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Graphical Abstract

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First practical synthesis of 2- or 3-fluoroalkylated indenols via cobalt-catalyzed [2+3] carbocyclization of fluorine-containing alkynes and 2-iodoaryl ketones

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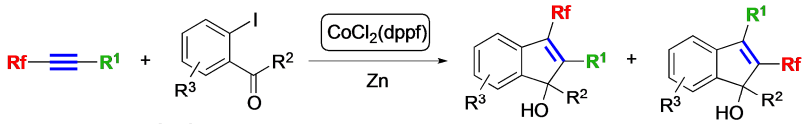

Rf = CF_3, CHF_2 R^2, R^3 = Me, 4-ClC_6H_4, 4-$MeOC_6H_4$, $PhMe_2Si$, etc.

ca. 70 : 30

19 examples (up to 98% yield)

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First practical synthesis of 2- or 3-fluoroalkylated indenols via cobalt-catalyzed [2+3] carbocyclization of fluorine-containing alkynes and 2-iodoaryl ketones

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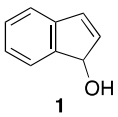
ABSTRACT

[2+3] Cycloaddition reaction of fluorine-containing alkynes with various 2-iodoaryl ketones in the presence of $CoCl_2$(dppf) catalyst proceeded very smoothly to give the corresponding 2- or 3-fluoroalkylated indenols in 57–98% yields. These regioisomers could be successfully separated and obtained in a pure form. From X-ray crystallographic and NOESY analyses, major or minor regioisomers were determined as 3- or 2-fluoroalkylated indenols, respectively.

1. Introduction

The indenol skeleton **1** (Fig. 1) is frequently found not only in the structure of naturally occurring substances but also in the framework of various biologically active materials, such as analgesics, insecticides or muscle relaxants.[1,2] Therefore, enormous attention has been paid to fluorine-containing indenol derivatives these days, since biological activities are often dramatically improved by introducing a small number of fluorine atoms into organic substances. However, there have been quite limited studies on the synthesis of fluoroalkylated indenols, despite such great pharmaceutical as well as agrochemical advantages imparted by fluorine atom(s).[3]

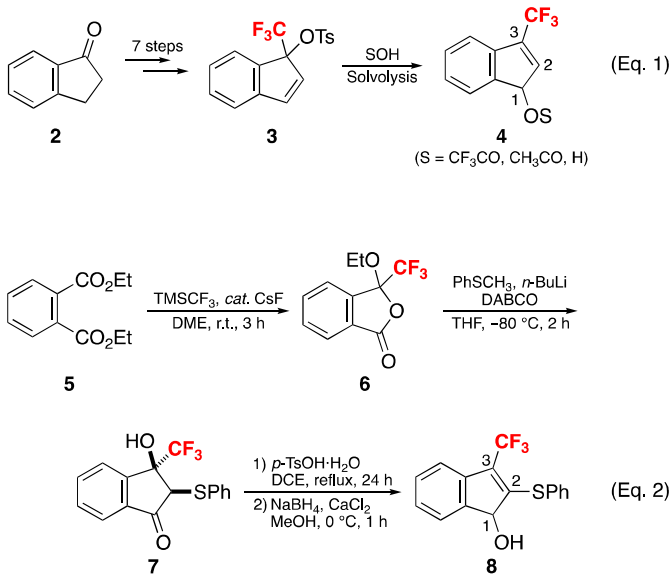


1

Fig. 1. Indenol skeleton.

Tidwell et al. have reported that the indenol derivative **3** having a trifluoromethyl (CF_3) group at the same carbon with a tosyloxy group, which could be prepared in 7 steps from the corresponding indanone **2**, underwent acid solvolysis to yield 3-CF_3 indenol derivatives **4** (Scheme 1. Eq. 1).[4] According to Yamazaki et al., on the other hand, the phthalide **6**, readily prepared from the reaction of diethyl phthalate **5** with the Ruppert-Prakash reagent ($TMSCF_3$) in the presence of a catalytic amount of cesium fluoride, reacts smoothly with phenylthiomethyllithium at –80 °C to give the corresponding CF_3-indanone **7**. Then, a dehydration reaction of **7** and the subsequent carbonyl-reduction provide the 3-CF_3 indenol **8** (Eq. 2).[5]

However, these are multi-step reaction-involved scheme, and the total yields are also extremely low. In addition, they are the only reports on the synthesis of 3-fluoroalkyl indenols. To the best of our knowledge, no publication has been made on indenols having a fluoroalkyl group at the 2 position at all so far.[6]



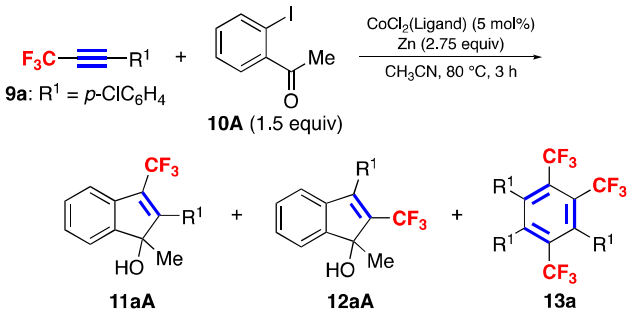
Scheme 1. Precedent works for the preparation of CF_3-containing indenols.

Herein we report a facile and practical synthetic protocol for 2- and 3-fluoroalkylated indenols *via* cobalt-catalyzed [2+3] carbocyclization reaction which was developed by Cheng *et al*. as a pioneering work,[7] using fluorine-containing internal alkynes with various 2-iodoaryl ketones in detail.

2. Results and discussion

An initial screening of the reaction conditions for the cobalt-catalyzed [2+3] carbocyclization reaction was performed using trifluoromethylated internal alkyne **9a**[8] and 2-iodoacetophenone **10A**. The results are summarized in Table 1.

Table 1. Screening for the reaction conditions of [2+3] carbocyclization.



Entry	Ligand	Yield[a] /%	
		11aA+12aA [**11aA/12aA**][b]	**13a**
1	None	15 [72/28]	53
2	dppe	73 [66/34]	14
3	dppb	83 [73/27]	13
4	(*S*)-BINAP	84 [73/27]	13
5	dppf	95 [72/28]	trace
6	phen	81 [80/20]	9
7	PPh_3	81 [80/20]	9
8[c]	dppf	89 [71/29]	trace
9[d]	dppf	99 [71/29]	trace
10[e]	dppf	84 [72/28]	8
11[f]	dppf	75 [70/30]	trace
12[g]	dppf	54 [73/27]	6
13[h]	–	0	0
14[i]	dppf	98 [70/30]	trace
15[j]	dppf	32 [67/33]	31

[a] Determined by ^{19}F NMR.
[b] Values in brackets are isomeric ratios of **11aA** and **12aA**.
[c] With $CoBr_2$(dppf).
[d] With CoI_2(dppf).
[e] Carried out at 50 ℃.
[f] With 1.0 equiv of Zn.
[g] With 3 mol% of $CoCl_2$(dppf).
[h] Without any cobalt catalyst.
[i] With 1.1 equiv of 2-iodoacetophenone.
[j] With 1.1 equiv of 2-bromoacetophenone.

To a solution of 5 mol% of $CoCl_2$ and 2.75 equiv of zinc powder in acetonitrile was added 1.0 equiv of **9a** and 1.5 equiv of 2-iodoacetophenone **10A**, and the mixture was heated at 80 °C for 3 h. As a result, [2+3] carbocyclization took place to give the desired cyclized products **11aA** and **12aA** in only 15% yield as a regioisomeric mixture (72:28), together with an undesired formation of alkyne trimerization product **13a** in 53% yield (Entry 1). As shown in Entries 2–6, we carried out the reaction using cobalt catalysts containing various bidentate phosphine ligands. Carbocyclizations in the presence of cobalt catalysts coordinated by 1,2-bis(diphenylphosphino)ethane (dppe), 1,4-bis(diphenylphosphino)butane (dppb), or (*S*)-2,2'-bis(diphenylphosphino)-1,1'-binaphthyl ((*S*)-BINAP) resulted in a significant improvement of the yield of the desired indenol derivatives (Entries 2-4). When 1,1'-bis(diphenylphosphino)ferrocene (dppf) was used as a ligand, in particular, desired cycloadducts **11aA**/**12aA** were obtained in 95% combined yields, together with very small amount of trimerization adduct **13a** (Entry 5). The use of 1,10-phenanthroline (phen) as a ligand was also found to be efficient, though the yield of fluorine-containing indenol derivatives was slightly decreased (Entry 6). Even when the ligand was switched from a bidentate to a monodentate ligand, like PPh_3, the yield or isomeric ratio of the reaction products did not change drastically (Entry 7).

It should be noted that cobalt catalyst substituted by other halogens (X = Br, I) also did not affect the yields and regioselectivity (Entries 8 and 9). Lower temperature deterred the reaction proceeding (Entry 10). Yields were somewhat eroded with decreasing the amount of zinc powder (1.0 equiv, Entry 11) or catalyst loading (3 mol%, Entry 12). Additionally, **11aA** and **12aA** were not obtained at all in the absence of cobalt catalyst, and the starting alkyne was completely recovered (Entry 13). Finally, the desired cyclization products were obtained in an excellent yield even when only 1.1 equiv of 2-iodoacetophenone was used (Entry 14). However, the use of 1.1 equiv of 2-bromoacetophenone caused a significant decrease in the yield, leading to trimerization product **13a** in 31% yield (Entry 15). In all cases, almost the same regioselectivity was detected.

With the optimal reaction conditions (Table 1, Entry 14), we carried out cobalt-catalyzed [2+3] carbocyclization reaction using various fluoroalkylated internal alkynes **9** and 2-iodoacetophenone **10A**. The results are summarized in Table 2.

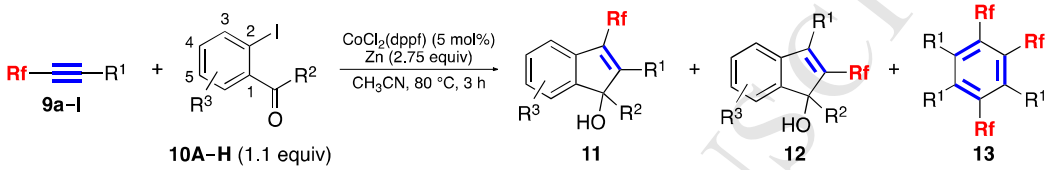
As shown in Entries 1–3, the position of the substituent on the benzene ring in the fluorinated alkynes, like *para*-, *meta*-, or *ortho*-position, did not affect the reaction at all, giving the corresponding products **11A**/**12A** in excellent yields. Substrates having various substituents on the benzene ring of the fluoroalkylated alkynes, such as electron-donating (MeO) or electron-withdrawing (CO_2Et) group, were found to be applicable in the present [2+3] cyclization to afford the fluoroalkylated indenol derivatives (Entries 4 and 5), though a slight decrease in the yield was observed in the case of the fluorinated alkynes having a 4-biphenyl or a dimethylphenylsilyl group as an R^1 (Entries 6 and 7). It should be noted that fluoroalkylated aliphatic alkyne **9h** could also be applied, giving the corresponding products **11hA**/**12aH** in moderate yield with the reverse of regioselectivity (22:77) (Entry 8). Besides, fluoroalkylated propargyl alcohols with a bulky substituent as an R^1 were found to be unsuitable for the cobalt-catalyzed [2+3] carbocyclization reaction (Entries 9 and 10). Difluoromethylated alkyne could be successfully applied to the present reaction (Entry 11), while *n*-perfluorobutyl (*n*-C_4F_9)-containing alkyne was not suitable for the reaction, resulting in complex mixtures (Entry 12).

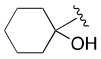
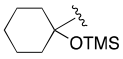
Subsequently, we examined the cobalt-catalyzed [2+3] carbocyclization reaction using alkyne **9a** (R^1 = 4-ClC_6H_4) and alkyl or variously substituted aryl 2-iodoaryl ketones. The 2-iodoaryl ketone **10B** bearing a cyclohexyl group as an R^2 also provided the corresponding cycloadducts **11aB** and **12aB** in high yield (Entry 13), whereas the reaction using 2-iodobenzophenone **10C** (R^2 = Ph) became somewhat sluggish, resulting in 57% combined yields of **11aC** and **12aC**, along with a formation of the trimerization product **13a** in 26% yield (Entry 14). As shown in Entries 15-17, electron-rich acetophenones **10D**–**F** possessing an electron-donating group on the aromatic ring gave the corresponding fluoroalkylated indenols in acceptable yields,

while a significant retard of the reaction was observed in the case of electron-deficient substrates, e.g., **10G** and **10H**, with an electron-withdrawing group on the aromatic ring, leading to the corresponding **11a** and **12a** only in around 28% combined yields (Entries 18 and 19). It was noteworthy that regioisomers **11** and **12** were easily separated from each other in many cases by simple silica gel column chromatography, which becomes a strong point for the practical applications.

Stereochemical assignment of the indenols **11** and **12** was carried out by double elucidation using X-ray crystallographic analysis and NMR technique. Thus, the major regioisomer **11aA** obtained through the reaction of **9a** (Rf = CF_3, R^1 = 4-ClC_6H_4) with **10A** (R^2 = Me, R^3 = H) formed single crystal suitable for X-ray crystallographic analysis by recrystallization from hexane/CH_2Cl_2. As shown in Fig. 2, the major regioisomer **11aA** was found to possess a CF_3 group at the 3-position. Additionally, NOESY analysis of the major regioisomer **11aF** obtained *via* the carbocyclization reaction of **9a** (Rf = CF_3, R^1 = 4-ClC_6H_4) and **10F** (R^2 = Me, R^3 = 4,5-OCH_2O) was carried out (For the detail, see Supporting Information), and as shown in Fig. 3, two strong correlations between H_c and H_e, and H_d and H_e were detected, whereas no cross-peak was observed between H_e and H_g, strongly indicating that the major compound **11aF** possessed a CF_3 group at the 3-position. The stereochemical assignments of other products were performed on the basis of the chemical shifts in ^{19}F NMR. Thus, comparing the chemical shifts in ^{19}F NMR for **11aA**/**12aA** or **11aF**/**12aF**, the signals of the major isomers, **11aA**, **11aF** appear at higher magnetic field than those of the minor regioisomers, **12aA**, **12aF**, respectively.[9] The difference of the chemical shifts was found to be qualitatively analogous to the situation in other regioisomers **11**/**12**. Therefore, the major isomers **11** or the minor ones **12** were safely assigned as 3- or 2-fluoroalkylated products, respectively.

Table 2. Cobalt-catalyzed [2+3] carbocyclization reaction of various fluorinated alkynes with various 2-iodoaryl ketones.



Entry	Rf	R^1	R^2	R^3	Product	Combined yield[a]/% of **11**+**12** [Isolated yield of **11**, **12**]	Ratio[a] of **11**/**12**	Yield[a]/% of **13**
1	CF_3	4-ClC_6H_4	Me	H	**11aA/12aA**	98 [52, 25]	70/30	trace
2	CF_3	3-ClC_6H_4	Me	H	**11bA/12bA**	93 [57, 25]	68/32	trace
3	CF_3	2-ClC_6H_4	Me	H	**11cA/12cA**	90 [77][b,c]	78/22	0
4	CF_3	4-$MeOC_6H_4$	Me	H	**11dA/12dA**	91 [73][c]	75/25	8
5	CF_3	4-$EtO_2CC_6H_4$	Me	H	**11eA/12eA**	82 [73][c]	72/28	8
6	CF_3	4-PhC_6H_4	Me	H	**11fA/12fA**	66 [40, 14]	71/29	20
7[d]	CF_3	$PhMe_2Si$	Me	H	**11gA/12gA**	61 [49][c]	64/36	5
8	CF_3	*n*-C_6H_{13}	Me	H	**11hA/12hA**	48[e]	22/77	39
9	CF_3		Me	H	**11iA/12iA**	23	82/18	0
10	CF_3		Me	H	**11jA/12jA**	14	71/29	0
11	CHF_2	4-ClC_6H_4	Me	H	**11kA/12kA**	78 [61, 10]	88/12	0
12	*n*-C_4F_9	4-ClC_6H_4	Me	H	**11lA/12lA**	16	75/25	0
13	CF_3	4-ClC_6H_4	Cy	H	**11aB/12aB**	84 [57, 23]	71/29	0
14	CF_3	4-ClC_6H_4	Ph	H	**11aC/12aC**	57 [37, 12]	73/27	26
15	CF_3	4-ClC_6H_4	Me	4-Me	**11aD/12aD**	88 [41, 24]	70/30	10
16	CF_3	4-ClC_6H_4	Me	4-MeO	**11aE/12aE**	62 [23, 16]	63/37	20
17	CF_3	4-ClC_6H_4	Me	4,5-OCH_2O	**11aF/12aF**	63 [31, 20]	59/41	33
18	CF_3	4-ClC_6H_4	Me	4-Cl	**11aG/12aG**	27	64/36	59
19	CF_3	4-ClC_6H_4	Me	4-CF_3	**11aH/12aH**	28	67/33	64

[a] Determined by ^{19}F NMR.
[b] Atropisomers of **11cA** and **12cA** were detected.
[c] Combined isolated yield.
[d] Performed using 2.0 equiv of **10A** and 10 mol% of cobalt catalyst.
[e] Unable to be purified because of undesired byproducts.

The above results allow us to propose the following reaction mechanism which is similar to the previously reported one,[10] as shown in Scheme 2. Thus, the reaction presumably proceeds as follows: (1) reduction of cobalt(II) catalyst by zinc metal generates the cobalt(I) species, (2) oxidative addition of Co(I) to C–I bond of 2-iodoaryl ketone gives the corresponding arylcobalt complex **Int-1**, (3) insertion of alkyne **9** into the Co-C_{Ar} bond (**Int-2**),[11] (4) intramolecular nucleophilic addition of carbon attached with Co metal to the carbonyl moiety to afford the corresponding cobalt alkoxide **Int-3**, (5) reduction of cobalt(III) complex by zinc metal brings about a cobalt(I) alkoxide **Int-4**, (6) transmetalation with ZnX_2 (X = Cl or I) forms zinc alkoxide **Int-5**, together with regeneration of Co(I) species, and (7)

hydrolysis of **Int-5** gives rise to the desired fluoroalkylated indenol derivatives **11** or **12**.

The formation of tris(trifluoromethyl)benzene derivative **13** as a side product can be explained by cobalt-catalyzed [2+2+2] cyclotrimerization of fluorinated alkynes of **9**, as described in the previous literature.[12] Thus, the generated Co(I) interacts with two molecules of fluorinated alkyne **9** to form cobaltacyclopentadiene complex **Int-1'**. Subsequent [4+2] cycloaddition of **Int-1'** with another molecule of the alkyne furnishes cobaltanorbornadiene **Int-2'**, followed by the reductive elimination, affording the corresponding trimerization product **13**.

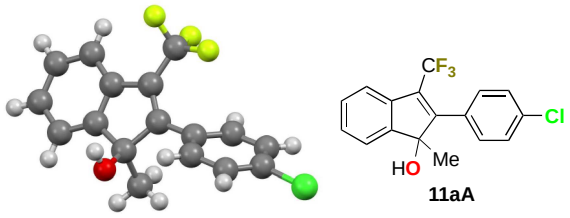


Fig. 2. X-ray crystallographic analysis of **11aA**.

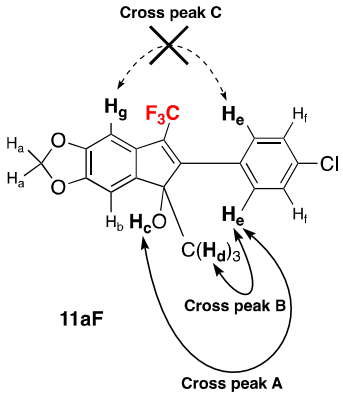


Fig. 3. NOE correlations of **11aF** observed by NOESY measurement.

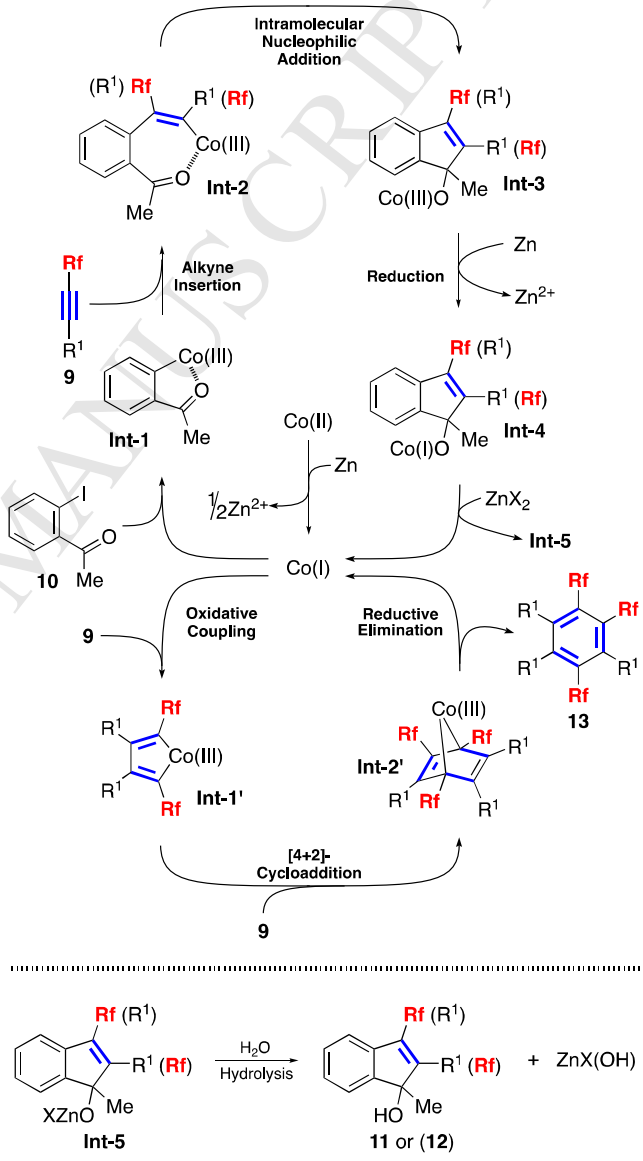
3. Conclusion

In conclusion, we accomplished the convenient synthesis of 2- and 3-fluoroalkylated indenols *via* cobalt-catalyzed [2+3] carbocyclization reaction of fluorine-containing alkynes with 2-iodoaryl ketones. Although the reaction did not proceed regioselectively, 2- and 3-fluoroalkylated indenol derivatives could be successfully separated in many cases by a simple silica gel column chromatography. The present cobalt-catalyzed carbocyclization was also applicable for various fluorinated alkynes and 2-iodoaryl ketones, giving rise to various fluorine-containing indenols in good to high yields. This process would become useful synthetic protocol for fluorine-containing carbocycles of biological interest.

4. Experimental section

4.1. General information

^{1}H and ^{13}C NMR spectra were obtained using an AVANCE III 400 NMR spectrometer (^{1}H: 400 MHz and ^{13}C: 100 MHz) in chloroform-*d* ($CDCl_3$) (Bruker, Germany), and the chemical shifts are reported in parts per million (ppm) based on the residual proton signal of the NMR solvent. ^{19}F NMR (376 MHz) spectra were obtained using AVANCE III 400 NMR spectrometer in $CDCl_3$ with $CFCl_3$ (δ_F = 0 ppm) as an internal standard (Bruker, Germany). The Bruker AVANCE III 400 NMR spectrometer was used for determining the yield of the products with trifluoromethylbenzene ($CF_3C_6H_5$) or hexafluorobenzene (C_6F_6) as internal references. IR spectra were recorded using the KBr method with FT/IR-4100 typeA spectrometer (JASCO, Japan); all spectra are reported in wavenumbers (cm^{-1}). High-resolution mass spectra were recorded on a JMS-700MS spectrometer (JEOL, Japan) using the fast- atom bombardment (FAB) method.



Scheme 2. Proposed reaction mechanism.

All reactions were carried out using dried glassware with a magnetic stirrer bar and routinely monitored by ^{19}F NMR spectroscopy or thin-layer chromatography (TLC). All chemicals were of reagent grade and, if necessary, purified in the usual manner prior to use. Cobalt catalysts used in this research were prepared according to the literature.[13] Column chromatography was carried out on silica gel (Wako gel® 60N, 38–100 μm) and

TLC analysis was performed on silica gel TLC plates (Merck, Silica gel 60F_{254}).

X-ray Crystallography: A colorless prismic crystal of **11aA** having approximate dimensions of 0.13×0.12×0.10 mm was mounted on a glass fiber. All measurements for **11aA** were made on a diffractometer with filtered MoKα radiation (λ= 0.71073 Å) and a rotating anode generator using a VariMax with PILATUS/DW (Rigaku); Compound **11aA**. tetragonal, a = 23.8638(15) Å, b = 23.8638(15) Å, c = 10.6175(12) Å, α = 90°, β = 90°, γ = 90°, V = 6046.5(10) Å^3, T = 173(2) K, space group $I4_1/a$ (no. 88), Z = 16 reflection measured, 3726 unique which were used in all calculations. The final R_1 and wR_2 were 0.1645 and 0.1909 ($I > 2\sigma(I)$). All calculations were performed using the CrystalStructure crystallographic software package. The structure was solved by direct methods and expanded using Fourier techniques. The structural model was refined by a full-matrix least-squares method using SHELXL-2014/6.[14] All calculations were performed using the SHELXL program. Crystallographic data for this compound has been deposited with the Cambridge Crystallographic Data Centre as supplementary data no. CCDC 1817768. Copy of the data can be obtained free of charge by applying to The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK (https://summary.ccdc.cam.ac.uk/structure-summary-form).

4.2. Typical procedure for the [2+3] carbocyclization of fluoroalkylated alkynes and 2-iodophenyl ketones

In a 30 mL two-necked round bottomed-flask, equipped with a magnetic stirring bar, were placed fluoroalkylated alkyne **9a** (0.123 g, 0.60 mmol), 2-iodoacetophenone **10A** (0.089 mL, 0.66 mmol), zinc powder (0.108 g, 1.65 mmol), and $CoCl_2$(dppf) (21 mg, 31 μmol) in acetonitrile (3.0 mL), and the resulting mixture was stirred at 80 °C with an oil bath. After 3 h, the reaction mixture was cooled to r.t., diluted with CH_2Cl_2 and then stirred in the air for 15 min. Subsequently, the reaction mixture was subjected to flash column chromatography using silica gel as stationary phase and CH_2Cl_2 as mobile phase. After removal of the solvent from the eluent under reduced pressure, the residue was purified by silica gel column chromatography (Hexane/AcOEt = 5:1) to give the corresponding 2-(4-chlorophenyl)-1-methyl-3-trifluoromethyl-1H-inden-1-ol **11aA** (0.102 g, 0.314 mmol) and 3-(4-chlorophenyl)-1-methyl-2-trifluoromethyl-1H-inden-1-ol **12aA** (0.049 g, 0.15 mmol).

*4.2.1. 2-(4-Chlorophenyl)-1-methyl-3-trifluoromethyl-1H-inden-1-ol (**11aA**).*

Yield: 52%; white solid, M.p. 105.1–105.3 °C, eluent of the column chromatography: Hexane/EtOAc = 5/1; ^{1}H NMR ($CDCl_3$): δ 1.41 (s, 3H, CH_3), 2.21 (s, 1H, OH), 7.29–7.43 (m, 6H, ArH), 7.45–7.50 (m, 2H, ArH); ^{13}C NMR ($CDCl_3$): δ 23.6 (*C*H$_3$), 83.4 (*C*-OH), 121.3 (Ar), 122.56 (Ar), 122.63 (q, J = 272.5 Hz, *C*F$_3$), 127.88 (Ar), 127.93 (q, J = 32.6 Hz, CF$_3$-*C*), 128.6 (Ar), 129.4 (Ar), 130.0 (Ar), 131.0 (Ar), 135.0 (Ar), 136.2 (Ar), 147.8 (Ar), 154.0 (q, J = 4.1 Hz, CF$_3$-C=*C*); ^{19}F NMR ($CDCl_3$, $CFCl_3$): δ –60.16 (s, 3F); IR (KBr) 3347, 3070, 2973, 2926, 1493, 1474, 1375, 1335, 1200, 1128, 1092, 773, 762, 725, 697 cm^{-1}; HRMS (FAB): calcd for [M$^+$] $C_{17}H_{12}ClF_3O$: 324.0529, Found: 324.0533.

*4.2.2. 3-(4-Chlorophenyl)-1-methyl-2-trifluoromethyl-1H-inden-1-ol (**12aA**).*

Yield: 25%; yellow oil, eluent of the column chromatography: Hexane/EtOAc = 5/1; ^{1}H NMR ($CDCl_3$): δ 1.82 (s, 3H, CH_3), 2.16 (s, 1H, OH), 7.04 (d, J = 7.5 Hz, 1H, ArH), 7.29–7.34 (m, 3H, ArH), 7.40 (tm, J = 7.5 Hz, 1H, ArH), 7.46 (d, J = 8.6 Hz, 2H, ArH), 7.54 (d, J = 7.5 Hz, 1H, ArH); ^{13}C NMR ($CDCl_3$): δ 24.4 (*C*H$_3$), 82.3 (*C*-OH), 122.2 (Ar), 122.7 (Ar), 123.5 (q, J = 272.3 Hz, *C*F$_3$), 128.90 (Ar), 129.2 (Ar), 129.4 (Ar), 129.8 (d, J = 1.3 Hz, Ar), 130.6 (Ar), 135.07 (Ar), 135.09 (q, J = 32.9 Hz, CF$_3$-*C*), 139.7 (Ar), 146.7 (q, J = 4.9 Hz, CF$_3$-C=*C*), 149.0 (Ar); ^{19}F NMR ($CDCl_3$, $CFCl_3$): δ –55.94 (s, 3F); IR (neat) 3371, 3073, 2982, 2934, 1632, 1491, 1353, 1253, 1195, 1147, 1022, 817, 762, 727 cm^{-1}; HRMS (FAB): calcd for [M$^+$] $C_{17}H_{12}ClF_3O$: 324.0529, Found: 324.0529.

*4.2.3. 2-(3-Chlorophenyl)-1-methyl-3-trifluoromethyl-1H-inden-1-ol (**11bA**).*

Yield: 57%; white solid, M.p. 89.8–90.1 °C, eluent of the column chromatography: Hexane/EtOAc = 5/1; ^{1}H NMR ($CDCl_3$): δ 1.46 (s, 3H, CH_3), 2.00 (s, 1H, OH), 7.26 (dt, J = 7.3, 2.1 Hz, 1H, ArH), 7.32–7.43 (m, 5H, ArH), 7.44–7.55 (m, 2H, ArH); ^{13}C NMR ($CDCl_3$): δ 23.6 (*C*H$_3$), 83.5 (*C*-OH), 121.8 (d, J = 1.3 Hz, Ar), 122.55 (q, J = 272.6 Hz, *C*F$_3$), 122.64 (Ar), 127.0 (d, J = 1.4 Hz, Ar), 128.0 (Ar), 128.2 (q, J = 32.8 Hz, CF$_3$-*C*), 128.6 (d, J = 1.2 Hz, Ar), 129.0 (Ar), 129.4 (Ar), 129.6 (Ar), 134.3 (Ar), 134.4 (Ar), 136.1 (Ar), 147.8 (Ar), 154.0 (q, J = 4.1 Hz, CF$_3$-C=*C*); ^{19}F NMR ($CDCl_3$, $CFCl_3$): δ –60.23 (s, 3F); IR (KBr) 3360, 3073, 2968, 1564, 1471, 1373, 1334, 1198, 1171, 1156, 1088, 760, 735, 716 cm^{-1}; HRMS (FAB): calcd for [M$^+$] $C_{17}H_{12}ClF_3O$: 324.0529, Found: 324.0520.

*4.2.4. 3-(3-Chlorophenyl)-1-methyl-2-trifluoromethyl-1H-inden-1-ol (**12bA**).*

Yield: 25%; white solid, M.p. 70.8–71.2 °C, eluent of the column chromatography: Hexane/EtOAc = 5/1; ^{1}H NMR ($CDCl_3$): δ 1.82 (s, 3H, CH_3), 2.24 (s, 1H, OH), 7.05 (d, J = 7.5 Hz, 1H), 7.24–7.30 (m, 1H, ArH), 7.31 (td, J = 7.5, 1.0 Hz, 1H, ArH), 7.36–7.47 (m, 4H, ArH), 7.54 (d, J = 7.4 Hz, 1H, ArH); ^{13}C NMR ($CDCl_3$): δ 24.4 (*C*H$_3$), 82.3 (*C*-OH), 122.2 (Ar), 122.8 (Ar), 123.5 (q, J = 272.2 Hz, *C*F$_3$), 126.7 (d, J = 1.4 Hz, Ar) , 128.4 (d, J = 1.7 Hz, Ar), 129.15 (Ar), 129.23 (Ar), 129.4 (Ar), 129.9 (Ar), 134.0 (Ar), 134.6 (Ar), 135.3 (q, J = 29.9 Hz, CF$_3$-*C*), 139.6 (Ar), 146.3 (q, J = 5.0 Hz, CF$_3$-C=*C*), 148.9 (Ar); ^{19}F NMR ($CDCl_3$, $CFCl_3$): δ –56.03 (s, 3F); IR (neat) 3377, 3072, 2983, 2935, 1636, 1588, 1566, 1475, 1461, 1419, 1352, 1250, 1198, 1119, 1055, 1021, 790, 502 cm^{-1}; HRMS (FAB): calcd for [M$^+$] $C_{17}H_{12}ClF_3O$: 324.0529, Found: 324.0524.

*4.2.5. 2-(2-Chlorophenyl)-1-methyl-3-trifluoromethyl-1H-inden-1-ol (**11cA**) and 3-(2-chlorophenyl)-1-methyl-2-trifluoromethyl-1H-inden-1-ol (**12cA**).*

Combined yield: 77%; Isometric ratio (**11cA**:**12cA**) = 78:22 (inseparable), yellow oil, eluent of the column chromatography: Hexane/EtOAc/Benzene = 5/1/2; **11cA**: (atropisomer 1): ^{1}H NMR ($CDCl_3$): δ 1.52 (s, 3H, CH_3), 1.96–2.40 (m, 1H, OH), 7.20–7.60 (m, 8H, ArH); ^{19}F NMR ($CDCl_3$): δ –63.48 (s, 3F); (atropisomer 2): ^{1}H NMR ($CDCl_3$): δ 1.56 (s, 3H, CH_3), 2.17–2.23 (m, 1H, OH), 7.20–7.60 (m, 8H, ArH); ^{19}F NMR ($CDCl_3$): δ –62.51 (s, 3F); **12cA**: (atropisomer 1): ^{1}H NMR ($CDCl_3$): δ 1.86 (s, 3H, CH_3), 2.17–2.23 (m, 1H, OH), 7.10–7.60 (m, 8H, ArH); ^{19}F NMR ($CDCl_3$): δ –57.95 (s, 3F); (atropisomer 2): ^{1}H NMR ($CDCl_3$): δ 1.83 (s, 3H, CH_3), 2.44–2.47 (m, 1H, OH), 7.10–7.60 (m, 8H, ArH); ^{19}F NMR ($CDCl_3$): δ –57.83 (s, 3F); IR (neat) 3402, 3390, 3056, 2981, 1378, 1200, 1173, 1147, 1131, 1118, 1093, 1064, 1052, 752, 752 cm^{-1}; HRMS (FAB): calcd for [M$^+$] $C_{17}H_{12}ClF_3O$: 324.0529, Found: 324.0519.

*4.2.6. 2-(4-Methoxyphenyl)-1-methyl-3-trifluoromethyl-1H-inden-1-ol (**11dA**) and 3-(4-methoxyphenyl)-1-methyl-2-trifluoromethyl-1H-inden-1-ol (**12dA**).*

Combined yield: 73%; Isometric ratio (**11dA**:**12dA**) = 75:25 (inseparable), yellow oil, eluent of the column chromatography: Hexane/EtOAc = 5/1; **11dA**: ^{1}H NMR ($CDCl_3$): δ 1.45 (s, 3H, HO-C-CH_3), 2.00 (s, 1H, O*H*), 3.85 (s, 3H, OCH_3), 6.96 (d, *J* = 8.8 Hz, 2H, Ar*H*), 7.26–7.41 (m, 4H, Ar*H*), 7.45 (d, *J* = 7.2 Hz, 1H, Ar*H*), 7.50 (d, *J* = 7.3 Hz, 1H, Ar*H*); ^{13}C NMR ($CDCl_3$): δ 23.7 (HO-C-*C*H_3), 55.2 (O*C*H_3), 83.3 (*C*-OH), 113.7 (Ar), 121.4 (d, *J* = 1.17, Ar), 122.5 (Ar), 123.8 (q, *J* = 272.0 Hz, *C*F_3), 124.8 (Ar), 126.6 (q, *J* = 32.3 Hz, CF_3-*C*), 127.4 (Ar), 129.1 (Ar), 136.5 (Ar), 140.1 (Ar), 147.9 (Ar), 155.2 (d, *J* = 3.5 Hz, CF_3-C=*C*), 159.9 (Ar); ^{19}F NMR ($CDCl_3$, $CFCl_3$): δ -60.07 (s, 3F); **12dA**: ^{1}H NMR ($CDCl_3$): δ 1.82 (s, 3H, HO-C-CH_3), 2.18 (s, 1H, O*H*), 3.87 (s, 3H, OCH_3), 7.00 (d, *J* = 8.8 Hz, 2H, Ar*H*), 7.12 (d, *J* = 7.4 Hz, 1H, Ar*H*), 7.26–7.40 (m, 4H, Ar*H*), 7.53 (d, *J* = 7.3 Hz, 1H, Ar*H*); ^{13}C NMR ($CDCl_3$): δ 24.1 (HO-C-*C*H_3), 55.2 (O*C*H_3), 82.1 (*C*-OH), 113.9 (Ar), 122.0 (Ar), 122.8 (Ar), 123.3 (q, *J* = 272.6 Hz, *C*F_3), 124.3 (d, *J* = 2.7 Hz, Ar), 128.9 (Ar), 129.0 (Ar), 129.8 (d, *J* = 1.0 Hz, Ar), 133.9 (q, *J* = 29.2 Hz, CF_3-*C*), 140.1 (Ar), 147.4 (d, *J* = 4.8 Hz, CF_3-C=*C*), 149.2 (Ar), 159.9 (Ar); ^{19}F NMR ($CDCl_3$, $CFCl_3$): δ –55.76 (s, 3F); IR (neat) 3377, 3074, 2976, 2934, 2840, 1606, 1511, 1461, 1377, 1356, 1335, 1290, 1252, 1199, 1174, 1146, 1121, 1035, 762, 733, cm^{-1}; HRMS (FAB): calcd for [M$^+$] $C_{18}H_{15}F_3O_2$: 320.1024, Found: 320.1033.

*4.2.7. Ethyl 4-(1-hydroxy-1-methyl-3-trifluoromethyl-1H-inden-2-yl)benzoate (**11eA**) and ethyl 4-(1-hydroxy-1-methyl-2-trifluoromethyl-1H-inden-3-yl)benzoate (**12eA**).*

Combined yield: 73%; Isometric ratio (**11eA**:**12eA**) = 72:28 (inseparable), yellow solid, eluent of the column chromatography: Hexane/EtOAc/benzene = 5/1/2; **11eA**: ^{1}H NMR ($CDCl_3$): δ 1.38–1.43 (m, 3H, CH_2C*H*$_3$), 1.45 (s, 3H, C-C*H*$_3$), 2.23 (s, 1H, O*H*), 4.35–4.42 (m, 2H, C*H*$_2$CH$_3$), 7.27–7.55 (m, 6H, Ar*H*), 8.08 (d, *J* = 6.7 Hz, 2H, Ar*H*); ^{13}C NMR ($CDCl_3$): δ 14.3 (CH_2*C*H$_3$), 23.6 (C-*C*H$_3$), 61.4 (*C*H$_2$CH$_3$), 83.5 (*C*-OH), 121.7 (Ar), 122.576 (Ar), 122.582 (q, *J* = 272.6 Hz, *C*F_3), 127.9 (Ar), 128.0 (q, *J* = 30.7 Hz, CF_3-*C*), 128.7 (d, *J* = 1.1 Hz, Ar), 129.3 (Ar), 129.7 (Ar), 130.5 (Ar), 136.0 (Ar), 137.6 (Ar), 148.1 (Ar), 154.4 (q, *J* = 4.0 Hz, CF_3-C=*C*), 166.4 (*C*=O); ^{19}F NMR ($CDCl_3$, $CFCl_3$): δ –60.23 (s, 3F); **12eA**: ^{1}H NMR ($CDCl_3$): δ 1.38–1.43 (m, 3H, CH_2C*H*$_3$), 1.83 (s, 3H, C-C*H*$_3$), 2.33 (s, 1H, O*H*), 4.35–4.42 (m, 2H, C*H*$_2$CH$_3$), 6.99 (d, *J* = 7.5 Hz, 1H, Ar*H*), 7.25–7.60 (m, 5H, Ar*H*), 8.13 (d, *J* = 6.7 Hz, 2H, Ar*H*); ^{13}C NMR ($CDCl_3$): δ 14.3 (CH_2*C*H$_3$), 24.3 (C-*C*H$_3$), 61.3 (*C*H$_2$CH$_3$), 82.3 (*C*-OH), 122.2 (Ar), 122.6 (Ar), 123.4 (q, *J* = 272.4 Hz, *C*F_3), 128.4 (d, *J* = 1.2, Ar), 129.1 (Ar). 129.2 (Ar), 129.3 (Ar), 130.8 (Ar), 135.4 (q, *J* = 29.8 Hz, CF_3-*C*), 136.9 (Ar), 139.5 (Ar), 146.7 (q, *J* = 4.7 Hz, CF_3-C=*C*), 149.1 (Ar), 166.5 (*C*=O); ^{19}F NMR ($CDCl_3$, $CFCl_3$): δ –56.03 (s, 3F); IR (KBr) 3461, 3074, 2980, 2931, 1698, 1606, 1310, 1297, 1201, 1173, 1115, 1058, 1023, 762, 717 cm^{-1}; HRMS (FAB): calcd for [M$^+$] $C_{20}H_{17}F_3O_3$: 362.1130, Found: 362.1118.

*4.2.8. 2-(4-Biphenyl)-1-methyl-3-trifluoromethyl-1H-inden-1-ol (**11fA**).*

Yield: 40%; yellow solid, M.p. 117.5–118.2 °C, eluent of the column chromatography: Hexane/EtOAc = 17/3; ^{1}H NMR ($CDCl_3$): δ 1.51 (s, 3H, C*H*$_3$), 2.06 (s, 1H, O*H*), 7.31–7.43 (m, 3H, Ar*H*), 7.44–7.56 (m, 6H, Ar*H*), 7.62–7.72 (4H, Ar-*H*); ^{13}C NMR ($CDCl_3$): δ 23.8 (*C*H$_3$), 83.6 (*C*-OH), 121.7 (d, *J* = 1.3 Hz, Ar), 122.6 (Ar), 122.8 (q, *J* = 272.7 Hz, *C*F_3), 127.0 (Ar), 127.2 (Ar), 127.68 (q, *J* = 32.0 Hz, CF_3-*C*), 127.71 (Ar), 129.0 (Ar), 129.1 (d, *J* = 1.2 Hz, Ar), 129.3 (Ar), 131.6 (Ar), 136.5 (Ar), 140.6 (Ar), 141.6 (Ar), 147.9 (Ar), 155.1 (q, *J* = 4.0 Hz, CF_3-C=*C*), the signal of one carbon was overlapped with other signals.; ^{19}F NMR ($CDCl_3$, $CFCl_3$): δ –60.09 (s, 3F); IR (KBr) 3278, 3032, 2981, 2928, 1376, 1200, 1158, 1113, 1061, 908, 828, 759, 733, 705 cm^{-1}; HRMS (FAB): calcd for [M$^+$] $C_{23}H_{17}F_3O$: 366.1232, Found: 366.1238.

*4.2.9. 3-(4-Biphenyl)-1-methyl-2-trifluoromethyl-1H-inden-1-ol (**12fA**).*

Yield: 14%; yellow solid, M.p. 142.7–143.0 °C, eluent of the column chromatography: Hexane/EtOAc = 17/3; ^{1}H NMR ($CDCl_3$): δ 1.86 (s, 3H, C*H*$_3$), 2.21 (s, 1H, O*H*), 7.15 (d, *J* = 7.4 Hz, 1H, Ar*H*), 7.32 (td, *J* = 7.5, 1.1 Hz, 1H, Ar*H*), 7.34–7.44 (m, 2H, Ar*H*), 7.45–7.52 (m, 4H, Ar*H*), 7.56 (d, *J* = 7.3 Hz, 1H, Ar*H*), 7.64–7.69 (m, 2H, Ar*H*), 7.71 (d, *J* = 8.5 Hz, 2H, Ar*H*); ^{13}C NMR ($CDCl_3$): δ 24.5 (*C*H$_3$), 82.3 (*C*-OH), 122.2 (Ar), 122.4 (q, *J* = 272.16 Hz, *C*F_3), 123.0 (Ar), 127.2 (Ar), 127.3 (Ar), 127.8 (Ar), 128.9 (d, *J* = 1.7 Hz, Ar), 129.0 (Ar), 129.1 (Ar) 129.2 (Ar), 131.1 (Ar), 134.6 (q, *J* = 29.6 Hz, CF_3-*C*), 140.1 (Ar), 140.6 (Ar), 141.8 (Ar), 147.6 (q, *J* = 4.8 Hz, CF_3-C=*C*), 149.1 (Ar); ^{19}F NMR ($CDCl_3$, $CFCl_3$): δ –55.79 (s, 3F); IR (KBr) 3549, 3933, 2990, 2942, 1489, 1357, 1319, 1253, 1209, 1195, 1149, 1109, 1027, 1014, 765, 732 cm^{-1}; HRMS (FAB): calcd for [M$^+$] $C_{23}H_{17}F_3O$: 366.1232, Found: 366.1231.

*4.2.10. 2-(Dimethylphenylsilyl)-1-methyl-3-trifluoromethyl-1H-inden-1-ol (**11gA**) and 3-(dimethylphenylsilyl)-1-methyl-2-trifluoromethyl-1H-inden-1-ol (**12gA**).*

Combined yield: 49%; Isometric ratio (**11gA**:**12gA**) = 64:36 (inseparable), yellow oil, eluent of the column chromatography: Hexane/EtOAc = 9/1; **11gA**: ^{1}H NMR ($CDCl_3$): δ 0.66 (s, Si-C*H*$_3$, 6H), 1.63 (s, 3H, C-C*H*$_3$), 1.93 (s, 1H, O*H*), 7.28–7.48 (m, 7H, Ar*H*), 7.57–7.65 (m, 2H, Ar*H*); ^{19}F NMR ($CDCl_3$, $CFCl_3$): δ –60.01 (s, 3F); **12gA**: ^{1}H NMR ($CDCl_3$): δ 0.66 (s, 6H, Si-C*H*$_3$), 1.75 (s, 3H, C-C*H*$_3$), 2.14 (s, 1H, O*H*), 7.01 (d, *J* = 7.68 Hz, 1H, Ar*H*), 7.09 (td, *J* = 7.57, 1.03 Hz, 1H, Ar*H*), 7.25 (t, 7.08 Hz, 1H, Ar*H*) 7.28–7.48 (m, 4H, Ar*H*), 7.53–7.65 (m, 2H, Ar*H*); ^{19}F NMR ($CDCl_3$, $CFCl_3$): δ –54.43 (s, 3F); (**11gA**+**12gA**): ^{13}C NMR ($CDCl_3$): δ –0.87 (q, *J* = 8.8 Hz, Si-*C*H$_3$), –0.53 (q, *J* = 9.0 Hz, Si-*C*H$_3$), –0.40 (m, 2C, Si-*C*H$_3$), 24.8 (C-*C*H$_3$), 25.3 (C-*C*H$_3$), 83.6 (*C*-OH), 87.5 (*C*-OH), 121.2 (d, *J* = 1.9 Hz, Ar), 121.89 (Ar), 121.94 (Ar), 123.1 (q, *J* = 272.8 Hz, *C*F_3), 124.0 (q, *J* = 273.0 Hz, *C*F_3), 125, 5 (Ar), 128.0 (Ar), 128.1 (Ar), 128.3 (Ar), 128.6 (Ar), 129.0 (Ar), 129.5 (Ar), 129.7 (Ar), 134.0 (Ar), 134.1 (Ar), 136.6 (Ar), 137.5 (Ar), 138.0 (Ar), 140.6 (q, *J* = 29.8 Hz, CF_3-*C*, Ar), 142.0 (Ar), 146.9 (q, *J* = 14.3 Hz, CF_3-C=*C*), 149.3 (Ar), 149.8 (q, *J* = 30.2 Hz, CF_3-*C*), 151.9 (Ar), 157.1 (q, *J* = 3.5 Hz, CF_3-C=*C*), the signal of one carbon was overlapped with other signals. ; IR (neat) 3348, 3071, 2980, 1428, 1363, 1336, 1311, 1254, 1196, 1168, 1156, 1119, 826, 785, 759 cm^{-1}; HRMS (FAB): calcd for [M+Na]$^+$ $C_{19}H_{19}F_3NaOSi$: 371.1055, Found: 371.1057.

*4.2.11. 2-Hexyl-3-trifluoromethyl-1H-inden-1-ol (**11hA**) and 3-Hexyl-2-trifluoromethyl-1H-inden-1-ol (**12hA**).*

Combined yield: 48%; Isometric ratio (**11hA**:**12hA**) = 77:23 (inseparable), yellow oil, eluent of the column chromatography: Hexane/EtOAc = 9/1; **11hA**: ^{1}H NMR ($CDCl_3$): δ 0.82-0.98 (m, 3H, CH_2-C*H*$_3$, 6H), 1.21-1.77 (m, 9H, CH_2-C_4H_8-CH_3, O*H*) 1.54 (s, 3H, C(OH)-C*H*$_3$), 2.39–2.61 (m, 2H, C=C-CH_2), 7.21–7.56 (m, 4H, Ar*H*), 7.71–7.84 (m, 1H, Ar*H*); ^{19}F NMR ($CDCl_3$, $CFCl_3$): δ –61.55 (s, 3F); **12hA**: ^{1}H NMR ($CDCl_3$): δ 0.82–0.98 (m, 3H, CH_2-C*H*$_3$, 6H), 1.21–1.77 (m, 8H, CH_2-C_4H_8-CH_3) 1.73 (s, 3H, C(OH)-C*H*$_3$), 2.01 (s, 1H, O*H*), 2.61–2.70 (m, 2H, C=C-CH_2), 7.21–7.56 (m, 3H, Ar*H*), 7.71–7.84 (m, 1H, Ar*H*); ^{19}F NMR ($CDCl_3$, $CFCl_3$): δ –57.03 (s, 3F); HRMS (FAB): calcd for [M$^+$] $C_{17}H_{21}F_3O$: 298.1544, Found: 298.1545.

*4.2.12. 2-(4-Chlorophenyl)-3-difluoromethyl-1-methyl-1H-inden-1-ol (**11kA**).*

Yield: 61%; yellow solid, M.p. 52.0–53.0 °C, eluent of the column chromatography: Hexane/EtOAc = 7/3; ^{1}H NMR ($CDCl_3$): δ 1.47 (s, 3H, CH_3), 1.95 (s, 1H, O*H*), 6.46 (t, J = 54.1 Hz, 1H, CF_2H), 7.32 (td, J = 7.4, 1.4 Hz, 1H Ar*H*), 7.36 (td, J = 7.4, 1.4 Hz, 1H, Ar*H*), 7.44 (d, J = 8.6 Hz, 2H, Ar*H*), 7.49 (d, J = 8.6 Hz, 2H, Ar*H*), 7.50 (d, J = 7.4 Hz, 1H Ar*H*), 7.60 (d, J = 7.4 Hz, 1H, Ar*H*); ^{13}C NMR ($CDCl_3$): δ 23.6 (*C*H$_3$), 83.4 (*C*-OH), 112.6 (q, J = 233.2 Hz, *C*F_2H), 122.3 (Ar), 122.4 (d, J = 2.17 Hz, Ar), 127.6 (Ar), 129.1 (Ar), 129.2 (Ar), 130.3 (Ar), 130.9 (Ar), 131.6 (dd, J = 25.0, 23.0 Hz, CF_2H-*C*), 135.3 (Ar), 136.7 (Ar), 148.4 (Ar), 153.2 (t, J = 10.2 Hz, CF_2H-C=*C*); ^{19}F NMR ($CDCl_3$, $CFCl_3$): δ –116.99 (dd, J = 321.2, 54.1 Hz, 2F), –114.45 (dd, J = 321.2, 54.1 Hz, 2F); IR (KBr) 3351, 3068, 2974, 2926, 1490, 1379, 1119, 1092, 1073, 1027, 823, 759, 731 cm^{-1}; HRMS (FAB): calcd for [M$^+$] $C_{17}H_{13}ClF_2O$: 306.0623, Found: 306.0625.

*4.2.13. 3-(4-Chlorophenyl)-2-drifluoromethyl-1-methyl-1H-inden-1-ol (**12kA**).*

Yield: 10%; yellow oil, eluent of the column chromatography: Hexane/EtOAc = 7/3; ^{1}H NMR ($CDCl_3$): δ 1.84 (s, 3H, CH_3), 2.30 (s, 1H, O*H*), 6.47 (t, J = 54.0 Hz, 1H, CF_2H), 7.14 (d, J = 7.4 Hz, 1H, Ar*H*), 7.31 (td, J = 7.4, 1.1 Hz, 1H, Ar*H*), 7.34–7.41 (m, 3H, Ar*H*), 7.49 (d, J = 8.5 Hz, 2H Ar*H*), 7.54 (d, J = 7.4 Hz, 1H, Ar*H*); ^{13}C NMR ($CDCl_3$): δ 24.8 (*C*H$_3$), 82.3 (*C*-OH), 113.7 (dd, J = 234.1, 231. 1 Hz, *C*F_2H), 122.1 (Ar), 122.3 (Ar), 127.6 (t, J = 77.2 Hz, CF_2H-*C*), 128.8 (t, J = 34.4 Hz, Ar), 128.9 (d, J = 2.5 Hz, Ar), 129.2 (Ar), 130.2 (Ar), 135.3 (Ar), 138.0 (dd, J = 21.7, 20.0 Hz, Ar), 139.7 (Ar), 145.6 (t, J = 10.3 Hz, Ar), 149.5 (Ar); ^{19}F NMR ($CDCl_3$, $CFCl_3$): δ –115.94 (dd, J = 316.6, 54.0 Hz, 1F), –109. 55 (dd, J = 316.6, 54.0 Hz, 1F); IR (neat) 3584, 3385, 3070, 2978, 2930, 2866, 1491, 1403, 1377, 1347, 1178, 1129, 1088, 1017, 806, 761, 733, 427 cm^{-1}; HRMS (FAB): calcd for [M$^+$] $C_{17}H_{13}ClF_2O$: 306.0623, Found: 306.0614.

*4.2.14. 2-(4-Chlorophenyl)-1-cyclohexyl-3-trifluoromethyl-1H-inden-1-ol (**11aB**).*

Yield: 57%; yellow oil, eluent of the column chromatography: Hexane/EtOAc = 9/1; ^{1}H NMR ($CDCl_3$): δ 0.30–0.43 (m, 1H, Cy), 0.85–1.18 (m, 3H, Cy), 1.25–1.66 (m, 5H, Cy), 1.70–1.80 (m, 1H, Cy), 1.97 (s, 1H, O*H*), 2.01–2.11 (m, 1H, Cy), 7.30 (td, J = 7.4, 1.2 Hz, 1H, Ar*H*), 7.34–7.47 (m, 6H, Ar*H*), 7.50 (d, J = 7.2 Hz, 1H, Ar*H*); ^{13}C NMR ($CDCl_3$): δ 26.1 (Cy), 26.2 (Cy), 26.4 (Cy), 26.5 (Cy), 26.7 (Cy), 44.2 (Cy), 88.7 (*C*-OH), 121.6 (d, J = 1.7 Hz, Ar), 122.6 (q, J = 272.8 Hz, *C*F_3), 123.8 (Ar), 127.2 (Ar), 128.6 (Ar), 129.2 (Ar), 129.4 (q, J = 32.1 Hz, CF_3-*C*), 130.0 (d, J = 1.1 Hz, Ar), 131.6 (Ar), 134.9 (Ar), 137.6 (Ar), 145.9 (Ar), 153.4 (q, J = 4.0 Hz, CF_3-C=*C*); ^{19}F NMR ($CDCl_3$, $CFCl_3$): δ –60.29 (s, 3F); IR (neat) 3443, 3073, 2932, 2855, 1490, 1471, 1378, 1203, 1169, 1126, 1094, 1021, 945, 813, 762, 732 cm^{-1}; HRMS (FAB): calcd for [M$^+$] $C_{22}H_{20}ClF_3O$: 392.1155, Found: 392.1144.

*4.2.15. 3-(4-Chlorophenyl)-1-cyclohexyl-2-trifluoromethyl-1H-inden-1-ol (**12aB**).*

Yield: 23%; yellow oil, eluent of the column chromatography: Hexane/EtOAc = 9/1; ^{1}H NMR ($CDCl_3$): δ 0.43–0.58 (m, 1H, Cy), 0.83–1.45 (m, 4H, Cy), 1.56–1.72 (m, 3H, Cy), 1.80–1.90 (m, 1H, Cy), 2.15–2.34 (m, 2H, Cy), 2.19 (s, 1H, O*H*), 6.99 (d, J = 7.3 Hz, 1H, Ar*H*), 7.25–7.37 (m, 4H, Ar*H*), 7.45 (d, J = 8.5 Hz, 2H, Ar*H*), 7.52 (d, J = 7.1 Hz, 1H, Ar*H*); ^{13}C NMR ($CDCl_3$): δ 26.4 (Cy), 26.5 (Cy), 26.8 (Cy), 27.1 (Cy), 27.4 (Cy), 45.0 (Cy), 88.3 (*C*-OH), 122.5 (Ar), 123.6 (q, J = 272.5 Hz, *C*F_3), 124.1 (Ar), 128.6 (Ar), 128.88 (Ar), 128.94 (Ar), 129.8 (d, J = 1.3 Hz, Ar), 130.9 (Ar), 134.6 (q, J = 29.4 Hz, CF_3-*C*), 135.0 (Ar), 141.2 (Ar), 146.7 (Ar), 148.2 (q, J = 4.9 Hz, CF_3-C=*C*); ^{19}F NMR ($CDCl_3$, $CFCl_3$): δ –55.97 (s, 3F); IR (neat) 3459, 3071, 2932, 2855, 1633, 1491, 1454, 1399, 1349, 1251, 1200, 1150, 1104, 1091, 826, 789, 764 cm^{-1}; HRMS (FAB): calcd for [M$^+$] $C_{22}H_{20}ClF_3O$: 392.1155, Found: 392.1154.

*4.2.16. 2-(4-Chlorophenyl)-1-phenyl-3-trifluoromethyl-1H-inden-1-ol (**11aC**).*

Yield: 37%; yellow oil, eluent of the column chromatography: Hexane/EtOAc = 9/1; ^{1}H NMR ($CDCl_3$): δ 2.38 (s, 1H, O*H*), 6.93 (d, J = 8.9 Hz, 2H, Ar*H*), 7.18–7.32 (m, 9H, Ar*H*), 7.39 (td, J = 7.5, 1.4 Hz, 1H, Ar*H*), 7.52–7.54 (m, 1H, Ar*H*); ^{13}C NMR ($CDCl_3$): δ 87.6 (*C*-OH), 121.9 (d, J = 1.4 Hz, Ar), 122.6 (q, J = 272.8 Hz, *C*F_3), 124.0 (Ar), 125.5 (Ar), 128.1 (Ar), 128.3 (Ar), 128.4 (Ar), 128.6 (Ar), 129.0 (q, J = 32.7 Hz, CF_3-*C*), 129.6 (Ar), 130.1 (d, J = 1.3 Hz, Ar), 130.6 (Ar), 135.0 (Ar), 137.3 (Ar), 138.5 (Ar), 149.2 (Ar), 155.1 (q, J = 3.9 Hz, CF_3-C=*C*); ^{19}F NMR ($CDCl_3$, $CFCl_3$): δ –60.13 (s, 3F); IR (neat) 3541, 3454, 3067, 3030, 1597, 1491, 1375, 1329, 1202, 1170, 1124, 1095, 729, 699 cm^{-1}; HRMS (FAB): calcd for [M$^+$] $C_{22}H_{14}ClF_3O$: 386.0685, Found: 386.0676.

*4.2.17. 3-(4-Chlorophenyl)-1-phenyl-2-trifluoromethyl-1H-inden-1-ol (**12aC**).*

Yield: 12%; yellow oil, eluent of the column chromatography: Hexane/EtOAc = 9/1; ^{1}H NMR ($CDCl_3$): δ 2.68 (s, 1H, O*H*), 7.08–7.14 (m, 1H, Ar*H*), 7.21–7.39 (m, 6H, Ar*H*), 7.41–7.47 (m, 2H, Ar*H*), 7.47–7.55 (m, 4H, Ar*H*); ^{13}C NMR ($CDCl_3$): δ 86.0 (*C*-OH), 122.9 (Ar), 123.1 (q, J = 272.4 Hz, *C*F_3), 123.6 (Ar), 124.5 (Ar), 128.0 (Ar), 128.8 (Ar), 129.1 (Ar), 129.2 (Ar), 129.9 (Ar), 130.3 (Ar), 135.4 (Ar), 136.1 (q, J = 29.6 Hz, CF_3-*C*), 139.3 (Ar), 140.1 (Ar), 148.6 (q, J = 4.6 Hz, CF_3-C=*C*), 150.2 (Ar), the signal of one carbon was overlapped with other signals. ; ^{19}F NMR ($CDCl_3$, $CFCl_3$): δ –55.11 (s, 3F); IR (neat) 3550, 3457, 3069, 3030, 3452, 1722, 1631, 1589, 1491, 1458, 1350, 1281, 1250, 1190, 1149, 1121, 1090, 1043, 1016, 857, 835, 800, 761 cm^{-1}; HRMS (FAB): calcd for [M$^+$] $C_{22}H_{14}ClF_3O$: 386.0685, Found: 386.0687.

*4.2.18. 2-(4-Chlorophenyl)-1,5-dimethyl-3-trifluoromethyl-1H-inden-1-ol (**11aD**).*

Yield: 41%; white solid, M.p. 129.6–130.4 °C, eluent of the column chromatography: Hexane/EtOAc = 9/1; ^{1}H NMR ($CDCl_3$): δ 1.42 (s, 3H, HO-C-CH_3), 1.91 (s, 1H, O*H*), 2.42 (s, 3H, Ar-CH_3), 7.15 (d, J = 7.5 Hz, 1H, Ar*H*), 7.27 (s, 1H, Ar*H*), 7.34 (d, J = 8.6 Hz, 2H, Ar*H*), 7.38 (d, J = 7.5 Hz, 1H, Ar*H*), 7.40 (d, J = 8.6 Hz, 2H, Ar*H*); ^{13}C NMR ($CDCl_3$): δ 21.7 (HO-C-*C*H$_3$), 23.7 (Ar-*C*H$_3$), 83.2 (*C*-OH), 122.3 (Ar), 122.5 (d, J = 1.2 Hz, Ar), 122.7 (q, J = 272.7 Hz, *C*F_3), 127.9 (q, J = 32.6 Hz, CF_3-*C*), 128.4 (Ar), 128.6 (Ar), 130.1 (d, J = 1.2 Hz, Ar), 131.2 (Ar), 134.9 (Ar), 136.4 (Ar), 139.5 (Ar), 145.0 (Ar), 154.2 (q, J = 3.9 Hz, CF_3-C=*C*); ^{19}F NMR ($CDCl_3$, $CFCl_3$): δ –60.11 (s, 3F); IR (KBr) 3333, 3034, 2976, 2927, 1483, 1369, 1224, 1176, 1129, 1063, 940, 823, 728 cm^{-1}; HRMS (FAB): calcd for [M$^+$] $C_{18}H_{14}ClF_3O$: 338.0685, Found: 338.0690.

*4.2.19. 3-(4-Chlorophenyl)-1,5-dimethyl-2-trifluoromethyl-1H-inden-1-ol (**12aD**).*

Yield: 24%; yellow oil, eluent of the column chromatography: Hexane/EtOAc = 9/1; ^{1}H NMR ($CDCl_3$): δ 1.80 (s, 3H, HO-C-CH_3), 2.15 (s, 1H, O*H*), 2.32 (s, 3H, ArCH_3), 6.83 (s, 1H, Ar*H*), 7.20 (d, J = 7.5 Hz, 1H, Ar*H*), 7.32 (d, J = 8.5 Hz, 2H, Ar*H*), 7.42 (d, J = 7.5 Hz, 1H, Ar*H*), 7.47 (d, J = 8.5 Hz, 2H, Ar*H*); ^{13}C NMR ($CDCl_3$): δ 21.6 (HO-C-*C*H$_3$), 24.4 (Ar-*C*H$_3$), 82.0 (HO-*C*), 122.0 (Ar), 123.4 (Ar), 123.6 (q, J = 272.3 Hz, *C*F_3), 128.9

(Ar), 129.8 (d, *J* = 1.5 Hz, Ar), 130.0 (Ar), 130.7 (Ar), 135.0 (Ar), 135.3 (q, *J* = 29.7 Hz, CF_3-*C*), 139.3 (Ar), 139.9 (Ar), 146.2 (Ar), 146.7 (q, *J* = 5.0 Hz, CF_3-C=*C*); ^{19}F NMR ($CDCl_3$, $CFCl_3$): δ −55.93 (s, 3F); IR (neat) 3384, 2980, 2927, 1491, 1354, 1254, 1223, 1186, 1153, 1116, 1090, 1022, 837, 822, 734 cm^{-1}; HRMS (FAB): calcd for [M$^+$] $C_{18}H_{14}ClF_3O$: 338.0685, Found: 338.0688.

*4.2.20. 2-(4-Chlorophenyl)-5-methoxy-1-methyl-3-trifluoromethyl-1H-inden-1-ol (**11aE**).*

Yield: 23%; white solid, M.p. 141.2–141.8 °C, eluent of the column chromatography: Hexane/EtOAc = 5/1; ^{1}H NMR ($CDCl_3$): δ 1.42 (s, 3H, HO-C-C*H*$_3$), 1.85 (s, 1H, O*H*), 3.85 (s, 3H, OC*H*$_3$), 6.84 (dd, *J* = 8.2, 2.3 Hz, 1H, Ar*H*), 7.00 (m, 1H, Ar*H*), 7.35 (d, *J* = 8.6 Hz, 2H, Ar*H*), 7.40–7.42 (m, 3H, Ar*H*); ^{13}C NMR ($CDCl_3$): δ 23.8 (HO-C-*C*H$_3$), 55.8 (O*C*H$_3$), 82.9 (HO-*C*), 108.2 (d, *J* = 1.4 Hz, Ar), 112.7 (Ar), 122.6 (q, *J* = 272.7 Hz, *C*F$_3$), 123.3 (Ar), 127.6 (q, *J* = 31.9 Hz, CF_3-*C*), 128.6 (Ar), 130.0 (d, *J* = 1.4 Hz, Ar), 131.1 (Ar), 135.0 (Ar), 137.7 (Ar), 139.8 (Ar), 155.3 (q, *J* = 3.8 Hz, CF_3-C=*C*), 160.9 (Ar); ^{19}F NMR ($CDCl_3$, $CFCl_3$): δ −60.05 (s, 3F); IR (KBr) 3461, 2983, 2948, 1478, 1434, 1374, 1334, 1226, 1197, 1174, 1149, 1106, 1092, 1058, 1024, 1016, 815 cm^{-1}; HRMS (FAB): calcd for [M$^+$] $C_{18}H_{14}ClF_3O_2$: 354.0634, Found: 354.0637.

*4.2.21. 3-(4-Chlorophenyl)-5-methoxy-1-methyl-2-trifluoromethyl-1H-inden-1-ol (**12aE**).*

Yield: 16%; yellow oil, eluent of the column chromatography: hexane/EtOAc = 5/1; ^{1}H NMR ($CDCl_3$): δ 1.80 (s, 3H, HO-C-C*H*$_3$), 2.04 (s, 1H, O*H*), 3.75 (s, 3H, OC*H*$_3$), 6.54 (d, *J* = 2.3 Hz, 1H, Ar*H*), 6.89 (dd, *J* = 8.2, 2.3 Hz, 1H, Ar*H*), 7.31 (d, *J* = 8.5 Hz, 2H, Ar*H*), 7.43 (d, *J* = 8.2 Hz, 1H, Ar*H*), 7.46 (d, *J* = 8.5 Hz, 2H, Ar*H*); ^{13}C NMR ($CDCl_3$): δ 24.5 (HO-C-*C*H$_3$), 55.8 (O*C*H$_3$), 81.8 (HO-*C*), 109.1 (Ar), 114.1 (Ar), 123.0 (Ar), 123.5 (q, *J* = 271.6 Hz, *C*F$_3$), 128.9 (Ar), 129.8 (d, *J* = 1.5 Hz, Ar), 130.1 (Ar), 135.1 (Ar), 136.6 (q, *J* = 29.7 Hz, CF_3-*C*), 141.0 (Ar), 141.3 (Ar), 146.3 (q, *J* = 4.9 Hz, CF_3-C=*C*), 160.9 (Ar); ^{19}F NMR ($CDCl_3$, $CFCl_3$): δ −56.09 (s, 3F); IR (neat) 3412, 2978, 2938, 2839, 1607, 1594, 1490, 1465, 1353, 1256, 1221, 1192, 1154, 1117, 1090, 1019, 835, 811, 750 cm^{-1}; HRMS (FAB): calcd for [M$^+$] $C_{18}H_{14}ClF_3O_2$: 354.0634, Found: 354.0639.

*4.2.22. 6-(4-Chlorophenyl)-5-methyl-7-trifluoromethyl-5H-indeno[5,6-d]-1,3-dioxol-5-ol (**11aF**).*

Yield: 31%; brown solid, M.p. 174.2–174.9 °C, eluent of the column chromatography: Hexane/EtOAc = 9/1; ^{1}H NMR ($CDCl_3$): δ 1.38 (s, 3H, C*H*$_3$), 2.00 (s, 1H, O*H*), 6.00 (d, *J* = 1.3 Hz, 1H, C*H*$_2$), 6.03 (d, *J* = 1.3 Hz, 1H, C*H*$_2$), 6.93 (d, *J* = 1.3 Hz, 1H, Ar*H*), 6.98 (s, 1H, Ar*H*), 7.32 (d, *J* = 8.6 Hz, 2H, Ar*H*), 7.39 (d, *J* = 8.6 Hz, 2H, Ar*H*); ^{13}C NMR ($CDCl_3$): δ 23.9 (*C*H$_3$), 82.9 (*C*-OH), 101.8 (Ar), 103.7 (d, *J* = 1.2 Hz, Ar), 104.3 (Ar), 122.6 (q, *J* = 272.6 Hz, *C*F$_3$), 127.7 (q, *J* = 32.6 Hz, CF_3-*C*), 128.6 (Ar), 129.6 (Ar), 130.1 (d, *J* = 1.4 Hz, Ar), 131.2 (Ar), 134.9 (Ar), 142.3 (Ar), 147.8 (Ar), 148.6 (Ar), 153.0 (q, *J* = 4.0 Hz, CF_3-C=*C*); ^{19}F NMR ($CDCl_3$, $CFCl_3$): δ −60.25 (s, 3F); IR (KBr) 3321, 3014, 2974, 2900, 1505, 1382, 1299, 1240, 1187, 1108, 1093, 1017, 940, 830 cm^{-1}; HRMS (FAB): calcd for [M$^+$] $C_{18}H_{12}ClF_3O_3$: 368.0427, Found: 368.0439.

*4.2.23. 7-(4-Chlorophenyl)-5-methyl-6-trifluoromethyl-5H-indeno[5,6-d]-1,3-dioxol-5-ol (**12aF**).*

Yield: 20%; brown solid, M.p. 107.2–108.0 °C, eluent of the column chromatography: Hexane/EtOAc = 9/1; ^{1}H NMR ($CDCl_3$): δ 1.76 (s, 3H, C*H*$_3$), 2.18 (s, 1H, O*H*), 5.98 (d, *J* = 1.6 Hz, 1H, C*H*$_2$), 5.97 (d, *J* = 1.6 Hz, 1H, C*H*$_2$), 6.47 (s, 1H, Ar*H*), 7.01 (s, 1H, Ar*H*), 7.29 (d, *J* = 8.5 Hz, 2H, Ar*H*), 7.44 (d, *J* = 8.5 Hz, 2H, Ar*H*); ^{13}C NMR ($CDCl_3$): δ 24.6 (*C*H$_3$), 81.7 (*C*-OH), 101.9 (Ar), 103.6 (Ar), 103.9 (Ar), 123.4 (q, *J* = 271.6 Hz, *C*F$_3$), 128.9 (Ar), 129.7 (d, *J* = 1.4 Hz, Ar), 130.7 (Ar), 133.3 (Ar), 133.9 (q, *J* = 29.8 Hz, CF_3-*C*), 135.1 (Ar), 143.9 (d, *J* = 1.7 Hz, Ar), 146.4 (q, *J* = 4.9 Hz, CF_3-C=*C*), 148.5 (Ar), 149.1 (Ar); ^{19}F NMR ($CDCl_3$, $CFCl_3$): δ −55.82 (s, 3F); IR (neat) 3395, 3070, 2979, 2898, 1614, 1592, 1502, 1398, 1371, 1330, 1301, 1263, 1232, 1176, 1107, 1230, 1014, 1003 cm^{-1}.

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Supplementary Material

Supplementary data to this article can be found online at https://.

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[9] Generally, the signal of the major isomers (3-CF_3-indenols) appears at −60 ppm, and that of the minor isomers (2-CF_3-indenols) appears at −54 to −56 ppm.

[10] a) M.-F. Chiou, J. Jayakumar, C.-H. Cheng, S.-C. Chuang, J. Org. Chem. 83 (2018) 7814–7824; b) S. Mannathan, C.-H. Cheng, J. Chin. Chem. Soc. 61 (2014) 59–66; c) W. J. Ang, C.-H. Tai, L.-C. Lo, Y. Lam, RSC Adv. 4 (2014) 4921-4929; d) K.-J. Chang, D. K. Rayabarapu, C.-H. Cheng, Org. Lett. 5 (2003) 3963-3966; e) D. K. Rayabarapu, C.-H. Yang, C.-H. Cheng, J. Org. Chem. 68 (2003) 6726-6731; f) D. J. Rayabarapu, C.-H. Cheng, Chem. Commun. (2002) 942–943.

[11] Larock' group has reported that alkyne insertion occurs to generate the least steric strain in the vicinity of the shorter, developing carbon-carbon bond rather than the longer carbon-metal bond. Also, it has been well known that a Ph group is bulkier than a CF_3 group based on Tordeux's work. Therefore, the regioselectivity of the present reaction might be explained on the basis of the above works, that is, 3-fluoroalkylated indenol derivatives are obtained as a major product because of a steric hindrance between the R^1 of alkyne **9** and the aryl moiety of ketone **10**. see: a) R. C. Larock, E. K. Yum, M. D. Refvik, J. Org. Chem. 63 (1998) 7652–7662; b). Y. Carcenac, P. Diter, C. Wakselman, M. Tordeux, New J. Chem. 30 (2006) 442–446.

[12] T. Kumon, S. Yamada, T. Agou, T. Kubota, T. Konno, J. Fluorine Chem. 213 (2018) 11–17.

[13] Cobalt complexes were prepared according to the literature. See: a) M.M.P. Grutters, C. Müller, D. Vogt, J. Am. Chem. Soc. 128 (2006) 7414–7415; b) B. Raya, S. Jing, V. Balasanthiran, T.V. RajanBabu, ACS Catal. 7 (2017) 2275–2283; c) S. Biswa, J.P. Page, K.R. Dewese, T.V. RajanBabu, J. Am. Chem. Soc. 137 (2015) 14268–14271; e) B. Brewer, N.R. Brooks, S. Abdul-Halim, A.G. Sykes, J. Chem. Crystallogr. 33 (2003) 651–662; f) V.V. Pagar, T.V. RajanBabu, Science 361 (2018) 68–75.

[14] a) G.M. Sheldrick, SHELXS-2014, Program for Crystal Structure Solution, University of Göttingen, 2014; b) G. M. Sheldrick, Acta Crystallogr., Sect. A 64 (2008) 112–122.