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SF_5-Enolates in Ti(IV)-Mediated Aldol Reactions

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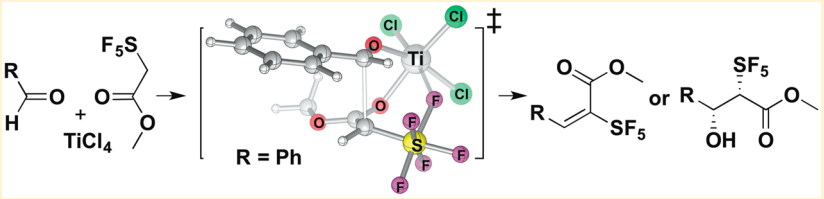
Supporting Information



ABSTRACT: The F···Ti bonding in the transition structures determines high *trans*- and *syn*-diastereoselectivities for aldol reactions of SF_5-acetates with aldehydes in the presence of $TiCl_4$ in the non-nucleophilic solvent CH_2Cl_2. Such bonding is canceled in nucleophilic solvents where opposite *cis*-stereochemistry is observed. The potential of thus obtained stereoisomeric SF_5-aryl acrylates as dipolarophiles in the preparation of SF_5-containing heterocycles is demonstrated.

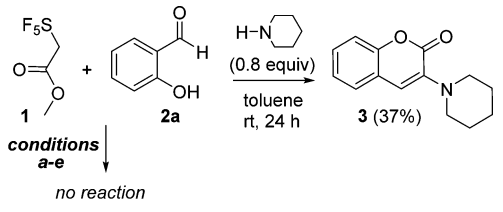
Pentafluoro-λ^6-sulfanyl-containing organic compounds attract substantial interest with respect to their potential in organic electronics, pharmaceuticals, and agrochemicals,[1] as well as due to the constantly growing impact of organofluorides in up-to-date materials.[2] The most recent development is associated with the availability of the SF_5-building blocks that were previously difficult to access. However, the number of SF_5-containing aliphatic compounds is still limited.[1c,e]

Enolization−aldolization reactions are one of the most versatile, century-old, carbon−carbon bond forming tools for natural product synthesis and drug discovery.[3] The studies of stereoselective aldol reactions are a particularly important area examining enolate geometries, the influence of mediators, and reaction conditions. The lack of methods for α-functionalization of the α-SF_5 carbonyl compounds may be attributed to instability of the starting material when reactions can be accompanied by the elimination of the SF_5 group under basic or nucleophilic conditions.[4] Despite the progress in aldol addition reactions of fluorinated[5] and trifluoromethylated enolates,[6] the number of reports on reactions through SF_5-enolates is limited. The first approach toward α-functionalized α-SF_5 carboxyl compounds is based on Ireland−Claisen rearrangement.[7] Recently, the first examples of *anti*-diastereoselective boron-mediated aldol additions of α-SF_5-esters were reported,[8] where the observed *anti*-diastereoselectivities were explained[8b] through the Zimmerman−Traxler model.[9] However, as the configuration of the resulting aldol not necessary is associated with the structure of the intermediate enolate,[3] the mechanistic interpretations of the stereochemical outcome still require rigorous scrutiny. Herein, we found experimental and computational evidence that the stereochemistry of the aldol reactions of model SF_5-acetate promoted by $TiCl_4$ is determined by the coordination of titanium with the SF_5 moiety of the enol in *Z*-configuration.

The stability of SF_5 intermediates plays a key role[4a,b,7,8] in the reactivity of the enols generated from α-SF_5-acetates. The reaction of methyl SF_5-acetate (**1**)[10] with salicylaldehyde (**2a**) leads to complete elimination of the SF_5 group, and only product **3** and starting **2a** were isolated from the reaction mixture (Scheme 1). No reaction was observed in the presence of various soft mediators[3] where **1** and **2a** almost fully recovered (Scheme 1).

$TiCl_4$ in the presence of tertiary amines has been shown to be an effective system for enolization−aldolization reactions,[3c] especially of α-fluorinated, and α-trifluoromethylated acetates[11] where Ti···F interactions in the transition structures not only result in high diastereoselectivities but also prevent the fluorine group loss.[11c,d]

Scheme 1. Reactivity of Methyl SF_5-Acetate



[a]Neat, Al_2O_3, 12 h, rt. [b]Ph_3P, toluene, 80 °C, 6 h. [c]Et_3N (2 equiv), CH_2Cl_2, 2 weeks, rt. [d]$TiCl_4$ (2 equiv), 6 h, rt. [e]BF_3-Et_2O (2 equiv), 24 h, rt.

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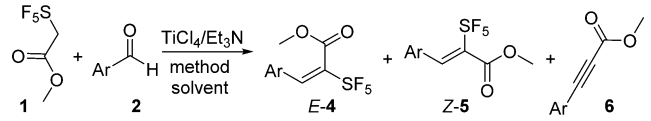
Table 1. Aldol Condensation of 1 with Aldehydes 2b−f



entry	Ar (2)	method[a]/t (h)/T (°C)/solvent	4/5/6 (%)[b]	4/5 ratio[c]
1	C_6H_5 (**b**)	***A***/4/−30/THF		27/73
2	C_6H_5 (**b**)	***A***/4/rt/THF	19/5/38	62/38
3	C_6H_5 (**b**)	***B***/4/0/THF	21/44/21	32/68
4	C_6H_5 (**b**)	***C***/4/0/THF	17/50/4	28/72
5	3,5-ClC_6H_3 (**c**)	***C***/2/0/THF	12/7/-	29/71
6	4-anisyl (**d**)	***C***/8/0/THF	30/50/7	37/63
7	2-furyl (**e**)	***C***/3/0/THF	44/47/-	44/56
8[d]	4-$NO_2C_6H_4$ (**f**)	***C***/2/0/THF		
9	C_6H_5 (**b**)	***B***/6/0/CH_2Cl_2	58/-/-	91/9
10	C_6H_5 (**b**)	***D***/6/0/CH_2Cl_2	79/-/-	90/10
11	3,5-ClC_6H_3 (**c**)	***B***/6/0/CH_2Cl_2	49/-/2	95/5
12	3,5-ClC_6H_3 (**c**)	***D***/4/0/CH_2Cl_2	68/-/-	96/4
13	4-anisyl (**d**)	***D***/12/0/CH_2Cl_2	93/-/-	97/3
14	2-furyl (**e**)	***D***/6/0/CH_2Cl_2	54/3	94/6
15	4-$NO_2C_6H_4$ (**f**)	***D***/4/0/CH_2Cl_2	50/-/3	

[a]***A***: Et_3N (4 equiv) was slowly added to **1**/$TiCl_4$ (2 equiv, 1 M, CH_2Cl_2)/**2** (1.5 equiv)/solvent; ***B***: Et_3N (4 equiv) was added in one portion to **1**/$TiCl_4$ (2 equiv, 1 M, CH_2Cl_2)/**2** (1.5 equiv)/solvent; ***C***: Et_3N (4 equiv) was added in one portion to **1**/$TiCl_4$ (neat, 2 equiv)/**2** (1.5 equiv)/THF; ***D***: $TiCl_4$ (2 equiv, 1 M, CH_2Cl_2) was added to **1**/**2** (1.2 equiv)/Et_3N (3 equiv)/solvent. [b]Isolated yields of pure individual products. [c]Observed by ^1H and ^{19}F NMR of crude mixtures after workup. [d]See the Experimental Section.

We assumed that involvement of the SF_5 group into the Ti···F interaction may enhance stability of the intermediates in the aldol reactions of the SF_5-enol generated from **1**. We found that, when an excess of Et_3N was slowly added to a suspension of **1**, **2b**, and $TiCl_4$ (1 M in CH_2Cl_2) in THF at −30 °C, the SF_5-containing products were observed only as admixtures. The aldehyde **2b** was almost fully recovered after workup, and the starting SF_5-ester **1** was not detected by NMR (Table 1, entry 1). In contrast, the reaction with neat $TiCl_4$ occurs with the formation of two isomeric SF_5-olefins *E*-**4b** and *Z*-**5b** isolated in low yields together with acetylene derivative **6b** as a main product (entry 2). The fact that olefins *E*-**4b** and *Z*-**5b** were not changed while exposed in a mixture of $TiCl_4$/Et_3N, as well as with excess of Et_3N in THF, shows that acetylene **6b** forms independently.

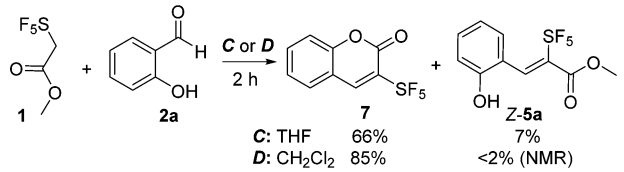
The yields of the SF_5-containing products increase if an excess of Et_3N is added in one portion into the vigorously stirred mixture of the starting materials in THF at 0 °C (entry 3, Table 1). The use of neat $TiCl_4$ in THF[12] slightly increases the formation of the *Z*-**5b** isomer (entry 4). Similar results were obtained in reactions of aromatic aldehydes **2c−e** carried out under the same conditions (entries 5−7). In all cases, *Z*-**5b−e** isomers were formed as the main products.

However, the reactions of aldehydes **2c,f**, which contain electron-withdrawing groups (Cl, NO_2) in the aromatic ring, proceed nonselectively, giving complex mixtures of products (entries 5 and 8). Along with the formation of *E*-**4**, *Z*-**5**, and **6**, aldol adducts of the SF_5-ester **1** (*syn*/*anti*-ArCH(OH)-CH-(SF_5)CO_2CH_3) were observed in up to 10% yield by NMR. In both reactions, about half of the starting aldehydes were recovered in spite of full consumption of the ester **1**.

Utilization of CH_2Cl_2 as a solvent displays dramatic changes in the stereochemical outcome and results in the formation of the α-SF_5-α,β-unsaturated esters **4** with *E*-configuration (Table 1, entries 9−15). Even the reactions of the aldehydes **2c,f**, which react nonselectively under similar conditions in THF (entries 5 and 8), now proceed selectively. These results are in sharp contrast to the aldol condensations of CF_3-,[11a] CN-,[13] halo-acetates (halo = F, Cl, Br, I),[11b] and other acetic acid derivatives[14] that give *Z*-derivatives almost exclusively in the $TiCl_4$/Et_3N system.

To our surprise, a reaction of salicylaldehyde (**2a**) with the SF_5-ester **1** in the $TiCl_4$/Et_3N system in both solvents, THF and CH_2Cl_2 (methods ***C*** and ***D***, Table 1), results in the formation of 3-SF_5-substituted coumarin **7**, which was isolated in good yields (Scheme 2). The 3-SF_5-coumarin **7** is likely the

Scheme 2. Synthesis of 3-SF_5-coumarin 7



product of the aldol condensation of **1** with **2a**, giving the corresponding α-SF_5-α,β-unsaturated *E*-**4** ester, followed by the intramolecular *trans*-esterification.

Unfortunately, the aldol condensation of isovaleraldehyde (**2g**) chosen as an example of aliphatic aldehyde was accompanied by tarring, which likely occurs due to polymerization of the olefins formed in the presence of Lewis acid. Only the *Z*-SF_5-olefin **5g** was isolated in ca. 3% yield when the reaction of **2g** with **1** was carried out in THF.

The configuration of *E*-**4** and *Z*-**5**-isomers was unambiguously confirmed by an X-ray crystallographic study of coumarin **7** and olefin *Z*-**5d** (see the SI) and helped to interpret unexpected interactions observed in the ^1H NMR spectra of *Z*-**5**-olefins. For instance, in the ^1H NMR spectra of *Z*-**5** products, the distinct quintet of vinyl proton at 7.78−7.95 ppm resulting from a $^4J_{HF}$-coupling (2.9−4.3 Hz) on four equatorial fluorine atoms of the SF_5 group is observed. This quintet is more

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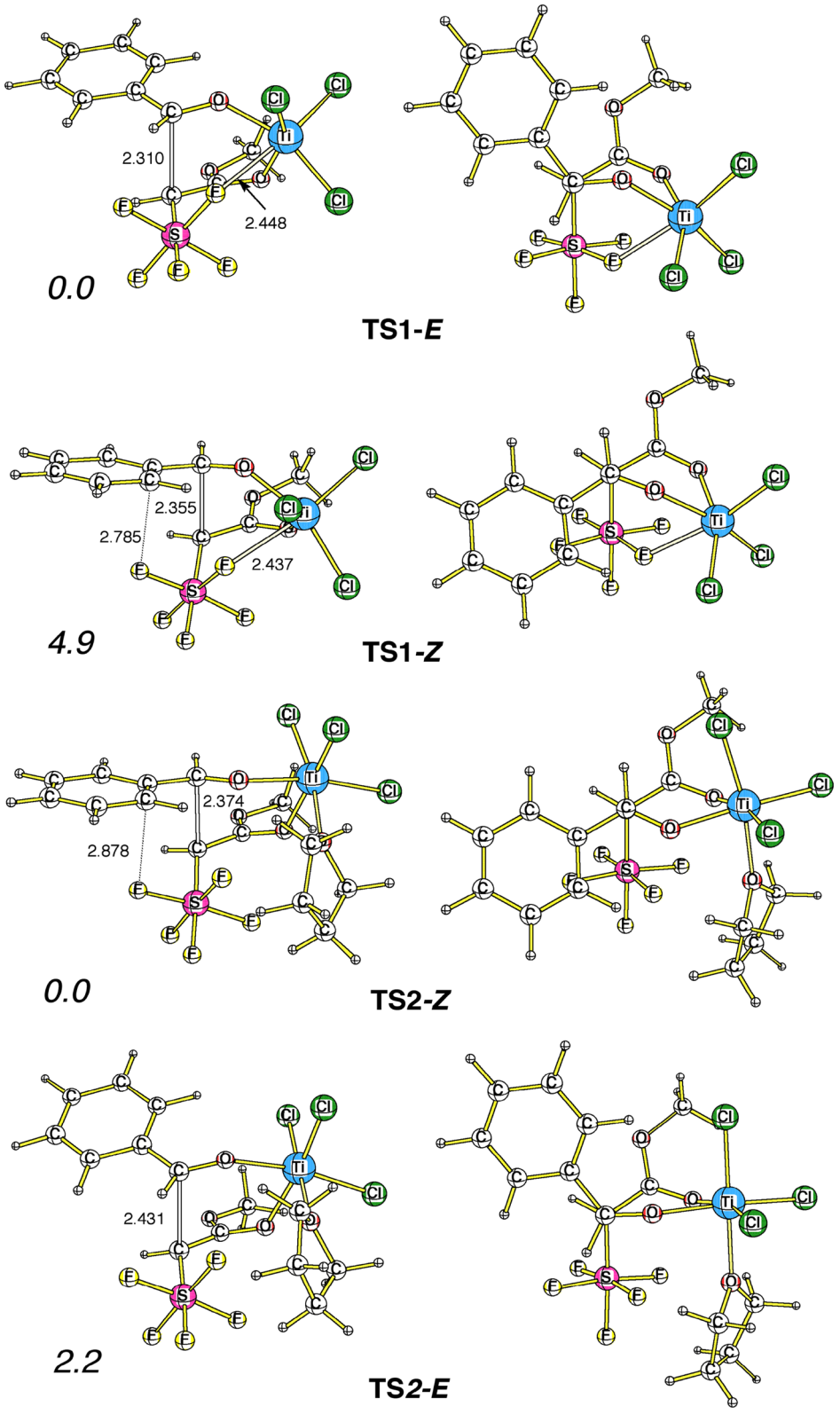

Figure 1. M06-2X/cc-pVDZ optimized transition structures for the Ti(IV)-promoted aldol condensations of *Z*-SF_5-enolate of **1** and aldehyde **2b** in the absence (**TS1**) and in the presence (**TS2**) of THF (critical bond distances in Å and relative ΔH^{298} in kcal mol^{-1} (italic), two projections shown for each TS).

downfield shifted, comparing to a singlet (7.16−7.56 ppm) of the same proton in *E*-**4**-structures.

In order to understand the stereoselectivity observed experimentally, we optimized the transition structures for the Ti(IV)-promoted aldol condensations between the *Z*-enolate of **1** and aldehyde **2b**.[15] To account for intermolecular interactions properly, we utilize the DFT method M06-2X[16] in combination with the correlation consistent basis set cc-

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pVDZ. The addition occurs through the transition structures **TS1** where strong F···Ti bonding[17] is present from the Atoms-in-Molecules analysis[18] (Figure 1).[19] Among four transition structures located (only two are shown for clarity in two projections each), the **TS1-*E*** is 4.9 kcal/mol lower in energy than the next lowest **TS1-*Z***. Despite **TS1-*E*** being partially eclipsed (around the newly formed CC bond), substantial steric repulsions between the phenyl and SF_5 groups (the closest C···F contact is 2.78 Å) increase the energy of staggered conformation **TS1-*Z***. Relative barriers for the cyclization are in accord with the experiment in poorly coordinating solvent CH_2Cl_2 where *trans*-olefin *E*-**4** resulting from **TS1-*E*** dominates in the reaction mixture (Table 1, entries 9 and 10).

The complexation of Ti(IV) with THF[12] causes substantial structural changes switching off the F···Ti interactions in more flexible transition structures **TS2**, where **TS2-*Z*** is now ca. 2 kcal/mol more stable than **TS2-*E*** (other conformeric TSs are higher in energy). The shortest C···F contact between the phenyl and SF_5 groups in **TS2-*Z*** increases to 2.88 Å, thus reducing the repulsion. Despite the absence of such interactions, **TS2-*E*** is 2.2 kcal/mol less stable than **TS2-*Z*** because of partial eclipse (around the forming CC bond). Higher stability of **TS2-*Z*** is in accord with the experiment where *cis*-olefin *Z*-**5** predominantly forms. The relatively small energetic gap between **TS2-*Z*** and **TS2-*E*** leads to the formation of substantial amounts of *trans*-product *E*-**4** (Table 1, entries 3 and 4).

Additionally, the antiperiplanar orientation of the hydrogen atom of the aldehyde fragment and the SF_5 group in the product derived from **TS2-*Z*** may facilitate Et_3N-mediated E_N2-elimination of the SF_5 group, yielding acetylenes **6**. This side reaction is more operative for the electron-poor aldehydes **2c,f**.

To the best of our knowledge, the aldol condensation between ester **1** and aldehydes **2** mediated by $TiCl_4$ represents the first one-pot synthetic approach toward a family of α-SF_5-α,β-unsaturated carbonyl derivatives that are potentially useful in the chemistry of biologically active compounds,[20] especially coumarines,[21] and new materials.[13] To appreciate the reactivity of SF_5-olefins *E*-**4** and *Z*-**5**, we tested several reactions typical for electron-poor α,β-unsaturated carbonyl compounds.[20a,b,22] Under the Michael reaction conditions with hydrazine hydrate, piperidine, NaCN/AcOH system, and TMSCN, the SF_5 group loss was observed (see the Experimental Section). However, the electron-poor double bond of *E*-**4b** and *Z*-**5b** shows appreciable reactivity in the classical 1,3-dipolar cycloaddition reaction with an azomethine ylide synthone *N*-(methoxymethyl)-*N*-[(trimethylsilyl)methyl]-*N*-benzylamine (**8**),[23] where SF_5-pyrrolidines **9** and **10** were formed in good yields (Scheme 3).

The ability of *E*-**4** and *Z*-**5** SF_5-olefins to undergo the cycloaddition reactions opens convenient ways to various SF_5-substituted heterocycles.[4a,23,24]

The formation of aldol adducts, methyl β-hydroxy-α-SF_5-β-arylpropanoates, as byproducts in the condensation of **1** with aldehydes **2c,f** (entries 5 and 8, Table 1) prompted us to study the $TiCl_4$-mediated reactions toward synthesis of corresponding α-SF_5-aldols. We assumed that the strong F···Ti bonding in **TS1** (Figure 1) for the condensation in CH_2Cl_2 may provide high diastereoselectivities similarly to the aldol addition of a Ti-enolate of α-CF_3 ketones with aldehydes.[11d] The enolization of the ester **1** did not proceed in THF, likely due to strong complexation of $TiCl_4$ with two THF-molecules and its insolubility at low temperatures. In contrast, in CH_2Cl_2, we indeed found that the enolate **I** (Table 2) can be generated *in situ* by adding only a slight excess of Et_3N to a mixture of α-SF_5-ester **1** and $TiCl_4$.

Scheme 3. 1,3-Dipolar Cycloaddition of *E*-4b and *Z*-5b

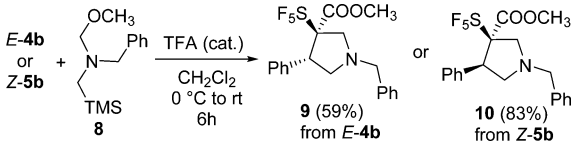
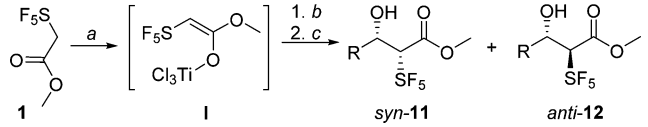


Table 2. Aldol Addition of 1 with Aldehydes 2



entry	R (**2**)	time (h)	**11** (%)[a]	*syn*/*anti*[b]
1	2-HO-C_6H_4 (**a**)	10	68	93/7
2	C_6H_5 (**b**)	7	71	98/2
3	3,5-ClC_6H_3 (**c**)	7	79	only *syn*
4	4-anisyl (**d**)	10	48	65/35
5	2-furyl (**e**)	10	52	only *syn*
6	4-$NO_2C_6H_4$ (**f**)	7	80	only *syn*
7	isobutyl (**g**)	10	82	94/6

[a]Isolated yields; entries 1, 4, 7: yields of **11**/**12** mixtures. [b]The *syn*-**11**/*anti*-**12** ratio was detected by ^{19}F and ^{1}H NMR of the reaction mixtures.

The enolate **I** is stable enough at −78 °C, and further addition of aldehydes **2a**−**e** and $TiCl_4$ results in the formation of β-hydroxy-α-SF_5-propanoates (**11** and **12**, Table 2) in good yields and high *syn*-diastereoselectivity. The later was confirmed through the X-ray crystallographic study of *syn*-**11f** (see the SI), and from spin−spin couplings of $^{\alpha}H-^{\beta}H$ protons observed in ^{1}H NMR spectra of *syn*-**11** ($^{3}J_{\alpha,\beta}$ = 8.4−9.6 Hz) comparing to *gauche*-$^{\alpha}H-^{\beta}H$ interaction in *anti*-**12** ($^{3}J_{\alpha,\beta}$ = 4.4 Hz).[8b] This transformation is suitable both for aromatic (**2a**−**f**) and for aliphatic (**2g**) aldehydes (Table 2).

In conclusion, we have developed an efficient synthetic approach toward α-SF_5-α,β-unsaturated carbonyl compounds (**4**, **5**, **7**) and *syn*-β-hydroxy-α-SF_5-propanoates (**11**) from aldehydes and methyl SF_5-acetate in the $TiCl_4$/Et_3N system. We demonstrated that the stereochemical outcome of the aldol reactions of SF_5-acetates is strongly determined by F···M bonding between the SF_5 group and Ti(IV) in the transition structures. This results in almost exclusive formation of *trans*-olefins and *syn*-aldols in poorly coordinating solvents like CH_2Cl_2. The nucleophilic THF switches off such intramolecular F···Ti coordination, giving predominantly *cis*-olefins. Thus, previously studied[8] formation of *anti*-aldols in the boron-mediated reactions of SF_5-acetates is not necessarily associated with participation of *E*-SF_5-enolate in the Zimmerman−Traxler transition state. The use of $TiCl_4$ as a mediator of aldol reactions gives access to stereoisomeric α-SF_5 esters, potentially useful for medicinal and material applications.

EXPERIMENTAL SECTION

General Information. All reagents from commercial suppliers were used without purification. ^{1}H NMR spectra were recorded on 400 or 401 MHz instruments. ^{13}C and ^{19}F NMR spectra were

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recorded on 100 or 101 MHz, and 376 or 377 MHz instruments, respectively. Chemical shifts are reported relative to TMS, $CHCl_3$ (δ = 7.26 ppm, ^{1}H NMR), $CDCl_3$ (δ = 77.16 ppm, ^{13}C NMR), and CCl_3F (^{19}F NMR) as internal standards. Column chromatography was performed on silica gel 60 (230−400 mesh). All nonaqueous reactions were carried out in an inert atmosphere of dry argon or nitrogen. THF and CH_2Cl_2 were preliminarily dried. HRMS (EI) spectra were obtained on a double-focusing mass spectrometer at 70 eV.

Methyl 2-(pentafluoro-λ^6-sulfanyl)acetate (**1**) was prepared according to the previously reported method.[10] The spectral data of **6f**,**c**,[25a] **6b**,[25b] and **6d**,[25c] correspond with the literature data.

General Procedures of the Aldol Condensations. *3-(Piperidin-1-yl)-2H-chromen-2-one (**3**).* 0.17g (2.00 mmol) of piperidine was added at 0 °C to a mixture of **2a** (0.30 g, 2.45 mmol) and **1** (0.49 g, 2.45 mmol) in 2 mL of toluene. The mixture was stirred for 24 h at room temperature; then it was filtered through a thin layer of SiO_2 eluting with CH_2Cl_2. Volatiles were removed under reduced pressure. The product **3** (0.21g, 37%) was crystallized from an *n*-hexane/CH_2Cl_2 mixture. Yellow crystals; mp = 134−135 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35 (dd, J_{HH} = 7.6, 1.3 Hz, 1H), 7.33−7.26 (m, 2H), 7.19 (td, J_{HH} = 7.5, 1.5 Hz, 1H), 6.81 (s, 1H), 3.13 (dd, J_{HH} = 5.4, 5.1 Hz, 4H), 1.75 (m, 4H), 1.61 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 159.0, 150.3, 139.0, 127.9, 126.2, 124.4, 120.7, 119.9, 119.9, 116.0, 50.8, 25.7, 24.3. HRMS (EI) Calcd for $C_{14}H_{15}NO_2$ $[M]^+$: 229.10973, found: 229.10989.

Method *A*. To a mixture of **2b** (0.35 g, 3.30 mmol) and **1** (0.44 g, 2.20 mmol) in 10 mL of THF was added a $TiCl_4$ solution (4.42 mL, 4.42 mmol, 1 M in CH_2Cl_2) at 0 °C. In 1−2 min, 0.895 g (8.85 mmol) of Et_3N was added slowly (15 min) to the mixture at the appropriate temperature (rt or −30 °C). Then, the cooling bath was removed, and the mixture was stirred for 4 h at room temperature. CH_2Cl_2 (30 mL) was added, and the resulting mixture was washed with water (3 × 5 mL). After drying over sodium sulfate and evaporating the solvent, the crude mixture was separated by column chromatography on SiO_2 (*n*-hexane/CH_2Cl_2 = 3/1), giving *E*-**4b** (0.120 g, 19%), *Z*-**5b** (0.320 g, 5%), and **6** (0.134 g, 38%).

Method *B*. Reactions were carried out similarly to method ***A*** in THF or CH_2Cl_2 solution. Et_3N was added to a vigorously stirred mixture of **2**/**1**/$TiCl_4$ (1 M, CH_2Cl_2) in one portion through a syringe at 0 °C. The cooling bath was removed in 15 min, and the mixture was stirred for 4−6 h at room temperature. The reaction mixture was worked up similarly to method ***A***. The products *E*-**4b**, *Z*-**5b**, **6**, and *E*-**4c** were isolated by column chromatography on SiO_2 (*n*-hexane/CH_2Cl_2 = 3/1).

Method *C*. THF (12 mL) was added slowly at 0 °C to neat $TiCl_4$ (0.8 g, 4.23 mmol) (exothermic). To the vigorously stirred yellow suspension of the $TiCl_4$/THF complex in THF were added **2b** (0.33 g, 3.11 mmol) and **1** (0.42 g, 2.10 mmol) quickly at 0 °C. In 1 min, Et_3N (0.85 g, 8.40 mmol) was added in one portion through a syringe to the mixture. The cooling bath was removed in 15 min, and the mixture was stirred for 4 h at room temperature. CH_2Cl_2 (50 mL) was added, and the resulting mixture was washed with water (3 × 10 mL). After drying over sodium sulfate, the solvent was evaporated to obtain the crude mixture of products that were separated by column chromatography on SiO_2 (*n*-hexane/CH_2Cl_2 = 3/1), giving *E*-**4b** (0.103 g, 17%), *Z*-**5b** (0.303 g, 50%), and **6** (0.013 g, 4%).

Method *D*. To a vigorously stirred mixture of **2b** (0.264 g, 2.49 mmol), **1** (0.42 g, 2.10 mmol), and Et_3N (0.637 g, 6.30 mmol) in CH_2Cl_2 (12 mL) was added a solution of $TiCl_4$ (4.23 mL, 1 M in CH_2Cl_2, 4.23 mmol) over 5 min at 0 °C. The cooling bath was removed in 15 min, and the mixture was stirred for 6 h at room temperature. CH_2Cl_2 (20 mL) was added, and the reaction mixture was washed with water (3 × 10 mL). After drying over sodium sulfate and evaporating the solvent, *E*-**4b** was isolated in 79% yield (0.478 g) by column chromatography on SiO_2 (*n*-hexane/CH_2Cl_2 = 1/1).

*Methyl (E)-2-(Pentafluoro-λ^6-sulfanyl)-3-phenylacrylate (E-**4b**).* Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.51 (s, 1H, H-C═CSF_5), 7.44−7.36 (m, 3H), 7.35−7.28 (m, 1H), 3.77 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 163.2 (quin, ^3J = 2.1 Hz, C═O), 146.1 (quin, ^2J = 17.4 Hz, C-SF_5), 137.2 (quin, ^3J = 6.1 Hz), 131.1, 130.8, 129.1, 128.7, 53.5 (OCH_3); ^{19}F NMR (376 MHz, $CDCl_3$): δ 81.4 (9 lines, A-part), 63.6 (d, $^2J_{FF}$ = 150.8 Hz, B_4-part); HRMS (EI) Calcd for $C_{10}H_9F_5O_2S$ $[M]^+$: 288.02434, found: 288.02329.

*Methyl (Z)-2-(Pentafluoro-λ^6-sulfanyl)-3-phenylacrylate (Z-**5b**).* Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.93 (quin, $^4J_{HF}$ = 4.3 Hz, 1H, H-C═CSF_5), 7.45−7.35 (m, 3H), 7.35−7.28 (m, 2H), 3.91 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 162.7 (quin, ^3J = 3.2 Hz, C═O), 145.2 (quin, ^2J = 16.5 Hz, C-SF_5), 145.2, 143.5 (quin, ^3J = 3.7 Hz), 133.5, 129.3, 128.4, 127.6 (quin, ^5J = 2.4 Hz), 53.8 (OCH_3); ^{19}F NMR (376 MHz, $CDCl_3$): δ 79.9 (9 lines, A-part), 69.9 (dm, $^2J_{FF}$ = 151.8 Hz, B_4-part); HRMS (EI) Calcd for $C_{10}H_9F_5O_2S$ $[M]^+$: 288.02434, found: 288.02575.

*Methyl (E)-3-(3,4-Dichlorophenyl)-2-(pentafluoro-λ^6-sulfanyl)-acrylate (E-**4c**).* *E*-**4c** was obtained from 0.398 g (1.99 mmol) of **1** by method ***D*** in 68% yield (0.482 g) after column chromatography (*n*-hexane/Et_2O = 10/1). Yellowish oil; ^{1}H NMR (401 MHz, $CDCl_3$): δ 7.47 (d, J_{HH} = 8.4 Hz, 1H), 7.42 (d, J_{HH} = 2.1 Hz, 1H), 7.39 (s, 1H, H-C═CSF_5), 7.15 (dd, J_{HH} = 8.4, 2.1 Hz, 1H), 3.79 (s, 1H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 162.6 (d, ^3J = 2.3 Hz, C═O), 147.6 (quin, ^2J = 17.8 Hz, C-SF_5), 135.1, 134.7 (quin, ^3J = 6.3 Hz), 133.6, 131.2, 131.1, 130.5, 127.7, 53.8 (OCH_3); ^{19}F NMR (377 MHz, $CDCl_3$): δ 79.30 (9 lines, A-part), 63.57 (d, $^2J_{FF}$ = 151.0 Hz, B_4-part); HRMS (EI) Calcd for $C_{10}H_7Cl_2F_5O_2S$ $[M]^+$: 355.94640, found: 355.94550.

*Methyl (Z)-3-(3,4-Dichlorophenyl)-2-(pentafluoro-λ^6-sulfanyl)-acrylate (Z-**5c**).* *Z*-**5c** was obtained from 0.598 g (2.99 mmol) of **1** by method ***C*** in 7% yield (0.075 g) after column chromatography (*n*-hexane/CH_2Cl_2 = 3/1). Yellowish oil; ^{1}H NMR (401 MHz, $CDCl_3$): δ 7.78 (quin, $^4J_{HF}$ = 4.2 Hz, 1H, H-C═CSF_5), 7.47 (d, J_{HH} = 8.4 Hz, 1H), 7.37 (s, 1H), 7.12 (d, J_{HH} = 8.4 Hz, 1H), 3.90 (s, 3H, OCH_3); ^{13}C NMR (101 MHz, $CDCl_3$): δ 162.1 (quin, ^3J = 3.1 Hz, C═O), 146.7 (quin, ^2J = 15.8 Hz, C-SF_5), 140.6 (quin, ^3J = 3.6 Hz), 133.7, 133.2, 132.9, 130.5, 129.4 (quin, ^5J = 2.1 Hz), 126.8 (quin, ^5J = 2.5 Hz), 54.0 (OCH_3); ^{19}F NMR (377 MHz, $CDCl_3$): δ 80.5 (9 lines, A-part), 71.12 (dm, $^2J_{FF}$ = 152.2 Hz, B_4-part); HRMS (EI) Calcd for $C_{10}H_7Cl_2F_5O_2S$ $[M]^+$: 355.94640, found: 355.94814.

*Methyl (E)-3-(4-Methoxyphenyl)-2-(pentafluoro-λ^6-sulfanyl)-acrylate (E-**4d**).* *E*-**4d** was obtained from 0.369 g (1.84 mmol) of **1** by method ***D*** in 93% yield (0.547 g) after column chromatography (CH_2Cl_2), as well as from 0.496 g (2.48 mmol) of **1** by method ***C*** in 30% yield (0.237 g) after column chromatography (*n*-hexane/CH_2Cl_2 = 1/1). Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.42 (s, 1H, H-C═CSF_5), 7.27 (dm, J_{HH} = 9.2 Hz, 2H), 6.90 (dm, J_{HH} = 8.9 Hz, 2H), 3.83 (s, 3H), 3.81 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 163.7 (quin, J = 2.0 Hz, C═O), 161.8, 144.1 (quin, ^2J = 17.3 Hz, C-SF_5), 136.9 (quin, ^3J = 6.0 Hz), 130.8, 123.2, 114.7, 55.5, 53.6; ^{19}F NMR (376 MHz, $CDCl_3$): δ 81.4 (9 lines, A-part), 64.1 (d, $^2J_{FF}$ = 150.7 Hz, B_4-part); HRMS (EI) Calcd for $C_{11}H_{11}F_5O_3S$ $[M]^+$: 318.03491, found: 318.03474.

*Methyl (Z)-3-(4-Methoxyphenyl)-2-(pentafluoro-λ^6-sulfanyl)-acrylate (Z-**5d**).* *Z*-**5d** was obtained from 0.496 g (2.48 mmol) of **1** by method ***C*** in 50% yield (0.394 g) after column chromatography (*n*-hexane/CH_2Cl_2 = 1/1). White crystals; mp = 64−65 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.84 (quin, $^4J_{HF}$ = 4.0 Hz, 1H, H-C═CSF_5), 7.49 (dm, J_{HH} = 8.8 Hz, 2H), 6.92 (d, J_{HH} = 8.9 Hz, 2H), 3.89 (s, 3H), 3.84 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 163.1 (quin, ^3J = 3.4 Hz, C═O), 161.5, 143.7 (quin, ^3J = 3.6 Hz), 142.0 (quin, ^2J = 16.9 Hz, C-SF_5), 132.1 (quin, ^5J = 3.2 Hz), 124.7, 114.1, 55.5, 53.6; ^{19}F NMR (376 MHz, $CDCl_3$): δ 81.4 (9 lines, A-part), 68.8 (dm, $^2J_{FF}$ = 152.0 Hz, B_4-part); HRMS (EI) Calcd for $C_{11}H_{11}F_5O_3S$ $[M]^+$: 318.03491, found: 318.03484.

*Methyl (E)-3-(Furan-2-yl)-2-(pentafluoro-λ^6-sulfanyl)acrylate (E-**4e**).* *E*-**4e** was obtained from 0.250 g (1.25 mmol) of **1** by method ***D*** in 54% yield (0.188 g) after column chromatography (*n*-hexane/CH_2Cl_2 = 1/1), as well as from 0.240 g (1.20 mmol) of **1** by method ***C*** in 44% yield (0.147 g) after column chromatography (*n*-hexane/Et_2O = 5/1). Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.51 (d, J_{HH} = 1.8 Hz, 1H), 7.16 (s, 1H, H-C═CSF_5), 6.73 (d, J_{HH} = 3.5 Hz, 1H), 6.50 (dd, J_{HH} = 3.5, 1.8 Hz, 1H), 3.93 (s, 3H, OCH_3); ^{13}C NMR (101 MHz, $CDCl_3$): δ 163.1 (quin, ^3J = 2.1 Hz, C═O), 146.5, 145.8, 142.3 (quin, ^2J = 18.6 Hz, C-SF_5), 123.1 (quin, ^3J = 6.5 Hz), 118.6, 112.7, 53.42

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(OCH_3); ^{19}F NMR (376 MHz, $CDCl_3$): δ 80.8 (9 lines, A-part), 64.6 (d, $^2J_{FF}$ = 151.0 Hz, B_4-part); HRMS (EI) Calcd for $C_8H_7F_5O_3S$ $[M]^+$: 278.00361, found: 278.00429.

*Methyl (Z)-3-(Furan-2-yl)-2-(pentafluoro-λ⁶-sulfanyl)acrylate (Z-**5e**).* *Z*-**5e** was obtained from 0.240 g (1.20 mmol) of **1** by method ***C*** in 47% yield (0.157 g) after column chromatography (*n*-hexane/Et_2O = 5/1). White crystals; mp = 54−55 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 7.95 (quin, $^4J_{HF}$ = 2.9 Hz, 1H, H-C═CSF_5), 7.69 (d, J_{HH} = 1.6 Hz, 1H), 7.36 (bs, 1H), 6.62 (dd, J_{HH} = 3.7, 1.6 Hz, 1H), 3.87 (s, 3H, OCH_3); ^{13}C NMR (101 MHz, $CDCl_3$): δ 162.2 (quin, ^3J = 3.0 Hz, C═O), 148.0, 147.4, 136.4 (quin, ^2J = 19.3 Hz, C-SF_5), 131.2 (quin, ^3J = 3.2 Hz), 123.0 (d, ^5J = 4.4 Hz), 114.0, 53.5 (OCH_3); ^{19}F NMR (376 MHz, $CDCl_3$): δ 80.7 (9 lines, A-part), 64.9 (dm, $^2J_{FF}$ = 151.3 Hz, B_4-part); HRMS (EI) Calcd for $C_8H_7F_5O_3S$ $[M]^+$: 278.00306, found: 278.00402.

*Methyl (E)-3-(4-Nitrophenyl)-2-(pentafluoro-λ⁶-sulfanyl)acrylate (E-**4f**).* *E*-**4f** was obtained from 0.399 g (1.99 mmol) of **1** by method ***D*** in 50% yield (0.333 g) after column chromatography (*n*-hexane/Et_2O = 5/1). When the same reaction was carried out at −78 °C for 4 h, the aldol adduct *syn*-**11f** was observed as a main product formed in 15−18% yield according to ^1H and ^{19}F NMR spectra of the reaction mixture. The olefin *E*-**4f** was observed in ca. 10% yield. Yellow oil; ^1H NMR (400 MHz, $CDCl_3$): δ 8.26 (dm, *J* = 8.7 Hz, 2H), 7.56 (s, 1H, H-C═CSF_5), 7.51 (dm, *J* = 8.7 Hz, 2H), 3.77 (s, 3H, OCH_3); ^{13}C NMR (101 MHz, $CDCl_3$): δ 162.3 (quin, ^3J = 2.0 Hz, C═O), 149.0 (quin, ^2J = 18.8 Hz, C-SF_5), 148.8, 137.6, 134.9 (quin, ^3J = 6.2 Hz), 129.5, 124.3, 54.0 (OCH_3); ^{19}F NMR (376 MHz, $CDCl_3$): δ 78.6 (9 lines, A-part), 63.4 (d, $^2J_{FF}$ = 151.1 Hz, B_4-part); HRMS (EI) Calcd for $C_{10}H_8F_5NO_4S$ $[M]^+$: 333.00942, found: 333.01115.

2f (0.47 g, 3.11 mmol) reacts with **1** (0.42 g, 2.10 mmol) in THF (method ***C***), giving a complex mixture of products, where *E*-**4f** (4%), *syn*-**11f** (8%), *anti*-**12f** (2%), **6f** (25%), and methyl (*Z*)-3-hydroxy-3-(4-nitrophenyl)acrylate[26] (**13**, 7%) were observed. Yields of these products were appreciated by ^1H and ^{19}F NMR spectra.

*Methyl (Z)-5-Methyl-2-(pentafluoro-λ⁶-sulfanyl)hex-2-enoate (Z-**5g**).* *Z*-**5g** was obtained from 0.333 g (1.66 mmol) of **1** by method ***C*** in 3% yield (0.012 g) after column chromatography (*n*-hexane/CH_2Cl_2 = 1/1). An appropriate sample for HRSM was not obtained due to difficulties in separation, and low yield of *Z*-**5g**. The structure was assigned based on characteristic multiples in ^1H NMR aroused from interactions with the SF_5 group observed also for other *Z*-**5** products. Yellow oil; 0.009 g (<3%, ∼80% of purity by NMR, from 0.333 g, 1.66 mmol of **1**); ^1H NMR (400 MHz, $CDCl_3$): δ 7.18 (m, $^4J_{HF}$ = 4.6 Hz, 1H, H-C═CSF_5), 3.83 (s, 3H, OCH_3), 2.49 (m, 2H), 1.84 (sep, $^3J_{HH}$ = 6.7 Hz, 1H), 0.97 (d, $^3J_{HH}$ = 6.7 Hz, 6H, $2CH_3$); ^{13}C NMR (101 MHz, $CDCl_3$): δ 161.9 (quin, ^3J = 3.3 Hz, C═O), 150.0 (quin, ^3J = 2.6 Hz), 145.8 (d, ^2J = 14.5 Hz, C-SF_5), 53.4 (OCH_3), 39.5 (quin, ^4J = 2.9 Hz), 28.5, 22.5; ^{19}F NMR (376 MHz, $CDCl_3$): δ 81.8 (9 lines, A-part), 67.61 (dm, $^2J_{FF}$ = 150.6 Hz, B_4-part).

*3-(Pentafluoro-λ⁶-sulfanyl)-2H-chromen-2-one (**7**).* **7** was obtained from 0.464 g (2.32 mmol) of **1** by method ***D*** in 85% yield (0.543 g) after crystallization of the crude product from a CH_2Cl_2/*n*-hexane mixture, as well as from 0.442 g (2.21 mmol) of **1** by method ***C*** in 66% yield (0.397 g) after column chromatography (*n*-hexane/CH_2Cl_2 = 3/1). White crystals; mp = 121−122 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 8.37 (s, 1H, H-C═CSF_5), 7.70 (dd, J_{HH} = 7.5, 1.6 Hz, 1H), 7.65 (dd, J_{HH} = 7.5, 1.4 Hz, 1H), 7.34−7.44 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 154.7, 152.9 (quin, ^3J = 1.4 Hz, C═O), 146.0 (quin, ^3J = 4.6 Hz), 139.6 (quin, ^2J = 17.8 Hz, C-SF_5), 135.2, 130.2, 125.6, 116.9, 116.4; ^{19}F NMR (376 MHz, $CDCl_3$): δ 79.1 (9 lines, A-part), 64.13 (d, $^2J_{FF}$ = 152.7 Hz, B_4-part); HRMS (EI) Calcd for $C_9H_5F_5O_2S$ $[M]^+$: 271.99249, found: 271.99219.

*Methyl (Z)-3-(2-Hydroxyphenyl)-2-(pentafluoro-λ⁶-sulfanyl)-acrylate (Z-**5a**).* *Z*-**5a** was obtained from 0.442 g (2.21 mmol) of **1** by method ***C*** in 7% yield (0.046 g) after column chromatography (*n*-hexane/CH_2Cl_2 = 3/1). Yellow oil; ^1H NMR (400 MHz, $CDCl_3$): δ 7.93 (quin, $^4J_{HF}$ = 4.3 Hz, 1H, H-C═CSF_5), 7.31−7.23 (m, 2H), 6.96 (td, J_{HH} = 7.5, 1.0 Hz, 1H), 6.82 (dd, J_{HH} = 8.6, 1.0 Hz, 1H), 5.54 (bs, 1H, OH), 3.90 (s, 3H, OCH_3); ^{13}C NMR (101 MHz, $CDCl_3$): δ 162.9 (quin, ^3J = 3.0 Hz, C═O), 152.7, 146.4 (quin, ^2J = 15.6 Hz, C-SF_5), 140.2 (quin, *J* = 3.5 Hz), 131.0, 128.8 (quin, *J* = 3.7 Hz), 120.9, 120.7, 115.4, 53.8 (OCH_3); ^9F NMR (376 MHz, $CDCl_3$): δ 80.0 (9 lines, A-part), 69.3 (dm, $^2J_{FF}$ = 152.5 Hz, B_4-part); HRMS (EI) Calcd for $C_{10}H_9F_5O_3S$ $[M]^+$: 304.01926, found: 304.01850.

Preparation of 9 and 10. TFA (0.07 mL, 1 M in CH_2Cl_2) was added to a stirred mixture of *E*-**4b** (0.154 g, 0.67 mmol) and **8** (0.192 g, 0.81 mmol) at 0 °C. The cooling bath was removed in 10−15 min, and the mixture was stirred for 6 h at room temperature. CH_2Cl_2 (20 mL) was added, and the mixture was washed with saturated aqua solution of $NaHCO_3$ (2 × 10 mL), then with water (3 × 10 mL). After drying over sodium sulfate, the solvent was evaporated, giving crude **9** mainly contaminated by *E*-**4b**. **9** was obtained in 59% yield (0.168 g) by column chromatography on SiO_2 (*n*-hexane/Et_2O = 1/1). In a similar manner, **10** was obtained in 83% yield (0.216 g) from 0.141 g (0.62 mmol) of *Z*-**5b**. It was difficult to obtain elemental analysis, as well as HRMS, of clean **9** and **10** due to their instability; the NMR spectra provided in the Supporting Information give evidence of the compounds' purities.

*Methyl (3,4)-1-Benzyl-3-(pentafluoro-λ⁶-sulfanyl)-4-phenylpyrrolidine-3-carboxylate (**9**).* Yellowish oil; ^1H NMR (400 MHz, $CDCl_3$): δ 7.43 (dm, J_{HH} = 8.3 Hz, 2H), 7.36 (tm, J_{HH} = 7.5 Hz, 4H), 7.28 (m, 3H), 7.21 (m, 1H), 4.24 (dd, $^3J_{HH}$ = 7.6, 1.6 Hz, 1H, C**H**Ph), 4.07 (d, $^2J_{HH}$ = 10.5 Hz, 1H), 3.78 (d, $^2J_{AB}$ = 13.2 Hz, 1H, CH_2Ph), 3.69 (d, $^2J_{AB}$ = 13.2 Hz, 1H, CH_2Ph), 3.07 (s, 3H, OCH_3), 3.04 (d, $^2J_{HH}$ = 10.5 Hz, 1H), 2.98 (bd, $^2J_{AB}$ = 8.8 Hz, 1H), 2.90 (dd, $^2J_{AB}$ = 8.8 Hz, $^3J_{HH}$ = 7.6 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 165.9 (C═O), 143.3, 138.1, 128.6, 128.5, 128.4, 128.4, 127.4, 127.2, 103.6 (quin, ^2J = 6.0 Hz, C-SF_5), 61.7, 61.1 (quin, ^3J = 4.5 Hz, CH_2), 59.7 (CH_2Ph), 52.3 (OCH_3), 52.3 (quin, ^3J = 2.9 Hz, CHPh); ^{19}F NMR (376 MHz, $CDCl_3$): δ 84.5 (9 lines, A-part), 57.88 (d, $^2J_{FF}$ = 144.3 Hz, B_4-part).

*Methyl (3,4)-1-Benzyl-3-(pentafluoro-λ⁶-sulfanyl)-4-phenylpyrrolidine-3-carboxylate (**10**).* Yellow oil; ^1H NMR (400 MHz, $CDCl_3$): δ 7.56 (d, J_{HH} = 7.4 Hz, 2H), 7.38−7.24 (m, 8H), 4.39 (dd, $^3J_{HH}$ = 6.0, 1.7 Hz, 1H, C**H**Ph), 3.93 (s, 3H, OCH_3), 3.91 (dm, $^2J_{AB}$ = 10.8 Hz, 1H), 3.88 (d, $^2J_{AB}$ = 13.5 Hz, 1H, CH_2Ph), 3.78 (d, $^2J_{AB}$ = 13.5 Hz, 1H, CH_2Ph), 3.70 (d, $^2J_{AB}$ = 10.8 Hz, 1H), 3.04 (dd, $^2J_{AB}$ = 9.7 Hz, $^3J_{HH}$ = 1.7 Hz, 1H), 2.93 (dd, $^2J_{AB}$ = 9.7 Hz, $^3J_{HH}$ = 6.2 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 168.4 (C═O), 141.1, 138.8, 129.8, 128.6, 128.4, 128.3, 127.4, 127.3, 99.8 (m, ^2J = 4.0 Hz, C-SF_5), 60.3 (CH_2Ph), 59.1, 56.2 (m, *J* = 4.3 Hz, CH_2), 54.2 (OCH_3), 52.40 (**C**HPh); ^{19}F NMR (376 MHz, $CDCl_3$): δ 82.3 (quin, $^2J_{FF}$ = 146.3 Hz, 1F), 65.6 (d, $^2J_{FF}$ = 146.3 Hz, 4F).

*Methyl 1-Benzyl-4-phenyl-2,5-dihydro-1H-pyrrole-3-carboxylate (**17**).* The products **9** and **10** decompose after 2 weeks of storage at room temperature, giving the product of a formal $[HSF_5]$ elimination **17**. The mixtures obtained after storage of **9** (0.150 g, 0.35 mmol) and **10** (0.180 g, 0.43 mmol) were diluted in CH_2Cl_2 (15 mL), and combined. The CH_2Cl_2 solution was washed with a saturated aqua solution of $NaHCO_3$ (2 × 10 mL), then with water (1 × 10 mL), and dried with Na_2SO_4. The solvent was evaporated. **17** was isolated in 49% yield (0.113 g) by column chromatography on SiO_2 (CH_2Cl_2/EtOAc = 10/1).

Yellow oil; ^1H NMR (400 MHz, $CDCl_3$): δ 7.53−7.19 (m, 10H), 3.92 (m, 4H, $2CH_2$), 3.85 (s, 2H, CH_2Ph), 3.64 (s, 3H, OCH_3); ^{13}C NMR (101 MHz, $CDCl_3$): δ 164.5, 150.9, 138.7, 133.8, 128.9, 128.8, 128.6, 128.2, 128.0, 127.4, 125.6, 65.3, 61.5, 60.1, 51.4; MS (EI, *m*/*z*): 291 ($C_{19}H_{17}NO_2^+$, 100), 260 ($C_{19}H_{17}NO_2-OCH_3^+$, 32), 232 ($C_{19}H_{17}NO_2-CO_2CH_3^+$, 7), 91($C_6H_5CH_2^+$, 80); Anal. Calcd for $C_{19}H_{19}NO_2$: C, 77.79; H, 6.53; N, 4.77. Found: C, 77.58; H, 6.51; N, 4.75.

*Michael Reactions of SF_5-olefins E-**4b** and Z-**5b**.*

1. Hydrazine monohydrate (0.019 g, 0.38 mmol) was added at 0 °C to a stirred solution of *Z*-**5b** (0.11 g, 0.38 mmol) in EtOH (3 mL). The mixture was stirred for 6 h at room temperature. Volatiles were removed in vacuo. SF_5 products and **6b** were not found in the mixture by ^1H and ^{19}F NMR.
2. Piperidine (0.008 g, 0.098 mmol) was added at 0 °C to a stirred solution of *E*-**4b** (0.014 g, 0.049 mmol) in CH_2Cl_2 (1 mL). The

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mixture was stirred for 2 h at 0 °C, and then for 12 h at room temperature. The resulting mixture was passed through a short column of SiO_2 (CH_2Cl_2/AcOEt = 5/1). After evaporation of the solvents, methyl *anti*-2,3-dipiperidino-3-phenyl propanoate[27] (**14**) was obtained in 63% yield (0.010 g).

3. TMSCN (0.031 g, 0.312 mmol) was added at −45 °C to a stirred solution of *Z*-**5b** (0.074 g, 0.257 mmol) in CH_2Cl_2 (5 mL). The cooling bath was removed in 1 h, and the mixture was stirred at room temperature for 5 days. After washing of the reaction mixture with aqua $NaHCO_3$ (3 × 2 mL), the CH_2Cl_2 layer was dried with Na_2SO_4, and then the solvent was evaporated in vacuo, giving only 0.07 g of the starting *Z*-**5b.** The same reaction carried out in the presence of $TiCl_4$ (0.26 mL, 1.0 M in CH_2Cl_2) led to full degradation of the starting olefin in 6 h.
4. A solution of NaCN (0.074 g, 1.5 mmol) in water (1 mL) was added at 0 °C to a stirred solution of *Z*-**5b** (0.108 g, 0.375 mmol) and acetic acid (0.045g, 0.750 mmol) in THF (5 mL). The cooling bath was removed after 15 min, and the reaction mixture was stirred for 24 h at room temperature. 10 mL of CH_2Cl_2 was added, and the mixture was washed with water (3 × 3 mL). The organic layer was dried with Na_2SO_4, and all volatiles were evaporated in vacuo. The resulting mixture was separated by column chromatography on SiO_2 (CH_2Cl_2), giving methyl (*Z*)-3-cyano-3-phenylacrylate[28] (40% yield, 0.028 g) and methyl (*E*)-3-cyano-3-phenylacrylate[25] (26% yield, 0.018 g).

General Procedure for the Aldol Addition. A solution of $TiCl_4$ (1.04 mL, 1 M in CH_2Cl_2, 1.04 mmol) was added at 0 °C to a stirred solution of **1** (0.173 g, 0.86 mmol) in 8 mL of CH_2Cl_2. In 5 min, the mixture was cooled down to −78 °C, and then Et_3N (0.122g, 1.21 mmol) was slowly added. In 15 min, to the dark-brown reaction mixture was added **2b** (0.11 g, 1.04 mmol), and then $TiCl_4$ (1.04 mL, 1 M in CH_2Cl_2, 1.04 mmol). The resulting mixture was stirred for 7 h at −78 °C, the cooling bath was removed, and at about −50 °C, 2 mL of water was added. The light-yellow mixture was stirred for a while; an additional 10 mL of CH_2Cl_2 was added. The CH_2Cl_2 layer was separated, washed with water (4 × 5 mL), and dried over sodium sulfate. The solvent was evaporated, giving a crude *syn*-**11b**/*anti*-**12b** mixture (98/2 according to ^{19}F NMR) contaminated mainly with the starting aldehyde. Pure *syn*-**11b** was isolated in 71% yield (0.187 g) by column chromatography on SiO_2 (*n*-hexane/CH_2Cl_2 = 1/1). When the aldol reaction of **1** and **2b** was carried out in a similar manner at −78 °C in THF, both starting materials were almost fully recovered.

*Methyl 3-Hydroxy-3-(2-hydroxyphenyl)-2-(pentafluoro-λ⁶-sulfanyl)propanoate (syn-**11a**).* *syn*-**11a**/*anti*-**12a** (93/7) were obtained from 0.337 g (1.68 mmol) of **1** in 68% yield (0.442 g) by crystallization of the crude reaction mixture from CH_2Cl_2 at −30 °C. White crystals; mp = 109−111 °C; *syn*-**11a**: ^1H NMR (400 MHz, $CDCl_3$): δ 7.21 (td, J_{HH} = 7.8, 1.7 Hz, 1H), 7.11 (dd, J_{HH} = 7.7, 1.5 Hz, 1H), 6.88 (td, J_{HH} = 7.6, 1.1 Hz, 1H), 6.83 (d, J_{HH} = 8.2 Hz, 1H), 6.82 (s, 1H, HOAr), 5.52 (dd, $^3J_{HH}$ = 9.4, 6.0 Hz, 1H, **H**COH), 5.07 (dquin, $^3J_{HH}$ = 9.4 Hz, $^3J_{HF}$ = 6.0 Hz, 1H, $HCSF_5$), 3.59 (d, $^3J_{HH}$ = 6.0 Hz, 1H, OH), 3.51 (s, 3H, OCH_3); ^{13}C NMR (101 MHz, $CDCl_3$): δ 164.6 (quin, ^3J = 3.3 Hz, C═O), 154.7, 130.7, 129.9, 122.8, 120.9, 117.6, 87.5 (quin, ^2J = 8.7 Hz, HC-SF_5), 73.5 (quin, ^3J = 2.4 Hz, HC-OH), 53.2 (OCH_3); ^{19}F NMR (376 MHz, $CDCl_3$): δ 80.5 (9 lines, A-part), 66.7 (dd, $^2J_{FF}$ = 146.2, $^3J_{FH}$ = 6.0 Hz, B_4-part); HRMS (EI) Calcd for $C_{10}H_{11}F_5O_4S$ $[M]^+$: 322.02982, found: 322.03021.

*Methyl 3-Hydroxy-2-(pentafluoro-λ⁶-sulfanyl)-3-phenylpropanoate (syn-**11b**).* Colorless oil; ^1H NMR (401 MHz, $CDCl_3$): δ 7.34 (m, 5H), 5.42 (dd, $^3J_{HH}$ = 9.4, 3.2 Hz, 1H, **H**COH), 4.77 (dquin, $^3J_{HH}$ = 9.4 Hz, $^3J_{HF}$ = 5.8 Hz, 1H, $HCSF_5$), 3.41 (s, 3H, OCH_3), 2.67 (d, $^3J_{HH}$ = 3.2 Hz, 1H, OH); ^{13}C NMR (101 MHz, $CDCl_3$): δ 164.1 (quin, ^3J = 3.2 Hz, C═O), 138.2 (quin, ^4J = 1.6 Hz), 129.4, 128.8, 127.6, 89.9 (quin, ^2J = 8.9 Hz, HC-SF_5), 73.6 (quin, ^3J = 2.4 Hz, HC-OH), 53.0 (OCH_3); ^{19}F NMR (376 MHz, $CDCl_3$): δ 81.7 (9 lines, A-part), 67.1 (dd, $^2J_{FF}$ = 146.7 Hz, $^3J_{FH}$ = 5.7 Hz, B_4-part); Anal. Calcd for $C_{10}H_{11}F_5O_3S$: C, 39.22; H, 3.62. Found: C, 39.10; H, 3.61.

*Methyl 3-(3,4-Dichlorophenyl)-3-hydroxy-2-(pentafluoro-λ⁶-sulfanyl)propanoate (syn-**11c**).* *syn*-**11c** was obtained from 0.345 g (1.72 mmol) of **1** in 79% yield (0.608 g) by column chromatography (*n*-hexane/CH_2Cl_2 = 3/1). Yellowish oil; ^1H NMR (400 MHz, $CDCl_3$): δ 7.49 (m, 1H), 7.42 (dd, *J* = 8.3, 1.9 Hz, 1H), 7.21 (dm, *J* = 8.3 Hz, 1H), 5.39 (dd, $^3J_{HH}$ = 9.1, 4.8 Hz, 1H, **H**COH), 4.68 (d, $^3J_{HH}$ = 9.1 Hz, $^3J_{HF}$ = 5.8 Hz, 1H, $HCSF_5$), 3.54 (s, 3H, OCH_3), 2.99 (bm, 1H, OH); ^{13}C NMR (101 MHz, $CDCl_3$): δ 164.2 (quin, ^3J = 3.0 Hz), 138.4, 133.6, 133.1, 130.8, 129.7, 127.0, 89.2 (quin, ^2J = 9.2 Hz), 72.5 (quin, ^3J = 2.1 Hz), 53.4 (OCH_3); ^{19}F NMR (376 MHz, $CDCl_3$): δ 80.1 (9 lines, A-part), 66.7 (dd, $^2J_{FF}$ = 146.8 Hz, $^3J_{FH}$ = 5.1 Hz, B_4-part); HRMS (EI) Calcd for $C_{10}H_9Cl_2F_5O_3S$ $[M]^+$: 373.95696, found: 373.95667.

*Methyl 3-Hydroxy-3-(4-methoxyphenyl)-2-(pentafluoro-λ⁶-sulfanyl)propanoates (syn-**11d**/anti-**12d**).* *syn*-**11d** and *anti*-**12d** were isolated as a mixture in 48% yield (0.259 g) by column chromatography on SiO_2 (CH_2Cl_2) of the crude reaction mixture obtained from 0.32 g (1.60 mmol) of **1** and 0.262 g (1.92 mmol) of **2d**. Yellowish oil; ^1H NMR (401 MHz, $CDCl_3$): δ 7.28 (dm, *J* = 8.7 Hz, 2H-*syn*), 7.22 (dm, *J* = 8.7 Hz, 2H-*anti*), 6.88 (dm, *J* = 8.7 Hz, 2H-*anti*), 6.85 (dm, *J* = 8.7 Hz, 2H-*syn*), 5.44 (dd, $^3J_{H\text{-}HO}$ = 8.5 Hz, $^3J_{HH}$ = 4.4 Hz, 1H, **H**COH-*anti*), 5.38 (dd, $^3J_{HH}$ = 9.6 Hz, $^3J_{H\text{-}HO}$ 3.0 Hz, 1H, **H**COH-*syn*), 4.73 (dquin, $^3J_{HH}$ = 9.6 Hz, $^3J_{HF}$ = 6.0 Hz, 1H, $HCSF_5$-*syn*), 4.63 (dquin, $^3J_{HH}$ = 4.4 Hz, $^3J_{HF}$ = 6.4 Hz, 1H, $HCSF_5$-*anti*), 4.07 (d, *J* = 8.5 Hz, 1H, OH-*anti*), 3.79 (s, 3H, Ar-OCH_3-*anti*), 3.78 (s, 3H, Ar-OCH_3-*syn*), 3.72 (s, 3H, $COOCH_3$-*anti*), 3.44 (s, 3H, $COOCH_3$-*syn*), 2.59 (d, $^3J_{HH}$ = 3.0 Hz, 1H, OH-*syn*); ^{13}C NMR (101 MHz, $CDCl_3$): δ 166.0 (quin, ^3J = 3.1 Hz, C═O-*anti*), 164.1 (quin, ^3J = 3.2 Hz, C═O-*syn*), 160.2 (*syn*), 159.8 (*anti*), 131.1 (quin, ^4J = 1.0 Hz, *anti*), 130.4 (quin, ^4J = 1.2 Hz, *syn*), 128.9 (*syn*), 127.4 (*anti*), 114.3 (*anti*), 114.2 (*syn*), 90.1 (quin, ^2J = 8.5 Hz, $HCSF_5$-*syn*), 86.6 (quin, ^2J = 8.9 Hz, $HCSF_5$-*anti*), 73.1 (d, ^3J = 2.4 Hz, CHOH-*syn*), 72.1 (d, ^3J = 3.1 Hz, HCOH-*anti*), 55.3 (*anti*), 55.3 (*syn*), 53.5 ($COO\mathbf{CH_3}$-*anti*), 52.9 ($COO\mathbf{CH_3}$-*syn*); ^{19}F NMR (376 MHz, $CDCl_3$): δ 81.9 (9 lines, A-part-*syn*), 80.8 (9 lines, A-part-*anti*), 66.8 (dd, $^2J_{FF}$ = 146.4, $^3J_{FH}$ = 5.8 Hz, B_4-part-*syn*), 66.5 (dd, $^2J_{FF}$ = 147.2 Hz, $^3J_{FH}$ = 6.2 Hz, B_4-part-*anti*); HRMS (EI) Calcd for $C_{11}H_{13}F_5O_4S$ $[M]^+$: 336.04492, found: 336.04221.

*Methyl 3-(Furan-2-yl)-3-hydroxy-2-(pentafluoro-λ⁶-sulfanyl)propanoate (syn-**11e**).* *syn*-**11e** was obtained from 0.379 g (1.89 mmol) of **1** in 52% yield (0.292 g) by column chromatography (CH_2Cl_2). Yellowish oil, stabile in solution for >3 days (eluent or $CDCl_3$), as well as on SiO_2; the neat product polymerizes spontaneously, giving a black solid residuum (*exothermic!*); ^1H NMR (400 MHz, $CDCl_3$): δ 7.39 (dd, *J* = 1.5, 1.1 Hz, 1H), 6.40−6.28 (m, 2H), 5.51 (dd, $^3J_{HH}$ = 9.5 Hz, $^3J_{H\text{-}OH}$ = 5.0 Hz, 1H, **H**COH), 4.88 (dquin, $^3J_{HH}$ = 9.6 Hz, $^3J_{HF}$ = 6.0 Hz, 1H, $HCSF_5$), 3.61 (s, 3H, OCH_3), 2.74 (d, ^3J = 5.0 Hz, 1H, OH); ^{13}C NMR (101 MHz, $CDCl_3$): δ 164.2 (m, C═O), 150.8 (m), 143.3, 110.8, 109.2, 87.0 (quin, ^2J = 10.1 Hz, HC-SF_5), 67.1 (HC-OH), 53.3 (OCH_3); ^{19}F NMR (376 MHz, $CDCl_3$): δ 80.0 (9 lines, A-part), 66.3 (dd, $^2J_{FF}$ = 146.8 Hz, $^3J_{FH}$ = 5.9 Hz, B_4-part); MS (EI, *m*/*z*): 296 (M^+, 9), 169 ($M^+ - SF_5$, 34), 151 ($M^+ - SF_5 - H_2O$, 19), 97 ($C_5H_5O_2^+$, 100).

*Methyl 3-Hydroxy-3-(4-nitrophenyl)-2-(pentafluoro-λ⁶-sulfanyl)propanoate (syn-**11f**).* *syn*-**11f** was isolated in 80% yield (0.535 g) by crystallization from CH_2Cl_2 of the crude reaction mixture obtained from 0.381 g (1.90 mmol) of **1** and 0.345 g (2.28 mmol) of **2f** added as a CH_2Cl_2 (3 mL) solution. White crystals; mp = 136−137 °C; ^1H NMR (401 MHz, $CDCl_3$): δ 8.23 (d, $^3J_{HH}$ = 8.8 Hz, 2H), 7.60 (d, $^3J_{HH}$ = 8.8 Hz, 2H), 5.57 (dd, ^3J = 8.4, 3.4 Hz, 1H, **H**COH), 4.76 (dquin, $^3J_{HH}$ = 8.4 Hz, $^3J_{HF}$ = 5.7 Hz, 1H, $HCSF_5$), 3.56 (s, 3H, OCH_3), 3.11 (d, $^3J_{HH}$ = 3.4 Hz, 1H, OH); ^{13}C NMR (101 MHz, $CDCl_3$): δ 164.4 (C═O), 148.3, 145.1, 128.7, 123.9, 88.8 (quin, ^2J = 9.6 Hz, HC-SF_5), 72.7 (quin, ^3J = 2.5 Hz, HC−OH), 53.6 (OCH_3); ^{19}F NMR (377 MHz, $CDCl_3$): δ 79.88 (9 lines, A-part), 67.27 (dd, $^2J_{FF}$ = 146.6 Hz, $^3J_{FH}$ = 5.5 Hz, B_4-part); MS (EI, *m*/*z*): 224 ($M^+ - SF_5$, 66), 152 ($M^+ - SF_5CHCO_2CH_3$, 100); Anal. Calcd for $C_{10}H_{10}F_5NO_5S$: C, 34.20; H, 2.87; N, 3.99. Found: C, 34.09; H, 2.86; N, 3.97.

*Methyl 3-Hydroxy-5-methyl-2-(pentafluoro-λ⁶-sulfanyl)hexanoate (syn-**11g**).* *syn*-**11g** was obtained from 0.432 g (2.16 mmol)

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of **1** in 82% yield (0.510 g) by column chromatography (*n*-hexane/CH_2Cl_2 = 1/1). Yellowish oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.47−4.30 (m, 2H, **H**CSF$_5$-C**H**OH), 3.82 (s, 1H, OCH_3), 2.49 (bs, 1H, OH), 1.98−1.87 (m, 1H, **H**C(CH_3)$_2$), 1.58−1.48 (m, 1H, A-part, CH_2), 1.18−1.10 (m, 1H, B-part, CH_2), 0.94 (d, $^3J_{HH}$ = 6.6 Hz, 3H, CH_3), 0.92 (d, $^3J_{HH}$ = 6.6 Hz, 3H, CH_3); ^{13}C NMR (101 MHz, $CDCl_3$): δ 165.4 (quin, ^3J = 3.2 Hz, C=O), 89.7 (quin, ^2J = 8.0 Hz, HCSF$_5$), 69.3 (quin, ^3J = 2.0 Hz, HCOH), 53.4 (OCH_3), 43.1 (quin, J = 1.4 Hz, CH_2), 24.6 (s, CH), 23.7 (CH_3), 21.0 (CH_3); ^{19}F NMR (376 MHz, $CDCl_3$): δ 81.1 (9 lines, A-part), 66.6 (dd, $^2J_{FF}$ = 148.4 Hz, $^3J_{FH}$ = 3.3 Hz, B_4-part); MS (EI, m/z): 229 (M^+ − *i*-Pr, 80), 159 (M^+ − SF_5, 35), 69 ($C_5H_9^+$, 100), 59 ($CO_2CH_3^+$, 35); Anal. Calcd for $C_8H_{15}F_5O_3S$: C, 33.57; H, 5.28. Found: C, 33.49; H, 5.26.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b00946.

X-ray crystallographic data of **11f** (CCDC 1454608) (CIF)

X-ray crystallographic data of **7** (CCDC 1454609) (CIF)

X-ray crystallographic data of *Z*-**5d** (CCDC 1454610) (CIF)

X-ray crystallographic data of **3** (CCDC 1454611) (CIF)

Experimental details, copies of ^{1}H, ^{13}C, ^{19}F, 2D NMR spectra of products, projections of X-ray structures of *Z*-**5d**, **7**, **11f**, interpretation of intermolecular interactions in the crystal packings, the AIM molecular graphs, bond-topological and atomic properties for **TS1-*E*** and **TS1-*Z*** (PDF)

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Notes

The authors declare no competing financial interest.

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