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A simple method for synthesis of 5-CF_3 substituted dienamides via rearrangement of 2*H*-pyran derivatives

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ABSTRACT

A simple and novel method for synthesis of 5-trifluoromethyl 2,4-dienamides with up to 95% yield under mild condition was first reported. With α,α-dicyanoalkenes and trifluoromethylketones as starting materials, the vinylogous aldol reaction was introduced and then followed by rearrangement of the 2*H*-pyran intermediate.

1. Introduction

The introduction of fluorine or fluoroalkyl group in organic moleculars may profoundly influence their physical, chemical and biological properties. For example, the fluorine-containing heterocycles are now widely used in medicinal and agricultural scientific fields.[1] As one of the most important methods, employing fluorine-containing building block as starting materials could successfully introduce fluorine into organic molecular. Because of not involving a C–F bond formation or breaking, this method was generally carried out to afford corresponding products with high selectivities and good yields.

Dienamides have always been recognised as key reactive intermediates due to their great diversities, potential synthetic values and commonly existence in nature. Therefore, dienamides could be used as electron-rich or electron-deficient dienes in Diels–Alder reactions effectively,[2] which have already been applied to asymmetric cycloaddition reactions regioselectively.[3]

Dienamides are also key constituents in a number of biologically active natural products and pharmaceutically relevant units. For examples, Apicularen A can induce apoptosis of RAW 264.7 cells; Salicylihalamide A (SA), a benzolactone enamide compound, possesses potent cytotoxicity against human tumour cell lines, while Zampanolide with potent cytotoxicity (IC_{50} 1–5 ng/mL) against P388, A549, HT29 and MEL28 cell lines. The Crocacins inhibit moderately the growth of a few grampositive bacteria and are potent inhibitors of animal cell cultures and several yeasts and fungi (Fig. 1).[4]

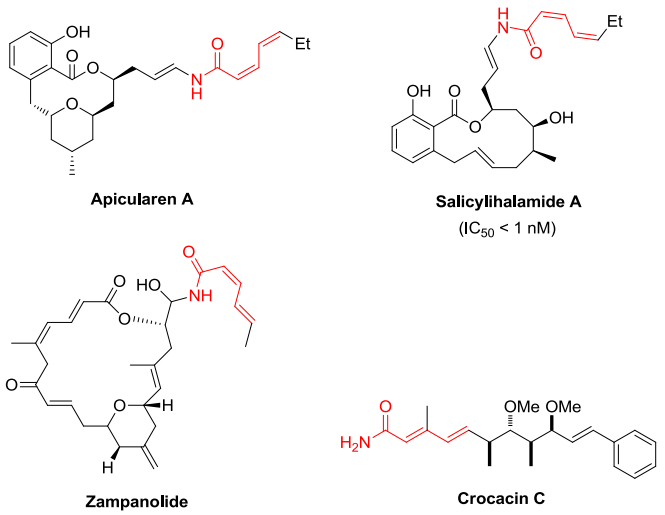

Fig. 1. Several natural products with a dieneamide structure.

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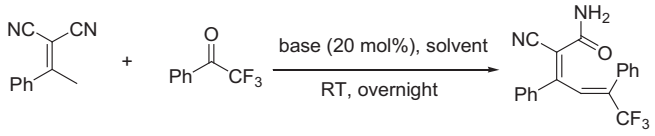
Although a number of preparative methods for dienamides have appeared in the literatures, mainly employing isocyanates as substrates and transition metals as catalysts, the development of mild synthetic approaches enabling facile access to these dieneamides is also desirable.[5] Recently, Perumal et al.[6] reported a novel one-pot approach to a variety dienamides from α,α-dicyanoalkenes and aldehydes via vinylogous aldol reaction by the electrolytic ring opening of the initially formed pyran derivatives under mild basic catalysis with good diastereoselectivity. However, to the best of our knowledges, the synthesis of 5-CF_3 substituted dienamides has not been reported. So herein we report the reaction of α,α-dicyanoalkenes and trifluoromethylketones catalyzed by organic bases, affording a series of 5-CF_3 substituted dienamides in high yields.

2. Results and discussion

The reaction of 2-(1-phenylethylidene)malononitrile (**1a**) and 2,2,2-trifluoro-1-phenylethanone (**2a**) was selected as a model reaction for catalyst evaluation. First, with $CHCl_3$ as solvent, several different bases as catalysts were evaluated at room temperature (Table 1, entries 1–6). To our pleasure, when Et_3N was used, the

Table 1
Optimization of reaction conditions[a]



1a **2a** **3a**

Entry	Base	Solvent	Yield[b] (%)
1	Et_3N	$CHCl_3$	90
2	DIPEA	$CHCl_3$	75
3	Piperidine	$CHCl_3$	45
4	TMEDA	$CHCl_3$	82
5	DBU	$CHCl_3$	45
6	DABCO	$CHCl_3$	52
7	Na_2CO_3	$CHCl_3$	Trace
8	Et_3N	DCM	95
9	Et_3N	EtOAc	92
10	Et_3N	THF	85
11	Et_3N	Toluene	82
12	Et_3N	EtOH	80
13	Et_3N	DMF	89
14	Et_3N	Et_2O	83
15	Et_3N	CH_3CN	88

[a] Unless otherwise noted, the reaction was carried out with **1a** (0.15 mmol) and **2a** (0.1 mmol) and base (20 mol %) at room temperature in solvent (1.0 mL) overnight.
[b] Yield of the isolated product after column chromatography on silica gel.

desired product **3a** was obtained with 90% yield (Table 1, entry 1). The configuration of product **3a**, was determined by X-ray crystallographic analysis (Fig. 2). While using DIPEA or TMEDA as organic base, the yield lowed slightly (Table 1, entries 2 and 3). But when changing the base from tertiary amine to secondary amine, such as piperidine, the yield decreased significantly (Table 1, entry 3). DBU or DABCO as base was also screened, which affording **3a** with only about 50% yield (Table 1, entries 5 and 6). Contrastively, Na_2CO_3 as inorganic base was also selected as catalyst, but no reaction was observed (Table 1, entry 7). Next, we examined the influence of different solvents on the isolated yield. Slightly higher yield was obtained in EtOAc (Table 1, entry 9), while with about 85% yield in ether, such as THF or Et_2O (Table 1, entries 10, 14). When using polar solvent, such as DMF, CH_3CN or EtOH, no more than 90% yield was obtained (Table 1, entries 12, 13 and 15). Fortunately, when using CH_2Cl_2 as the solvent, the yield could be improved to 95% (Table 1, entry 8). To summarize, the present reaction was best performed with 20 mol % of Et_3N in CH_2Cl_2 at room temperature overnight.

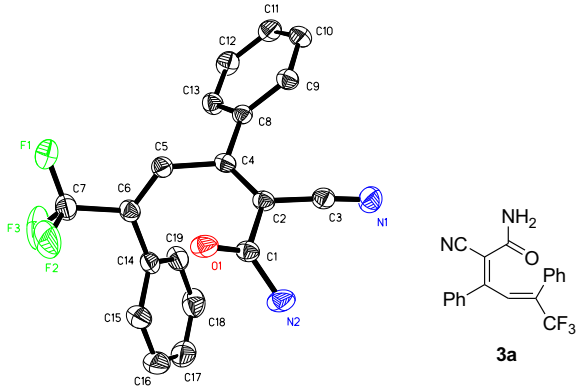
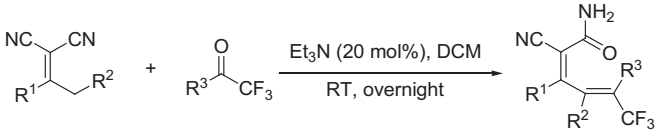


Fig. 2. ORTEP diagram of compound **3a**.

Having established the optimal conditions, we next explored the scope of the reaction and representative results are listed in Table 2. Generally, with 2,2,2-trifluoro-1-phenylethanone **2a**, for α,α-dicyanoalkenes **1a**–**h**, in which R^1 were differently substituted benzene rings, excellent yields were obtained irrespective of the electronic nature of the substituents on the benzene ring (Table 2, entries 1–8). Notably, when R^2 was a methyl group, the reaction still proceeded efficiently to give the desired product **3i** in high yield (Table 2, entry 9). Next, various trifluoromethylketones **2** were investigated with 2-(1-phenylethylidene)malononitrile **1a**. When R^3 was an aromatic group, both electron-donating and electron-withdrawing substituents on the benzene ring were tolerated to give the desired products, though with slightly lower yields (Table 2, entries 10–13). But when R^3 was methyl, the isolated yield decreased to 65% (Table 2, entry 14).

Table 2
Examination of the reaction scope[a]



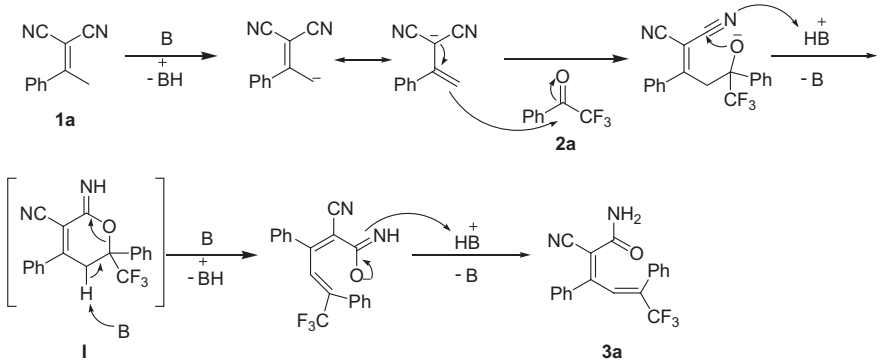
1 **2** **3**

Entry	**1**, R^1, R^2	**2**, R^3	Product	Yield[b] (%)
1	**1a**, Ph, H	**2a**, Ph	**3a**	95
2	**1b**, 4-ClC_6H_4, H	**2a**, Ph	**3b**	90
3	**1c**, 4-BrC_6H_4, H	**2a**, Ph	**3c**	92
4	**1d**, 4-$OMeC_6H_4$, H	**2a**, Ph	**3d**	90
5	**1e**, 3-$OMeC_6H_4$, H	**2a**, Ph	**3e**	90
6	**1f**, 1-Naphthyl, H	**2a**, Ph	**3f**	91
7	**1g**, 4-MeC_6H_4, H	**2a**, Ph	**3g**	89
8	**1h**, 4-$CF_3C_6H_4$, H	**2a**, Ph	**3h**	86
9	**1i**, Ph, Me	**2a**, Ph	**3i**	80
10	**1a**, Ph, H	**2b**, 2-Naphthyl	**3j**	83
11	**1a**, Ph, H	**2c**, 4-ClC_6H_4	**3k**	87
12	**1a**, Ph, H	**2d**, 4-BrC_6H_4	**3l**	85
13	**1a**, Ph, H	**2e**, 4-MeC_6H_4	**3m**	89
14	**1a**, Ph, H	**2f**, Me	**3n**	65

[a] Unless otherwise noted, the reaction was carried out with **1** (0.15 mmol) and **2** (0.1 mmol) and Et_3N (20 mol %) at room temperature in DCM (1.0 mL) overnight.
[b] Yield of the isolated product after column chromatography on silica gel.

A possible mechanism of this reaction was proposed in Scheme 1. Under an organic base, 2-(1-phenylethylidene)malononitrile **1a** was first deprotonated to form a nucleophile, which then attacked 2,2,2-trifluoro-1-phenylethanone **2a** through aldol reaction.

Subsequent intramolecular nucleophilic addition and protonation to afford the 2*H*-pyran intermediate I. A second deprotonation of active hydrogen of the intermediate I catalyzed by the organic base occurred and followed by rearrangement to provide the product **3a** after protonation once again.



Scheme 1. Proposed possible catalytic mechanism for the synthesis of product **3a**.

3. Conclusion

In summary, we have developed a simple method to synthesize a series of 5-trifluoromethyl 2,4-dienamides via vinylogous aldol reaction followed by the rearrangement of 2*H*-pyran derivatives intermediate. By using Et_3N as catalyst, the desired products were obtained with up to 95% yields in DCM under mild conditions. Efforts towards applications of the reaction to the synthesis of related biologically active natural products are in progress in our laboratories.

4. Experimental

4.1. General

^1H and ^{13}C NMR spectra were recorded at 300 and 100 MHz, respectively, with TMS as the internal standard. ^{19}F NMR spectra were recorded at 282 MHz with $CFCl_3$ as the external standard. IR spectra were recorded in cm^{-1}. Melting points were uncorrected.

All solvents were distilled prior to use unless otherwise noted. All reactions sensitive to moisture or oxygen were conducted under an atmosphere of nitrogen or argon.

4.2. General procedure for the preparation of 3-fluoro-4-aryl-2-pyridone (3)

A solution of compound **1** (0.15 mmol), **2** (0.1 mmol) and Et_3N (20 mmol%) in DCM (1.0 mL) was reacted at room temperature for appropriate times (monitored by TLC). After removal of the solvent under reduced pressure, the crude product was purified directly by column chromatography on silica gel (hexanes/EtOAc=5/1–2/1) to afford the desired products.

*4.2.1. (2E,4E)-2-Cyano-6,6,6-trifluoro-3,5-diphenylhexa-2,4-dienamide (**3a**).* Yield: 95%; yellow solid; mp: 161–162 °C; IR (CH_2Cl_2, film): 3448, 2997, 2212, 1693, 1582, 1445, 1174, 1030, 958 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ=7.86 (d, *J*=1.2 Hz, 1H), 7.21 (d, *J*=0.9 Hz, 1H), 7.19–7.18 (m, 3H), 7.13–7.03 (m, 4H), 6.87 (d, *J*=5.4 Hz, 2H), 6.45 (s, 1H), 6.40 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): 163.5, 162.5, 137.0, 136.8 (m, *J*=30 Hz), 134.0 (m, *J*=6 Hz), 131.6, 130.4, 129.4, 129.0, 128.9, 128.1, 128.0, 125.6 (m, *J*=272 Hz), 117.2, 108.0; ^{19}F NMR ($CDCl_3$): δ=−65.9 (s, 3F); MS (ESI) (*m*/*z*): 365 (M+Na^+); HRMS calcd for $C_{19}H_{13}F_3N_2ONa$: 365.0878, found: 365.0872.

*4.2.2. (2E,4E)-3-(4-Chlorophenyl)-2-cyano-6,6,6-trifluoro-5-phenylhexa-2,4-dienamide (**3b**).* Yield: 90%; yellow solid; mp: 163–164 °C; IR (CH_2Cl_2, film): 3475, 3162, 2221, 1683, 1593, 1444, 1172, 1073, 965 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ=7.85 (s, 1H), 7.18–7.07 (m, 5H), 6.97–6.94 (m, 3H), 6.88–6.86 (m, 2H), 6.49 (s, 1H), 6.39 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): 162.2, 162.1, 137.6 (m, *J*=30 Hz), 136.6, 135.3, 133.6 (m, *J*=6.6 Hz), 131.6, 130.1, 129.4, 129.2, 128.4, 128.1, 122.7 (m, *J*=273 Hz), 116.9, 108.3; ^{19}F NMR ($CDCl_3$): δ=−65.6 (s, 3F); MS (ESI) (*m*/*z*): 399 (M+Na^+); HRMS calcd for $C_{19}H_{12}ClF_3N_2ONa$: 399.0488, found: 399.0483.

*4.2.3. (2E,4E)-3-(4-Bromophenyl)-2-cyano-6,6,6-trifluoro-5-phenylhexa-2,4-dienamide (**3c**).* Yield: 92%; yellow solid; mp: 188–189 °C; IR (CH_2Cl_2, film): 3475, 3164, 2222, 1683, 1587, 1443, 1172, 1074, 964 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ=7.85 (s, 1H), 7.25–7.19 (m, 3H), 7.13–7.06 (m, 2H), 6.90–6.86 (m, 4H), 6.46 (s, 1H), 6.32 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): 162.2, 162.1, 137.6 (m, *J*=30 Hz), 135.8, 133.5 (m, *J*=6.9 Hz), 131.6, 131.4, 130.2, 129.4, 129.2, 128.1, 125.0, 122.7 (m, *J*=273 Hz), 116.9, 108.3; ^{19}F NMR ($CDCl_3$): δ=−65.9 (s, 3F); MS (ESI) (*m*/*z*): 443 (M+Na^+); HRMS calcd for $C_{19}H_{12}BrF_3N_2ONa$: 442.9983, found: 442.9977.

*4.2.4. (2E,4E)-2-Cyano-6,6,6-trifluoro-3-(4-methoxyphenyl)-5-phenylhexa-2,4-dienamide (**3d**).* Yield: 90%; yellow solid; mp: 167–168 °C; IR (CH_2Cl_2, film): 3480, 3202, 2217, 1680, 1547, 1463, 1168, 1074, 962 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ=7.81 (s, 1H), 7.19–7.08 (m, 5H), 6.95 (d, *J*=7.2 Hz, 2H), 6.68 (d, *J*=4.8 Hz, 2H), 6.38 (s, 1H), 6.10 (s, 1H), 3.78 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 163.1, 162.7, 136.4 (m, *J*=31 Hz), 134.4 (m, *J*=6.5 Hz), 131.8, 130.9, 129.2, 129.1, 128.9, 128.0, 123.9 (m, *J*=267 Hz), 118.9, 117.9, 114.0, 113.7, 105.6; ^{19}F NMR ($CDCl_3$): δ=−65.6 (s, 3F); MS (ESI) (*m*/*z*): 395 (M+Na^+); HRMS calcd for $C_{20}H_{15}F_3N_2O_2Na$: 395.0983, found: 395.0978.

*4.2.5. (2E,4E)-2-Cyano-6,6,6-trifluoro-3-(3-methoxyphenyl)-5-phenylhexa-2,4-dienamide (**3e**).* Yield: 90%; yellow solid; mp: 162–163 °C; IR (CH_2Cl_2, film): 3397, 3196, 2224, 1698, 1597, 1464, 1178, 1077, 961 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ=7.84 (s, 1H), 7.16–7.01 (m, 4H), 6.92–6.89 (m, 2H), 6.76–6.63 (m, 2H), 6.51 (s, 1H), 6.43 (s, 1H), 6.25 (s, 1H), 3.67 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 163.3, 162.3, 159.0, 138.1, 137.1 (m, *J*=30 Hz), 133.7 (m, *J*=6.2 Hz), 131.7, 129.5, 129.2, 129.0, 128.0, 122.8 (m, *J*=272 Hz), 121.4, 118.8, 117.1, 116.6, 114.1, 108.0, 55.3; ^{19}F NMR ($CDCl_3$): δ=−65.7 (s, 3F); MS (ESI) (*m*/*z*): 395 (M+Na^+); HRMS calcd for $C_{20}H_{15}F_3N_2O_2Na$: 395.0983, found: 395.0978.

*4.2.6. (2E,4E)-2-Cyano-6,6,6-trifluoro-3-(naphthalen-1-yl)-5-phenylhexa-2,4-dienamide (**3f**).* Yield: 91%; brown solid; mp: 201–202 °C; IR (CH_2Cl_2, film): 3443, 3093, 2222, 1694, 1547, 1443, 1174, 1026, 961 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ=8.28 (s, 1H),

7.73–7.46 (m, 6H), 7.09–6.76 (m, 5H), 6.54–6.49 (m, 3H), 6.15 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): 162.4, 162.0, 138.2 (m, J=31 Hz), 134.2, 133.3, 131.6 (m, J=6.5 Hz), 130.8, 130.4, 129.8, 128.8, 128.5, 128.4, 128.2, 127.4, 126.8, 126.3, 125.0, 124.7, 124.1, 122.0 (m, J=274 Hz), 116.7, 111.4; ^{19}F NMR ($CDCl_3$): δ=−66.6 (s, 3F); MS (ESI) (m/z): 415 ($M+Na^+$); HRMS calcd for, $C_{23}H_{15}F_3N_2ONa$: 415.1034 found: 415.1028.

*4.2.7. (2E,4E)-2-Cyano-6,6,6-trifluoro-5-phenyl-3-p-tolylhexa-2,4-dienamide (**3g**).* Yield: 89%; yellow solid; mp: 164–165 °C; IR (CH_2Cl_2, film): 3334, 2923, 2226, 1724, 1689, 1445, 1173, 1076, 962 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.80 (s, 1H), 7.17–7.03 (m, 4H), 6.99–6.87 (m, 6H), 6.40 (s, 1H), 6.19 (s, 1H), 2.25 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 163.7, 162.5, 141.1, 136.7 (m, J=31 Hz), 134.1 (m, J=5.7 Hz), 131.7, 129.7, 129.4, 128.9, 128.8, 128.8, 127.7, 122.9 (m, J=267 Hz), 117.5, 106.9, 21.3; ^{19}F NMR ($CDCl_3$): δ=−65.6 (s, 3F); MS (ESI) (m/z): 379 ($M+Na^+$); HRMS calcd for $C_{20}H_{15}F_3N_2ONa$: 379.1034, found: 379.1029.

*4.2.8. (2E,4E)-2-Cyano-6,6,6-trifluoro-3-(4-(trifluoromethyl)phenyl)-5-phenylhexa-2,4-dienamide (**3h**).* Yield: 86%; yellow solid; mp: 145–146 °C; IR (CH_2Cl_2, film): 3413, 3196, 2230, 1732, 1596, 1446, 1172, 1064, 965 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.92 (s, 1H), 7.35–7.32 (m, 3H), 7.13–7.01 (m, 5H), 6.83–6.80 (m, 3H), 6.49 (s, 1H), 6.35 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): 161.8, 161.7, 140.4, 138.4 (m, J=31 Hz), 133.1 (m, J=6.7 Hz), 131.7 (m, J=33 Hz), 131.5, 129.5, 129.3, 129.1, 128.2, 125.0 (m, J=3.7 Hz), 123.3 (m, J=270 Hz), 122.7 (m, J=273 Hz), 116.5, 109.5; ^{19}F NMR ($CDCl_3$): δ=−66.5 (s, 3F), −63.7 (s, 3F); MS (ESI) (m/z): 433 ($M+Na^+$); HRMS calcd for $C_{20}H_{12}F_6N_2ONa$: 433.0752, found: 433.0746.

*4.2.9. (2Z,4E)-2-Cyano-6,6,6-trifluoro-4-methyl-3,5-diphenylhexa-2,4-dienamide (**3i**).* Yield: 86%; yellow solid; mp: 165–166 °C; IR (CH_2Cl_2, film): 3453, 3154, 2211, 1697, 1582, 1444, 1186, 1027, 919 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.40–7.33 (m, 1H), 7.27–7.18 (m, 3H), 7.13–7.08 (m, 4H), 6.88 (d, J=6.9 Hz, 2H), 6.29 (s, 1H), 6.20 (s, 1H), 2.38 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 169.8, 161.9, 145.7 (m, J=6.9 Hz), 136.5, 134.0, 131.2, 129.3, 129.0 (m, J=27 Hz), 128.5, 128.2, 127.9, 123.4 (m, J=273 Hz), 117.6, 105.4, 21.0; ^{19}F NMR ($CDCl_3$): δ=−68.4 (s, 3F); MS (ESI) (m/z): 379 ($M+Na^+$); HRMS calcd for $C_{20}H_{15}F_3N_2ONa$: 379.1034, found: 379.1029.

*4.2.10. (2E,4E)-2-Cyano-6,6,6-trifluoro-5-(naphthalen-3-yl)-3-phenylhexa-2,4-dienamide (**3j**).* Yield: 83%; yellow solid; mp: 199–200 °C; IR (CH_2Cl_2, film): 3453, 3146, 2212, 1694, 1591, 1463, 1175, 1077, 946 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ=8.22 (s, 1H), 7.73 (t, J=7.8 Hz, 2H), 7.60 (d, J=8.4 Hz, 1H), 7.45–7.40 (m, 2H), 7.04–6.98 (m, 2H), 6.88–6.80 (m, 3H), 6.53 (d, J=8.1 Hz, 2H), 6.42 (s, 1H), 6.24 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): 163.9, 162.2, 136.6, 135.9 (m, J=5.9 Hz), 135.2 (m, J=31 Hz), 133.1, 132.0, 129.9, 129.3, 128.5, 128.1, 128.0, 127.9, 127.8, 127.7, 126.6, 126.0, 125.1, 124.5, 123.0 (m, J=273 Hz), 116.9, 107.6; ^{19}F NMR ($CDCl_3$): δ=−65.8 (s, 3F); MS (ESI) (m/z): 415 ($M+Na^+$); HRMS calcd for, $C_{23}H_{15}F_3N_2ONa$: 415.1034, found: 415.1028.

*4.2.11. (2E,4E)-5-(4-Chlorophenyl)-2-cyano-6,6,6-trifluoro-3-phenylhexa-2,4-dienamide (**3k**).* Yield: 87%; yellow solid; mp: 170–171 °C; IR (CH_2Cl_2, film): 3486, 3247, 2221, 1700, 1595, 1492, 1175, 1030, 963 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.88 (s, 1H), 7.26 (t, J=7.2 Hz, 2H), 7.16 (t, J=7.5 Hz, 1H), 7.06–7.02 (m, 5H), 6.79 (d, J=8.4 Hz, 2H), 6.48 (s, 1H), 6.26 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): 163.0, 162.2, 136.9, 136.4, 135.4 (m, J=30 Hz), 134.6 (m, J=6.5 Hz), 130.7, 130.6, 130.0, 128.9, 128.3, 128.2, 122.7 (m, J=270 Hz), 117.0, 108.1; ^{19}F NMR ($CDCl_3$): δ=−65.8 (s, 3F); MS (ESI) (m/z): 399 ($M+Na^+$); HRMS calcd for $C_{19}H_{12}ClF_3N_2ONa$: 399.0488, found: 399.0483.

*4.2.12. (2E,4E)-5-(4-Bromophenyl)-2-cyano-6,6,6-trifluoro-3-phenylhexa-2,4-dienamide (**3l**).* Yield: 85%; yellow solid; mp: 185–186 °C; IR (CH_2Cl_2, film): 3411, 2925, 2225, 1676, 1588, 1445, 1174, 1072, 964 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.87 (s, 1H), 7.29–7.25 (m, 1H), 7.20–7.15 (m, 3H), 7.05–7.03 (m, 3H), 6.72 (d, J=8.4 Hz, 2H), 6.44 (s, 1H), 6.11 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): 163.1, 162.1, 136.9, 135.9 (m, J=30 Hz), 134.6 (m, J=6.0 Hz), 133.1, 130.9, 130.7, 130.5, 128.9, 128.3, 124.7 (m, J=270 Hz), 123.6, 117.0, 108.1; ^{19}F NMR ($CDCl_3$): δ=−65.7 (s, 3F); MS (ESI) (m/z): 443 ($M+Na^+$); HRMS calcd for $C_{19}H_{12}BrF_3N_2ONa$: 442.9983, found: 442.9977.

*4.2.13. (2E,4E)-2-Cyano-6,6,6-trifluoro-3-phenyl-5-p-tolylhexa-2,4-dienamide (**3m**).* Yield: 89%; yellow solid; mp: 168–169 °C; IR (CH_2Cl_2, film): 3440, 3159, 2200, 1694, 1611, 1446, 1180, 1081, 961 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ=8.07 (s, 1H), 7.48–7.29 (m, 5H), 7.12–7.00 (m, 4H), 6.68 (s, 1H), 6.51 (s, 1H), 2.47 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 163.8, 162.4, 139.1, 137.2 (m, J=30 Hz), 137.1, 133.5 (m, J=5.9 Hz), 130.3, 129.3, 128.9, 128.7, 128.6, 128.0, 123.8 (m, J=273 Hz), 117.3, 107.8, 21.1; ^{19}F NMR ($CDCl_3$): δ=−65.6 (s, 3F); MS (ESI) (m/z): 379 ($M+Na^+$); HRMS calcd for $C_{20}H_{15}F_3N_2ONa$: 379.1034, found: 379.1029.

*4.2.14. (2E,4E)-2-Cyano-6,6,6-trifluoro-5-methyl-3-phenylhexa-2,4-dienamide (**3n**).* Yield: 65%; white solid; mp: 132–133 °C; IR (CH_2Cl_2, film): 3437, 3168, 2205, 1698, 1612, 1446, 1189, 1097, 896 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.51–7.48 (m, 6H), 6.41 (s, 1H), 6.26 (s, 1H), 1.36 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 162.2, 161.9, 136.9, 133.7 (m, J=30 Hz), 131.4, 129.4 (m, J=6.6 Hz), 129.2, 128.8, 123.9 (m, J=272 Hz), 117.4, 107.8, 13.0; ^{19}F NMR ($CDCl_3$): δ=−70.3 (s, 3F); MS (ESI) (m/z): 303 ($M+Na^+$); HRMS calcd for $C_{14}H_{11}F_3N_2ONa$: 303.0721, found: 303.0716.

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tet.2011.07.007. These data include MOL files and InChIKeys of the most important compounds described in this article.

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