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An unexpected highly diastereoselective double Baylis–Hillman reaction of per- (or poly)fluorophenyl aromatic aldimines with methyl vinyl ketone

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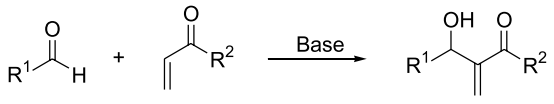
Abstract—Aza-Baylis–Hillman reaction of per- (or poly)fluorophenyl aromatic aldimines **1** with methyl vinyl ketone (MVK) was studied. It was found that both the used Lewis base and solvent can significantly affect the reaction. Using triphenylphosphine as a Lewis base, the reaction of **1** with MVK proceeded smoothly to give the normal Baylis–Hillman adduct **2** along with the double Baylis–Hillman adduct **3** as by-product in THF. When 1,4-diazabicyclo[2.2.2]octane was used as a Lewis base in DMF, the aza-Baylis–Hillman reaction of **1** with MVK gave the double aza-Baylis–Hillman adduct **3** exclusively in moderate to good yields with excellent diastereoselectivities. The double Baylis–Hillman adduct **3** was conveniently converted to fluorine-containing 4-alkylidene-2-cyclohexen-1-ones under mild reaction conditions in good yields.

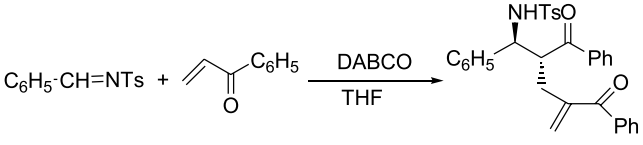
1. Introduction

Mild and selective carbon–carbon bond formations represent one of the major challenges in organic synthesis. In the same perspective, atom-economic reactions become more and more a need and a requirement.[1] One of the carbon–carbon bond forming reaction which fulfills the above criteria is the Baylis–Hillman reaction.[2,3] In this transformation, Michael acceptors are coupled with aldehydes to form highly functionalized α-methylene-β-hydroxycarbonyl compounds (Scheme 1).



Scheme 1.

Previously, Shi and co-workers reported that, in the reaction of sulfonated imines with phenyl vinyl ketone catalyzed by DABCO, the highly diastereselective double aza-Baylis–Hillman reaction products were formed in moderate to good yields. While using methyl vinyl ketone (MVK) as the active olefin, no such double aza-Baylis–Hillman reaction product could be formed at all (Scheme 2).[4] As part of our ongoing projects in fluorooganic chemistry,[5] we examined the Baylis–Hillman reaction of per- (or poly)fluorophenyl aromatic aldimines with MVK in the presence of different Lewis bases, and found that the double Baylis–Hillman reaction product could be exclusively formed with high diastereoselectivity in the presence of 1,4-diazabicyclo-[2.2.2]octane (DABCO).



Scheme 2.

It is well known that the biological properties of medicinal compounds can often be influenced by fluorine substitution.[6] The physical properties of several electronic and optical devices also depend immensely on the structure of fluoroorganic molecules.[7] Fluorine substitution provides organic chemists with an opportunity to study an extreme case of electronic effect in reactions.[6,7] Herein we report an unexpected highly diastereoselective double Baylis–

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Hillman reaction of per- (or poly)fluorophenyl aromatic aldimines with methyl vinyl ketone (MVK).

2. Results and discussion

The promoters and solvents for the aza-Baylis–Hillman reaction of *N*-pentafluorophenyl-pentafluorophenyl aldimine (**1a**) with methyl vinyl ketone were systematically examined first, and the results were summarized in Table 1. We found that every parameter, such as solvent and catalyst influenced the reaction of *N*-pentafluorophenyl-pentafluorophenyl aldimine (0.5 mmol) with MVK (1 mmol) drastically (Scheme 3; Table 1). Using 20 mol % of triphenylphosphine as a Lewis base in THF, the reaction proceeded very well to give the normal aza-Baylis–Hillman adduct **2a** as a major product in good yield (Table 1, entry 1). In DMF and CH_2Cl_2, the corresponding normal aza-Baylis–Hillman adduct **2a** was obtained in 63% and 48% yield along with the double aza-Baylis–Hillman adduct **3a** in 27 and 31% yield, respectively (Table 1, entries 2 and 3). In CH_3CN, the aza-Baylis–Hillman reaction of *N*-pentafluorophenyl-pentafluorophenyl aldimine with MVK was sluggish because of the poor solubility of **1a** in the reaction media (Table 1, entry 4). For the influence of Lewis bases, a variety of Lewis base catalysts (20 mol %) were also screened. The use of tertiary amines such as 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) as a Lewis base gave the corresponding normal aza-Baylis–Hillman adduct in low yield along with many unidentified products (Table 1, entry 5). While using DABCO (20 mol %) as a Lewis base in DMF, we delightfully found that the double aza-Baylis–Hillman adduct **3a** was formed exclusively in good yield (Table 1, entry 7). In contrast to other Lewis base, no reaction of **1a** with MVK occurred to give the corresponding adduct **2a** or **3a**, but only **1a** by itself decomposed in the presence of stronger Lewis base such as tri-*n*-butylphosphine (PBu_3) to provide a mixture of compounds (Table 1, entry 8). On the other hand, using DMAP, Et_3N or Me_2S, no reaction occurred under the same reaction conditions due to their low catalytic activity as a Lewis base to initiate the aza-Baylis–Hillman reaction (Table 1, entries 9–11). Thus, PPh_3 is the best Lewis base for this version of normal aza-Baylis–Hillman reaction in THF, while DABCO is the best Lewis base for this version of double aza-Baylis–Hillman reaction in DMF. Moreover, on the basis of the ^1H, ^{19}F and ^{13}C NMR spectroscopic data and X-ray diffraction analysis, we were pleased to find that, in this aza-Baylis–Hillman reaction, the double aza-Baylis–Hillman reaction product **3a** was formed diastereoselectively in the *anti*-configuration (Fig. 1).

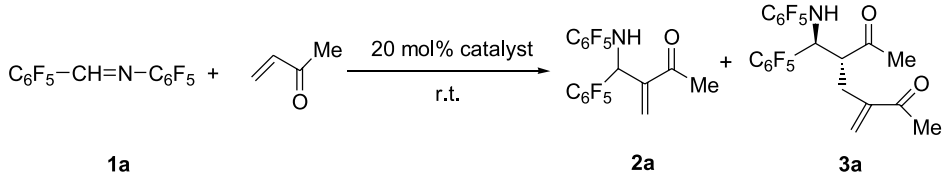
In Tables 2 and 3, the results of the aza-Baylis–Hillman reaction of per- (or poly)fluorophenyl aromatic aldimines with methyl vinyl ketone in the presence of Lewis bases PPh_3 and DABCO were summarized, respectively.

The other per- (or poly)fluorophenyl aromatic aldimines (**1b–1k**) (0.5 mmol) could react with MVK (1 mmol) smoothly in the presence of Lewis base PPh_3 under the optimized reaction conditions to give the corresponding normal aza-Baylis–Hillman adducts **2b–2k** and the double Baylis–Hillman adducts **3b–3h** in excellent to moderate yields; while the product ratio was dependent on electronic features of aryl substituents of the corresponding imines (Table 2). The aza-Baylis–Hillman adducts **2** and double Baylis–Hillman adducts **3** were formed in good yields in the reaction of MVK with imines with an electron-withdrawing group on the benzene ring (Table 2, entries 4–9), whereas an electron-donating substituent lowered the yields (entries

Table 1. Results of aza-Baylis–Hillman reactions of *N*-pentafluorophenyl-pentafluorophenyl aldimine with MVK[a]

Entry	Lewis base	Solvent	Time (h)	Yield of **2a**[b] (%)	Yield of **3a**[b] (%)
1	PPh_3	THF	12	80	18
2	PPh_3	DMF	12	63	27
3[c]	PPh_3	CH_2Cl_2	12	48	31
4	PPh_3	CH_3CN	12	Trace	Trace
5[c]	DBU	THF	6	30	0
6	DABCO	THF	12	12	72
7	DABCO	DMF	12	Trace	87
8[d]	PBu_3	THF	24	0	0
9	DMAP	THF	12	[e]	[e]
10	Et_3N	THF	12	[e]	[e]
11	Me_2S	THF	12	[e]	[e]

[a] All reactions carried out at room temperature; the molar ratio of **1a** to MVK was 1:2.
[b] Isolated yields.
[c] Determined by ^{19}F NMR.
[d] An unidentified mixture of products was obtained.
[e] No reaction occurred.



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

Scheme 3.

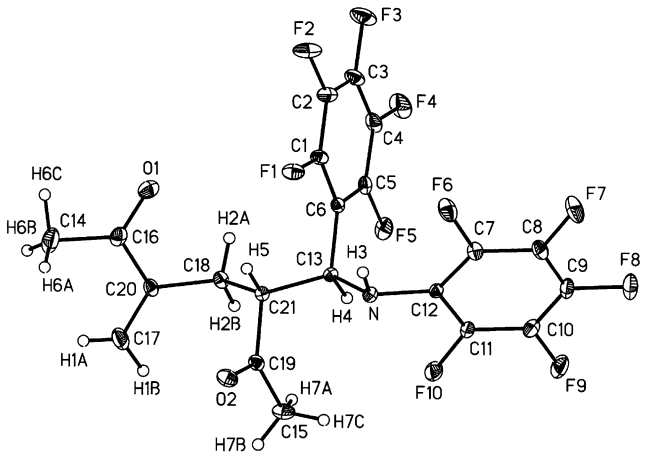
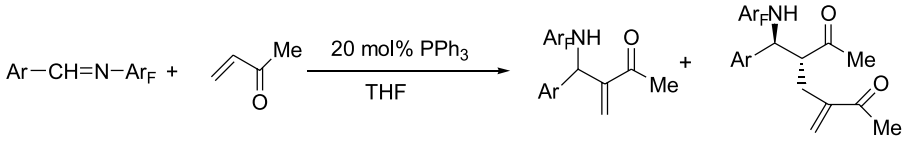


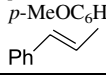
Figure 1. X-ray crystal structure of **3a**.

10–11). To our surprise, the aza-Baylis–Hillman reaction of *N*-(4-chloro-2,3,5,6-tetrafluoro) phenyl-4-nitrophenyl aldimine **1d** with MVK, under the similar reaction conditions, gave the normal Baylis–Hillman adduct **2d** exclusively (Table 2, entry 4). And decreasing the reaction temperature to 0 °C yielded 80% of the normal Baylis–Hillman adduct **2d** and no corresponding double aza-Baylis–Hillman adduct **3d** was isolated (entry 5). 4-Methylphenyl, 4-methoxyphenyl or 4-propenyl-phenyl aldimines **1i**–**1k** could also react with MVK to give the normal aza-Baylis–Hillman adducts **2i**–**2k** in moderate yields along with some unidentified products, respectively, but only if the reaction temperature was kept at 60 °C due to their low reactivity. None of the corresponding double aza-Baylis–Hillman adducts was formed, possibly due to the decomposition or side reaction at high reaction temperature (entries 10–12). The above results indicated that the substituents on Ar_F and

Table 2. Aza-Baylis–Hillman reactions of per- (or poly)fluorophenyl aromatic aldimines with MVK in THF in the presence of PPh_3[a]

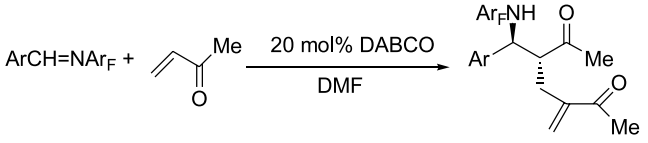


1(a-k) **2 (a-k)** **3(a-c, e-h)**

Entry	Ar	Ar_F	Time (h)	Temperature (°C)	Yield of **2**[b](%)	Yield of **3**[b](%)
1	C_6F_5	C_6F_5	12	rt	**2a**, 80	**3a**, 18
2	C_6H_5	C_6F_5	96	40	**2b**, 20	**3b**, 25
3	C_6H_5	4-ClC_6F_4	72	40	**2c**, 51	**3c**, 17
4	*p*-$NO_2C_6H_4$	4-ClC_6F_4	24	40	**2d**, 90	0
5	*p*-$NO_2C_6H_4$	4-ClC_6F_4	24	0	**2d**, 80	0
6	*o*-$NO_2C_6H_4$	4-ClC_6F_4	24	40	**2e**, 51	**3e**, 35
7	*p*-BrC_6H_4	4-ClC_6F_4	72	40	**2f**, 35	**3f**, 37
8	*o*-BrC_6H_4	4-ClC_6F_4	72	40	**2g**, 61	**3g**, 27
9	*o*-ClC_6H_4	4-ClC_6F_4	58	40	**2h**, 53	**3h**, 25
10	*p*-MeC_6H_4	4-ClC_6F_4	48	60	**2i**, 45	—[c]
11	*p*-$MeOC_6H_4$	4-ClC_6F_4	72	60	**2j**, 34	—[c]
12		4-ClC_6F_4	72	60	**2k**, 30	—[c]

[a] The molar ratio of imine with MVK was 1:2.
[b] Isolated yields.
[c] An unidentified mixture of products was obtained.

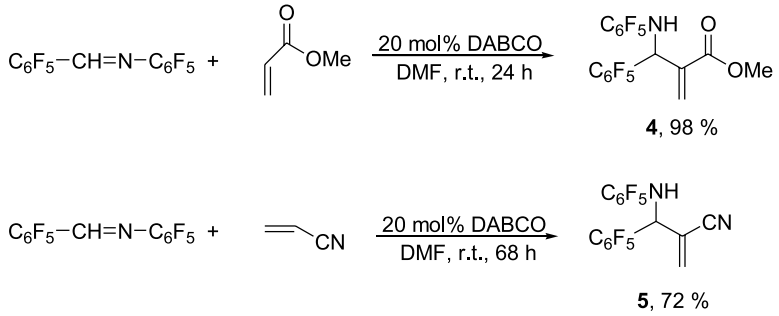
Table 3. Results of aza-Baylis–Hillman reactions of per- (or poly)fluorophenyl aromatic aldimines with MVK in DMF in the presence of DABCO[a]



1 **3**

Entry	Ar	ArF	Time (h)	Temperature (°C)	Yield of **3**[b] (%)[c]
1[d]	C_6F_5	C_6F_5	12	25	**3a**, 87
2	C_6H_5	C_6F_5	240	60	**3b**, 35
3	C_6H_5	4-ClC_6F_4	240	60	**3c**, 47
4	*p*-$NO_2C_6H_4$	4-ClC_6F_4	24	−78∼0	**3d**, 30
5	*o*-$NO_2C_6H_4$	4-ClC_6F_4	48	−78∼0	**3e**, 69
6	*p*-BrC_6H_4	4-ClC_6F_4	60	25	**3f**, 65
7	*o*-BrC_6H_4	4-ClC_6F_4	48	25	**3g**, 61
8	*o*-ClC_6H_4	4-ClC_6F_4	60	25	**3h**, 61

[a] The molar ratio of imine to MVK was 1:5.
[b] All the products **3** were *anti*-configuration.
[c] Isolated yields.
[d] The molar ratio of imine with MVK was 1:2.



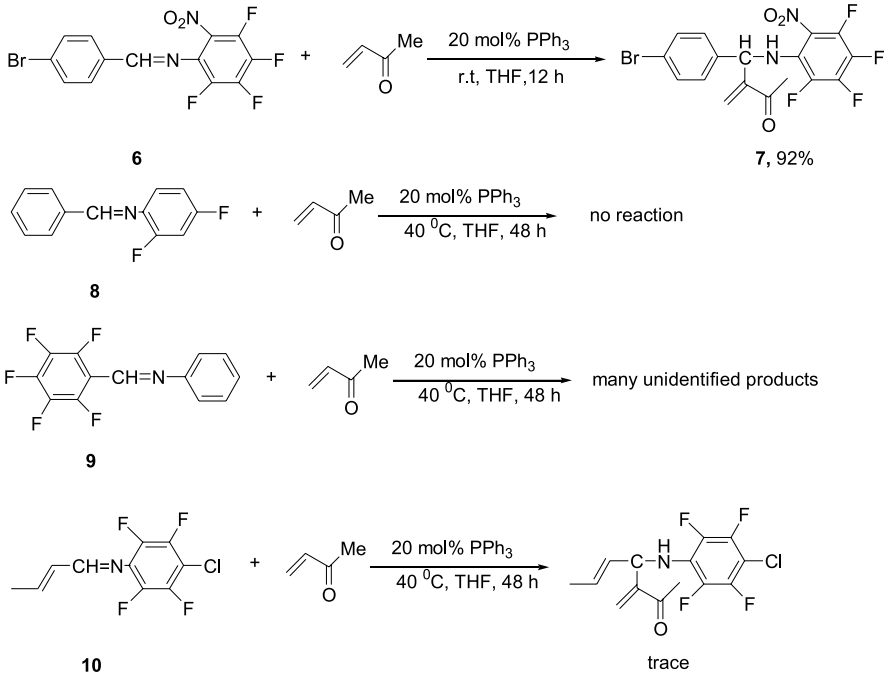
Scheme 4.

Ar affected the reactions, and electron-withdrawing substituents on the groups (Ar) would favor this version of the aza-Baylis–Hillman reaction.

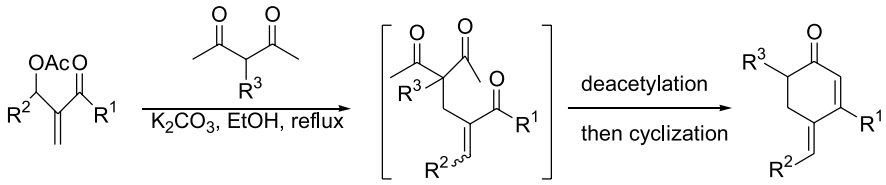
On the other hand, if using DABCO as a Lewis base in DMF, in all cases the corresponding double aza-Baylis–Hillman adducts were obtained exclusively as the sole product with the *anti*-configuration (Table 3). In order to obtain **3** in higher yields, 5 equiv of MVK was employed in all cases (Table 3). For substrates having an electron-withdrawing group on the benzene ring, the reaction proceeded very well to give **3** in good yields within shorter reaction time (Table 3, entries 5–8). Rising of the reaction temperature and prolonged reaction time were effective with less-reactive substrates like **1b**,**1c** (Table 3, entries 2–3). Specifically, when *N*-(4-chloro-2,3,5,6-tetrafluoro)phenyl-4-nitrophenyl aldimine **1d** bearing a strong electron-withdrawing nitro group on the benzene ring was used as the substrate, it was found that **1d** decomposed rapidly, and the corresponding double aza-Baylis–Hillman adduct **3d** could only be obtained in 30% yield along with many unidentified products, when the reaction temperature was kept at $-78\sim0$ °C (Table 3, entry 4).

It should be emphasized here that for other Michael acceptors such as methyl acrylate and acrylonitrile reacted with **1**, no such double aza-Baylis–Hillman reaction product could be observed at all. For example, the aza-Baylis–Hillman reaction of *N*-pentafluorophenyl-pentafluorophenyl aldimine **1a** with methyl acrylate in DMF in the presence of DABCO (20 mol %) was completed within 24 h to provide 98% yield of the product **4**. Under the same reaction conditions, it reacted with acrylonitrile within 68 h providing 2-(pentafluorophenyl-pentafluorophenylamino -methyl)-acrylonitrile **5** in 72% yield (Scheme 4).

This result stimulated us to seek out other versions of aza-Baylis–Hillman reactions using other fluorinated imines. Therefore, several fluorine-containing imines have been prepared and used as the substrates (Scheme 5). The reaction of [1-(4-bromophenyl)-meth-(*E*)-ylidene]-(2,3,4,5-tetrafluoro-6-nitrophenyl)-amine **6** which had an electron-withdrawing group (*o*-NO_2) on Ar_F with MVK proceeded smoothly under the same conditions as those described above, the corresponding normal aza-Baylis–Hillman adduct **7** was formed exclusively in 92% yield within 12 h. However, under the same reaction conditions,

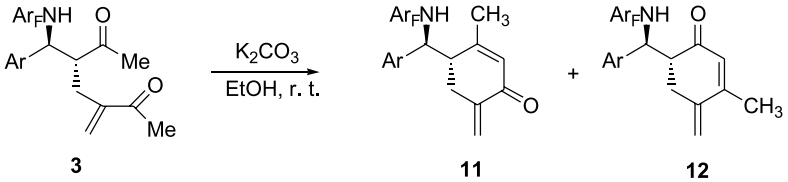


Scheme 5.



Scheme 6.

Table 4. Synthesis of fluorine-containing 4-alkylidene-2-cyclohexen-1-ones **11** and **12**



3 **11** **12**

Entry	Ar	ArF	Time (h)	Yield[a]/%	Ratio (**11**/**12**)
1	C_6F_5	C_6F_5	4	90	1:2[b]
2	*o*-BrC_6H_4	4-ClC_6F_4	4	79	37:42[c]
3	*o*-ClC_6H_4	4-ClC_6F_4	4	97	48:49[c]

[a] Isolated yield.
[b] Determined by ^{19}F NMR.
[c] Determined by isolated weight.

N-benzyliden-2, 4-difluor-anilin **8** did not react with MVK and even at higher temperature no reaction occurred to give the corresponding product due to its low reactivity. These results indicated that the electron-withdrawing nature of the *N*-substituent was necessary for a successful aza-Baylis–Hillman reaction. When *N*-phenyl-pentafluorophenyl aldimine **9** was subjected to similar reaction conditions, many unidentified products were formed, and none of the corresponding aza-Baylis–Hillman adduct was obtained. We also prepared trans-crotonaldehyde-4-chloro-2,3,5,6-tetrafluoro-phenylimine **10** which was very labile and must be used immediately for the reaction. In the aza-Baylis–Hillman reaction of **10** with MVK in the presence of PPh_3 under the same conditions, the corresponding normal aza-Baylis–Hillman adduct was formed in very low yield.

In 1998, Amri and co-workers reported a convenient synthesis of 4-alkylidene-2-cyclohexen-1-ones via the tandem three-step: S_N2' substitution–deacetylation–cyclization reactions (Scheme 6).[8] We intended to convert the double Baylis–Hillman adducts **3** to fluorine-containing 4-alkylidene-2-cyclohexen-1-ones, which represented the main structural feature of some natural and synthetic products[9–11] characterized by important biological activities[12] and considered as useful flavouring materials and perfumes.[13] However, under the reported reaction conditions, we found that the double aza-Baylis–Hillman adducts were transformed to the corresponding two isomers **11** and **12** in good yields at room temperature (Table 4). The structure of **12h** was determined by X-ray diffraction (Fig. 2). Specifically, when **3a** was used as a substrate, the aza-Baylis–Hillman adduct was transformed to the corresponding two isomers **11a** and **12a** in a ratio of 1:2 according to the ^{19}F NMR spectra which could not be separated by flash column chromatography. This transformation could provide a convenient method for the preparation of fluorine-containing 4-alkylidene-2-cyclohexen-1-one derivatives.

The double Baylis–Hillman reaction mechanism of electron deficient *N*-sulfonylimine and aldehyde had been proposed in Scheme 7.[4,14] The first mechanism is the Michael addition of enolate derived from DABCO and MVK to the Baylis–Hillman adduct, and the second is the aldol condensation reaction of enolate derived from DABCO and MVK (a MVK dimer type enloate) with the substrate.

To confirm the reaction mechanism of the formation of the

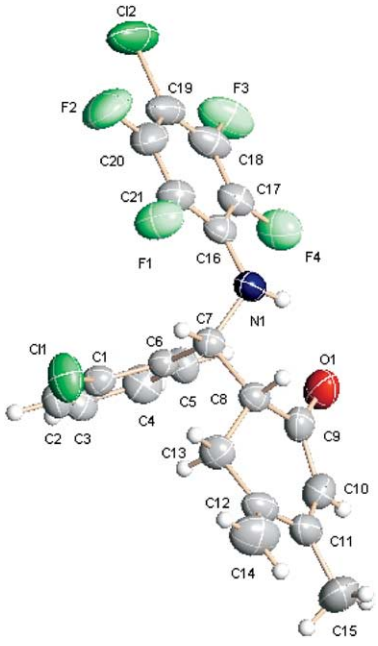
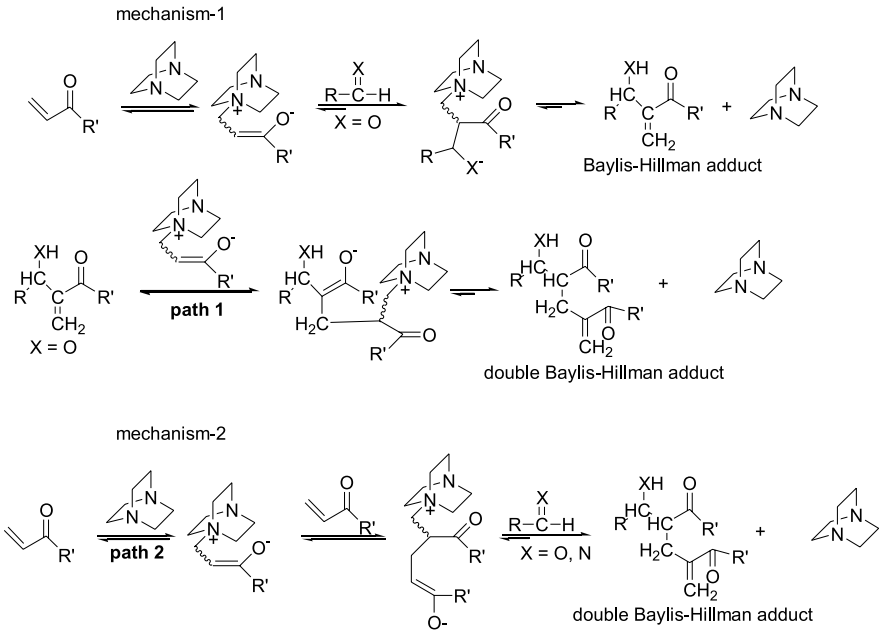
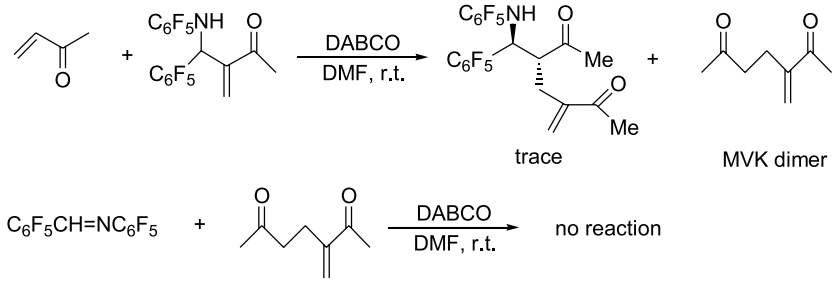


Figure 2. X-ray crystal structure of **12h**.



Scheme 7.



Scheme 8.

double aza-Baylis–Hillman product **3**, we conducted the reaction of MVK with the normal aza-Baylis–Hillman adduct **2a** under the same conditions (Scheme 8). To our surprise, only trace **3a** was obtained and the main product was the dimmer of MVK. We also confirmed that the MVK dimmer did not react with *N*-pentafluorophenyl-pentafluorophenyl aldimine **1a** in the presence of DABCO (Scheme 8). This was simply due to the fact that the MVK dimmer type enolate (show in mechanism 2 of Scheme 7) could not be formed from the MVK dimmer with DABCO. These results suggested that the double aza-Baylis–Hillman products **3** were not derived from the first mechanism as shown in Scheme 7, and this unexpected highly diastereoselective double aza-Baylis–Hillman reaction could only proceed via the second mechanism. Namely, a MVK dimmer type enolate was formed during the reaction which was further reacted with per- (or poly)fluorophenyl aromatic aldimines to give exclusively the double aza-Baylis–Hillman adduct (show in mechanism 2 of Scheme 7).

3. Conclusion

In conclusion, we have found that in the aza-Baylis–Hillman reaction of per- (or poly)fluorophenyl aromatic aldimines **1** with MVK, the Lewis base and solvent could significantly affect the reaction. Using triphenylphosphine as a Lewis base, the reaction of **1** with MVK proceeded smoothly to give the normal Baylis–Hillman adduct **2** along with the double Baylis–Hillman adduct **3** as by-product in THF. On the other hand, in the aza-Baylis–Hillman reaction of **1** with MVK using DABCO as a Lewis base, double aza-Baylis–Hillman adducts **3** were formed exclusively in the *anti*-configuration, which was confirmed to be derived from the Baylis–Hillman reaction of the enolate of the MVK dimmer induced by DABCO and MVK with per- (or poly)fluorophenyl aromatic aldimines. The double Baylis–Hillman adducts **3** were conveniently converted to fluorine-containing 4-alkylidene-2-cyclohexen-1-ones under mild reaction conditions in good yields. Further studies on applications of these aza-Baylis–Hillman reactions are underway.

4. Experimental

Unless otherwise stated, all reactions were carried out under an argon atmosphere. All per- (or poly)fluorophenyl aromatic aldimines[15] were prepared according to the literature. ^{1}H, ^{13}C and ^{19}F NMR spectra were recorded in

$CDCl_3$ on Bruker AM-300 instruments with Me_4Si and $CFCl_3$ (with upfield negative) as the internal and external standards, respectively. IR spectra were obtained with a Nicolet AV-360 spectrophotometer. Lower resolution mass spectrum or high-resolution mass spectra (HRMS) were obtained on a Finnigan GC-MS 4021 or a Finnigan MAT-8430 instrument using the electron impact ionization technique (70 ev), respectively. Elemental analyses were performed by this Institute. X-ray crystal structure analysis was performed on a Bruker P4 instrument. Melting points were measured in Temp-Melt apparatus and were uncorrected.

4.1. Typical reaction procedure for the triphenylphosphine-catalyzed Baylis–Hillman reaction of methyl vinyl ketone with per- (or poly)fluorophenyl aromatic aldimines

To a solution of *N*-pentafluorophenyl-pentafluorophenyl aldimine (181 mg, 0.5 mmol) and triphenylphosphine (26 mg, 0.1 mmol) in THF (1.0 mL) at room temperature was added methyl vinyl ketone (70 mg, 1 mmol). The reaction was monitored by TLC; when the imine disappeared, the solvent was removed under reduced pressure, and the residue was purified by flash chromatography [SiO_2, EtOAc–petroleum ether (1:20)] to yield **2a** (172 mg, 80%) as a colorless liquid and **3a** (45 mg, 18%) as a colorless solid.

4.1.1. 3-(Pentafluorophenyl-pentafluorophenylamino-methyl)-but-3-en-2-one (2a). Colorless liquid; IR (film) υ 1678 cm^{-1} (C=O); ^1H NMR ($CDCl_3$, TMS, 300 MHz) δ 2.39 (3H, s, Me), 4.29 (1H, d, $J=11.4$ Hz, NH), 6.03 (1H, d, $J=10.8$ Hz, CH), 6.24 (1H, s), 6.41 (1H, s); ^{19}F NMR ($CDCl_3$, TMS, 282 MHz) δ −143.0 (2F, d, $^3J_{FF}=18.9$ Hz), −154.2 (1F, t, $^3J_{FF}=21.4$ Hz), −157.7 (2F, d, $^3J_{FF}=24.5$ Hz), −161.3 (2F, m), −163.2 (2F, t, $^3J_{FF}=22.0$ Hz), −167.5 (1F, t, $^3J_{FF}=17.2$ Hz); ^{13}C NMR ($CDCl_3$, TMS, 75.44 MHz) δ 26.1, 50.9, 114.2, 121.3, 126.8, 135.3 (m, $^1J_{CF}=288.2$ Hz), 136.3, 137.8 (m, $^1J_{CF}=239.1$ Hz), 139.1, 141.7 (m, $^1J_{CF}=211.6$ Hz), 144.9 (m, $^1J_{CF}=245.9$ Hz), 145.8, 197.6; MS (EI) *m/e* 431 (M^+, 7.05), 43 (M^+-388, 100). Anal. Calcd for $C_{17}H_7NOF_{10}$: C, 47.35; H, 1.64; N, 3.25. Found: C, 47.71; H, 1.79; N, 3.26.

4.1.2. 3-(Pentafluorophenylamino-phenyl-methyl)-but-3-en-2-one (2b). Colorless liquid (34 mg, 20%); IR (film) υ 1681 cm^{-1} (C=O); ^1H NMR ($CDCl_3$, TMS, 300 MHz) δ 2.35 (3H, s, Me), 4.56 (1H, d, $J=9.3$ Hz, NH), 5.70 (1H, d, $J=9.6$ Hz, CH), 6.04 (1H, s), 6.26 (1H, s), 7.27–7.36 (5H, m, Ar); ^{19}F NMR ($CDCl_3$, TMS, 282 MHz) δ −158.20 (2F, d, $^3J_{FF}=25.4$ Hz), −164.2 (2F, t, $^3J_{FF}=22.8$ Hz), −170.6 (1F, m); ^{13}C NMR ($CDCl_3$, TMS, 75.44 MHz) δ 19.7, 60.6, 116.7, 122.6, 126.7, 126.8, 127.9, 128.8, 133.9 (m, $^1J_{CF}=241.9$ Hz), 138.3 (m, $^1J_{CF}=232.2$ Hz), 140.2, 148.3, 198.8; MS (EI) *m/e* 341 (M^+, 12.11), 159 (M^+-182, 61.39), 43 (M^+-298, 100). Anal. Calcd for $C_{17}H_{12}NOF_5$: C, 59.83; H, 3.54; N, 4.10. Found: C, 60.10; H, 3.48; N, 3.91.

4.1.3. 3-[(4-Chloro-2,3,5,6-tetrafluorophenylamino)-phenyl-methyl]-but-3-en-2-one (2c). Colorless liquid(91 mg, 51%); IR (film) υ 1680 cm^{-1} (C=O); ^1H NMR ($CDCl_3$, TMS, 300 MHz) δ 2.36 (3H, s, Me), 4.75 (1H, d, $J=9.6$ Hz, NH), 5.81 (1H, d, $J=9.3$ Hz, CH), 6.05 (1H, s), 6.28 (1H, s), 7.28–7.37 (5H, m, Ar); ^{19}F NMR ($CDCl_3$, TMS, 282 MHz) δ −143.8 (2F, d, $^3J_{FF}=20.6$ Hz), −156.7 (2F, d, $^3J_{FF}=19.7$ Hz); ^{13}C NMR ($CDCl_3$, TMS, 75.44 MHz) δ 26.6, 60.1, 99.9, 125.7, 126.8, 127.1, 128.0, 128.7, 138.0 (m, $^1J_{CF}=241.3$ Hz), 140.1, 144.6 (m, $^1J_{CF}=244.2$ Hz), 148.2, 198.8; MS (EI) *m/e* 357 (M^+, 6.06), 43 (M^+-314, 100). Anal. Calcd for $C_{17}H_{12}NOF_4Cl$: C, 57.08; H, 3.36; N, 3.92. Found: C, 57.21; H, 3.56; N, 3.66.

4.1.4. 3-[(4-Chloro-2,3,5,6-tetrafluorophenylamino)-(4-nitrophenyl)-methyl]-but-3-en-2-one (2d). Yellow solid (181 mg, 90%); mp 97–99 °C; IR (film) υ 1681 cm^{-1} (C=O); ^1H NMR ($CDCl_3$, TMS, 300 MHz) δ 2.37 (3H, s, Me), 4.90 (1H, d, $J=9.3$ Hz, NH), 5.75 (1H, d, $J=9.9$ Hz, CH), 6.13 (1H, s), 6.35 (1H, s), 7.56 (2H, d, $J=9.0$ Hz, Ar), 8.22 (2H, d, $J=8.7$ Hz, Ar); ^{19}F NMR ($CDCl_3$, TMS, 282 MHz) δ −142.8 (2F, d, $^3J_{FF}=13.0$ Hz), −156.9 (2F, d, $^3J_{FF}=16.9$ Hz); ^{13}C NMR ($CDCl_3$, TMS, 75.44 MHz) δ 26.5, 60.6, 101.2, 123.9, 125.1, 127.4, 128.8, 138.3 (m, $^1J_{CF}=232.5$ Hz), 144.6 (m, $^1J_{CF}=247.0$ Hz), 147.1, 147.4, 147.6, 198.77; MS (EI) *m/e* 402 (M^+, 2.89), 43 (M^+-359, 100). Anal. Calcd for $C_{17}H_{11}N_2O_3F_4Cl$: C, 50.70; H, 2.75; N, 6.96. Found: C, 50.62; H, 2.87; N, 6.85.

4.1.5. 3-[(4-Chloro-2,3,5,6-tetrafluorophenylamino)-(2-nitrophenyl)-methyl]-but-3-en-2-one (2e). Yellow solid (103 mg, 51%); mp 109–111 °C; IR (film) υ 1683 cm^{-1} (C=O); ^1H NMR ($CDCl_3$, TMS, 300 MHz) δ 2.37 (3H, s, Me), 4.46 (1H, d, $J=8.1$ Hz, NH), 5.90 (1H, s), 6.24 (1H, s), 6.43 (1H, d, $J=8.1$ Hz, CH), 7.49 (1H, m, Ar), 7.66 (1H, m, Ar), 7.76 (1H, m, Ar), 7.98 (1H, m, Ar); ^{19}F NMR ($CDCl_3$, TMS, 282 MHz) δ -143.2 (2F, d, $^3J_{FF}=18.8$ Hz), -157.9 (2F, d, $^3J_{FF}=16.6$ Hz); ^{13}C NMR ($CDCl_3$, TMS, 75.44 MHz) δ 26.0, 55.6, 100.4, 125.4, 125.6, 127.4, 128.4, 129.2,133.3, 135.3, 137.9 (m, $^1J_{CF}=241.1$ Hz), 144.4 (m, $^1J_{CF}=249.0$ Hz), 147.7, 148.1, 198.0; MS (EI) *m/e* 402 (M^+, 0.98), 43 (M^+-359, 100). Anal. Calcd for $C_{17}H_{11}N_2O_3F_4Cl$: C, 50.70; H, 2.75; N, 6.96. Found: C, 50.73; H, 3,04; N, 6.79.

4.1.6. 3-[(4-Bromophenyl)-(4-chloro-2,3,5,6-tetrafluorophenylamino)-methyl]-but-3-en-2-one (2f). Colorless liquid (76 mg, 35%); IR (film) υ 1680 cm^{-1} (C=O); ^1H NMR ($CDCl_3$, TMS, 300 MHz) δ 2.35 (3H, s, Me), 4.75 (1H, d, $J=9.0$ Hz, NH), 5.70 (1H, d, $J=9.0$ Hz, CH), 6.05 (1H, s), 6.27 (1H, s), 7.20 (2H, d, $J=8.1$ Hz, Ar), 7.47 (2H, d, $J=8.1$ Hz, Ar); ^{19}F NMR ($CDCl_3$, TMS, 282 MHz) δ −143.2 (2F, d, $^3J_{FF}=21.4$ Hz), −157.3 (2F, d, $^3J_{FF}=22.8$ Hz); ^{13}C NMR ($CDCl_3$, TMS, 75.44 MHz) δ 26.5, 60.0, 101.7, 121.8, 125.4, 127.4, 128.4, 131.9, 139.2, 138.0 (m, $^1J_{CF}=236.2$ Hz), 139.2, 144.5 (m, $^1J_{CF}=262.15$ Hz), 147.8, 198.7; MS (EI) *m/e* 435 (M^+, 2.90), 43 (M^+-392, 100). HRMS (MALDI) *m/e* calcd for $C_{17}H_{12}N_2O_3F_4Br$ $(M+H)^+$ 435.9727, found 435.9746.

4.1.7. 3-[(2-Bromophenyl)-(4-chloro-2,3,5,6-tetrafluorophenylamino)-methyl]-but-3-en-2-one (2g). Colorless liquid(133 mg, 61%); IR (film) υ 1680 cm^{-1} (C=O); ^1H NMR ($CDCl_3$, TMS, 300 MHz) δ 2.36 (3H, s, Me), 4.76 (1H, d, $J=9.3$ Hz, NH), 5.72 (1H, d, $J=9.0$ Hz, CH), 6.07 (1H, s), 6.30 (1H, s), 7.20–7.50 (4H, m, Ar); ^{19}F NMR ($CDCl_3$, TMS, 282 MHz) δ −143.2 (2F, d, $^3J_{FF}=21.4$ Hz),

−157.3 (2F, d, $^3J_{FF}$=22.8 Hz); ^{13}C NMR ($CDCl_3$, TMS, 75.44 MHz) δ 26.6, 60.2, 102.7, 122.9, 125.3, 126.4, 127.6, 129.7, 130.3, 131.0, 138.0 (m, $^1J_{CF}$=243.5 Hz), 142.4, 144.9 (m, $^1J_{CF}$=292.9 Hz), 147.6, 198.6; MS (EI) *m/e* 435 (M^+, 3.69), 43 (M^+−392, 100). Anal. Calcd for $C_{17}H_{11}NOF_4ClBr$: C, 46.76; H, 2.54; N, 3.21. Found: C, 47.18; H, 2.81; N, 2.97.

4.1.8. 3-[(2-Chlorophenyl)-(4-chloro-2,3,5,6-tetrafluorophenylamino)-methyl]-but-3-en-2-one (2h). Colorless liquid (104 mg, 53%); IR (film) υ 1681 cm^{-1} (C=O); ^{1}H NMR ($CDCl_3$, TMS, 300 MHz) δ 2.39 (3H, s, Me), 4.62 (1H, d, *J*=9.0 Hz, NH), 6.01 (1H, s), 6.23 (1H, d, *J*=8.7 Hz, CH), 6.32 (1H, s), 7.21–7.45 (4H, m, Ar); ^{19}F NMR ($CDCl_3$, TMS, 282 MHz) δ −143.5 (2F, d, $^3J_{FF}$=14.9 Hz), −158.1 (2F, d, $^3J_{FF}$=12.7 Hz); ^{13}C NMR ($CDCl_3$, TMS, 75.44 MHz) δ 26.6, 56.7, 100.6, 125.6, 127.2, 127.9, 128.2, 129.2, 130.2, 133.6, 137.5, 137.9 (m, $^1J_{CF}$=239.9 Hz), 144.5 (m, $^1J_{CF}$=246.3 Hz), 147.4, 198.5; MS (EI) *m/e* 391 (M^+, 13.14), 43 (M^+−348, 100). Anal. Calcd for $C_{17}H_{11}NOF_4Cl_2$: C, 52.06; H, 2.83; N, 3.57. Found: C, 52.25; H, 2.88; N, 3.50.

4.1.9. 3-[(4-Chloro-2,3,5,6-tetrafluorophenylamino)-*p*-tolyl-methyl]-but-3-en-2-one (2i). Colorless liquid (84 mg, 45%); IR (film) υ 1680 cm^{-1} (C=O); ^{1}H NMR ($CDCl_3$, TMS, 300 MHz) δ 2.34 (3H, s, Me), 3.35 (3H, s, Me), 4.71 (1H, d, *J*=8.7 Hz, NH), 5.78 (1H, d, *J*=9.3 Hz, CH), 6.04 (1H, s), 6.25 (1H, s), 7.16 (2H, d, *J*=7.8 Hz, Ar), 7.24 (2H, d, *J*=7.8 Hz, Ar); ^{19}F NMR ($CDCl_3$, TMS, 282 MHz) δ −143.7 (2F, d, $^3J_{FF}$=16.9 Hz), −157.7 (2F, d, $^3J_{FF}$=18.3 Hz); ^{13}C NMR ($CDCl_3$, TMS, 75.44 MHz) δ 21.1, 26.7, 59.8, 99.9, 125.6, 126.4, 126.7, 129.5, 137.1, 137.8, 137.9 (m, $^1J_{CF}$=225.4 Hz), 144.6 (m, $^1J_{CF}$=248.0 Hz), 148.4, 198.8; MS (EI) *m/e* 371 (M^+, 7.14), 173 (M^+− 198, 54.03), 43 (M^+−328, 100). Anal. Calcd for $C_{18}H_{14}NOF_4Cl$: C, 58.16; H, 3.80; N, 3.78. Found: C, 58.43; H, 3.87; N, 3.55.

4.1.10. 3-[(4-Chloro-2,3,5,6-tetrafluorophenylamino)-(4-methoxy-phenyl)-methyl]-but-3-en-2-one (2j). Colorless liquid (68 mg, 35%); IR (film) υ 1680 cm^{-1} (C=O); ^{1}H NMR ($CDCl_3$, TMS, 300 MHz) δ 2.35 (3H, s, Me), 3.80 (3H, s, Me), 4.67 (1H, d, *J*=8.7 Hz, NH), 5.78 (1H, d, *J*=8.7 Hz, CH), 6.03 (1H, s), 6.25 (1H, s), 6.88 (2H, d, *J*=6.6 Hz, Ar), 7.27 (2H, d, *J*=6.6 Hz, Ar); ^{19}F NMR ($CDCl_3$, TMS, 282 MHz) δ −143.6 (2F, d, $^3J_{FF}$=26.2 Hz), −157.6 (2F, d, $^3J_{FF}$=23.4 Hz); ^{13}C NMR ($CDCl_3$, TMS, 75.44 MHz) δ 26.7, 55.3, 59.5, 100.0, 114.2, 125.6, 126.1, 128.2, 132.2, 137.8 (m, $^1J_{CF}$=235.4 Hz), 144.5 (m, $^1J_{CF}$=254.8 Hz), 148.4, 159.3, 198.8; MS (EI) *m/e* 387 (M^+, 3.47), 318 (M^+−69, 100), 43 (M^+−344, 57.65). Anal. Calcd for $C_{18}H_{14}NO_2F_4Cl$: C, 55.76; H, 3.64; N, 3.61. Found: C, 56.09; H, 3.83; N, 3.42.

4.1.11. 3-(4-Chloro-2,3,5,6-tetrafluorophenylamino)-3-methylene-6-(*trans*)-phenyl-hex-5-en-2-one (2k). Colorless liquid (58 mg, 30%); IR (film) υ 1678 cm^{-1} (C=O); ^{1}H NMR ($CDCl_3$, TMS, 300 MHz) δ 2.39 (3H, s, Me), 4.78 (1H, d, *J*=9.9 Hz, NH), 5.23 (1H, dd, *J*=9.9, 7.2 Hz, CH), 6.06 (1H, s), 6.20 (1H, s), 6.34 (1H, dd, *J*=7.2, 6.9 Hz, CH), 6.59 (1H, d, *J*=6.9 Hz, CH), 7.23–7.39 (5H, m, Ar); ^{19}F NMR ($CDCl_3$, TMS, 282 MHz) δ −143.3 (2F, d, $^3J_{FF}$=26.2 Hz), −156.5 (2F, d, $^3J_{FF}$=24.8 Hz); ^{13}C NMR ($CDCl_3$, TMS, 75.44 MHz) δ 26.6, 59.8, 100.0, 125.6, 126.6, 127.4, 128.0, 128.6, 132.3, 136.1, 137.9 (m, $^1J_{CF}$=239.9 Hz), 138.8, 144.5 (m, $^1J_{CF}$=246.3 Hz), 147.6, 199.1; MS (EI) *m/e* 383 (M^+, 10.13), 185 (M^+−198, 100), 43 (M^+−340, 93.02); HRMS *m/e* calcd for $C_{19}H_{14}NOF_4Cl$ 383.0700, found. 383.06837.

4.2. Typical reaction procedure for the DABCO-catalyzed Baylis–Hillman reaction of methyl vinyl ketone with per- (or poly)fluorophenyl aromatic aldimines.

To a solution of *N*-pentafluorophenyl-pentafluorophenyl aldimine (181 mg, 0.5 mmol) and DABCO (12 mg, 0.1 mmol) in DMF (1.0 mL) at room temperature was added methyl vinyl ketone(175 mg, 2.5 mmol) under an argon atmosphere and the reaction mixture was stirred for 12 h at room temperature. The reaction mixture was washed with water (3×10 mL) and extracted with dichloromethane (2×10 mL). The organic layer was dried over anhydrous Na_2SO_4, the solvent was removed under reduced pressure, the residue was purified on silica gel using ethyl acetate (hexane (V/V: 1:20) as an elute to give a white solid product **3a**, which was further recrystallized from dichloromethane-hexane (V/V: 1:1) to give the pure product **3a** (218 mg, 87%) as a colorless crystal.

4.2.1. (*4,5-trans*)-3-Methylene-5-(pentafluorophenyl-pentafluorophenylamino-methyl)-heptane-2,6-dione (3a). Colorless solid; mp 102–104 °C; IR (film) υ 1713 cm^{-1} (C=O); 1670 cm^{-1} (C=O); ^{1}H NMR ($CDCl_3$, TMS, 300 MHz) δ 2.40 (3H, s, Me), 2.31 (1H, dd, *J*=13.8, 5.7 Hz), 2.34 (3H, s, Me), 2.50 (1H, dd, *J*=13.8, 9.0 Hz), 3.36 (1H, ddd, *J*=9.3, 9.0, 5.7 Hz), 4.56 (1H, d, *J*=11.7 Hz, NH), 5.27 (1H, dd, *J*=11.7, 9.3 Hz, CH), 5.82 (1H, s), 6.08 (1H, s); ^{19}F NMR ($CDCl_3$, TMS, 282 MHz) δ −143.9 (2F, d, $^3J_{FF}$=17.2 Hz), −152.8 (1F, t, $^3J_{FF}$=20.3 Hz), −157.7 (2F, d, $^3J_{FF}$=20.6 Hz), −160.4 (2F, m), −163.1 (2F, t, $^3J_{FF}$=17.8 Hz), −167.3 (1F, t, $^3J_{FF}$=18.1 Hz); ^{13}C NMR ($CDCl_3$, TMS, 75.44 MHz) δ 25.5, 30.7, 31.8, 53.2, 54.8, 114.2, 121.3, 128.5, 135.3 (m, $^1J_{CF}$=288.2 Hz), 136.3, 137.8 (m, $^1J_{CF}$=239.1 Hz), 139.1, 141.7 (m, $^1J_{CF}$=211.6 Hz), 144.6, 144.9 (m, $^1J_{CF}$=245.9 Hz), 198.8, 209.0; MS (EI) *m/e* 501 (M^+, 0.53), 362 (M^+−139, 55.76), 43 (M^+−458, 100). Anal. Calcd for $C_{21}H_{13}NO_2F_{10}$: C, 50.31; H, 2.61; N, 2.79. Found: C, 50.32; H, 2.62; N, 2.66.

4.2.2. (*4,5-trans*)-3-Methylene-5-(pentafluorophenyl-amino-phenyl-methyl)-heptane-2,6-dione (3b). Colorless solid (72 mg, 35%); mp 86–87 °C; IR (film) υ 1717 cm^{-1} (C=O); 1662 cm^{-1} (C=O); ^{1}H NMR ($CDCl_3$, TMS, 300 MHz) δ 1.92 (3H, s, Me), 2.37 (3H, s, Me), 2.56 (1H, dd, *J*=13.2, 6.3 Hz), 2.68 (1H, dd, *J*=13.2, 8.4 Hz), 3.24 (1H, ddd, *J*=8.4, 6.3, 5.7 Hz), 4.79 (1H, dd, *J*=10.5, 5.7 Hz, CH), 5.32 (1H, d, *J*=10.5 Hz, NH), 5.91 (1H, s), 6.13 (1H, s), 7.13–7.32 (5H, m, Ar); ^{19}F NMR ($CDCl_3$, TMS, 282 MHz) δ −158.0 (2F, d, $^3J_{FF}$=23.1 Hz), −164.4 (2F, t, $^3J_{FF}$=17.5 Hz), −170.60 (1F, m); ^{13}C NMR ($CDCl_3$, TMS, 75.44 MHz) δ 25.8, 31.7, 32.0, 56.1, 60.4, 116.7, 122.2, 126.2, 127.9, 128.7, 128.9, 133.9 (m, $^1J_{CF}$=241.9 Hz), 138.3 (m, $^1J_{CF}$=232.2 Hz), 140.4, 145.2,

199.4, 212.8; MS (EI) *m/e* 411 (M^+, 1.05), 272 (M^+-139, 100), 43 (M^+-368, 32.97). Anal. Calcd for $C_{21}H_{18}NO_2F_5$: C, 61.31; H, 4.41; N, 3.40. Found: C, 61.42; H, 4.31; N, 3.18.

4.2.3. (*4,5-trans*)-3-[(4-Chloro-2,3,5,6-tetrafluorophenylamino)-phenyl-methyl]-5-methylene-heptane-2,6-dione (3c). Colorless liquid (101 mg, 47%); IR (film) υ 1707 cm^{-1} (C=O); 1678 cm^{-1} (C=O); ^1H NMR ($CDCl_3$, TMS, 300 MHz) δ 1.90 (3H, s, Me), 2.37 (3H, s, Me), 2.59 (1H, dd, $J=13.2$, 6.9 Hz), 2.71 (1H, dd, $J=13.2$, 8.1 Hz), 3.26 (1H, ddd, $J=8.1$, 6.9, 5.1 Hz), 4.87 (1H, dd, $J=11.1$, 5.1 Hz, CH), 5.66 (1H, d, $J=11.1$ Hz, NH), 5.91 (1H, s), 6.14 (1H, s), 7.10 - 7.32 (5H, m, Ar); ^{19}F NMR ($CDCl_3$, TMS, 282 MHz) δ −143.8 (2F, d, $^3J_{FF}=25.4$ Hz), −157.3 (2F, d, $^3J_{FF}=25.9$ Hz); ^{13}C NMR ($CDCl_3$, TMS, 75.44 MHz) δ 25.9, 32.0, 32.1, 60.0, 65.9, 100.0, 125.5, 126.1, 127.9, 128.7, 129.0, 137.9 (m, $^1J_{CF}=241.1$ Hz), 142.9, 144.5 (m, $^1J_{CF}=248.0$ Hz), 145.2, 199.4, 213.0; MS (EI) *m/e* 427 (M^+, 4.26), 288 (M^+-139, 100), 43 (M^+-384, 55.18); HRMS (MALDI) *m/e* calcd for $C_{21}H_{18}NO_2F_4ClNa$ $(M+Na)^+$ 450.0860, found 450.0898.

4.2.4. (*4,5-trans*)-3-[(4-Chloro-2,3,5,6-tetrafluorophenylamino)-(4-nitrophenyl)-methyl]-5-methylene-heptane-2,6-dione (3d). Yellow solid (71 mg, 30%); mp 150–152 °C; IR (film) υ 1709 cm^{-1} (C=O); 1678 cm^{-1} (C=O); ^1H NMR ($CDCl_3$, TMS, 300 MHz) δ 1.94 (3H, s, Me), 2.39 (3H, s, Me), 2.57 (1H, dd, $J=13.2$, 7.2 Hz), 2.70 (1H, dd, $J=13.2$, 7.8 Hz), 3.24 (1H, ddd, $J=7.8$, 7.2, 4.5 Hz), 4.82 (1H, dd, $J=9.6$, 4.5 Hz, CH), 5.74 (1H, d, $J=9.6$ Hz, NH), 5.92 (1H, s), 6.16 (1H, s), 7.04 (2H, d, $J=8.7$ Hz, Ar), 7.42 (2H, d, $J=8.4$ Hz, Ar); ^{19}F NMR ($CDCl_3$, TMS, 282 MHz) δ −143.4 (2F, d, $^3J_{FF}=26.2$ Hz), −157.3 (2F, d, $^3J_{FF}=18.3$ Hz); ^{13}C NMR ($CDCl_3$, TMS, 75.44 MHz) δ 25.9, 31.8, 32.1, 55.5, 59.5, 100.2, 124.2, 125.5, 127.3, 127.4, 129.6, 137.9 (m, $^1J_{CF}=241.1$ Hz), 144.4 (m, $^1J_{CF}=249.0$ Hz), 144.7, 148.2, 199.5, 212.4; MS (EI) *m/e* 472 (M^+, 4.26), 333 (M^+-139, 88.90), 43 (M^+-429, 100); HRMS *m/e* calcd for $C_{21}H_{17}N_2O_4F_4Cl$ 472.0813, found 472.0815.

4.2.5. (*4,5-trans*)-3-[(4-Chloro-2,3,5,6-tetrafluorophenylamino)-(2-nitrophenyl)-methyl]-5-methylene-heptane-2,6-dione (3e). Yellow solid (163 mg, 69%); mp 144–146 °C; IR (film) υ 1704 cm^{-1} (C=O); 1678 cm^{-1} (C=O); ^1H NMR ($CDCl_3$, TMS, 300 MHz) δ 2.08 (3H, s, Me), 2.51 (3H, s, Me), 2.61 (1H, dd, $J=13.2$, 10.5 Hz), 2.97 (1H, dd, $J=13.2$, 3.6 Hz), 3.44 (1H, ddd, $J=10.5$, 3.6, 3.0 Hz), 5.50 (1H, dd, $J=10.2$, 3.0 Hz, CH), 5.94 (1H, s), 6.25 (1H, s), 6.58 (1H, d, $J=10.2$ Hz, NH), 7.38–7.59 (3H, m, Ar), 7.96–7.99 (1H, m, Ar); ^{19}F NMR ($CDCl_3$, TMS, 282 MHz) δ −143.1 (2F, d, $^3J_{FF}=23.1$ Hz), −158.7 (2F, d, $^3J_{FF}=22.3$ Hz); ^{13}C NMR ($CDCl_3$, TMS, 75.44 MHz) δ 25.8, 31.7, 32.0, 52.3, 53.8, 100.2, 125.5, 125.4, 128.5, 128.6, 129.0, 133.7, 136.7, 137.9 (m, $^1J_{CF}=241.1$ Hz), 144.4 (m, $^1J_{CF}=249.0$ Hz), 144.6, 148.2, 199.3, 213.8; MS (EI) *m/e* 333 (M^+-139, 20.47), 43 (M^+-429, 100). Anal. Calcd for $C_{21}H_{17}N_2O_4F_4Cl$: C, 53.35; H, 3.62; N, 5.92. Found: C, 52.93; H, 3.57; N, 5.70.

4.2.6. (*4,5-trans*)-3-[(4-Bromophenyl)-(4-chloro-2,3,5,6-tetrafluorophenylamino)-methyl]-5-methylene-heptane-2,6-dione (3f). Colorless solid (165 mg, 65%); mp 112–120 °C; IR (film) υ 1707 cm^{-1} (C=O); 1677 cm^{-1} (C=O); ^1H NMR ($CDCl_3$, TMS, 300 MHz) δ 1.95 (3H, s, Me), 2.42 (3H, s, Me), 2.63 (1H, dd, $J=13.2$, 8.1 Hz), 2.76 (1H, dd, $J=13.2$, 6.6 Hz), 3.31 (1H, ddd, $J=8.1$, 6.6, 4.2 Hz), 4.95 (1H, dd, $J=9.3$, 4.2 Hz, CH), 5.94 (1H, d, $J=9.3$ Hz, NH), 5.95 (1H, s), 6.20 (1H, s), 7.36 (2H, d, $J=8.7$ Hz, Ar), 8.17 (2H, d, $J=8.7$ Hz, Ar); ^{19}F NMR ($CDCl_3$, TMS, 282 MHz) δ −142.9 (2F, d, $^3J_{FF}=21.7$ Hz), −157.6 (2F, d, $^3J_{FF}=22.0$ Hz); ^{13}C NMR ($CDCl_3$, TMS, 75.44 MHz) δ 22.7, 29.7, 32.2, 55.1, 59.4, 100.1, 121.8, 125.5, 127.9, 129.1, 132.0, 138.1 (m, $^1J_{CF}=237.1$ Hz), 139.7, 144.5 (m, $^1J_{CF}=254.1$ Hz), 144.9, 199.4, 212.8; MS (EI) *m/e* 505 (M^+, 2.21), 366 (M^+-139, 69.72), 43 (M^+-462, 100); HRMS (MALDI) *m/e* calcd for $C_{21}H_{18}NO_2F_4ClBr$ $(M+H)^+$ 506.0146, found 506.0124.

4.2.7. (*4,5-trans*)-3-[(2-Bromophenyl)-(4-chloro-2,3,5,6-tetrafluorophenylamino)-methyl]-5-methylene-heptane-2,6-dione (3g). Colorless solid (155 mg, 61%); mp 124–126 °C; IR (film) υ 1705 cm^{-1} (C=O); 1673 cm^{-1} (C=O); ^1H NMR ($CDCl_3$, TMS, 300 MHz) δ 1.94 (3H, s, Me), 2.45 (3H, s, Me), 2.67 (1H, dd, $J=13.2$, 9.3 Hz), 2.90 (1H, dd, $J=13.2$, 5.1 Hz), 3.40 (1H, ddd, $J=9.3$, 5.1, 3.6 Hz), 5.30 (1H, dd, $J=10.2$, 3.6 Hz, CH), 6.02 (1H, s), 6.24 (1H, s), 6.26 (1H, d, $J=10.2$ Hz, NH), 7.09–7.28 (3H, m, Ar), 7.53–7.56 (1H, m, Ar); ^{19}F NMR ($CDCl_3$, TMS, 282 MHz) δ −143.5 (2F, d, $^3J_{FF}=26.2$ Hz), −158.2 (2F, d, $^3J_{FF}=22.0$ Hz); ^{13}C NMR ($CDCl_3$, TMS, 75.44 MHz) δ 25.6, 31.5, 32.2, 51.8, 58.0, 100.1, 122.6, 125.6, 127.5, 127.9, 128.7, 129.2, 133.5, 138.1 (m, $^1J_{CF}=239.5$ Hz), 139.3, 144.5 (m, $^1J_{CF}=262.2$ Hz), 145.0, 198.9, 213.2; MS (EI) *m/e* 505 (M^+, 2.21), 366 (M^+-139, 69.72), 43 (M^+-462, 100). Anal. Calcd for $C_{21}H_{17}NO_2F_4ClBr$: C, 49.78; H, 3.38; N, 2.76. Found: C, 49.76; H, 3.34; N, 2.55.

4.2.8. (*4,5-trans*)-3-[(2-Chlorophenyl)-(4-chloro-2,3,5,6-tetrafluorophenylamino)-methyl]-5-methylene-heptane-2,6-dione (3h). Colorless solid (141 mg, 61%); mp 88–90 °C; IR (film) υ 1706 cm^{-1} (C=O); 1674 cm^{-1} (C=O); ^1H NMR ($CDCl_3$, TMS, 300 MHz) δ 1.94 (3H, s, Me), 2.42 (3H, s, Me), 2.63 (1H, dd, $J=13.2$, 9.3 Hz), 2.87 (1H, dd, $J=13.2$, 5.1 Hz), 3.36 (1H, ddd, $J=9.3$, 5.1, 3.6 Hz), 5.33 (1H, dd, $J=9.9$, 3.6 Hz, CH), 5.98 (1H, s), 6.18 (1H, d, $J=9.9$ Hz, NH), 6.21 (1H, s), 7.14–7.36 (4H, m, Ar); ^{19}F NMR ($CDCl_3$, TMS, 282 MHz) δ −143.6 (2F, d, $^3J_{FF}=18.9$ Hz), −158.2 (2F, d, $^3J_{FF}=18.1$ Hz); ^{13}C NMR ($CDCl_3$, TMS, 75.44 MHz) δ 25.6, 31.5, 32.1, 51.9, 55.6, 99.6, 125.7, 125.3, 125.4, 128.8, 128.9, 130.2, 132.4, 137.8, 138.0 (m, $^1J_{CF}=224.9$ Hz), 144.5 (m, $^1J_{CF}=244.4$ Hz), 145.0, 199.0, 213.2; MS (EI) *m/e* 461 (M^+, 1.51), 322 (M^+-139, 100), 43 (M^+-458, 56.81). Anal. Calcd for $C_{21}H_{17}NO_2F_4Cl_2$: C, 54.56; H, 3.71; N, 3.03. Found: C, 54.86; H, 3.53; N, 2.95.

4.2.9. 2-(Pentafluorophenyl-pentafluorophenylamino-methyl)-acrylic acid methyl ester (4). Colorless liquid (219 mg, 98%); IR (film) υ 3408, 1728, 1525, 1504 cm^{-1}; ^1H NMR ($CDCl_3$, TMS, 300 MHz) δ 3.78 (3H, s, Me), 4.44 (1H, d, $J=11.1$ Hz, NH), 6.00 (1H, s), 6.04 (1H, d, $J=11.7$ Hz, CH), 6.54 (1H, s); ^{19}F NMR ($CDCl_3$, TMS, 282 MHz) δ −143.0 (2F, d, $^3J_{FF}=21.4$ Hz), −153.8 (1F, t, $^3J_{FF}=22.0$ Hz), −157.7 (2F, d, $^3J_{FF}=21.7$ Hz), −161.2 (2F, m), −163.2 (2F, t, $^3J_{FF}=20.9$ Hz), −167.5 (1F, t,

$^3J_{FF}$=21.7 Hz); MS (EI) *m/e* 447 (M^+, 91), 387 (60), 362 (100), 265 (50). Anal. Calcd for $C_{17}H_7N_2O_2F_{10}$: C, 45.66; H, 1.58; N, 3.13. Found: C, 45.85; H, 1.68; N, 3.11.

4.2.10. 2-(Pentafluorophenyl-pentafluorophenylamino-methyl)-acrylonitrile (5). Colorless liquid (149 mg, 72%); IR (film) υ 3396, 1510, 1505 cm^{-1}; ^1H NMR ($CDCl_3$, TMS, 300 MHz) δ 4.40 (1H, d, J=10.8 Hz, NH), 5.78 (1H, d, J=11.4 Hz, CH), 6.15 (1H, s), 6.25 (1H, s); ^{19}F NMR ($CDCl_3$, TMS, 282 MHz) δ −142.8 (2F, d, $^3J_{FF}$=12.7 Hz), −150.7 (1F, t, $^3J_{FF}$=20.9 Hz), −156.7 (2F, d, $^3J_{FF}$=22.8 Hz), −159.3 (2F, m), −162.2 (2F, t, $^3J_{FF}$=23.1 Hz), −165.2 (1F, t, $^3J_{FF}$=22.6 Hz); MS (EI) *m/e* 414 (M^+, 81), 362 (80), 232 (100), 182 (31). Anal. Calcd for $C_{16}H_4N_2F_{10}$: C, 46.40; H, 0.97; N, 6.76. Found: C, 46.75; H, 1.35; N, 7.00.

4.2.11. 2-[(4-Bromophenyl)-(2,3,4,5-tetrafluoro-6-nitro-phenylamino)-methyl]-but-3-en-2-one (7). Yellow liquid (206 mg, 92%); IR (film) υ 1681 cm^{-1} (C=O); ^1H NMR ($CDCl_3$, TMS, 300 MHz) δ 2.35 (3H, s, Me), 5.82 (1H, d, J=8.1 Hz, CH), 5.97 (1H, s), 6.27 (1H, s), 6.84 (1H, d, J=8.1 Hz, NH), 7.20 (2H, d, J=8.1 Hz, Ar), 7.48 (2H, d, J=8.7 Hz, Ar); ^{19}F NMR ($CDCl_3$, TMS, 282 MHz) δ −144.2 (1F, m), −146.6 (1F, m); −153.2 (1F, m), −168.8 (1F, m); ^{13}C NMR ($CDCl_3$, TMS, 75.44 MHz) δ 26.4, 59.6, 122.1, 127.2, 128.6, 130.4, 132.1, 134.7, 136.5, 138.8, 141.6, 143.2, 145.1, 148.2, 198.1; MS (EI) *m/e* 446 (M^+, 0.06), 43 (M^+−403, 100); HRMS (MALDI) *m/e* calcd for $C_{17}H_{12}N_2O_3F_4Br$ $(M+H)^+$ 446.9967, found 446.9973.

4.3. Typical experimental procedure for the synthesis of fluorine-containing 4-alkylidene-2-cyclohexen-1-ones 11 and 12

To absolute ethanol solution of anhydrous potassium carbonate was mixed with 3-methylene-5-(pentafluoro-phenyl-pentafluorophenylamino-methyl)-heptane-2,6-dione **3a**. The mixture was stirred at room temperature for a given time (TLC, see Table 4). After removed of ethanol in vacuo, the residue was shaken with water to dissolve the salts. The resulting mixture was extracted three times with 10 mL of ether. The organic phase was dried on $MgSO_4$, concentrated and the crude products **11a** and **12a** were purified by flash chromatogryphy (EtOAc/Hexane, 1:40).

4.3.1. 3-Methyl-4-methylene-6-(pentafluorophenyl-pentafluorophenylamino-methyl)-cyclohex-2-enone (12a). Yellow liquid (32 mg, 60%); IR (film) υ 1668 cm^{-1} (C=O); ^1H NMR ($CDCl_3$, TMS, 300 MHz) δ 2.10 (3H, s, Me), 2.93–3.11 (3H, m), 4.35 (1H, d, J=10.8 Hz, NH), 5.13–5.21 (1H, m, CH), 5.45 (1H, s), 5.52 (1H, s), 5.84 (1H, s); ^{19}F NMR ($CDCl_3$, TMS, 282 MHz) δ −143.7 (2F, d, $^3J_{FF}$=18.6 Hz), −154.2 (1F, t, $^3J_{FF}$=20.9 Hz), −157.5 (2F, d, $^3J_{FF}$=22.5 Hz), −161.6 (2F, m), −163.4 (2F, t, $^3J_{FF}$=21.4 Hz), −167.7 (1F, t, $^3J_{FF}$=20.3 Hz); ^{13}C NMR ($CDCl_3$, TMS, 75.44 MHz) δ 19.7, 34.1, 50.9, 51.8, 114.2, 118.3, 121.3, 126.8, 135.3 (m, $^1J_{CF}$=288.2 Hz), 136.3, 137.8 (m, $^1J_{CF}$=239.1 Hz), 139.0, 139.2, 141.7 (m, $^1J_{CF}$=211.6 Hz), 144.9 (m, $^1J_{CF}$=245.9 Hz), 154.8, 197.1; MS (EI) *m/e* 483 (M^+, 0.53), 362 (M^+−121, 61.10), 122 (M^+−361, 100), 107 (M^+−376, 53.12); HRMS (MALDI) *m/e* calcd for $C_{21}H_{11}NOF_{10}Na$ $(M+Na)^+$ 506.0579, found 506.0600.

4.3.2. 3-Methyl-6-methylene-4-(pentafluorophenyl-pentafluorophenylamino-methyl)-cyclohex-2-enone (11a). Yellow liquid (16 mg, 30%); IR (film) υ 1668 cm^{-1} (C=O); ^1H NMR ($CDCl_3$, TMS, 300 MHz) δ 2.14 (3H, s, Me), 2.35–2.42 (1H, m), 2.86–2.93 (1H, m), 2.99–3.11 (1H, m), 4.48 (1H, d, J=9.6 Hz, NH), 5.13–5.21 (1H, m, CH), 5.35 (1H, s), 5.56 (1H, s), 5.95 (1H, s); ^{19}F NMR ($CDCl_3$, TMS, 282 MHz) δ −142.9 (2F, d, $^3J_{FF}$=13.8 Hz), −153.5 (1F, t, $^3J_{FF}$=20.0 Hz), −158.0 (2F, d, $^3J_{FF}$=24.8 Hz), −161.0 (2F, m), −163.8 (2F, t, $^3J_{FF}$=15.6 Hz), −168.7 (1F, t, $^3J_{FF}$=17.2 Hz); ^{13}C NMR ($CDCl_3$, TMS, 75.44 MHz) δ 19.7, 34.6, 50.8, 52.0, 114.2, 118.3, 121.5, 126.1, 135.3 (m, $^1J_{CF}$=288.2 Hz), 136.3, 137.8 (m, $^1J_{CF}$=239.1 Hz), 138.8, 139.1, 141.7 (m, $^1J_{CF}$=211.6 Hz), 144.9 (m, $^1J_{CF}$=245.9 Hz), 154.4, 197.7; MS (EI) *m/e* 483 (M^+, 3.75), 362 (M^+−121, 61.10), 122 (M^+−361, 100), 107 (M^+−376, 53.12); HRMS (MALDI) *m/e* calcd for $C_{21}H_{11}NOF_{10}Na$ $(M+Na)^+$ 506.0579, found 506.0600.

4.3.3. 4-[(2-Bromophenyl)-(4-chloro-2,3,5,6-tetrafluoro-phenylamino)-methyl]-3-methyl-6-methylene-cyclohex-2-enone (11g). Colorless liquid (23 mg, 37%); IR (film) υ 1664 cm^{-1} (C=O); ^1H NMR ($CDCl_3$, TMS, 300 MHz) δ 2.10 (3H, s, Me), 2.94–2.97 (2H, m), 3.12–3.19 (1H, m), 5.13–5.18 (1H, m, CH), 5.33 (1H, d, J=10.8 Hz, NH), 5.45 (1H, s), 5.50 (1H, s), 5.91 (1H, s), 7.08–7.14 (1H, m, Ar), 7.27–7.35 (1H, m, Ar), 7.50–7.63 (2H, m, Ar); ^{19}F NMR ($CDCl_3$, TMS, 282 MHz) δ −143.6 (2F, d, $^3J_{FF}$=26.5 Hz), −156.5 (2F, d, $^3J_{FF}$=21.7 Hz); ^{13}C NMR ($CDCl_3$, TMS, 75.44 MHz) δ 19.6, 36.3, 51.4, 60.4, 100.9, 117.4, 123.2, 125.8, 127.5, 127.7, 129.0, 133.1, 133.2, 138.6 (m, $^1J_{CF}$=252.0 Hz), 141.1, 142.7, 144.4 (m, $^1J_{CF}$=237.9 Hz), 154.2, 200.0; MS (EI) *m/e* 487 (M^+, 0.84), 366 (M^+−121, 32.48), 210 (M^+−277, 27.63), 122 (M^+−365, 100), 107 (M^+−380, 44.84); HRMS (MALDI) *m/e* calcd for $C_{21}H_{15}NOF_4ClBrNa$ $(M+Na)^+$ 509.9859, found 509.9879.

4.3.4. 6-[(2-Bromophenyl)-(4-chloro-2,3,5,6-tetrafluoro-phenylamino)-methyl]-3-methyl-4-methylene-cyclohex-2-enone (12g). Colorless solid (26 mg, 42%); mp 127 °C; IR (film) υ 1652 cm^{-1} (C=O); ^1H NMR ($CDCl_3$, TMS, 300 MHz) δ 2.05 (3H, s, Me), 2.61–2.69 (1H, m), 2.82–2.89 (1H, m), 3.15–3.22 (1H, m), 5.42 (2H, s), 5.62 (1H, brs, NH), 5.70–5.75 (1H, m), 5.96 (1H, s), 7.08–7.54 (4H, m, Ar); ^{19}F NMR ($CDCl_3$, TMS, 282 MHz) δ −143.7 (2F, d, $^3J_{FF}$=16.9 Hz), −157.2 (2F, d, $^3J_{FF}$=19.5 Hz); ^{13}C NMR ($CDCl_3$, TMS, 75.44 MHz) δ 19.7, 32.6, 49.8, 58.2, 100.0, 117.2, 124.0, 125.8, 127.7, 128.4, 128.8, 129.2, 133.4, 138.6 (m, $^1J_{CF}$=252.0 Hz), 138.9, 140.9, 144.4 (m, $^1J_{CF}$=237.9 Hz), 154.6, 198.6; MS (EI) *m/e* 487 (M^+, 1.68), 366 (M^+−121, 34.82), 210 (M^+−277, 34.17), 122 (M^+−365, 100), 107 (M^+−380, 37.99); HRMS (MALDI) *m/e* calcd for $C_{21}H_{15}NOF_4ClBrNa$ $(M+Na)^+$ 509.9859, found 509.9883.

4.3.5. 4-[(2-Chlorophenyl)-(4-chloro-2,3,5,6-tetrafluoro-phenylamino)-methyl]-3-methyl-6-methylene-cyclohex-2-enone (11h). Colorless liquid (21 mg, 48%); IR (film) υ 1664 cm^{-1} (C=O); ^1H NMR ($CDCl_3$, TMS, 300 MHz) δ 2.03 (3H, s, Me), 2.76–2.84 (2H, m), 3.00–3.07 (1H, m),

5.07–5.12 (1H, m), 5.18 (1H, brs, NH), 5.34 (1H, s), 5.43 (1H, s), 5.84 (1H, s), 7.10–7.27 (3H, m, Ar), 7.45–7.48 (1H, m, Ar); ^{19}F NMR ($CDCl_3$, TMS, 282 MHz) δ −143.4 (2F, d, $^3J_{FF}$=22.8 Hz), −156.3 (2F, d, $^3J_{FF}$=19.5 Hz); ^{13}C NMR ($CDCl_3$, TMS, 75.44 MHz) δ 14.1, 35.9, 51.4, 58.2, 100.0, 117.6, 125.7, 127.0, 127.4, 128.4, 128.8, 129.9, 132.9, 138.2, 138.4 (m, $^1J_{CF}$=228.1 Hz), 140.9, 144.5 (m, $^1J_{CF}$=253.7 Hz), 154.3, 200.0; MS (EI) *m/e* 443 (M^+, 0.65), 322 (M^+-121, 39.24), 210 (M^+-233, 28.66), 122 (M^+-321, 100), 107 (M^+-336, 49.97); HRMS (MALDI) *m/e* calcd for $C_{21}H_{15}NOF_4Cl_2$ Na $(M+Na)^+$ 466.0365, found 466.0383.

4.3.6. 6-[(2-Chlorophenyl)-(4-chloro-2,3,5,6-tetrafluorophenylamino)-methyl]-3-methyl-4-methylene-cyclohex-2-enone (12h). Colorless solid (22 mg, 49%); mp 122 °C; IR (film) υ 1648 cm^{-1} (C=O); ^{1}H NMR ($CDCl_3$, TMS, 300 MHz) δ 1.96 (3H, s, Me), 2.51–2.60 (1H, m), 2.75–2.82 (1H, m), 3.08–3.15 (1H, m), 5.33 (2H, s), 5.61–5.67 (1H, m), 5.85 (1H, s), 5.71 (1H, brs, NH), 7.06–7.30 (4H, m, Ar); ^{19}F NMR ($CDCl_3$, TMS, 282 MHz) δ −143.5 (2F, d, $^3J_{FF}$=23.4 Hz), −157.1 (2F, d, $^3J_{FF}$=22.8 Hz); ^{13}C NMR ($CDCl_3$, TMS, 75.44 MHz) δ 14.1, 32.9, 49.9, 56.9, 100.0, 117.2, 125.6, 127.2, 128.3, 128.8, 128.9, 130.0, 133.7, 137.2, 138.3 (m, $^1J_{CF}$=242.4 Hz), 140.9, 144.4 (m, $^1J_{CF}$=246.05 Hz), 154.7, 198.4; MS (EI) *m/e* 443 (M^+, 1.36), 322 (M^+-121, 42.69), 210 (M^+-233, 27.45), 122 (M^+-321, 100), 107 (M^+-336, 43.94); HRMS (MALDI) *m/e* calcd for $C_{21}H_{15}NOF_4Cl_2Na$ $(M+Na)^+$ 466.0365, found 466.0403.

4.4. X-ray crystal structure data of compounds (3a) and (12h)

Intensity data were collected at 293(2) K on Bruker P4 diffractometer with graphite monochromator and Mo Kα radiation (λ=0.71073 Å). The structure was solved by direct methods and explained using Fourier techniques. The nonhydrogen atoms were refined anisotropically, hydrogen atoms were included but not refined. The final cycle of full matrix least-squares refinement was based on F^2, respectively. All calculations were performed using SHELXS-97 and SHELXL-97 programs. X-ray data for compounds **3a** and **12h** are listed in Table 5.

Table 5. X-ray data collection and processing parameters for compounds **3a** and **12h**

Compound	**3a** CCDC 260807	**12h** CCDC 260807
Formula	$C_{21}H_{13}F_{10}NO_2$	$C_{21}H_{15}Cl_2F_4NO$
Size (mm)	0.27×0.22×0.16	0.51×0.44×0.41
Space group	*P*2 (1)/*C*	*P*2 (1)/*n*
Crystal system	Monoclinic	Monoclinic
a (Å)	9.748(2)	19.201(1)
b (Å)	25.814(5)	8.1936(5)
c (Å)	9.028(2)	26.4171(17)
α (°)	90.00	90.00
β (°)	111.00(3)	110.6980(10)
γ (°)	90.00	90.00
V (Å^3)	2120.9(7)	3887.8(4)
Z-value	4	8
D_{calc} (g cm^{-3})	1.570	1.518
μ (mm^{-1})	0.16	0.384
T (K)	293(2)	293(2)
2θ range (°)	3–55	4–54
Total reflections	6033	22164
F(000)	1008	1808
Independent reflections	4872	8430
R_{int}	0.0343	0.0756
$I>2\sigma$ (*I*)	1535	8430
Parameters	360	533
Goodness of fit	0.904	0.875
Final *R* indices ($I>2\sigma$ (*I*))	0.2000; 0.0530	0.0476; 0.1122
R indices (all data)	0.1479; 0.1062	0.0889; 0.1264

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