated in a separate fraction (0.036 g, 3.9%) as colorless crystals, Mp 112–114 °C. ^1H and ^{13}C NMR data: see tables XIII and XIV.

Table XIII. ^{1}H NMR spectra ($CDCl_3$, 250 MHz) of fluorinated dienes **16**–**17**. Ph-CH$^{1'}$=CF-CH$^{3'}$=CH$^{4'}$-R.

Compound	*R*	$H^{1'}$ [a]	$H^{3'}$ [b]	$H^{4'}$ [a]	*Ph*	*R*
(***E,E***)-**16**	4-Me-Ph	6.37 (20.0)	6.93 (25.0, 16.0)	7.08 (16.0)	7.30 (m, 5H)	2.32 (s, 3H), 7.13 (d, 8.7 Hz, 2H), 7.52 (d, 8.7 Hz, 2H)
(***Z,E***)-**16**	4-Me-Ph	5.79 (39.9)	6.61 (25.3, 15.9)	6.98 (15.9)	7.38 (m, 5H)	2.40 (s, 3H), 7.20 (d, 8.7 Hz, 2H), 7.62 (d, 8.7 Hz, 2H)
(***E,E***)-**17**	COOEt	6.65 (20.0)	7.55 (28.0, 15.0)	6.38 (15.0)	7.30–7.62 (m, 5H)	1.32 (t, 5.0 Hz, 3H), 1.50 (q, 5.0 Hz, 2H)

[a] Doublet. In parentheses: $^3J_{HH}$. [b] Doublet of doublets. In parentheses: $^3J_{HF}$, $^3J_{HH}$. [c] Doublet. In parentheses: $^3J_{HH}$.

Table XIV. ^{13}C NMR spectra ($CDCl_3$, 300.5 MHz) of fluorinated dienes **16**–**17**. Ph-C$^{1'}$H=C$^{2'}$F-C$^{3'}$H=C$^{4'}$H-R.

Compound	*R*	$C^{1'}$ [a]	$C^{2'}$ [a]	$C^{3'}$ [a]	$C^{4'}$ [a]	*Ph* [b]	*R*
(***E,E***)-**16**	4-Me-Ph	115.9 (22)	157.7 (245)	110.5 (30)	131.8	131.1 (13), 127.1, 129.0 (2.5), 128.6	21.3 (CH_3), 127.0 (2 CH), 129.5 (2CH), 133.3 (C), 138.6 (C)
(***Z,E***)-**16**	4-Me-Ph	119.8 (23)	157.7 (248)	110.1 (10)	129.6	133.9 (3.5), 127.2, 128.8 (8), 128.5	21.3 (CH_3), 126.7 (2 CH), 129.6 (2 CH), 133.1 (C), 138.3 (C)
(***E,E***)-**17**	COOEt	117.0 (18)	154.1 (240)	117.7 (55)	121.2	132.5 (10), 128.2, 129.1 (1), 128.7	14.1 (CH_3), 60.7 (CH_2), 166.3 (C)

[a] Doublet due to $^2J_{CF}$ coupling. In parentheses: coupling constant in Hz. [b] Successively: $C^{1''}$, $^3J_{CF}$ in Hz; $C^{2''}$, $C^{3''}$, $^4J_{CF}$ in Hz; $C^{4''}$.

IR (KBr): 3020, 2965, 2920, 1680, 1635, 1605, 1595, 1510, 1490, 1450, 1415, 1350, 1320, 1260, 1175, 1160, 1110, 1020, 975, 965, 920, 900, 840, 810, 750, 700, 690, 620 cm^{-1}.

MS (EI, 70 eV): *m/z* 248 (M^+), 223, 222, 220, 202, 161, 159, 147, 146, 119, 95, 91, 77, 65, 57.

Anal. calc. for $C_{17}H_{17}F$: C, 85.71; H, 6.40. Found: C, 85.56; H, 6.42.

• *Ethyl (2Z,4E)-2-fluoro-5-phenylpenta-2,4-dienoate (**E,E**)-**17***

A mixture of palladium diacetate (4.1 mg, 0.24 mmol, 0.03 equiv), triphenylphosphine (118 mg, 0.45 mmol, 0.06 equiv), bromofluoroalkene (**Z**)-**3b** (1.51 g, 7.5 mmol, 1 equiv), ethyl acrylate (0.97 g, 9.7 mmol, 1.3 equiv) and triethylamine (2 mL) was stirred at reflux temperature for 18 h. After the same work-up as for the preparation of enynes **10**–**13**, purification by flash chromatography on silica gel (pentane–ethyl acetate 95:5) gave (***E,E***)-**17** (1.17 g, 71%) as a colorless oil. ^{1}H and ^{13}C NMR data: see tables XIII and XIV.

IR (film): 3050, 2980, 1720, 1645, 1600, 1580, 1450, 1400, 1300, 1275, 1200, 1175, 1110, 1060, 1030, 980, 860, 830, 750, 715, 690, 650 cm^{-1}.

MS (EI, 70 eV): *m/z* 220 (M^+), 175, 147, 146, 145, 143, 127, 120, 115, 105, 101, 91, 78, 77, 76, 75, 74, 73, 69, 68, 64, 51.

• *(1E,3E)-1,4-Diphenyl-2-fluorobuta-1,3-diene (**E,E**)-**18a** and (2Z,4E)-1,4-diphenyl-2-fluorobuta-1,3-diene (**Z,E**)-**18a***

The procedure used was the same as for the preparation of **16**, starting from **1a** (1.0 g, 5 mmol, 1 equiv) as a 92:8 *E*/*Z* mixture, and styrene (0.624 g, 6 mmol, 1.2 equiv). The ^{1}H NMR spectrum of the raw product showed a 92:8 (*E,E*)/(*Z,E*) mixture of the expected diene. Purification by chromatography on silica gel (pentane) gave (***E,E***)-**18a** (0.795 g, 71%) as a colorless oil. ^{1}H and ^{13}C NMR data: see tables XV and XVI.

IR (film): 3020, 2960, 2920, 1645, 1590, 1485, 1330, 1320, 1280, 1260, 1190, 1150, 1100, 1075, 1035, 1000, 965, 910, 860, 800, 790, 760, 750, 685, 650, 620, 610 cm^{-1}.

MS (EI, 70 eV): *m/z* 224 (M^+), 223, 203, 146, 109, 101, 91.

Anal. calc. for $C_{16}H_{13}F$: C, 85.71; H, 5.80. Found: C, 85.62; H, 5.96.

The minor isomer (**Z,E**)-**18a** could be isolated in a separate fraction (0.052 g, 14%) as colorless crystals, Mp 128–129 °C. ^{1}H and ^{13}C NMR data: see tables XV and XVI.

IR (KBr): 3025, 2960, 2930, 1630, 1595, 1485, 1430, 1320, 1280, 1260, 1190, 1150, 1105, 1075, 1030, 1005, 995, 915, 910, 860, 800, 790, 760, 750, 685, 650, 620, 610 cm^{-1}.

MS (EI, 70 eV): *m/z* 224 (M^+), 223, 203, 146, 109, 101, 91.

Anal. calc. for $C_{16}H_{13}F$: C, 85.71; H, 5.80. Found: C, 85.57; H, 5.89.

• *(1E,3E)-1-Phenyl-2-fluoronona-1,3-diene (**E,E**)-**18b***

The procedure used was the same as for the preparation of **16**, starting from (**E**)-**5b** (0.471 g, 1.96 mmol, 1 equiv) and styrene (0.306 g, 2.91 mmol, 2 equiv). Purification by chromatography on silica gel (pentane) gave (***E,E***)-**18b** (0.350 g, 82%) as a colorless oil. ^{1}H NMR data: table XV.

MS (EI, 70 eV): *m/z* 218 (M^+), 161, 147, 146, 141, 129, 128, 115, 101, 91, 83, 77, 75.

• *Ethyl (2E,4E)-2-fluoro-5,5-diphenylpenta-2,4-dienoate (**E,E**)-**19** and ethyl (2Z,4E)-2-fluoro-5,5-diphenylpenta-2,4-dienoate (**Z,E**)-**19***

A mixture of palladium diacetate (13.7 mg, 0.06 mmol, 0.05 equiv), triphenylphosphine (32 mg, 0.12 mmol, 0.10 equiv), bromofluoroester (**Z**)-**9a** (0.334 g, 1.22 mmol, 1 equiv), styrene (0.380 g, 3.66 mmol, 3 equiv) and triethylamine (3 mL) was stirred at reflux temperature for 1 h.

Table XV. ^{1}H NMR spectra ($CDCl_3$, 250 MHz) of fluorinated dienes **18–19**. $R^{(1)}$-$CF{=}CR^{(2)}$-$CH^{(3)}{=}CH^{(4)}$-Ph.

Compound	$R^{(1)}$	$R^{(2)}$	$H^{(3)a}$	$H^{(4)a}$	$R^{(2)}$	*Ph*	$R^{(1)}$
(*E,E*)-**18a**	Ph	H	7.02 (15.5, 11.0)	6.75 (15.5)	6.38 (dd, 20.0 Hz, 11.0 Hz)	7.30–7.75 (m, 10H)	
(*Z,E*)-**18a**	Ph	H	7.19 (15.0, 11.0)	6.60 (15.0)	6.20 (dd, 34.8 Hz, 11.0 Hz)	7.15–7.57 (m, 10H)	
(*E,E*)-**18b**	*n*-C_5H_{11}	H	6.72 (17.7, 10.9)	5.75 (17.7)	5.29 (dd, 23.2 Hz, 10.9 Hz)	7.30 (m, 5H)	0.90 (t, 7.0 Hz, 3H), 1.31 (m, 2H), 1.52 (m, 2 H), 2.25 (dt, 17.4 Hz, 7.1 Hz, 2H)
(*E,E*)-**19**	$COOEt$	Ph	8.25 (16.1, 1.7)	6.35 (16.1)		7.20–7.40 (m, 10H)	1.42 (t, 7.1 Hz, 3H), 4.38 (q, 7.1 Hz, 2H)
(*Z,E*)-**19**	$COOEt$	Ph	7.50 (16.1, 1.7)	6.40 (16.1)		7.25–7.43 (m, 10H)	1.10 (t, 7.1 Hz, 3H), 4.30 (q, 7.1 Hz, 2H)

[a] Doublet of doublets. In parentheses: $^3J_{HH}$, $^3J_{HF}$ in Hz. [b] Doublet. In parentheses: $^3J_{HH}$ in Hz.

Table XVI. ^{13}C NMR spectra ($CDCl_3$, 100.5 MHz) of fluorinated dienes **18–19**. $R^{(1)}$-$C^{(1)}F{=}C^{(2)}R^{(2)}$-$C^{(3)}H{=}C^{(4)}H$-Ph.

Compound	$R^{(1)}$	$R^{(2)}$	$C^{(1)a,b}$	$C^{(2)a,b}$	$C^{(3)a,b}$	$C^{(4)a,b}$	$R^{(1)}$	$R^{(2)}$, *Ph*
(*E,E*)-**18a**	Ph	H	159.2 (246)	110.1 (30)	122.5 (10)	133.3 (10)	127.9 (2CH, d, 5 Hz), 128.6[c] (2CH), 129.5 (CH), 131.9 (C, d, $^2J_{CF}$ = 28 Hz)	126.3 (2CH), 127.5 (CH), 128.7[c] (2CH), 137.2 (C)
(*Z,E*)-**18a**	Ph	H	157.1 (255)	106.9 (14)	120.9 (6)	132.3 (4)	123.9 (2CH, d, 8 Hz), 128.5[c] (2CH), 128.9 (CH), 132.0 (C, d, $^2J_{CF}$ = 27 Hz)	126.5 (2CH), 127.7 (CH), 128.6b (2CH), 137.3 (C)
(*E,E*)-**19**	$COOEt$	Ph	143.9 (260)	132.6 (10)	123.2 (7)	138.6 (6)	13.5 (CH_3), 61.0 (CH_2), 160.7 (C, d, $^2J_{CF}$ = 35 Hz)	127.2 (2 CH), 127.9 (CH), 128.0 (2 CH), 128.6 (2 CH), 128.8 (CH), 129.3 (2 CH), 134.0 (C, d, $^3J_{CF}$ = 5 Hz), 136.2 (C)
(*Z,E*)-**19**	$COOEt$	Ph	143.5 (260)	134.7 (20)	117.4 (5)	138.7 (12)	14.1 (CH_3), 61.5 (CH_2), 161.6 (C, d, $^2J_{CF}$ = 35 Hz)	127.0 (2 CH), 128.2 (2 CH), 128.3 (2 CH), 128.5 (CH), 128.6 (CH), 129.4 (2 CH), 133.3 (C, d, $^3J_{CF}$ = 4 Hz), 136.6 (C)

[a] Doublet due to C–F coupling. In parentheses: coupling constant in Hz. [b] Assignment may be reversed.

After the same work-up as for preparation of **14**, purification by chromatography on silica gel (pentane/ethyl acetate (95:5)) gave the two isomers separately. ^{1}H and ^{13}C NMR data, see tables XV and XVI.

(E,E)-19 (101 mg, 28%)

MS (EI, 70 eV): *m/z* 296 (M^+), 276, 231, 222, 221, 220, 204, 203, 202, 191, 146, 133, 115, 108, 105, 102, 101, 91, 77, 51.

(Z,E)-19 (190 mg, 53%)

MS (EI, 70 eV): *m/z* 296 (M^+), 276, 231, 222, 221, 220, 204, 203, 202, 191, 146, 133, 115, 108, 105, 102, 101, 91, 77, 51.

• *(1E)-2-Fluoro-1-phenylpenta-1,3-diene (E)-20*

A mixture of (**Z**)-**3a** (1.0 g, 5 mmol), prop-2-enyltributyltin (3.31 g, 10 mmol, 2 equiv) and tetrakis(triphenylphosphine)palladium (289.7 mg, 0.25 mmol, 0.05 equiv) in THF (5 mL) was stirred at reflux temperature for 18 h. Water was added to the cooled mixture, the organic phase was extracted with pentane and dried ($MgSO_4$). After evaporation of the solvent under reduced pressure the residue was purified by chromatography on silica gel (pentane) to give (**E**)-**20** (640 mg, 79%).

IR (film): 3095, 3060, 3025, 2960, 2925, 2880, 1685, 1645, 1600, 1580, 1500, 1450, 1425, 1360, 1245, 1200, 1170, 1085, 1075, 995, 920, 880, 850, 750, 700, 665, 660, 500 cm^{-1}.

^{1}H NMR ($CDCl_3$, 250 MHz): δ 3.34 (ddt, J = 23.9 Hz, 6.0 Hz and 1.6 Hz, 2H), 5.32 (dt, J = 10.1 Hz and 1.6 Hz, 1 H), 5.40 (dt, J = 17.1 Hz and 1.6 Hz, 1H), 6.06 (ddt, J = 17.1 Hz, 10.1 Hz and 6.0 Hz, 1H), 6.43 (d, J = 21.2 Hz, 1H), 7.30 (m, 3H), 7.48 (m, 2H).

^{13}C NMR ($CDCl_3$, 62.8 MHz): δ 33.6 (CH_2, d, J = 27.5 Hz), 109.2 (CH, d, J = 27.6 Hz), 117.5 (CH), 126.8 (CH), 128.3 (2CH, d, $^3J_{CF}$ = 3.5 Hz), 128.5 (2CH), 132.1 (CH, d, $^3J_{CF}$ = 1.7 Hz), 134.0 (C, d, $^3J_{CF}$ = 13.4 Hz), 159.8 (C, d, $^1J_{CF}$ = 253.5 Hz).

MS (EI, 70 eV): 162 (M^+), 161, 159, 148, 147, 146, 141, 134, 133, 129, 128, 127, 115, 109, 91, 89, 84, 83, 63, 57, 51.

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