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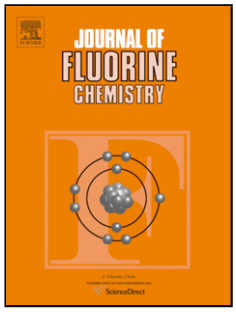

Title: Highly regioselective cobalt-catalyzed [2+2+2] cycloaddition of fluorine-containing internal alkynes to construct various fluoroalkylated benzene derivatives

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Highly regioselective cobalt-catalyzed [2+2+2] cycloaddition of fluorine-containing internal alkynes to construct various fluoroalkylated benzene derivatives

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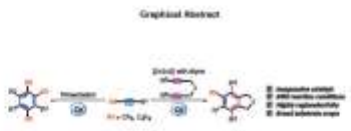
Graphical abstract



Highlight

1. Cobalt-catalyzed [2+2+2] cycloaddition using fluorine-containing alkynes proceeded under mild reaction conditions.
2. The reaction can be performed at low catalyst loading.
3. High regioselection was observed in the trimerization of fluorine-containing alkynes.
4. Cycloaddition of fluorinated alkynes with non-fluorinated diynes proceeded very smoothly.

Abstract: Novel cobalt-catalyzed [2+2+2] cycloaddition using fluorine-containing alkynes was described. Cyclotrimerization of fluorinated alkynes under the influence of $CoCl_2$(dppb) in acetonitrile at 80 °C for 3 h took place smoothly, affording the corresponding benzene derivatives in excellent yields with high regioselectivity. Additionally, intermolecular cycloaddition of fluorinated alkynes with non-fluorinated diynes also proceeded in the presence of a catalytic amount of $CoCl_2$((*S*)-BINAP) and ZnI_2 to give various bicyclic aromatic compounds in high yields.

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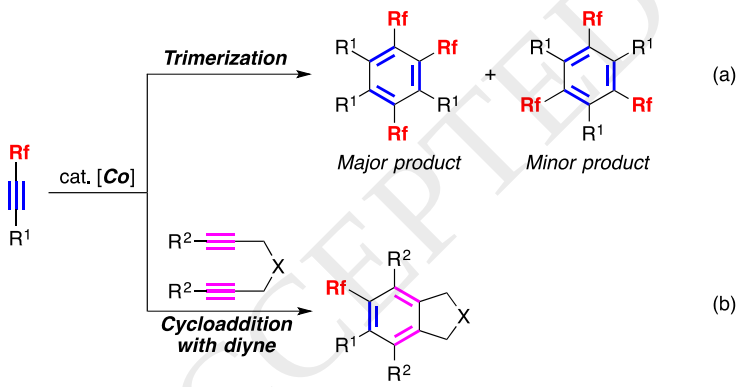
Keyword: Fluorine-containing alkynes, cobalt catalysts, [2+2+2] cycloaddition, regioselective

1. Introduction

Benzene derivatives bearing a fluoroalkyl (Rf) group have been recognized as one of the most important fluorinated frameworks because they are widely distributed in the skeleton of pharmaceuticals, agrochemicals, and functional materials and have a unique physicochemical and biochemical property, such as significantly enhanced lipophilicity, stability, and binding affinity [1]. Consequently, tremendous efforts have been devoted to the development of novel synthetic approaches to various classes of fluoroalkylated benzene materials so far [2].

Transition metal-catalyzed [2+2+2] cycloaddition reactions using alkynes have been widely considered as one of the most efficient and convenient protocols for the construction of various aromatic rings [3]. There have been numerous studies on the reaction with non-fluorinated alkynes under the influence of various transition metals, such as Ni [4], Rh [5], Au [6], Ru [7], Co [8], Ti [9], Ir [10], Fe [11], and Nb [12]. Despite of their potent utility, on the other hand, very little attention has been paid to the [2+2+2] cycloaddition reactions of fluorine-containing alkynes [13]. Although there have been reported several examples on the fluorinated version of [2+2+2] cycloaddition reactions, they still have drawbacks, like the use of expensive catalysts, prolonged reaction times, or poor atom efficiency. Accordingly, the development of more efficient and convenient cycloaddition reactions using fluorine-containing alkynes remains highly desirable.

In this article, we describe a highly regioselective trimerization of CF_3-alkynes in the presence of inexpensive cobalt catalysts under mild reaction conditions (Scheme 1 (a)) [14]. In addition, it is also disclosed that the efficient access to various mono-substituted fluoroalkylated bicyclic aromatic compounds *via* the cobalt-catalyzed [2+2+2] cycloaddition reaction of fluoroalkylated alkynes with various diynes (Scheme 1 (b)).



Scheme 1. Cobalt-Catalyzed [2+2+2] Cycloaddition Reactions of Fluorine-Containing Alkynes.

2. Results and discussion

An initial screening of the reaction conditions for the cobalt-catalyzed [2+2+2] cyclotrimerization was performed using trifluoromethylated internal alkyne **1a**. The results are summarized in Table 1.

Thus, treatment of **1a** in the presence of 5 mol% of $CoCl_2$ and 2.75 equiv. of zinc powder in acetonitrile at 80 °C for 3 h gave an inseparable mixture of isomeric trimerization products **2a** and **3a** in 60% combined yield

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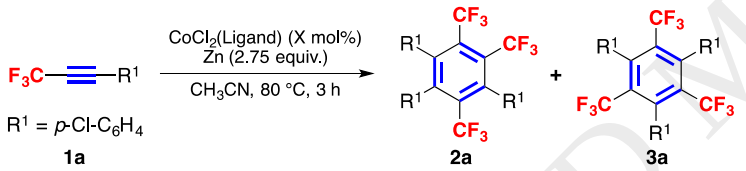
(**2a**:**3a** = 87:13) (Entry 1). While the use of cobalt catalyst coordinated with a monodentate ligand, such as PPh_3, did not drastically improve the yield or isomeric ratio of the reaction product (Entry 2), changing the ligand from a monodentate to a bidentate ligand, e.g. 1,2-bis(diphenylphosphino)ethane (dppe), led to a significant increase in the yield (Entry 3). It should be noted that the length of the carbon linker in the bidentate ligand significantly affected the regioselectivity. Thus, cyclotrimerization in the presence of cobalt catalyst coordinated with 1,3-bis(diphenylphosphino)propane (dppp) or 1,4-bis(diphenylphosphino)butane (dppb) afforded the corresponding benzene derivatives in excellent yields with high regioselectivity (Entries 4 and 5). 1,1'-Bis(diphenylphosphino)ferrocene (dppf) was also found to be a suitable ligand for the present trimerization reaction (Entry 6); however, the use of (*S*)-2,2'-bis(diphenylphosphino)-1,1'-binaphthyl ((*S*)-BINAP) as ligand decreased the yield of the desired cycloadducts (Entry 7). A decrease in the catalyst loading (3 mol%) also afforded the trimerization products in high yield (Entry 8). However, further decreasing the catalyst loading to 1 mol% resulted in the sluggish formation of cycloadducts along with the recovery of unreacted **1a** (Entry 9). Additionally, **2a** and **3a** were not obtained in the absence of cobalt catalyst (Entry 10). Finally, the best yield was obtained when the reaction was carried out using less amount of zinc powder (1.0 equiv.) (Entry 11).

Table 1

Initial screening of the cyclotrimerization conditions.



Entry	Ligand	X	Yield[a]/% of **2a**+**3a**	Ratio[b] of **2a**:**3a**
1	None	5	60	87:13
2	$2PPh_3$	5	64	88:12
3	dppe	5	88	84:16
4	dppp	5	90	96:4
5	dppb	5	93	96:4
6	dppf	5	86	96:4
7	(*S*)-BINAP	5	64	92:8
8	dppb	3	95	96:4
9	dppb	1	73	96:4
10	dppb	0	0	-
11[c]	dppb	3	97 (95)	96:4

[a] Determined by ^{19}F NMR. Value in parentheses is of isolated yield of **2a**+**3a**.
[b] Determined by ^{19}F NMR.
[c] The reaction was carried out using 1.0 equiv. of Zn.

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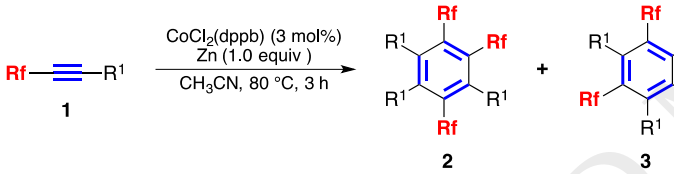
We next examined the substrate scope in the present cobalt-catalyzed [2+2+2] cyclotrimerization under the optimized reaction conditions (Table 2).

Alkynes **1b**, **c**, which have a phenyl or methoxy group at the *para* position on the benzene ring, participated efficiently in the present cyclotrimerization to give the corresponding trimerization adducts in good to excellent yields with an isomeric ratio of 95:5 (Entries 2 and 3). While *meta* substitution on the benzene ring of the substrate did not affect significantly the outcome of the reaction (Entry 4), *ortho* substitution completely retarded the formation of **2e**, **3e** (Entry 5). The introduction of a strongly electron-withdrawing group onto the benzene ring of the substrate, e.g. **1f**, also impeded the reaction to progress completely (Entry 7). In both cases, the addition of 30 mol% of zinc iodide caused a significant improvement of the chemical yields and the corresponding products were obtained in 58% and 83% yields, respectively, with high regioselectivity (Entries 6 and 8). On the other hand, alkynes **1g** and **1h** with a bulky dimethylphenylsilyl or *n*-nonafluorobutyl groups were found to be unsuitable for the reaction and the starting materials were recovered quantitatively (Entries 9 and 10).

Table 2

Cobalt-catalyzed cyclotrimerization of various fluorine-containing alkynes.



a : Rf = CF_3, R^1 = *p*-Cl-C_6H_4
b : Rf = CF_3, R^1 = *p*-Ph-C_6H_4
c : Rf = CF_3, R^1 = *p*-MeO-C_6H_4
d : Rf = CF_3, R^1 = *m*-Cl-C_6H_4
e : Rf = CF_3, R^1 = *o*-Cl-C_6H_4
f : Rf = CF_3, R^1 = *p*-EtO_2C-C_6H_4
g : Rf = CF_3, R^1 = $PhMe_2Si$
h : Rf = *n*-C_4F_9, R^1 = *p*-Cl-C_6H_4

Entry	Substrate	Yield[a]/% of **2**+**3**	Ratio[b] of **2**:**3**
1	**1a**	97 (95)	96:4
2	**1b**	92 (90)	95:5
3	**1c**	74 (69)	95:5
4	**1d**	95 (84)	95:5
5	**1e**	trace	N.D.[c]
6[d]	**1e**	58 (56)	98:2[e]
7	**1f**	trace	N.D.[c]
8[d]	**1f**	83 (70)	96:4
9[d]	**1g**	trace	N.D.[c]
10[d]	**1h**	trace	N.D.[c]

[a] Determined by ^{19}F NMR. Values in parentheses are of isolated yield of **2**+**3**.
[b] Determined by ^{19}F NMR.
[c] Not determined.
[d] 30 mol% of ZnI_2 was used.

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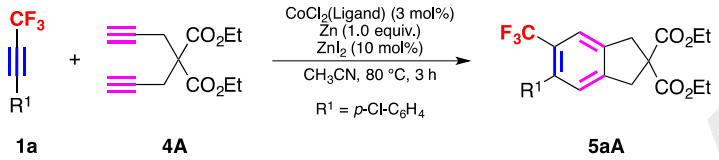
[e] Many atropisomers of **2e** and **3e** were detected.

With deep literature investigations, it was strictly limited an efficient intermolecular [2+2+2] cycloaddition using a fluorinated alkyne and non-fluorinated diynes [13]. Very interestingly, present cobalt-catalytic system was found to sufficiently applicable to the intermolecular [2+2+2] cycloaddition reaction, leading to fluoroalkylated bicyclic compounds well. Table 3 describes the ligand screening for the optimal reaction conditions.

Thus, treatment of 1.2 equiv. of **1a** and 1.0 equiv. of **4A** in the presence of 3 mol% of $CoCl_2$(dppb) and 1.0 equiv. of zinc powder in acetonitrile at 80 °C for 3 h gave only a trace amount of cycloadduct **5aA** (Entry 1). However, the yield of **5aA** significantly improved when 10 mol% of zinc iodide was used as an additive (55% ^{19}F NMR yield, Entry 2). The cycloaddition also proceeded using cobalt catalyst with no ligand to give the corresponding adduct **5aA** in 57% yield (Entry 3). As shown in Entries 4–9, we carried out the reaction using cobalt catalysts with various phosphine ligands. The best result was obtained when (*S*)-BINAP was used as a ligand and the desired cycloadduct **5aA** was obtained in 83% isolated yield (Entry 9).

Table 3

Ligand screening for the cycloaddition of CF_3-alkyne **1a** with diyne **4A**[a].



Entry	Ligand	Yield[b]/% of **5aA**
1[c]	dppb	trace
2	dppb	55
3	None	57
4	$2PPh_3$	71
5	$2P(t\text{-}Bu)_3$	71
6	dppe	12
7	dppp	71
8	dppf	20
9	(*S*)-BINAP	88 (83)

[a] Reaction conditions: **1a** (1.2 equiv.), **4A** (1.0 equiv.).
[b] Determined by ^{19}F NMR. Value in parentheses is of isolated yield of **5aA**.
[c] Without ZnI_2.

With the optimized reaction conditions in hand (Table 3, Entry 9), we next investigated the cycloaddition of various fluorine-containing alkynes **1** with diyne **4A**. The results are summarized in Table 4.

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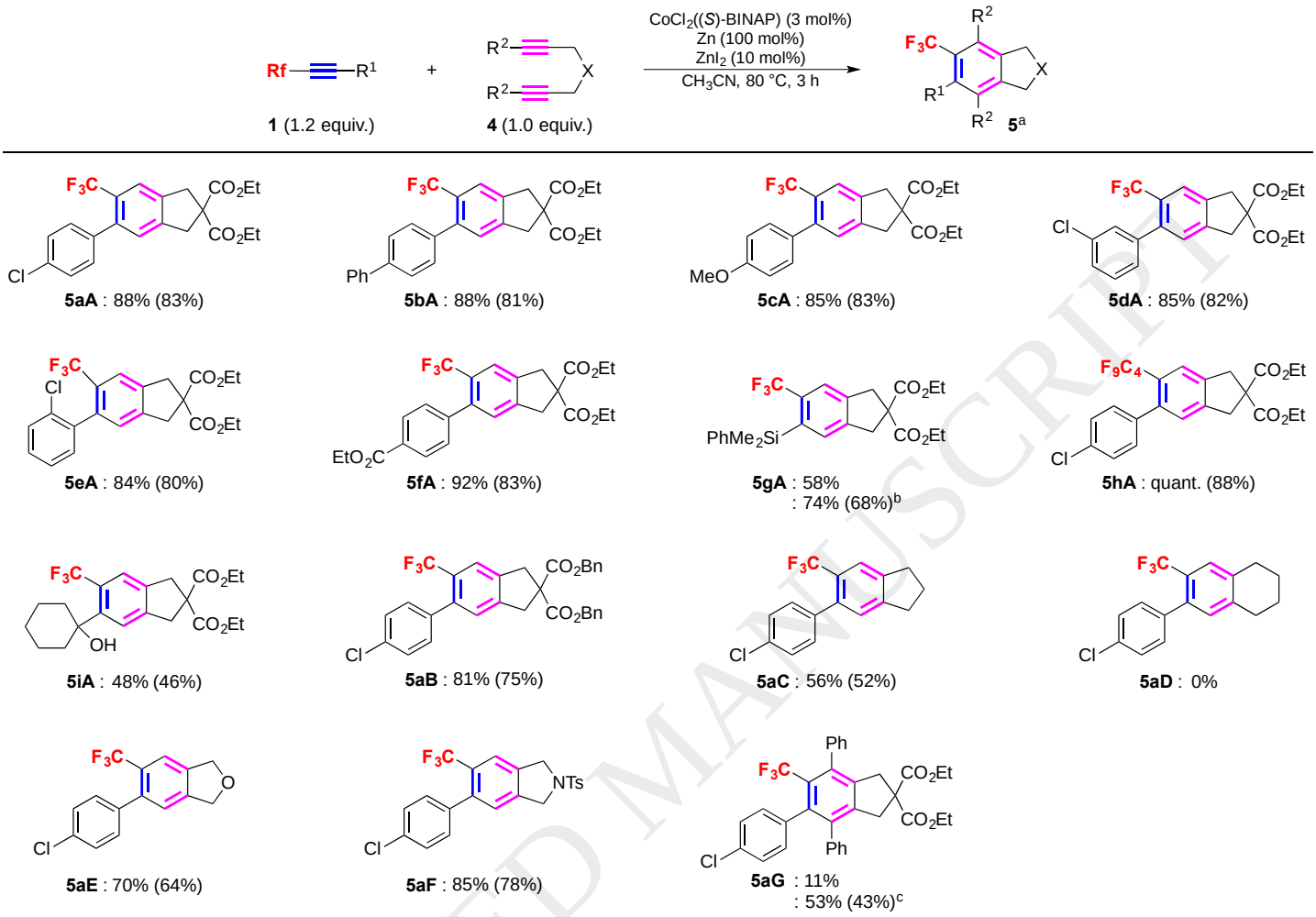
Table 4

Cobalt-catalyzed cycloaddition of various fluorinated alkynes with various diynes.



[a] Determined by ^{19}F NMR. Values in parentheses are of isolated yield of **5**.
[b] 2.4 equiv. of **1g** was used.
[c] The reaction was carried out for 9 h using 3.6 equiv. of **1a**, 10 ml% of $CoCl_2$((*S*)-BINAP), and 30 mol% of ZnI_2.

Various substituents on the benzene ring of the fluoroalkylated alkynes, such as electron-withdrawing (Ph, CO_2Et) or electron-donating groups (MeO) did not influence considerably the [2+2+2] cycloaddition, giving the corresponding products **5bA**, **5fA**, and **5cA** in excellent yields. Notably, the position of the substituent on the benzene ring did not affect the reaction (**5aA**, **5dA**, **5eA**). Although the cycloaddition of fluorine-containing alkyne **1g** having a bulky silyl group with diyne **4A** was somewhat sluggish, the isolated yield of the product **5gA** could increase to 68% when the reaction was carried out using 2.4 equiv. of **1g**. The cycloaddition of alkyne **1h** bearing a *n*-C_4F_9 substituent with diyne **4A** proceeded efficiently to afford the corresponding perfluorobutylated benzene derivative **5hA** in excellent yield. On the other hand, the fluorinated propargyl alcohol **1i** was found to be less reactive, affording the desired product **5iA** in moderate yield.

Subsequently, we examined the cobalt-catalyzed [2+2+2] cycloaddition using alkyne **1a** with a variety of diynes (**4B**–**G**). Thus, cycloaddition of **1a** with dibenzyl dipropargylmalonate (**4B**) proceeded well to give the corresponding adduct (**5aB**) in good yield (75% isolated yield). In sharp contrast, the reaction with 1,6-heptadiyne (**4C**) was less efficient, leading to the formation of **5aC** in only 52% isolated yield. Disappointingly, 1,7-octadiyne (**4D**) was an unsuitable substrate for this

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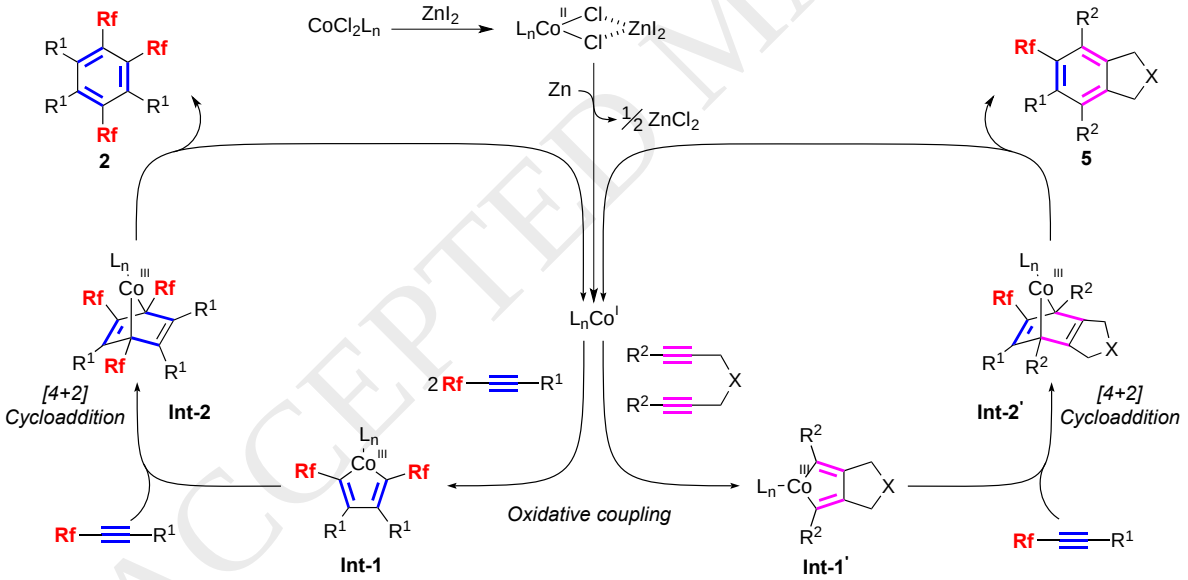
cycloaddition. It should be noted that the [2+2+2] cycloaddition of **1a** with dipropargyl ether (**4E**) or *N*,*N*-dipropargyl tosylamide (**4F**) proceeded smoothly to give the corresponding heterocyclic aromatics **5aE** or **5aF** in 64% or 78% isolated yields, respectively. The internal diyne **4G** was less reactive in the present cycloaddition and corresponding **5aG** was obtained in only 11% yield. After several attempts to improve the reaction efficiency, cycloadduct **5aG** could be isolated in 43% yield when the reaction was conducted with 3.6 equiv. of **1a** in the presence of 10 mol% of $CoCl_2$((*S*)-BINAP), 1.0 equiv. of zinc powder, and 30 mol% of zinc iodide for 9 h.

A possible reaction mechanism for the cobalt-catalyzed [2+2+2] cyclotrimerization of fluorinated alkynes or cycloaddition with diynes is shown in Scheme 2 [15].

First, the cobalt(II) catalyst is reduced by zinc metal to generate the cobalt(I) species (L_nCo^I). This reduction process is possibly accelerated by ZnI_2 because the formation of a $CoCl_2$•••ZnI_2 complex might weaken a Co–Cl bond [16]. In the case of the trimerization reaction, the generated Co(I) species interacts with two molecules of the fluorinated alkyne through a strong π-back donation to form cobaltacyclopentadiene complex **Int-1** [13(c),17, 18]. Subsequent [4+2] cycloaddition of **Int-1** with another fluorinated alkyne furnishes cobaltanorbornadiene **Int-2**, which immediately undergoes reductive elimination to afford the desired tris(trifluoromethyl)benzene derivative **2** in a regioselective manner [13(c),(d)]. On the other hand, when a non-fluorinated diyne is employed, the generated Co(I) species possibly interacts with the diyne much faster than with the fluorinated alkyne, resulting in the formation of cobaltacyclopentadiene complex **Int-1'**. Then, a [4+2] cycloaddition with the fluorinated alkyne proceeds to give cobaltanorbornadiene **Int-2'**, followed by the subsequent reductive elimination, affording the corresponding cyclized product **5**.



Scheme 2. Possible reaction mechanism.

3. Conclusion

In summary, we have developed a novel cobalt-catalyzed [2+2+2] cycloaddition using fluorinated alkynes, which have comparative advantages, like reaction efficiency, regioselectivity, and low catalyst loading, rather than the reported procedures. Trimerization of fluorinated alkynes took place smoothly in the presence of a catalytic

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amount of $CoCl_2$(dppb) and 1.0 equiv. of zinc metal, affording the corresponding cycloadducts in excellent yields with high regioselectivity. Additionally, the intermolecular cycloaddition of fluorinated alkynes with non-fluorinated diynes also proceeded smoothly in the presence of $CoCl_2$((*S*)-BINAP), zinc metal, and ZnI_2, to provide various bicyclic aromatic compounds in high yields.

4. Experimental sections

4.1. General experimental procedures

Infrared spectra (IR) were obtained on liquid films on a NaCl plate with a JASCO FT/IR-4100 type A spectrometer and all spectra are reported in wavenumber (cm^{-1}). ^1H and ^{13}C NMR spectra were recorded with a Bruker AVANCE III 400 NMR spectrometer (^1H: 400 MHz and ^{13}C: 100 MHz) in chloroform-*d* ($CDCl_3$) and the chemical shifts are reported in parts per million (ppm) and are referenced to the residual proton of the NMR solvent. ^{19}F NMR (376 MHz) spectra were recorded with a Bruker AVANCE III 400 NMR spectrometer in $CDCl_3$ with $CFCl_3$ (δ_F = 0 ppm) as internal standard. 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_6H_6) as internal references. High-resolution mass spectra (HRMS) were recorded on a JEOL JMS-700MS spectrometer using the fast atom bombardment (FAB) method.

4.1.1. Materials

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. 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 $60F_{254}$).

4.2. Typical procedure for the cobalt-catalyzed cyclotrimerization of fluoroalkylated alkynes.

In a 30 mL two-necked round bottomed-flask, equipped with a magnetic stirring bar, were placed fluoroalkylated alkyne (**1a**, 0.099 g, 0.48 mmol), zinc powder (0.033 g, 0.50 mmol), and $CoCl_2$(dppb) (8.34 mg, 15 μmol) in acetonitrile (1.5 mL), and the resulting mixture was stirred at 80 °C with an oil bath. After 3 h, 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 column chromatography (hexane/AcOEt = 50:1) to give an inseparable mixture of 3,5,6-tris(4-chlorophenyl)-1,2,4-tris(trifluoromethyl)benzene (**2a**) and 2,4,6-tris(4-chlorophenyl)-1,3,5-tris(trifluoromethyl)benzene (**3a**) in 95% combined yield (0.094 g, 0.15 mmol) as a white solid.

*4.3. X-Ray structural analysis of **2a**•CH_2Cl_2.*

A colorless prismic crystal of **2a**•CH_2Cl_2 having approximate dimensions of 0.13×0.12×0.10 mm was mounted on a glass fiber. All measurements for **2a**•CH_2Cl_2 were made on a diffractometer with filtered Mo*K*α radiation (λ= 0.71075 Å) and a rotating anode generator using a VariMax with PILATUS/DW (Rigaku); Compound **2a**•CH_2Cl_2. monoclinic, a = 16.7701(9) Å, b = 8.4760(4) Å, c = 21.2137(13) Å, α = 90°, β = 109.939(6)°, γ = 90°, V = 2834.6(3) Å^3, T = 173(2) K, space group $P\,2_1/c$ (no. 14), Z = 4, 5272 reflection measured, 3626 unique which were used in all calculations. The final R^1 and wR^2 were 0.071 and 0.203 ($I > 2\sigma(I)$). All calculations were performed using the CrystalStructure crystallographic software

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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 [19] . 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).

4.4. Typical procedure for the cobalt-catalyzed cycloaddition of fluoroalkylated alkynes with diynes.

In a nitrogen-filled glove box, a 30 mL two-necked round bottomed-flask, equipped with a magnetic stirring bar, was charged with zinc iodide (0.016 g, 0.050 mmol). Subsequently the flask was taken out of the gloved box and zinc powder (0.033 g, 0.50 mmol), fluorinated alkyne **1a** (0.123 g, 0.60 mmol), diethyl dipropargylmalonate **4A** (0.117 g, 0.50 mmol), and acetonitrile (1.5 mL) were added to the mixture. The resulting mixture was stirred at 80 °C with an oil bath. After 3 h, 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 solvent from the eluent under reduced pressure, the residue was purified by column chromatography (hexane/AcOEt = 10/1) to give diethyl 6-(4-chlorophenyl)-5-trifluoromethyl-1*H*-indene-2,2(3H)-dicarboxylate **5aA** in 83% yield (0.181 g, 0.41 mmol) as colorless oil.

*4.4.1. Diethyl 6-(3-chlorophenyl)-5-trifluoromethyl-1H-indene-2,2(3H)-dicarboxylate (**5dA**)*

Yield: 82%; Colorless oil; ^{1}H NMR: δ 1.27 (t, J = 7.1 Hz, 6H), 3.65 (s, 2H), 3.68 (s, 2H), 4.23 (q, J = 7.1 Hz, 4H), 7.12 (s, 1H), 7.18 (d, J = 7.3 Hz, 1H), 7.27–7.37 (m, 3H), 7.57 (s, 1H); ^{13}C NMR: δ 14.1, 40.2, 40.4, 60.5, 62.1, 122.1 (q, J = 5.3), 124.2 (q, J = 273.75 Hz), 127.4 (d, J = 1.1 Hz), 127.5 (q, J = 29.6 Hz), 127.75, 127.80, 129.0, 129.2 (d, J = 1.26 Hz), 133.7, 139.0, 140.2, 141.7, 144.1, 171.3; ^{19}F NMR: δ –56.90 (s, 3F); IR (neat): ν 1734, 1346, 1297, 1281, 1247, 1205, 1190, 1156, 1136, 1124, 1097, 1065 cm^{-1}; HRMS (FAB): calcd for $[M+H]^+$ $C_{22}H_{21}ClF_3O_4$: 441.1080, Found: 441.1096.

*4.4.2. Diethyl 6-(2-chlorophenyl)-5-trifluoromethyl-1H-indene-2,2(3H)-dicarboxylate (**5eA**)*

Yield: 80%; White solid; M.p. 73–75 °C; ^{1}H NMR: δ 1.30 (td, J = 7.1, 2.0 Hz, 6H), 3.62–3.80 (m, 4H), 4.27 (quint, J = 7.1 Hz, 4H), 7.13 (s, 1H), 7.22–7.37 (m, 3H), 7.42–7.52 (m, 1H), 7.63 (s, 1H); ^{13}C NMR: δ 14.1, 40.3, 40.4, 60.4, 62.0, 122.0 (q, J = 5.1 Hz), 124.1 (q, J = 273.9 Hz), 126.0, 127.6, 127.8 (q, J = 29.9 Hz), 129.2, 129.3, 131.3, 133.6, 137.2 (d, J = 2.0 Hz), 138.2, 140.4, 144.0, 171.2, 171.4; ^{19}F NMR: δ –59.11 (s, 3F); IR (KBr): ν 1728, 1435, 1367, 1347, 1300, 1289, 1257, 1240, 1189, 1163, 1137, 1120, 1078, 1057, 768 cm^{-1}; HRMS (FAB): calcd for $[M+H]^+$ $C_{22}H_{21}ClF_3O_4$: 441.1080, Found: 441.1073.

*4.4.3. Diethyl 6-(4-ethoxycarbonylphenyl)-5-trifluoromethyl-1H-indene-2,2(3H)-dicarboxylate (**5fA**).*

Yield: 83%; Colorless oil; ^{1}H NMR: δ 1.27 (t, J = 7.2 Hz, 6H), 1.39 (t, J = 7.1 Hz, 3H), 3.64 (s, 2H), 3.68 (s, 2H), 4.23 (q, J = 7.2 Hz, 4H), 4.39 (q, J = 7.1 Hz, 2H), 7.13 (s, 1H), 7.36 (d, J = 8.2 Hz, 2H), 7.57 (s, 1H), 8.05 (d, J = 8.2 Hz, 2H); ^{13}C NMR: δ 14.1, 14.4, 40.2, 40.4, 60.4, 61.1, 62.1, 122.1 (q, J = 5.2 Hz), 124.2 (q, J = 273.5 Hz), 127.4 (q, J = 30.5 Hz), 127.5, 129.0, 129.2, 129.8, 139.5, 140.2, 144.1, 144.6, 166.4, 171.2; ^{19}F NMR: δ –56.84 (s, 3F); IR (neat): ν 2983, 1734, 1367, 1347, 1297, 1277, 1246, 1206, 1189, 1157, 1135, 1103, 1063, 1021, 738, 710 cm^{-1}; HRMS (FAB): calcd for $[M+H]^+$ $C_{25}H_{26}F_3O_6$: 479.1681, Found: 479.1682.

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*4.4.4. Diethyl 6-dimethylphenylsilyl-5-trifluoromethyl-1H-indene-2,2(3H)-dicarboxylate (**5gA**).*

Yield: 68%; Colorless oil; ^{1}H NMR: δ 0.60 (d, J = 1.2 Hz, 6H), 1.26 (t, J = 7.1 Hz, 6H), 3.57 (s, 2H), 3.63 (s, 2H), 4.21 (q, J = 7.1 Hz, 4H), 7.30–7.38 (m, 3H), 7.40 (s, 1H), 7.43–7.50 (m, 2H), 7.54 (s, 1H); ^{13}C NMR: δ –0.7 (q, J = 2.8 Hz), 14.1, 40.5, 40.6, 60.2, 62.0, 122.4 (q, J = 5.4 Hz), 125.2 (q, J = 273.5 Hz), 127.8, 129.1, 133.1, 134.1, 134.4 (q, J = 30.9 Hz), 135.3 (d, J = 1.9 Hz), 138.7, 141.8, 143.2, 171.4; ^{19}F NMR: δ –57.56 (s, 3F); IR (neat): ν 1735, 1333, 1297, 1254, 1232, 1190, 1162, 1147, 1119, 1095, 1069, 948, 818, 404 cm^{-1}; HRMS (FAB): calcd for [M+H]$^{+}$ $C_{24}H_{28}F_3O_4Si$: 465.1709, Found: 465.1694.

*4.4.5. Diethyl 6-(4-chlorophenyl)-5-nonafluorobutyl-1H-indene-2,2(3H)-dicarboxylate (**5hA**).*

Yield: 88%; Yellow oil; ^{1}H NMR: δ 1.27 (t, J = 7.1 Hz, 6H), 3.64 (s, 2H), 3.69 (s, 2H), 4.24 (q, J = 7.1 Hz, 4H), 7.05 (s, 1H), 7.14 (d, J = 8.3 Hz, 2H), 7.30 (d, J = 8.3 Hz, 2H), 7.44 (s, 1H); ^{13}C NMR: δ 14.0, 40.2, 40.4, 60.4, 62.1, 105.0–114.0 (m, 2C), 117.5 (qt, J = 288.3, 33.4 Hz), 117.0 (tt, J = 259.3, 34.1 Hz), 124.2 (t, J = 8.1 Hz), 125.3 (t, J = 22.2 Hz), 127.5, 128.6, 130.6, 133.4, 139.0, 140.4, 140.7, 144.3, 171.3; ^{19}F NMR: δ –126.35 (t, J = 14.1 Hz, 2F), –121.06 (d, J = 8.24 Hz, 2F), –103.03 (d, J = 14.1 Hz, 2F), –81.51 (t, J = 9.6 Hz, 3F); IR (neat): ν 1736, 1483, 1352, 1237, 1209, 1191, 1134, 1093, 1072, 1016, 841, 732 cm^{-1}; HRMS (FAB): calcd for [M+H]$^{+}$ $C_{25}H_{21}ClF_9O_4$: 591.0985, Found: 591.0989.

*4.4.6. Diethyl 6-(1-hydroxycyclohexan-1-yl)-5-trifluoromethyl-1H-indene-2,2(3H)-dicarboxylate (**5iA**).*

Yield: 46%; Colorless oil; ^{1}H NMR: δ 1.25 (t, J = 7.1 Hz, 6H), 1.56–1.90 (m, 11H), 3.59 (s, 2H), 3.60 (s, 2H), 4.20 (q, J = 7.1 Hz, 4H), 7.40 (s, 1H), 7.56 (s, 1H); ^{13}C NMR: δ 14.1, 22.0, 25.5, 39.3 (d, J = 1.0 Hz), 40.2, 40.7, 60.5, 62.0, 74.6, 123.6, 124.0 (q, J = 7.67 Hz), 125.3 (q, J = 273.2 Hz), 126.4 (q, J = 30.7 Hz), 138.8, 144.0, 148.4, 171.4; ^{19}F NMR: δ –53.35 (s, 3F); IR (neat): ν 3539, 2981, 2934, 2860, 1731, 1446, 1368, 1352, 1334, 1292, 1252, 1190, 1151, 1130, 1111, 1070, 1054, 990, 906, 734 cm^{-1}; HRMS (FAB): calcd for [M+H]$^{+}$ $C_{22}H_{28}F_3O_5$: 429.1889, Found: 429.1898.

*4.4.7. Dibenzyl 6-(4-chlorophenyl)-5-trifluoromethyl-1H-indene-2,2(3H)-dicarboxylate (**5aB**).*

Yield: 75%; Yellow oil; ^{1}H NMR: δ 3.71 (s, 2H), 3.74 (s, 2H), 5.20 (s, 4H), 7.14 (s, 1H), 7.21–7.42 (m, 14H), 7.60 (s, 1H); ^{13}C NMR: δ 40.3, 40.5, 60.7, 67.8, 122.2 (q, J = 5.59 Hz), 124.3 (q, J = 273.3 Hz), 127.6 (d, J = 30.0 Hz), 127.8, 128.0, 128.2, 128.6, 128.7, 130.5, 133.8, 135.3, 138.4, 139.4, 139.9, 143.9, 170.9; ^{19}F NMR: δ –56.92 (s, 3F); IR (neat): ν 1735, 1485, 1347, 1298, 1281, 1234, 1206, 1184, 1156, 1134, 1104, 1091, 1061, 907, 734, 697 cm^{-1}; HRMS (FAB): calcd for [M+H]$^{+}$ $C_{32}H_{25}ClF_3O_4$: 565.1393, Found: 565.1395.

*4.4.8. 6-(4-Chlorophenyl)-5-trifluoromethyl-1H-indene (**5aC**).*

Yield: 52%; Colorless oil; ^{1}H NMR: δ 2.18 (quint, J = 7.4 Hz, 2H), 2.99 (t, J = 7.4 Hz, 2H), 3.0 (t, J = 7.4 Hz, 2H), 7.16 (s, 1H), 7.27 (d, J = 8.4 Hz, 2H), 7.37 (d, J = 8.4 Hz, 2H), 7.61 (s, 1H); ^{13}C NMR: δ 25.6, 32.7, 32.9, 122.1 (q, J = 4.9 Hz), 124.6 (q, J = 273.9 Hz), 126.6 (q, J = 29.7 Hz), 127.9, 128.0, 130.6, 133.6, 138.4, 139.0, 144.1, 148.3; ^{19}F NMR: δ –56.65 (s, 3F); IR (neat): ν 2957, 1484, 1417, 1341, 1288, 1267, 1242, 1200, 1154, 1119, 1094, 1058, 1016, 889, 833 cm^{-1}; HRMS (FAB): calcd for [M^{+}] $C_{16}H_{12}ClF_3$: 296.0580, Found: 296.0585.

*4.4.9. 5-(4-Chlorophenyl)-6-trifluoromethyl-1,3-dihydroisobenzofuran (**5aE**)*

Yield: 64%; Colorless oil; ^{1}H NMR: δ 5.13 (s, 2H), 5.16 (s, 2H), 7.14 (s, 1H), 7.22 (d, J = 8.4 Hz, 2H), 7.34 (d, J = 8.4 Hz, 2H), 7.60 (s, 1H); ^{13}C NMR: δ 73.3, 73.4, 119.1 (q, J = 5.5 Hz), 124.2 (q, J = 273.8 Hz), 124.7, 128.07 (q, J = 30.0 Hz),

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128.13, 130.5 (d, J = 1.2 Hz), 134.0, 138.2, 139.2, 139.9, 143.1; ^{19}F NMR: δ –57.00 (s, 3F); IR (neat): ν 1484, 1425, 1320, 1264, 1243, 1209, 1160, 1131, 1093, 1052, 1016, 885, 830, 591 cm^{-1}; HRMS (FAB): calcd for [M$^+$] $C_{15}H_{10}ClF_3O$: 298.0372, Found: 298.0370.

*4.4.10. Experimental procedure for the cobalt-catalyzed cycloaddition of the fluoroalkylated alkyne **1a** with the diyne **4G**.*

In a nitrogen-filled glove box, a 30 mL two-necked round bottomed-flask, equipped with a magnetic stirring bar, was charged with zinc iodide (0.048 g, 0.150 mmol). Subsequently the flask was taken out of the gloved box and zinc powder (0.033 g, 0.50 mmol), fluorinated alkyne **1a** (0.370 g, 1.8 mmol), diethyl dipropargylmalonate **4G** (0.194 g, 0.50 mmol), and acetonitrile (1.5 mL) were added to the mixture. The resulting mixture was stirred at 80 °C with an oil bath. After 9 h, 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 solvent from the eluent under reduced pressure, the residue was purified by column chromatography (hexane/AcOEt = 10/1) to give diethyl 5-(4-chlorophenyl)-4,7-diphenyl-6-trifluoromethyl-1H-indene-2,2(3H)-dicarboxylate **5aG** in 43% yield (0.128 g, 0.216 mmol) as white solid.

*Diethyl 5-(4-chlorophenyl)-4,7-diphenyl-6-trifluoromethyl-1H-indene-2,2(3H)-dicarboxylate (**5aG**)*

Yield: 43%; White solid; M.p. 233–234 °C; ^{1}H NMR: δ 1.19 (t, J = 7.1 Hz, 6H), 3.32 (s, 2H), 3.39 (s, 2H), 4.15 (q, J = 7.1 Hz, 4H), 6.90–7.02 (m, 4H), 7.10 (d, J = 8.3 Hz, 2H), 7.12–7.24 (m, 3H), 7.31 (d, J = 8.3 Hz, 2H), 7.39 (t, J = 7.3 Hz, 1H), 7.46 (t, J = 7.2 Hz, 2H); ^{13}C NMR: δ 14.1, 41.0, 41.2, 59.6, 62.0, 124.5 (q, J = 277.2), 126.6 (q, J = 27.5 Hz), 127.0, 127.3, 127.5, 128.1, 128.4, 129.5, 131.6 (d, J = 1.2 Hz), 132.8, 137.38, 137.41, 137.44, 138.3, 138.9 (d, J = 1.4 Hz), 139.18, 139.21, 140.7, 142.6, 171.3; ^{19}F NMR: δ –48.19 (s, 3F); IR (KBr): ν 1731, 1443, 1348, 1329, 1298, 1280, 1243, 1215, 1189, 1151, 1124, 1098, 1016, 753, 703, 523 cm^{-1}; HRMS (FAB): calcd for [M+H]$^+$ $C_{34}H_{29}ClF_3O_4$: 593.1706, Found: 593.1704.

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In addition, we also attempted [2+2+2] cycloaddition reaction using the alkyne **1a** and the diene **4A** in the presence of CoI_2(dppe) instead of $CoCl_2$((*S*)-BINAP)/ZnI_2. As a result, it was found that the reaction proceeded smoothly to give the corresponding benzene derivative **5aA** in 84% yield, while the use of $CoCl_2$(dppe) retarded the reaction from proceeding (Table 3, Entry 6). This result implies that the smooth reduction from Co(II) to Co(I) makes the progress of the reaction easier, that is, zinc iodide may also promote the reduction.

[17] The regioselective formation of **Int-1** may be stemmed from an efficient decrease of LUMO energy level at the sp-hybridized carbon adjacent to CF_3, which is due to a strong electron-withdrawing character of a CF_3 group. It was reported that the formation of similar metalacyclopentadiene from CF_3-alkyne and Ru-catalyst by Kawatsura and Itoh's

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group, see: Ref. 13(c).

[18] When alkynes with bulky substituents as R^1 are used, the trimerization reaction does not proceed well. This might be due to the suppression of formation of cobaltacyclopentadiene **Int-1** by large steric repulsion between R^1 substituents. Since such steric repulsion does not exist in the case of using diyne, on the other hand, the reaction proceeds without problem, even if a bulky perfluorobutylated alkyne etc. are used as substrates.

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