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A FACILE SYNTHESIS OF 4-ARYL-1,1,1-TRIFLUOROBUT-3-EN-2-ONES VIA 4-ARYL SUBSTITUTED CF_3 - CONTAINING DIHYDROPYRAN DERIVATIVES: A VERSATILE METHOD FOR THE INTRODUCTION OF FLUORINE-CONTAINING C_4- AND C_6- UNIT TO AROMATIC COMPOUNDS

Norio Ota, Etsuji Okada,* Dai Shibata, Satoru Adachi, and Shohei Saikawa

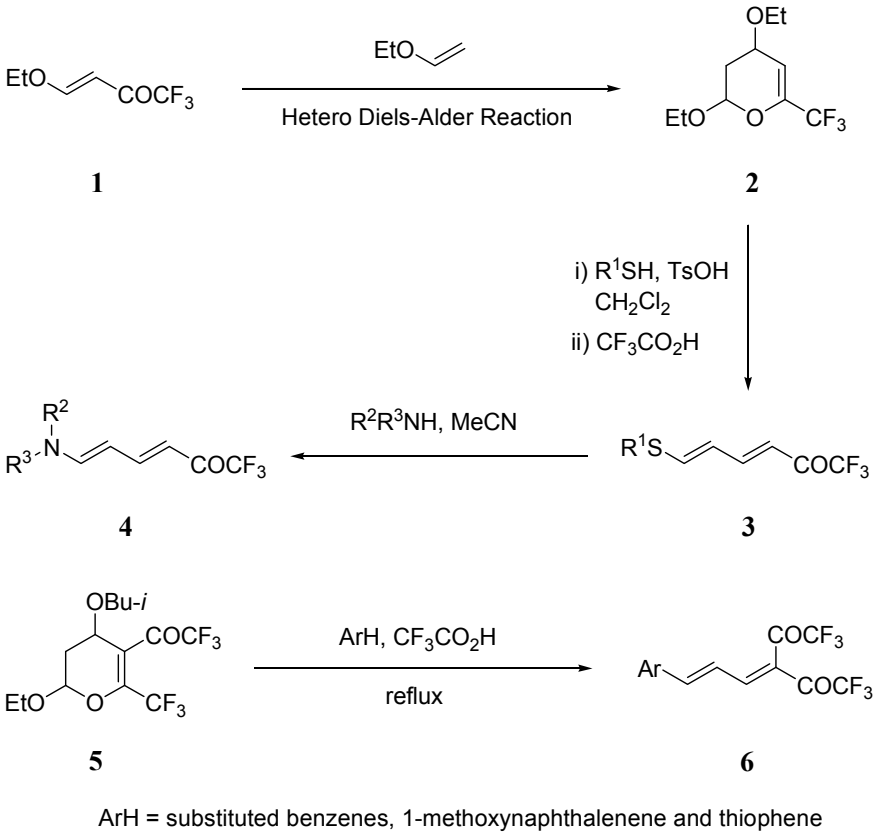
Department of Chemical Science and Engineering, Graduate School of Engineering, Kobe University, Rokkodai-cho, Nada-ku, Kobe 657-8501, Japan
Fax: +81(78)8036194; E-mail: okaetsu@kobe-u.ac.jp

Abstract – The CF_3 - containing dihydropyran derivative (**2**) reacted easily with various aromatic compounds in trifluoroacetic acid to give novel 4-aryl substituted dihydropyran derivatives (**7**) in moderate to high yields. Retro hetero Diels-Alder reaction of thus obtained **7** proceeded readily by heating at 300 °C to afford the corresponding 4-aryl-1,1,1-trifluorobut-3-en-2-ones (**12**) in good to excellent yields. With the use of *p*-toluenesulfonic acid instead of trifluoroacetic acid together with dihydropyran (**2**) in acetonitrile, 4-trifluoroacetyl-1,3-butadienylation of 1,3-dimethoxybenzene occurred successfully. The bimolecular reaction of dihydropyran (**2**) in the presence of *p*-toluenesulfonic acid was also examined.

INTRODUCTION

Many new methodologies for carbon-carbon bond formation are developed in the field of organic synthesis since the carbon-carbon bond formation has been one of the most interesting challenges in organic chemistry.[1-3] On the other hand, 6-arylhexa-3,5-dien-2-one systems are useful building blocks for the synthesis of various heterocycles. For instance, it has been reported that the reaction of 6-arylhexa-3,5-dien-2-ones with *N*-tosyliminophenyliodinane give aziridine derivatives.[4] Moreover, the syntheses of 1,2-dihydropyridines,[5] 2-pyridones,[6] and 2-aminopyrimidines[7] from various 6-arylhexa-3,5-dien-2-one derivatives have been reported. 6-Arylhexa-3,5-dien-2-ones and 1,2,4-triazole-3,5-dione are also known to undergo Diels-Alder reaction to give the corresponding

[1,2,4]triazolo[1,2-*a*]pyridazines.[8] In our previous papers, we reported that the ring-opening reactions of fluorine-containing dihydropyran derivative (**2**), which was easily prepared by the hetero Diels-Alder reaction of trifluoroacetylvinyl ether (**1**) with ethyl vinyl ether,[9] with mercaptans in the presence of *p*-toluenesulfonic acid afforded the corresponding 4-trifluoroacetyl-1,3-butadienyl sulfides (**3**).[10] These butadienyl sulfides (**3**) are easily converted to 4-trifluoroacetyl-1,3-butadienylamines (**4**) by *S*-*N* exchange reactions[11] as depicted in Scheme 1. Very recently, we have reported a facile and convenient synthetic method for 4,4-bis(trifluoroacetyl)-1,3-butadienylated aromatic compounds (**6**) by the one step C_8-unit introduction to aromatic rings by making use of fluorine-containing dihydropyran derivative (**5**)[12] in trifluoroacetic acid.[13] These findings prompted us to research on the new carbon-carbon bond formation through the acid-catalyzed reaction of dihydropyran derivative (**2**).



ArH = substituted benzenes, 1-methoxynaphthalenene and thiophene

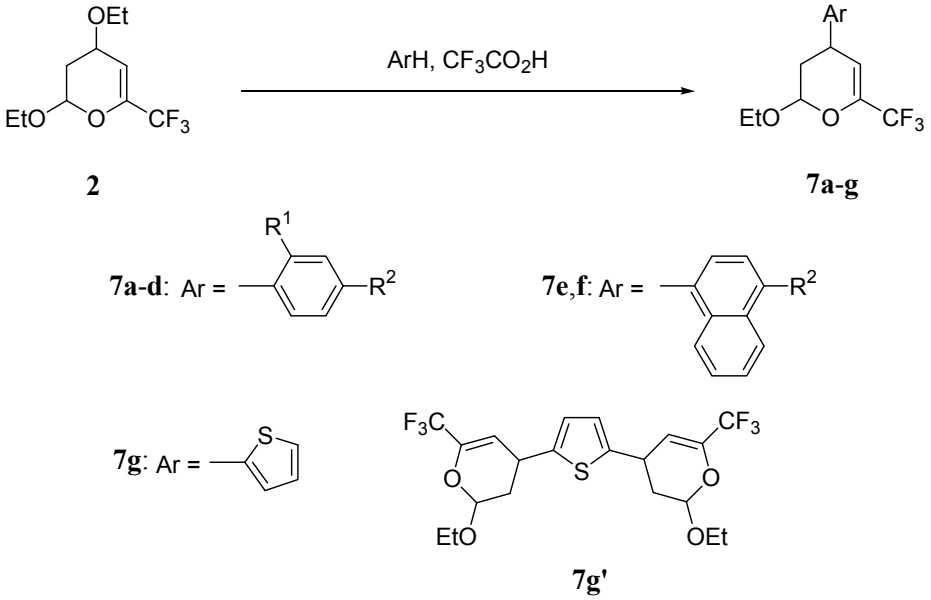
Scheme 1

We here wish to present a synthesis of novel 4-aryl substituted dihydropyrans (**7**) which obtained unexpectedly by the reaction of fluorine-containing dihydropyran (**2**) with various aromatic compounds in trifluoroacetic acid. The synthesis of 4-aryl-1,1,1-trifluorobut-3-en-2-ones (**12**) from dihydropyrans (**7**) by retro hetero Diels-Alder reactions is also described. In addition, a new synthetic method for 6-(2,4-dimethoxyphenyl)-1,1,1-trifluorohexa-3,5-dien-2-one (**8**), by making use of fluorine-containing dihydropyran derivative (**2**), is briefly discussed in this report. Possibly, these aromatic compounds

having fluorine-containing ethene and butadiene fragments prepared by our novel C_4- and C_6-unit introduction method can serve as versatile building blocks for the construction of CF_3 -containing heterocycles, which may be expected to show interesting biological activities.[14-17]

RESULTS AND DISCUSSION

The results of the reaction of dihydropyran derivative (**2**) with various aromatic compounds in trifluoroacetic acid are shown in Scheme 2 and summarized in Table 1. The *O*-*C* exchange reaction of **2** with anisole easily proceeded at -15 °C for 18 h to give the corresponding 4-(4- and 2-methoxyphenyl) substituted dihydropyran derivatives as a mixture of two regioisomers, **7a** and **7a'**, in 26% and 23% yields, respectively (entry 1). *m*-Xylene also exhibited almost the same reactivity with anisole to afford the dihydropyran (**7b**) in 53% yield (entry 2). The reaction of **2** with 1-methoxy-3-methylbenzene occurred at ambient temperature within 15 min to provided a mixture of two kinds of regioisomers, **7c** and **7c'**, in 72% as a combined yield (entry 3). Separation of the mixtures into **7c** and **7c'** was hardly performed by column chromatography. The reaction with 1,3-dimethoxybenzene proceeded quite rapidly to afford **7d** in 60% yield, selectively (entry 4). It was, moreover, found that this type of *O*-*C* exchange reaction at 4-*C* of dihydropyran (**2**) had application to other aromatic compounds, as 1-methylnaphthalene and 1-methoxynaphthalene (naphthalenes) and thiophene (heteroaromatics), to provide **7e-g** in high yields (entries 5-7). The reactions of **2** with benzene, naphthalene, and aromatic



Scheme 2

compounds having electron-withdrawing group were unsuccessful to give decomposed products.

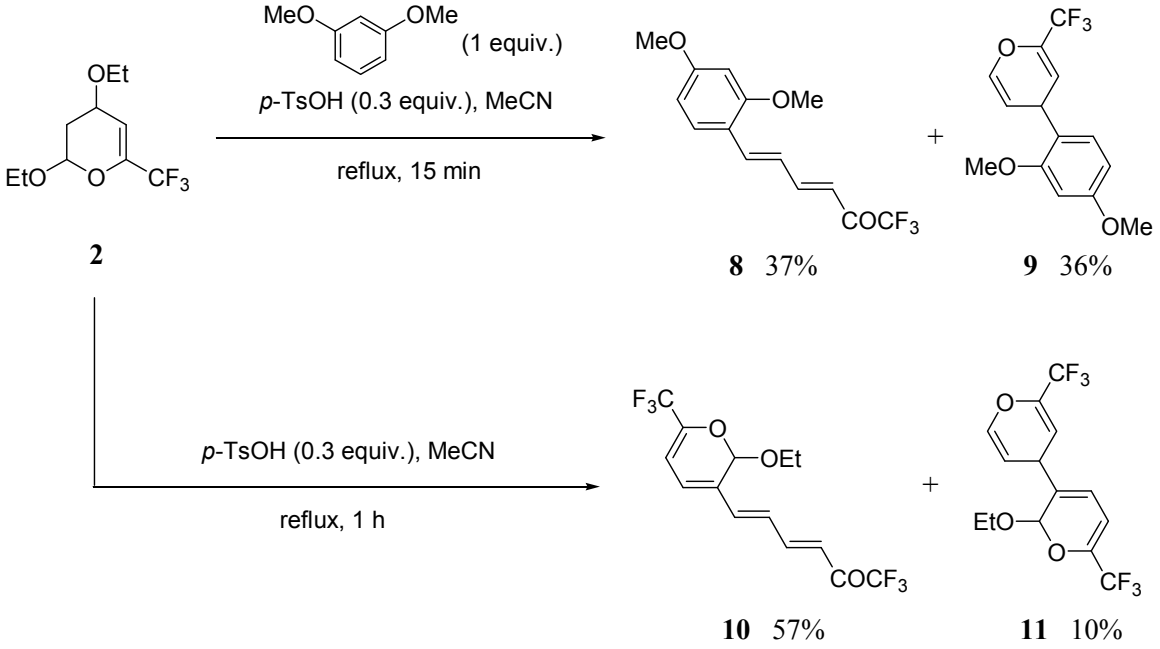
In all cases in Table 1, 4-aryl substituted dihydropyrans (**7**) were obtained selectively under very mild conditions without any products of ring-opening reaction of dihydropyran system, types of **3** and **6**.

Table 1. Synthesis of 4-aryl-2-ethoxy-6-trifluoromethyl-3,4-dihydro-2*H*-pyrans (**7a-g'**).

Entry	R^1	R^2	ArH (equiv.)	Temp. (°C)	Time (min)	Product	Yield (%)[a]
1	H	OMe	5	-15	18 h	**7a**	26[b]
	OMe	H				**7a'**	23[b]
2	Me	Me	5	-15	24 h	**7b**	53
3	Me	OMe	1	rt	15	**7c**[c]	72[d]
	OMe	Me				**7c'**[c]	
4	OMe	OMe	1	0	5	**7d**	60
5	-	Me	1	rt	15	**7e**	74
6	-	OMe	1	rt	15	**7f**	88
7	-	-	5	rt	15	**7g**	73
	-	-				**7g'**	17

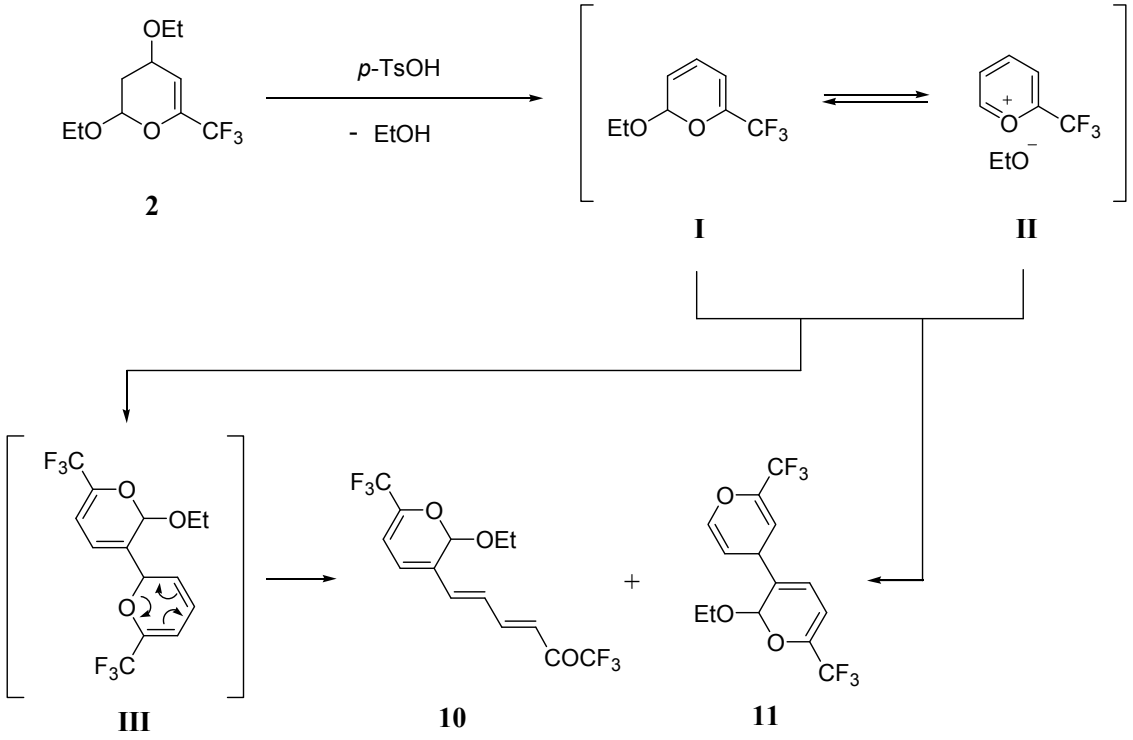
[a] Isolated yield after column chromatography.
[b] The fraction of a mixture of **7a** and **7a'** (combined yield: 8%) was accompanied.
[c] The regiochemistry and the ratio were not determined yet due to the impossibility of the separation of the two regioisomers, **7c** and **7c'**.
[d] Combined yield (NMR yield) of two regioisomers.

These results of our approaches on the reactions of **2** with various aromatic compounds show sharp contrast to the reaction of **5** with aromatic compounds in refluxing trifluoroacetic acid (see Scheme 1).[13] Also, we tried the reactions of **2** with various aromatic compounds in trifluoroacetic acid under reflux in stead of at -15 °C to room temperatures, which resulted in failure to give complex mixtures without any formation of 1,3-butadinene derivatives. So, we attempted the acid-catalyzed reaction of **2** with *p*-toluenesulfonic acid in place of trifluoroacetic acid in acetonitrile under reflux.



Scheme 3

As shown in Scheme 3, the reaction of **2** with 1,3-dimethoxybenzene in the presence of *p*-toluenesulfonic acid was found to occur in refluxing acetonitrile to afford a mixture of 4-trifluoroacetyl-1,3-butadiene derivative (**8**) and 2-trifluoromethyl-4*H*-pyran derivative (**9**) in almost same yields, respectively. Contrary to our expectation, the similar 4-trifluoroacetyl-1,3-butadienylation of the other aromatic compounds by the *p*-toluenesulfonic acid catalyzed reaction of **2** was unsuccessful to give decomposed products. Next, we tried the reaction of **2** without aromatic compounds in the presence of *p*-toluenesulfonic acid in refluxing acetonitrile to afford the bimolecular reaction products, 2*H*-pyran (**10**) and 4*H*-pyran (**11**).

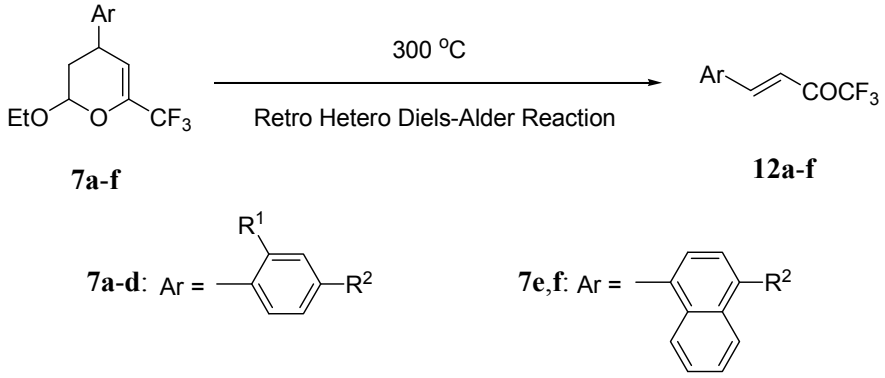


Scheme 4

A possible pathway for the formation of **10** and **11** is depicted in Scheme 4. Elimination of alcohols from **2** by *p*-toluenesulfonic acid occurs first to form 2*H*-pyran (**I**) and pyrylium (**II**) at equilibrium, electrophilic substitution on 3-*C* of **I** by 6-*C* of **II** gives 2*H*-pyran (**III**), and finally **III** undergoes electrocyclic ring-opening reaction to afford **10**. Meanwhile, electrophilic substitution on 3-*C* of **I** by 4-*C* of **II** simply gives 4*H*-pyran (**11**).

Lastly, we tried to carry out the retro hetero Diels-Alder reaction of 4-aryl substituted dihydropyrans (**7**) at 300 °C under atmospheric pressure, as depicted in Scheme 5 and summarized in Table 2. The desired retro hetero Diels-Alder reactions of **7a-f** were thoroughly proceeded at 300 °C within 30-60 min to

provide the corresponding 4-aryl-1,1,1-trifluorobut-3-en-2-ones (**12a-f**) in medium to excellent yields. Thus, we achieved a new method for the synthesis of trifluoroacetylvinylated aromatics (**12**) which were easily obtained in two steps from dihydropyran (**2**) via the novel 4-arylated dihydropyrans (**7**). The present C_4-unit introduction method is one of the versatile and unique methods for the synthesis of various trifluoroacetylvinylated aromatic compounds.[18,19]



Scheme 5

Table 2. Synthesis of (*E*)-4-aryl-1,1,1-trifluorobut-3-en-2-one (**12a-f**).

Entry	Substrate	R^1	R^2	Time (min)	Product	Yield (%)[a]
1	**7a**	H	OMe	60	**12a**	79
2	**7a'**	OMe	H	60	**12a'**	78
3	**7b**	Me	Me	60	**12b**	68
4	**7c** and **7c'**[b,c]	Me / OMe	OMe / Me	60	**12c** and **12c'**[c]	79[d]
5	**7d**	OMe	OMe	30	**12d**	83
6	**7e**	-	Me	30	**12e**	96
7	**7f**	-	OMe	30	**12f**	87

[a] Isolated yield after column chromatography.
[b] A mixture of two regioisomers (**7c** and **7c'**) was used as a starting material.
[c] The regiochemistry and the ratio were not determined yet.
[d] Combined yield of two regioisomers.

In conclusion, we succeeded in the synthesis of novel 4-aryl substituted dihydropyran derivatives (**7**), which were successfully converted to 4-aryl-1,1,1-trifluorobut-3-en-2-ones (**12**). So we have developed a simple method for the introduction of fluorine-containing C_4-unit, 2-trifluoracetylvinyl system, to various aromatic rings in two steps. The first step is the *O-C* exchange at 4-*C* of CF_3-containing dihydropyran derivative (**2**), and the following step is retro hetero Diels-Alder reactions of 4-aryl substituted dihydropyran (**7**). We also found a novel method for the introduction of fluorine-containing C_6-unit, 4-trifluoroacetyl-1,3-butadienyl system, to 1,3-dimethoxybenzene using **2**. Moreover, by a

bimolecular reaction of dihydropyran (**2**) in the presence of *p*-toluenesulfonic acid, novel 2*H*-pyran (**10**) and 4*H*-pyran (**11**), which are not easily accessible by other methods, were synthesized. Further work is under progress in our laboratory on the synthetic application of **7**, **8**, and **10** to the fluorine-containing heterocycles of potentially biological importance.

EXPERIMENTAL

All melting points were determined on an electrothermal digital melting point apparatus and are uncorrected. ^{1}H NMR spectra were obtained with JEOL PMX60SI and Bruker AVANCE500 instruments. All chemical shifts are reported in ppm downfield from internal tetramethylsilane. IR spectra were recorded on Hitachi EPI-G3 and PerkinElmer Spectrum ONE spectrophotometers. Elemental analyses were performed by the Microanalyses Center of Kyoto University or taken with a YANACO CHN-Corder MT-5 analyzer. Chromatographic separations were carried out on a silica gel column (Fuji Silysia Chemical BW-127ZH; 100-270 mesh). All reagents were obtained commercially and used without further purification. Final purification of products for elemental analyses was done by recrystallization or Kugelrohr distillation.

Synthesis of 4-aryl-2-ethoxy-6-(trifluoromethyl)-3,4-dihydro-2*H*-pyrans (7).

To a mixture of **2** (661 mg, 2.75 mmol) and substituted benzenes (13.75 mmol or 2.75 mmol), naphthalenes (2.75 mmol) and thiophene (13.75 mmol) was added dropwise trifluoroacetic acid (3.8 mL) and this solution was stirred under the conditions as shown in Table 1. The reaction mixture was washed with 10% aq. Na_2CO_3 (30 mL) and H_2O (30 mL), extracted with CH_2Cl_2 (30 mL) and dried (Na_2SO_4). The solvent was removed under reduced pressure and the crude mixture was chromatographed on silica gel column using *n*-hexane/benzene (1:1) as eluent to give **7a-g'**.

2-Ethoxy-4-(4-methoxyphenyl)-6-trifluoromethyl-3,4-dihydro-2*H*-pyran (7a): bp 110 °C / 1 mmHg (oven temperature); ^{1}H NMR ($CDCl_3$): δ 7.04 (d, 2H, *J* = 10.0 Hz, H-2', H-6'), 6.72 (d, 2H, *J* = 10.0 Hz, H-3', H-5'), 5.42 (br s, 1H, H-5), 5.22 (t, 1H, *J* = 3.0 Hz, H-2), 4.26-3.30 (m, 3H, H-4, OC<u>H</u>$_2$CH$_3$), 3.71 (s, 3H, OCH_3), 2.81-2.49 (m, 2H, H-3), 1.23 (t, 3H, *J* = 6.6 Hz, OCH_2C<u>H</u>$_3$); IR (neat): 1684, 1608 cm^{-1}. Anal. Calcd for $C_{15}H_{17}O_3F_3$: C, 59.60; H, 5.67; F, 18.85. Found: C, 59.75; H, 5.59; F, 19.06.

2-Ethoxy-4-(2-methoxyphenyl)-6-trifluoromethyl-3,4-dihydro-2*H*-pyran (7a'): bp 125 °C / 2 mmHg (oven temperature); ^{1}H NMR ($CDCl_3$): δ 7.07 (d, 1H, *J* = 8.0 Hz, H-6'), 6.97 (dd, 1H, *J* = 8.0, 6.0 Hz, H-4'), 6.86 (dd, 1H, *J* = 8.0, 6.0 Hz, H-5'), 6.74 (d, 1H, *J* = 8.0 Hz, H-3'), 5.46 (br s, 1H, H-5), 5.10 (t, 1H, *J* = 3.0 Hz, H-2), 4.31-3.42 (m, 3H, H-4, OC<u>H</u>$_2$CH$_3$), 3.73 (s, 3H, OCH_3), 2.39-1.55 (m, 2H, H-3), 1.23 (t, 3H, *J* = 6.8 Hz, OCH_2C<u>H</u>$_3$); IR (neat): 1680, 1582 cm^{-1}. Anal. Calcd for $C_{15}H_{17}O_3F_3$: C, 59.60; H, 5.67; F, 18.85. Found: C, 59.67; H, 5.65; F, 19.25.

4-(2,4-Dimethylphenyl)-2-ethoxy-6-trifluoromethyl-3,4-dihydro-2*H*-pyran (7b): bp 100 °C / 1 mmHg

(oven temperature); ^{1}H NMR ($CDCl_3$): δ 6.89 (s, 3H, H-3', H-5', H-6'), 5.50 (br s, 1H, H-5), 5.15 (t, 1H, *J* = 3.0 Hz, H-2), 4.01-3.45 (m, 3H, H-4, OC<u>H</u>$_2$CH$_3$), 2.28 (s, 3H, CH_3), 2.25 (s, 3H, CH_3), 2.22-1.46 (m, 2H, H-3), 1.23 (t, 3H, *J* = 6.8 Hz, OCH$_2$C<u>H</u>$_3$); IR (neat): 1680, 1610 cm^{-1}. Anal. Calcd for $C_{16}H_{19}O_2F_3$: C, 63.99; H, 6.38; F, 18.98. Found: C, 64.27; H, 6.53; F, 19.20.

A mixture of 2-ethoxy-4-(4-methoxy-2-methylphenyl)-6-trifluoromethyl-3,4-dihydro-2*H*-pyran (7c) and 2-ethoxy-4-(2-methoxy-4-methylphenyl)-6-trifluoromethyl-3,4-dihydro-2*H*-pyran (7c'): bp 130 °C / 2 mmHg (oven temperature); ^{1}H NMR ($CDCl_3$): δ 7.16-6.67 (m, 3H, H-3', H-5', H-6'), 5.60 (br s, 1H, H-5), 5.23 (t, 1H, *J* = 3.0 Hz, H-2), 4.40-3.50 (m, 3H, H-4, OC<u>H</u>$_2$CH$_3$), 3.83, 3.77 (s, 3H, OCH_3), 2.50-1.55 (m, 2H, H-3), 2.33 (s, 3H, C<u>H</u>$_3$), 1.27, 1.23 (t, 3H, *J* = 7.0 Hz, OCH$_2$C<u>H</u>$_3$); IR (neat): 1675, 1605 cm^{-1}. Anal. Calcd for $C_{16}H_{19}O_3F_3$: C, 60.75; H, 6.05; F, 18.02. Found: C, 60.54; H, 6.01; F, 18.29.

4-(2,4-Dimethoxyphenyl)-2-ethoxy-6-trifluoromethyl-3,4-dihydro-2*H*-pyran (7d): bp 140 °C / 2 mmHg (oven temperature); ^{1}H NMR ($CDCl_3$): δ 6.92 (d, 1H, *J* = 8.4 Hz, H-6'), 6.43 (d, 1H, *J* = 8.4 Hz, H-5'), 6.39 (s, 1H, H-3'), 5.46 (br s, 1H, H-5), 5.11 (t, 1H, *J* = 3.0 Hz, H-2), 4.13-3.44 (m, 3H, H-4, OC<u>H</u>$_2$CH$_3$), 3.72 (s, 3H, OCH_3), 3.69 (s, 3H, OCH_3), 2.47-1.52 (m, 2H, H-3), 1.23 (t, 3H, *J* = 7.0 Hz, OCH$_2$C<u>H</u>$_3$); IR (neat): 1682, 1610 cm^{-1}. Anal. Calcd for $C_{16}H_{19}O_4F_3$: C, 57.83; H, 5.76; F, 17.15. Found: C, 57.59; H, 5.89; F, 17.30.

2-Ethoxy-4-(4-methylnaphthalen-1-yl)-6-trifluoromethyl-3,4-dihydro-2*H*-pyran (7e): bp 150 °C / 3 mmHg (oven temperature); ^{1}H NMR ($CDCl_3$): δ 8.02-7.75 (m, 2H, H_{arom}), 7.52-7.29 (m, 2H, H_{arom}), 7.10 (s, 2H, H-2', H-3'), 5.65 (br s, 1H, H-5), 5.15 (t, 1H, *J* = 3.0 Hz, H-2), 4.68-4.16 (m, 1H, H-4), 4.05-3.78 (m, 2H, OC<u>H</u>$_2$CH$_3$), 2.65 (s, 3H, CH_3), 2.30-1.56 (m, 2H, H-3), 1.26 (t, 3H, *J* = 8.0 Hz, OCH$_2$C<u>H</u>$_3$); IR (neat): 1680, 1596 cm^{-1}. Anal. Calcd for $C_{19}H_{19}O_2F_3$: C, 67.85; H, 5.69; F, 16.95. Found: C, 68.06; H, 5.72; F, 17.11.

2-Ethoxy-4-(4-methoxynaphthalen-1-yl)-6-trifluoromethyl-3,4-dihydro-2*H*-pyran (7f): bp 190 °C / 2 mmHg (oven temperature); ^{1}H NMR ($CDCl_3$): δ 8.30-7.81 (m, 2H, H_{arom}), 7.55-7.33 (m, 2H, H_{arom}), 7.14 (d, 1H, *J* = 8.0 Hz, H-2'), 6.65 (d, 1H, *J* = 8.0 Hz, H-3'), 5.66 (br s, 1H, H-5), 5.16 (t, 1H, *J* = 3.0 Hz, H-2), 4.60-4.15 (m, 1H, H-4), 3.90 (s, 3H, OCH_3), 4.06-3.47 (m, 2H, OC<u>H</u>$_2$CH$_3$), 2.53-1.63 (m, 2H, H-3), 1.27 (t, 3H, *J* = 7.0 Hz, OCH$_2$C<u>H</u>$_3$); IR (neat): 1680, 1590 cm^{-1}. Anal. Calcd for $C_{19}H_{19}O_3F_3$: C, 64.77; H, 5.44; F, 16.18. Found: C, 65.03; H, 5.38; F, 16.44.

2-Ethoxy-4-(thiophen-2-yl)-6-trifluoromethyl-3,4-dihydro-2*H*-pyran (7g): bp 85 °C / 1 mmHg (oven temperature); ^{1}H NMR ($CDCl_3$): δ 6.95 (d, 1H, *J* = 5.4 Hz, H-5'), 6.71 (dd, 1H, *J* = 5.4, 4.0 Hz, H-4'), 6.70 (d, *J* = 4.0 Hz, H-3'), 5.56 (br s, 1H, H-5), 5.19 (t, 1H, *J* = 3.0 Hz, H-2), 4.19-3.66 (m, 1H, H-4), 3.68 (q, 2H, *J* = 7.0 Hz, OC<u>H</u>$_2$CH$_3$), 2.47-1.67 (m, 2H, H-3), 1.22 (t, 3H, *J* = 7.0 Hz, OCH$_2$C<u>H</u>$_3$); IR (neat): 1680, 1578 cm^{-1}. Anal. Calcd for $C_{12}H_{13}O_2F_3S$: C, 51.79; H, 4.71; F, 20.48. Found: C, 51.86;

H, 4.68; F, 20.65.

2,5-Bis(2-ethoxy-6-trifluoromethyl-3,4-dihydro-2*H*-pyran-4-yl)thiophene (7g'): ^{1}H NMR ($CDCl_3$): δ 6.62 (s, 2H, $H_{thienyl}$), 5.56 (br s, 2H, H-5), 5.19 (t, 2H, *J* = 2.8 Hz, H-2), 4.20-3.56 (m, 2H, H-4), 3.67 (q, 4H, *J* = 7.6 Hz, $OC\underline{H}_2CH_3$), 2.46-1.66 (m, 4H, H-3), 1.22 (t, 6H, *J* = 7.6 Hz, $OCH_2C\underline{H}_3$); IR (neat): 1680, 1582 cm^{-1}.

Reaction of 2 with 1,3-dimethoxybenzene in the presence of *p*-toluenesulfonic acid.

To a stirred solution of **2** (697 mg, 2.90 mmol) and 1,3-dimethoxybenzene (401 mg, 2.90 mmol) in MeCN (7 mL) was added *p*-toluenesulfonic acid (150 mg, 0.87 mmol) and the mixture was refluxed for 15 min. The reaction mixture was washed with 10% aq. Na_2CO_3 (30 mL) and H_2O (30 mL), extracted with CH_2Cl_2 (30 mL) and dried (Na_2SO_4). The solvent was removed under reduced pressure and the crude mixture was chromatographed on silica gel column using *n*-hexane/benzene (4:1) as eluent to give **8** (307 mg, 37 %) and **9** (299 mg, 36 %).

(*E*,*E*)-6-(2,4-Dimethoxyphenyl)-1,1,1-trifluorohexa-3,5-dien-2-one (8): bp 150 °C / 2 mmHg (oven temperature); ^{1}H NMR ($CDCl_3$): δ 7.61 (dd, 1H, *J* = 14.4, 10.4 Hz, H-4), 7.28 (d, 1H, *J* = 14.4 Hz, H-3), 7.10 (d, 1H, *J* = 15.2 Hz, H-6), 6.77 (dd, 1H, *J* = 15.2, 10.4 Hz, H-5), 6.41 (d, 1H, *J* = 7.8 Hz, H-6'), 6.37 (d, 1H, *J* = 7.8 Hz, H-5'), 6.31 (s, 1H, H-3'), 3.77 (s, 3H, OCH_3), 3.75 (s, 3H, OCH_3); IR (neat): 1680 cm^{-1}. Anal. Calcd for $C_{14}H_{13}O_3F_3$: C, 58.74; H, 4.58; F, 19.91. Found: C, 58.91; H, 4.63; F, 20.17.

4-(2,4-Dimethoxyphenyl)-2-trifluoromethyl-4*H*-pyran (9): bp 170 °C / 2 mmHg (oven temperature); ^{1}H NMR ($CDCl_3$): δ 7.02 (d, 1H, *J* = 9.0 Hz, H-6), 6.42 (d, 1H, *J* = 7.2 Hz, H-6'), 6.39 (d, 1H, *J* = 7.2 Hz, H-5'), 6.28 (s, 1H, H-3'), 5.47-5.37 (m, 1H, H-3), 5.93-5.69 (m, 1H, H-5), 4.54-4.30 (m, 1H, H-4), 3.69 (s, 6H, OCH_3); IR (neat): 1600, 1582 cm^{-1}. Anal. Calcd for $C_{14}H_{13}O_3F_3$: C, 58.74; H, 4.58; F, 19.91. Found: C, 58.59; H, 4.52; F, 19.58.

Reaction of 2 in the presence of *p*-toluenesulfonic acid.

To a stirred solution of **2** (2964 mg, 12.34 mmol) in MeCN (30 mL) was added *p*-toluenesulfonic acid (637 mg, 3.70 mmol) and the mixture was refluxed for 1 h. The reaction mixture was washed with 10% aq. Na_2CO_3 (120 mL) and H_2O (120 mL), extracted with CH_2Cl_2 (100 mL) and dried (Na_2SO_4). The solvent was removed under reduced pressure and the crude mixture was chromatographed on silica gel column using *n*-hexane/benzene (4:1) as eluent to give **10** (1204 mg, 57 %) and **11** (211 mg, 10 %).

(*E*,*E*)-6-(2-Ethoxy-6-trifluoromethyl-2*H*-pyran-3-yl)-1,1,1-trifluorohexa-3,5-dien-2-one (10): mp 110-112 °C (*n*-hexane); ^{1}H NMR ($CDCl_3$): δ 7.55 (dd, 1H, *J* = 14.2, 10.0 Hz, H-4), 6.87-5.95 (m, 5H, H-3, H-5, H-6, H-4', H-5'), 4.10-3.50 (m, 2H, $OC\underline{H}_2CH_3$), 1.26 (t, 3H, *J* = 7.0 Hz, $OCH_2C\underline{H}_3$); ^{13}C NMR ($CDCl_3$): δ 179.9 (q, J_{CF} = 35.4 Hz), 149.2, 142.2, 142.2 (q, J_{CF} = 37.8 Hz), 128.1, 126.6, 126.4, 120.8, 119.8 (q, J_{CF} = 272.2 Hz), 116.5 (q, J_{CF} = 291.8 Hz), 103.2 (q, J_{CF} = 3.7 Hz), 96.4, 64.4, 15.1; IR (KBr): 1702 cm^{-1}. Anal. Calcd for $C_{14}H_{12}O_3F_6$: C, 49.13; H, 3.53; F, 33.31. Found: C, 48.85; H, 3.48; F,

33.22.

2-Ethoxy-6-trifluoromethyl-3-(2-trifluoromethyl-4*H*-pyran-4-yl)-2*H*-pyran (11): bp 90 °C / 1 mmHg (oven temperature); ^{1}H NMR ($CDCl_3$): δ 6.46 (d, 1H, *J* = 6.0 Hz, H-6'), 6.00 (s, 2H, H-4, H-5), 5.56 (s, 1H, H-2), 5.43-5.35 (m, 1H, H-3'), 4.90-4.65 (m, 1H, H-5'), 4.03-3.43 (m, 3H, H-4', $OC\underline{H}_2CH_3$), 1.21 (t, 3H, *J* = 7.0 Hz, $OCH_2C\underline{H}_3$); IR (KBr): 1645 cm^{-1}. Anal. Calcd for $C_{14}H_{12}O_3F_6$: C, 49.13; H, 3.53; F, 33.31. Found: C, 48.99; H, 3.48; F, 33.71.

Synthesis of (*E*)-4-aryl-1,1,1-trifluorobut-3-en-2-one (12a-f).

The retro hetero Diels-Alder reaction of **7** was successfully carried out at 300 °C without solvent. The reaction times were as shown in Table 2. The crude mixture was chromatographed on silica gel column using *n*-hexane/EtOAc (100:1) as eluent to give products (**12a**, **12a'**, and **12d**) and *n*-hexane as eluent to give **12b**. For products (**12c**, **12c'**, **12e**, and **12f**), *n*-hexane/benzene (1:1) was used as eluent.

(*E*)-1,1,1-Trifluoro-4-(4-methoxyphenyl)but-3-en-2-one (12a): mp 35-37 °C (*n*-hexane/benzene); ^{1}H NMR ($CDCl_3$): δ 8.00 (d, 1H, *J* = 16.0 Hz, H-4), 7.67 (d, 2H, *J* = 9.0 Hz, H-2', H-6'), 7.00 (d, 2H, *J* = 9.0 Hz, H-3', H-5'), 6.92 (d, 1H, *J* = 16.0 Hz, H-3), 3.88 (s, 3H, OCH_3); IR (KBr): 1713 cm^{-1}. Anal. Calcd for $C_{11}H_9O_2F_3$: C, 57.40; H, 3.94. Found: C, 57.23; H, 4.03.

(*E*)-1,1,1-Trifluoro-4-(2-methoxyphenyl)but-3-en-2-one (12a'): bp 190 °C / 5 mmHg (oven temperature); ^{1}H NMR ($CDCl_3$): δ 8.37 (d, 1H, *J* = 16.0 Hz, H-4), 7.70-6.90 (m, 5H, H-3, H_{arom}), 3.93 (s, 3H, OCH_3); IR (KBr): 1712 cm^{-1}. Anal. Calcd for $C_{11}H_9O_2F_3$: C, 57.40; H, 3.94. Found: C, 57.57; H, 4.18.

(*E*)-4-(2,4-Dimethylphenyl)-1,1,1-trifluorobut-3-en-2-one (12b): bp 200 °C / 5 mmHg (oven temperature); ^{1}H NMR ($CDCl_3$): δ 8.35 (d, 1H, *J* = 16.0 Hz, H-4), 7.63 (d, 1H, *J* = 8.0 Hz, H-6'), 7.30-6.77 (m, 3H, H-3, H-3', H-5'), 2.40 (s, 3H, CH_3), 2.33 (s, 3H, CH_3); IR (KBr): 1698 cm^{-1}. Anal. Calcd for $C_{12}H_{11}OF_3$: C, 63.16; H, 4.86. Found: C, 63.12; H, 4.50.

A mixture of (*E*)-1,1,1-trifluoro-4-(4-methoxy-2-methylphenyl)but-3-en-2-one (12c) and (*E*)-1,1,1-trifluoro-4-(2-methoxy-4-methylphenyl)but-3-en-2-one (12c'): bp 95 °C / 2 mmHg (oven temperature); ^{1}H NMR ($CDCl_3$): δ 8.26-8.00 (m, 1H, H-4), 7.63-7.50 (m, 1H, H-6'), 6.83-6.60 (m, 3H, H-3, H-3', H-5'), 3.87, 3.80 (s, 3H, OCH_3), 2.47, 2.37 (s, 3H, CH_3); IR (KBr): 1697 cm^{-1}. Anal. Calcd for $C_{12}H_{11}O_2F_3$: C, 59.02; H, 4.54; F, 23.34. Found: C, 59.39; H, 4.54; F, 23.46.

(*E*)-4-(2,4-Dimethoxyphenyl)-1,1,1-trifluorobut-3-en-2-one (12d): mp 65-66 °C (*n*-hexane/benzene); ^{1}H NMR ($CDCl_3$): δ 8.04 (d, 1H, *J* = 15.0 Hz, H-4), 7.37 (d, 1H, *J* = 9.2 Hz, H-6'), 6.87 (d, 1H, *J* = 15.0 Hz, H-3), 6.41 (d, 1H, *J* = 9.2 Hz, H-5'), 6.32 (s, 1H, H-3'), 3.78 (s, 3H, OCH_3), 3.76 (s, 3H, OCH_3); IR (KBr): 1697 cm^{-1}. Anal. Calcd for $C_{12}H_{11}O_3F_3$: C, 55.39; H, 4.26; F, 21.90. Found: C, 55.11; H, 4.13; F, 21.77.

(*E*)-1,1,1-Trifluoro-4-(4-methylnaphthalen-1-yl)but-3-en-2-one (12e): mp 68-69 °C (*n*-hexane/benzene);

^{1}H NMR ($CDCl_3$): δ 8.38 (d, 1H, *J* = 13.4 Hz, H-4), 7.81-7.56 (m, 2H, H_{arom}), 7.33 (d, 1H, *J* = 8.0 Hz, H-2'), 7.36-7.13 (m, 2H, H_{arom}), 6.89 (d, 1H, *J* = 8.0 Hz, H-3'), 6.76 (d, 1H, *J* = 13.4 Hz, H-3), 2.43 (s, 3H, CH_3); IR (KBr): 1708 cm^{-1}. Anal. Calcd for $C_{15}H_{11}OF_3$: C, 68.18; H, 4.20; F, 21.57. Found: C, 67.89; H, 4.06; F, 21.37.

(*E*)-1,1,1-Trifluoro-4-(4-methoxynaphthalen-1-yl)but-3-en-2-one (12f): mp 88-89 °C (*n*-hexane/benzene); ^{1}H NMR ($CDCl_3$): δ 8.06 (d, 1H, *J* = 15.0 Hz, H-4), 8.24-7.91 (m, 2H, H_{arom}), 7.75 (d, 1H, *J* = 8.2 Hz, H-2'), 7.35-7.20 (m, 2H, H_{arom}), 6.88 (d, 1H, *J* = 15.0 Hz, H-3), 6.70 (d, 1H, *J* = 8.2 Hz, H-3'), 3.96 (s, 3H, OCH_3); IR (KBr): 1694 cm^{-1}. Anal. Calcd for $C_{15}H_{11}O_2F_3$: C, 64.29; H, 3.96. Found: C, 64.58; H, 4.09.

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