MICHAEL ADDITION REACTIONS TO 3-(4-CHLORO-4,4-DIFLUOROBUT-2-ENOYL)OXAZOLIDIN-2-ONE

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Dedicated to Professor Oldřich Paleta on the occasion of his 70th birthday in recognition of his outstanding contributions to the area of organofluorine chemistry.

1,4-Addition reactions to chlorodifluorinated Michael acceptor **1b** containing a chiral oxazolidinone auxiliary were found to proceed smoothly either with alkyllithium or Grignard reagents in the presence of CuY (Y = I or CN) or $ZnCl_2$. In contrast to the corresponding cuprates, R_2Zn or $R_3ZnMgBr$ species (prepared from 2 or 3 equiv. of RMgX and $ZnCl_2$, respectively) were quite effective in suppression of the unfavorable β-elimination mechanism leading to the terminally difluorinated byproduct **3**.

Keywords: Michael addition; Cuprates; Organozinc reagents; Chlorodifluoromethyl.

Development of novel preparation methods for fluorine-containing materials is one of the most important issues[1] because of their potential use as biologically active materials, optical devices, and so forth where fluorine atoms play a significantly important role which cannot be usually attained by any other elements or groups. We have previously reported[2] successful diastereoselective conjugate addition reactions of cuprates to chiral 3-(4,4,4-trifluorobut-2-enoyl)oxazolidin-2-one **1a**, and our continuing interest in this area prompted us to further investigate the 4-chloro-4,4-difluorinated derivative **1b**. In spite of close similarity of **1b** to **1a**, substitution of fluorine with chlorine could seriously affect the behavior of this substrate in Michael addition reactions of adequate nucleophiles. As shown in Scheme 1, migration of R groups in the initial intermediate **Int** is considered as the plausible pathway to afford the conjugate addition product **2**, but attachment of the more potent leaving element X would prefer to follow the elimination mechanism to furnish the terminally difluorinated

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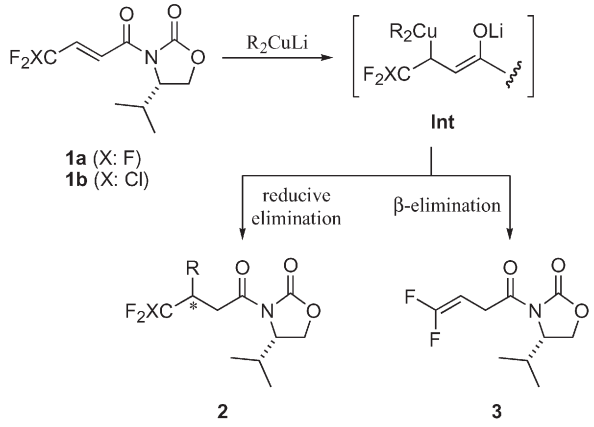
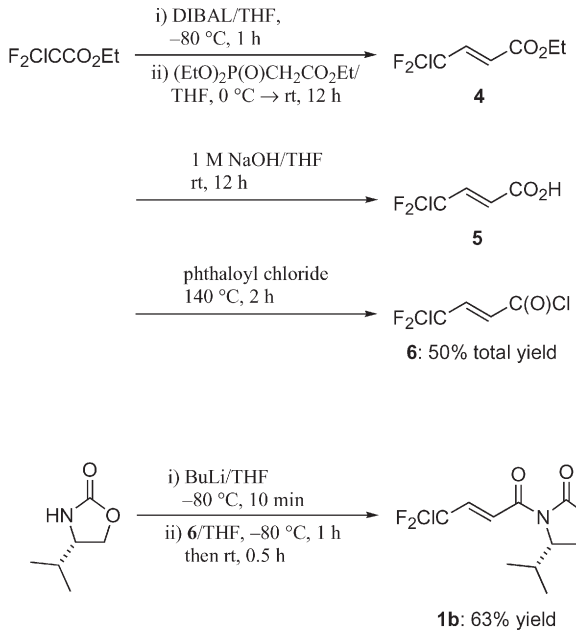
olefin **3** in a preferential manner. Thus, it is probable that introduction of Cl instead of F would possibly render this Michael addition process more problematic in spite of the usefulness of this chlorine atom as the key functional element for reductive conversion to a difluoromethyl group[3] and formation of new carbon-carbon bonds[3,4] via Bu_3SnH-mediated radical processes. In this article is reported our extensive work in this area which clearly disclosed the interesting reactivity difference between **1a** and **1b**, and appropriate conditions for construction of new carbon–carbon bonds with **1b** by Michael addition reactions of various organometallic species.



SCHEME 1

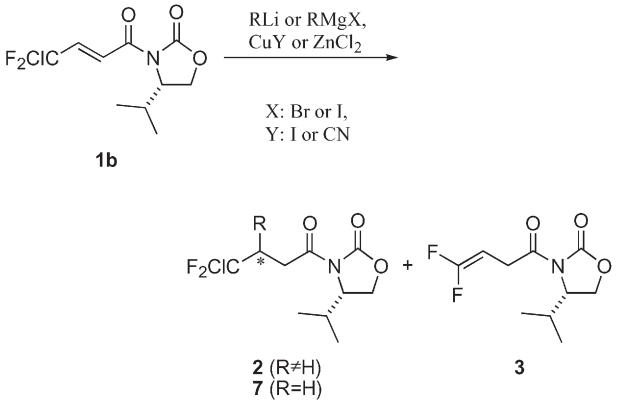
RESULTS AND DISCUSSION

The key substrate **1b** was prepared as shown in Scheme 2. Thus, following to the previously reported procedure[5], the modified Horner–Wadsworth–Emmons reaction[6] was performed directly with the aluminum acetal readily obtained from the controlled DIBAL reduction of the commercially available ethyl 2-chloro-2,2-difluoroacetate. This intermediate nicely acted as the convenient aldehyde precursor to smoothly afford the corresponding but-2-enoate **4** as a single (*E*)-stereoisomer[7]. With regard to its relatively low boiling point and high volatility, the compound **4** was subjected to alkaline hydrolysis[8] without further purification. The obtained acid chloride **6** was readily isolated by distillation under atmospheric pressure after phthaloyl-dichloride-mediated conversion of the resulting crude acid **5** in 50% total yield based on chlorodifluoroacetate. Construction of the α,β-unsaturated imide **1b** was eventually realized in 63% yield by condensation of **6** with the well-known oxazolidin-2-one[9] derived from L-valine.



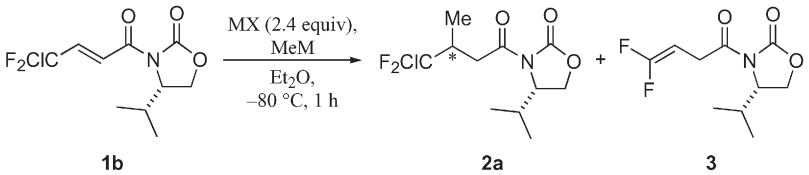
SCHEME 2

With the requisite Michael acceptor **1b** in hand, our attention was at first focused on finding out the appropriate reaction conditions for the 1,4-addition of Me-based organometallic species (Scheme 3). It is clearly understood from entries 1–4 in Table I that combination of CuI and MeLi [10] in various ratios did not furnish the conjugate adduct **2a** at all. Instead, the



SCHEME 3

TABLE I
Reaction conditions for the reaction of **1b**



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

Entry	MX	MeM	Equiv.	Yield[a], %			Conversion %
					2a[b]	**3**	
1	CuI	MeLi	2.4	0	–	19	100
2	CuI	MeLi	4.8	0	–	77	97
3[c]	CuI	MeLi	4.8	0	–	75	100
4	CuI	MeLi	7.2	0	–	90	100
5[d]	CuI	MeMgI	2.4	0	–	0	43
6[d]	CuI	MeMgI	4.8	17	(68:32)	6	41
7[d]	CuI	MeMgI	7.2	26	(52:48)	38	100
8	CuCN	MeLi	2.4	0	–	39	99
9	CuCN	MeLi	4.8	0	–	82	98
10	CuCN	MeLi	7.2	11	–	60	100
11[e]	CuCN	MeMgI	1.2	3	(58:42)	3	6
12[e]	CuCN	MeMgI	2.4	24	(63:37)	14	55
13[e]	CuCN	MeMgI	3.6	36	(74:26)	35	100
14	CuCN	MeMgI	2.4	24	(57:43)	33	100
15	CuCN	MeMgI	4.8	25	(59:41)	40	97
16	CuCN	MeMgI	7.2	19	(66:34)	32	100
17[d]	CuCN	MeMgI	7.2	51	(62:38)	29	100
18	$ZnCl_2$	MeLi	2.4	12	–	0	100
19	$ZnCl_2$	MeLi	4.8	66	(60:40)	0	100
20	$ZnCl_2$	MeLi	7.2	64	(61:39)	trace	100
21	$ZnCl_2$	MeMgI	2.4	0	–	0	0
22	$ZnCl_2$	MeMgI	4.8	39 [32]	(64:36)	0	63
23	$ZnCl_2$	MeMgI	7.2	71 [65]	(63:37)	0	100

[a] Yields determined by ^{19}F NMR are shown and the isolated yield is depicted in the brackets. [b] The diastereomer ratios determined by ^{19}F NMR are shown in parentheses. [c] The reaction was performed at 0 °C in THF. [d] Reaction was carried out at temperatures from –80 to –30 °C for 3 h. [e] 1.2 equiv. of CuCN was used.

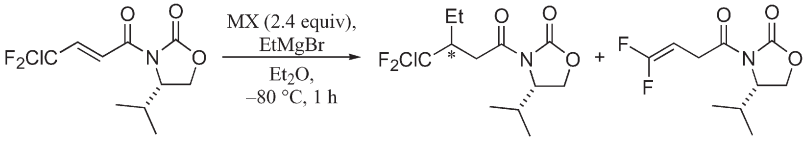
difluorinated alkene **3** was obtained in high to excellent yields which increased when using a larger amount of MeLi. These phenomena would be a reflection of the lower migration ability of a CH_3 group. The formation of byproduct **3** could be mechanistically explained as the result of the conjugate addition of the cuprate species, followed by smooth departure of the more potent Cl atom with "Cu" via β-elimination rather than "CuF" elimination or competing CH_3 migration. A similar tendency was also observed when CuCN was employed instead of CuI (entries 8–10), which led us to clear conclusion that MeLi-based organocuprates would not be the method of choice for effective construction of the Michael adduct **2a**. However, the corresponding Grignard reagent changed the situation and formation of the desired 1,4-adduct **2a** was noticed in 51% yield by mixing CuCN and MeMgI in a 1:3 molar ratio along with 29% of **3** when 2.4 equiv. of CuCN was employed under the conditions of a gradual temperature increase from –80 to –30 °C in the course of 3 h (entry 17). These improved results allowed further investigation of organozinc species[11] both from MeLi and MeMgI (entries 18–23). Although MeZnCl did not work properly, the use of 2 or 3 molar equiv. of MeLi or 3 equiv. of MeMgI per 1 equiv. of $ZnCl_2$ led to the selective formation of **2a** and complete suppression of the undesirable byproduct **3**. Entry 23 recorded the best isolated yield of **2a** (65%) as a 63:37 diastereomer mixture determined by ^{19}F NMR when 2.4 equiv. of Me_3ZnMgI was employed.

In the next stage, we employed EtMgBr as a representative Grignard reagent with higher migration ability than the methyl group (Table II). In accord with our expectation, EtMgBr was found to possess better reactivity than MeMgI and even the corresponding organocuprates furnished the desired compound **2b** in good yields both from CuI and CuCN (entries 1–5), in spite of the exclusive formation of **3** from MeLi or MeMgI under the same conditions. Lower-order cuprates were found preferable giving better yields as well as a higher **2b**/**3** selectivity while the difference was not quite significant. The inherently higher transposition ability of an ethyl group would result in its smoother bond formation prior to "CuCl" β-elimination to attain good to excellent product selectivity of **2b**/**3** from 57:17 to 74:4. Combination of EtMgBr and $ZnCl_2$ in 1:2 or 1:3 ratios proved to effectively inhibit the formation of **3** again and, as shown in entry 8, the desired ethylated compound **2b** was isolated in 74% yield as an almost stereorandom mixture.

Since we have found out appropriate reaction conditions for both Me- and Et-based organometals in the presence of copper or zinc salts as described above, introduction of a variety of alkyl groups has been carried

out. The results are summarized in Table III. Although many instances usually afforded the product **2** in good to high chemical yields, this reaction seemed to be sensitive to bulkiness of the incoming nucleophile, and the desired product was formed only in low yields when *i*-PrMgCl was employed (entries 6 and 7). The lower-ordered cuprate from PhMgBr and CuI also suffered from lower reactivity furnishing at most 30% conversion (entry 12), while $ZnCl_2$ led to appreciable improvement to afford the adduct **2f** in a good isolated yield. Entries 9–11 were the special cases: the major product in entry 10 was the terminal difluoroolefin **3** in 51% yield instead of the desired conjugate addition product **2e** (37% yield), possibly as a result of the increased activation energy due to migration of the bulky *i*-Bu group, rendering this process slower and predominating the "CuCl"

TABLE II
Reaction conditions for the reaction of **1b**



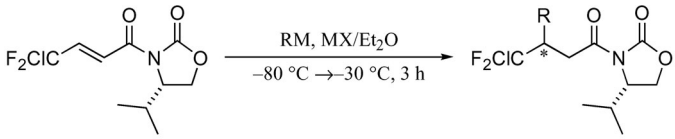
1b **2b** **3**

Entry	MX	EtMgBr Equiv.	Yield[a], %			Conversion %
			2b[b]		**3**	
1	CuCN	2.4	60	(56:44)	10	99
2	CuCN	4.8	57	(56:44)	17	100
3	CuI	2.4	74	(55:45)	4	96
4	CuI	4.8	68	(57:43)	5	96
5	CuI	7.2	60	(58:42)	5	100
6	$ZnCl_2$	2.4	56	(56:44)	3	85
7	$ZnCl_2$	4.8	67	(50:50)	–	94
8[c]	$ZnCl_2$	4.8	73 [74]	(53:47)	–	100
9	$ZnCl_2$	7.2	67	(54:46)	–	98

[a] Yields determined by ^{19}F NMR are shown and the isolated yield is depicted in the brackets. [b] The diastereomer ratios determined by ^{19}F NMR are shown in parentheses. [c] The reaction was carried out at temperatures from –80 to –30 °C for 3 h.

β-elimination. Interestingly enough, the saturated product **7** was isolated in 10 and 43% yields in entries 9 and 11, respectively. It was pointed out[12] that Bu-based cuprates generally showed a higher preference to such reduction than the corresponding Me-based species due to their higher electron transfer ability, which at least qualitatively explained our observation that the latter nucleophiles furnished the compound **7** only in a trace amount. Since the present 1,4-addition pathway produced two inseparable diastereomers almost in an equal amount and we could not obtain any suitable crystals for X-ray analysis in the case of separable stereoisomers like **2c**, it is quite unfortunate not to reach to the stage for determination of the stereochemical preference of the Michael adducts **2** at present.

TABLE III
Michael addition reactions of RM to **1b**

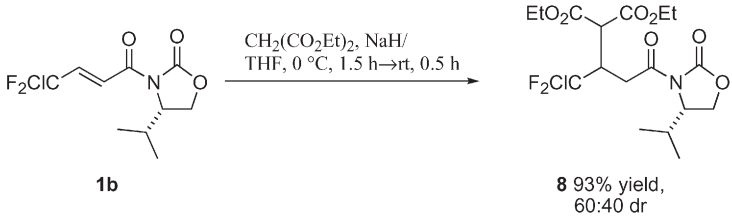


Entry	RM	Equiv.	MX	Equiv.	Product	Yield[a] %	Diastereomer ratio
1	MeMgI	7.2	CuCN	2.4	**2a**	51	(62:38)
2	MeMgI	7.2	$ZnCl_2$	2.4	**2a**	71 [65]	(63:37)
3[b]	MeLi	4.8	$ZnCl_2$	2.4	**2a**	66	(60:40)
4	EtMgBr	2.4	CuI	2.4	**2b**	73 [71]	(54:46)
5	EtMgBr	4.8	$ZnCl_2$	2.4	**2b**	73 [74]	(53:47)
6	*i*-PrMgCl	2.2	CuI	2.2	**2c**	complex	
7	*i*-PrMgCl	4.4	$ZnCl_2$	2.2	**2c**	[28]	(68:32)
8	BuMgBr	2.2	CuI	2.2	**2d**	47 [40]	(52:48)
9	BuMgBr	4.4	$ZnCl_2$	2.2	**2d**	70 [62]	(62:38)
10	*i*-BuMgBr	2.2	CuI	2.2	**2e**	37	(62:38)
11	*i*-BuMgBr	4.4	$ZnCl_2$	2.2	**2e**	48 [42]	(85:15)
12	PhMgBr	2.2	CuI	2.2	**2f**	19	–
13	PhMgBr	4.4	$ZnCl_2$	2.2	**2f**	59 [60]	(83:17)

[a] Yields determined by ^{19}F NMR are shown and the isolated yield is depicted in the brackets.
[b] The reaction was performed at –80 °C for 1 h.

The most important result noticed in this study was that the reactions of organozinc species could nicely participate in effective suppression of unfavorable byproduct (terminal olefin **3**) formation while this compound was obtained in every instances as long as **1b** was subjected to a solution of appropriate cuprates. Such characteristics eventually led to preferential construction of the desired Michael products **2** without contamination of **3**. This phenomenon could be consistently elucidated as a consequence of the intramolecular interaction of the chlorine atom and the metals. Actually, the bond energy difference[13] between Cu–Cl and Zn–Cl is approximately as much as 150 kJ/mol, the former bond being stronger. This trend would allow cuprates to construct a firmer Cl···Metal contact after the initial conjugate addition, resulting in the production of **3** whose amount would be dependent on the migration rate of the alkyl groups from the above intermediate.

Acceptor **1b** was found to smoothly react with diethyl malonate in the presence of a catalytic amount of sodium hydride to form the corresponding conjugate adduct **8** in 93% yield as a chromatographically separable 60:40 diastereomer mixture (Scheme 4).



1b **8** 93% yield, 60:40 dr

SCHEME 4

Although improvement of diastereoselectivities of products **2** and **8** and their stereochemical determination were regarded as the task to be promptly realized, it is worthwhile to note that the high reactivity of **1b** with both organometallics and enolates would open promising ways to construct chlorodifluoromethylated materials with good to excellent product selectivity by Michael addition reactions.

EXPERIMENTAL

General Procedure

Unless otherwise noted, materials were obtained from commercial suppliers and were used without further purification. All manipulations involving air-sensitive materials were performed under argon, with such materials being exposed only to anhydrous Et_2O, THF and

CH_2Cl_2 which were purchased and were used without further purification. ^1H, ^{13}C and ^{19}F NMR spectra were recorded at room temperature in $CDCl_3$ (^1H: 300 MHz, ^{13}C: 75 MHz, ^{19}F: 282 MHz). ^1H, ^{13}C and ^{19}F NMR data were reported as follows: chemical shift (δ-scale) in ppm downfield from tetramethylsilane, TMS, (δ 0.00) as an internal standard for ^1H and ^{13}C NMR, and internal hexafluorobenzene and benzotrifluoride (δ –163 and –64, respectively) for ^{19}F NMR, the number of protons or fluorines, multiplicity (s, singlet; d, doublet; t, triplet; q, quartet; quint, quintet; sep, septet; m, multiplet; br, broad peak); coupling constant (*J*) in Hz. IR spectra were reported in wavenumbers (cm^{-1}). Melting points were determined without correction and were obtained on a capillary apparatus. Column chromatography was conducted with spherical and neutral silica gel 60 N (63–210 nm).

When diastereomers were inseparable (except for the case of **2c**, **2f**, and **9**), the spectroscopic data for minor isomers may be incomplete because unfavorable overlap of peaks sometimes makes their correct analysis difficult or even impossible.

Preparation of (*E*)-4-Chloro-4,4-difluorobut-2-enoyl Chloride (**6**)

To a solution of ethyl 2-chloro-2,2-difluoroacetate (15.85 g, 100 mmol) in THF (100 ml), 104 ml of DIBAL (0.97 M in hexanes, 101 mmol) at –80 °C were slowly added, and the mixture was stirred at the same temperature for 1 h. To a premixed solution of LiBr (11.29 g, 130 mmol) and ethyl diethylphosphonoacetate (19.9 ml, 100 mmol) in THF (130 ml), Et_3N (14.7 ml, 105 mmol) at 0 °C was slowly added and after 10-min stirring at room temperature, the reduced crude material was added at 0 °C. After stirring at room temperature overnight, the reaction mixture was quenched with aqueous 1 M HCl and extracted three times with ether. The combined organic phase was dried over anhydrous $MgSO_4$ and the volatiles were distilled off at atmospheric pressure.

To a concentrated solution containing **4** [5] in THF (100 ml), aqueous 1 M NaOH (100 ml) was added, and the mixture was stirred at room temperature overnight. Removal of THF on a rotary evaporator was followed by the extraction with ether, and the separated water phase was again extracted with ether after acidification by aqueous 6 M HCl. Dried over anhydrous $MgSO_4$ and concentrated on a rotary evaporator, the crude **5** [14] was obtained which was used in the next step without further purification.

The crude **5** was added to a flask containing phthaloyl dichloride (21.6 ml, 50 mmol) and the mixture was heated at 140 °C under an argon atmosphere for 2 h. The condenser was replaced with a distillation head and the crude material was distilled at 150 °C (bath temperature) under atmospheric pressure to furnish (*E*)-4-chloro-4,4-difluorobut-2-enoyl chloride **6** (8.770 g, 50.1 mmol, total yield 50%). ^1H NMR: 7.06 (dt, 1 H, $^3J_{HH}$ = 15.3, $^3J_{HF}$ = 8.7); 6.59 (dt, 1 H, $^3J_{HH}$ = 15.0, $^4J_{HF}$ = 1.5). ^{13}C NMR: 164.6, 140.6 (t, $^1J_{CF}$ = 292.0); 129.5 (t, $^3J_{CF}$ = 6.2); 122.6 (t, $^2J_{CF}$ = 29.5). ^{19}F NMR: –56.09 (d, $^3J_{HF}$ = 9.0). IR (neat): 3505, 3083, 1766, 1652, 1272, 1234, 1193, 1087, 1027, 970, 865, 834, 790, 714, 652, 625.

Preparation of (*S*)-3-[(*E*)-4-Chloro-4,4-difluorobut-2-enoyl]-4-isopropyl-oxazolidin-2-one (**1b**)

To a solution of (*S*)-4-isopropyloxazolidin-2-one (6.587 g, 51.0 mmol) in THF (80 ml), BuLi (35.0 ml, 1.6 M in hexane) at –80 °C was added, and the mixture was stirred at the same temperature for 10 min. To this solution, **6** (8.770 g, 50.1 mmol) was added and, after stirring at –80 °C for 1 h, the mixture was allowed to warm to ambient temperature over a 30-min period. The reaction mixture was quenched with an addition of saturated aqueous

NH_4Cl, and then extracted twice with AcOEt. The combined organic phase was dried over anhydrous $MgSO_4$ and concentrated on a rotary evaporator. The resulting crude oil was purified by silica gel column chromatography (hexane–AcOEt, 3:1) to afford **1b** (8.50 g, 31.8 mmol, 62%) as a white solid. M.p. 47.0–49.0 °C. $[\alpha]_D^{18}$ 71.9 (*c* 1.00, $CHCl_3$). ^{1}H NMR: 7.84 (dt, 1 H, $^3J_{HH}$ = 15.2, $^4J_{HF}$ = 1.8); 7.03 (dt, 1 H, $^3J_{HH}$ = 15.2, $^3J_{HF}$ = 9.3); 4.52 (dt, 1 H, $^3J_{HH}$ = 8.1, 3.3); 4.34 (t, 1 H, $^2J_{HH}$ = $^3J_{HH}$ = 8.6); 4.28 (dd, 1 H, $^2J_{HH}$ = 9.2, $^3J_{HH}$ = 3.3); 2.43 (sepd, 1 H, $^3J_{HH}$ = 7.0, 3.8); 0.93 (d, 3 H, $^3J_{HH}$ = 6.9); 0.88 (d, 3 H, $^3J_{HH}$ = 6.9). ^{13}C NMR: 162.6, 153.6, 137.3 (t, $^2J_{CF}$ = 28.5); 124.3 (t, $^3J_{CF}$ = 6.2); 123.7 (t, $^1J_{CF}$ = 287.2); 63.7, 58.7, 28.8, 17.9, 14.4. ^{19}F NMR: –54.72 (d, $^3J_{HF}$ = 9.1). IR (KBr): 3055, 2986, 2685, 2305, 1782, 1693, 1656, 1487, 1421, 1389, 1369, 1345, 1265, 1207, 1143, 1107, 1060, 1029, 976, 896, 739, 705. For $C_{10}H_{12}ClF_2NO_3$ (267.7) calculated: 44.87% C, 4.52% H, 5.23% N; found: 45.12% C, 4.62% H, 5.12% N.

Michael Addition Reactions. General Procedure

An appropriate amount of organometallics was added to a solution of CuI (or CuCN or $ZnCl_2$) in Et_2O (3 ml) at 0 °C and stirred for 10 min. To this solution, **1b** (1.0 mmol) in Et_2O (2 ml) at –80 °C was added dropwise and, after stirring at the same temperature for 1 h, the reaction mixture was gradually warmed to –30 °C for 2 h. After quenching with aqueous 1 M HCl and filtration, the crude mixture was extracted with Et_2O. The usual work-up and purification by silica gel column chromatography furnished the desired products.

(S)-3-(4-Chloro-4,4-difluoro-3-methylbutanoyl)-4-isopropyloxazolidin-2-one (**2a**). IR (neat): 2966, 2878, 2359, 1784, 1703, 1487, 1466, 1390, 1254, 1206, 1099, 1023, 999, 973, 954, 912, 888, 773, 754, 717, 692, 664, 638. For $C_{11}H_{16}ClF_2NO_3$ (283.7) calculated: 46.57% C, 5.68% H, 4.94% N; found: 47.39% C, 5.84% H, 4.74% N.

Major diastereomer: ^{1}H NMR: 4.43 (dt, 1 H, $^3J_{HH}$ = 10.5, 3.9); 4.30 (t, 1 H, $^2J_{HH}$ = $^3J_{HH}$ = 10.5); 4.23 (dd, 1 H, $^2J_{HH}$ = 10.5, $^3J_{HH}$ = 3.0); 3.26 (dd, 1 H, $^2J_{HH}$ = 16.8, $^3J_{HH}$ = 9.0); 3.10 (dd, 1 H, $^2J_{HH}$ = 16.8, $^3J_{HH}$ = 6.0); 3.07 (m, 1 H); 2.43 (sepd, 1 H, $^3J_{HH}$ = 6.6, 3.3); 1.24 (d, 3 H, $^3J_{HH}$ = 6.6); 0.96 (d, 3 H, $^3J_{HH}$ = 5.7); 0.91 (d, 3 H, $^3J_{HH}$ = 5.7). ^{13}C NMR: 170.0, 153.9, 132.0 (t, $^1J_{CF}$ = 293.3); 63.5, 58.5, 40.7 (t, $^2J_{CF}$ = 23.0); 37.0 (t, $^3J_{CF}$ = 3.1); 28.3, 17.8, 14.6, 14.5. ^{19}F NMR: –57.10 (dd, 1 F, $^2J_{FF}$ = 161.9, $^3J_{HF}$ = 9.3); –57.81 (dd, 1 F, $^2J_{FF}$ = 161.6, $^3J_{HF}$ = 9.3).

Minor diastereomer: ^{1}H NMR: 4.45 (dt, 1 H, $^3J_{HH}$ = 7.2, 3.0); 4.30 (t, 1 H, $^2J_{HH}$ = $^3J_{HH}$ = 9.0); 4.24 (dd, 1 H, $^2J_{HH}$ = 9.3, $^3J_{HH}$ = 3.3); 4.00 (dd, 1 H, $^2J_{HH}$ = 17.1, $^3J_{HH}$ = 3.3); 3.07 (m, 1 H); 2.97 (dd, 1 H, $^2J_{HH}$ = 17.1, $^3J_{HH}$ = 9.0); 2.38 (sepd, 1 H, $^3J_{HH}$ = 6.9, 3.6); 1.22 (d, 3 H, $^3J_{HH}$ = 6.6); 0.93 (d, 3 H, $^3J_{HH}$ = 6.6); 0.88 (d, 3 H, $^3J_{HH}$ = 6.6). ^{13}C NMR: 153.8, 63.4, 40.5 (t, $^2J_{CF}$ = 23.6); 37.0 (t, $^3J_{CF}$ = 3.8); 28.2, 14.5. ^{19}F NMR: –57.25 (dd, 1 F, $^2J_{FF}$ = 146.1, $^3J_{HF}$ = 9.0); –58.07 (dd, 1 F, $^2J_{FF}$ = 146.1, $^3J_{HF}$ = 9.0).

(S)-3-(4-Chloro-3-ethyl-4,4-difluorobutanoyl)-4-isopropyloxazolidin-2-one (**2b**). IR (KBr): 3059, 2970, 2881, 2307, 1782, 1705, 1487, 1465, 1389, 1367, 1303, 1267, 1208, 1099, 1060, 1024, 996, 922, 888, 852, 830, 740, 704, 668, 640. For $C_{12}H_{18}ClF_2NO_3$ (297.7) calculated: 48.41% C, 6.09% H, 4.70% N; found: 48.84% C, 6.33% H, 4.64% N.

Major diastereomer: ^{1}H NMR: 4.47 (dt, 1 H, $^3J_{HH}$ = 7.5, 3.5); 4.31 (t, 1 H, $^2J_{HH}$ = $^3J_{HH}$ = 8.4); 4.26 (dd, 1 H, $^3J_{HH}$ = 9.0, $^3J_{HH}$ = 5.7); 3.42 (dd, 1 H, $^2J_{HH}$ = 20.5, $^3J_{HH}$ = 12.4); 3.00 (m, 1 H); 2.97 (dd, 1 H, $^2J_{HH}$ = 17.6, $^3J_{HH}$ = 5.9); 2.38 (sepd, 1 H, $^3J_{HH}$ = 7.0, 3.1); 1.83 (dqd, 1 H, $^2J_{HH}$ = 16.7, $^3J_{HH}$ = 7.6, 5.1); 1.51 (dquint, 1 H, $^2J_{HH}$ = 14.1, $^3J_{HH}$ = 7.5); 1.01 (t, 3 H, $^3J_{HH}$ = 6.7); 0.93 (d, 3 H, $^3J_{HH}$ = 7.0); 0.88 (d, 3 H, $^3J_{HH}$ = 7.0). ^{13}C NMR: 170.3, 153.9, 132.2 (t,

$^{1}J_{CF}$ = 294.0); 63.4, 58.5, 46.1 (t, $^{2}J_{CF}$ = 21.7); 35.1 (t, $^{3}J_{CF}$ = 3.1); 28.2, 23.0, 17.8, 14.5, 11.2. ^{19}F NMR: –52.96 (d, $^{3}J_{HF}$ = 9.1).

Minor diastereomer: ^{1}H NMR: 4.46 (dt, 1 H, $^{3}J_{HH}$ = 8.1, 3.3); 4.31 (t, 1 H, $^{2}J_{HH}$ = $^{3}J_{HH}$ = 8.1); 4.24 (dd, 1 H, $^{2}J_{HH}$ = 9.0, $^{3}J_{HH}$ = 3.3); 3.27 (dd, 1 H, $^{2}J_{HH}$ = 18.0, $^{3}J_{HH}$ = 5.3); 3.11 (dd, 1 H, $^{2}J_{HH}$ = 18.1, $^{3}J_{HH}$ = 6.2); 3.02 (m, 1 H); 2.37 (sepd, 1 H, $^{3}J_{HH}$ = 7.0, 3.8); 1.85 (dqd, 1 H, $^{2}J_{HH}$ = 14.1, $^{3}J_{HH}$ = 7.7, 5.0); 1.51 (dq, 1 H, $^{2}J_{HH}$ = 14.2, $^{3}J_{HH}$ =7.4); 1.01 (t, 3 H, $^{3}J_{HH}$ = 7.5); 0.93 (d, 3 H, $^{3}J_{HH}$ = 7.0); 0.91 (d, 3 H, $^{3}J_{HH}$ = 7.0). ^{13}C NMR: 45.8 (t, $^{2}J_{CF}$ = 21.7); 28.3. ^{19}F NMR: –54.91 (d, $^{3}J_{HF}$ = 9.1).

(S)-3-(4-Chloro-4,4-difluoro-3-isopropylbutanoyl)-4-isopropyloxazolidin-2-one (**2c**).

Major diastereomer: M.p. 57.0–59.0 °C. $[\alpha]_D^{18}$ 68.3 (*c* 1.00, $CHCl_3$). ^{1}H NMR: 4.47 (dt, 1 H, $^{3}J_{HH}$ = 7.5, 3.6); 4.31 (t, 1 H, $^{2}J_{HH}$ = $^{3}J_{HH}$ = 8.4); 4.23 (dd, 1 H, $^{2}J_{HH}$ = 9.3, $^{3}J_{HH}$ = 3.6); 3.43 (dd, 1 H, $^{2}J_{HH}$ = 18.3, $^{3}J_{HH}$ = 6.6); 3.12 (m, 1 H); 2.93 (dd, 1 H, $^{2}J_{HH}$ = 18.6, $^{3}J_{HH}$ = 4.2); 2.38 (sepd, 1 H, $^{3}J_{HH}$ = 6.9, 3.9); 2.24 (sepd, 1 H, $^{3}J_{HH}$ = 6.9, 3.9); 1.01 (d, 3 H, $^{3}J_{HH}$ = 6.9); 1.00 (d, 3 H, $^{3}J_{HH}$ = 6.9); 0.99 (d, 3 H, $^{3}J_{HH}$ = 6.9); 0.88 (d, 3 H, $^{3}J_{HH}$ = 6.9). ^{13}C NMR: 170.9, 153.9, 132.1 (t, $^{1}J_{CF}$ = 295.8); 63.3, 58.6, 49.7 (t, $^{2}J_{CF}$ = 20.4); 31.5 (t, $^{3}J_{CF}$ = 3.1); 28.1, 28.0, 21.2, 18.4, 17.8, 14.4. ^{19}F NMR: –52.72 (dd, 1 F, $^{2}J_{FF}$ = 164.2, $^{3}J_{HF}$ = 13.6); –54.17 (dd, 1 F, $^{2}J_{FF}$ = 164.2, $^{3}J_{HF}$ = 11.6). IR (KBr): 2967, 2880, 2360, 1784, 1705, 1487, 1468, 1389, 1373, 1303, 1277, 1249, 1206, 1142, 1119, 1100, 1060, 1038, 1020, 985, 972, 925, 849, 771, 702, 663, 644. For $C_{13}H_{20}ClF_2NO_3$ (311.8) calculated: 50.08% C, 6.47% H, 4.49% N; found: 50.70% C, 6.68% H, 4.43% N.

Minor diastereomer: ^{1}H NMR: 4.46 (dt, 1 H, $^{3}J_{HH}$ = 8.1, 3.9); 4.31 (t, 1 H, $^{2}J_{HH}$ = $^{3}J_{HH}$ = 9.0); 4.24 (dd, 1 H, $^{2}J_{HH}$ = 9.0, $^{3}J_{HH}$ = 3.0); 3.25 (dd, 1 H, $^{2}J_{HH}$ = 19.5, $^{3}J_{HH}$ = 7.5); 3.14 (m, 1 H); 3.11 (dd, 1 H, $^{2}J_{HH}$ = 19.2, $^{3}J_{HH}$ = 3.3); 2.38 (sepd, 1 H, $^{3}J_{HH}$ = 6.9, 3.9); 2.24 (sepd, 1 H, $^{3}J_{HH}$ = 6.6, 3.9); 1.02 (d, 3 H, $^{3}J_{HH}$ = 8.4); 0.99 (d, 3 H, $^{3}J_{HH}$ = 7.2); 0.93 (d, 3 H, $^{3}J_{HH}$ = 6.9); 0.89 (d, 3 H, $^{3}J_{HH}$ = 6.9). ^{13}C NMR: 170.9, 154.0, 132.1 (t, $^{1}J_{CF}$ = 295.8); 63.5, 58.7, 49.7 (t, $^{2}J_{CF}$ = 20.4); 31.7 (t, $^{3}J_{CF}$ = 2.5); 28.3, 28.2, 21.2, 18.3, 17.9, 14.6. ^{19}F NMR: –52.35 (dd, 1 F, $^{2}J_{FF}$ = 162.0, $^{3}J_{HF}$ = 11.3); –53.72 (dd, 1 F, $^{2}J_{FF}$ = 164.2, $^{3}J_{HF}$ = 11.6). IR (neat): 3056, 2968, 2936, 2879, 2306, 1781, 1706, 1487, 1467, 1389, 1374, 1303, 1266, 1208, 1142, 1119, 1101, 1061, 1019, 985, 972, 92–8096, 741, 705, 666, 645.

(S)-3-(3-Butyl-4-chloro-4,4-difluorobutanoyl)-4-isopropyloxazolidin-2-one (**2d**). IR (neat): 2962, 2875, 2359, 1785, 1704, 1488, 1467, 1389, 1302, 1284, 1248, 1207, 1107, 1059, 1019, 972, 942, 890, 773, 754, 715, 670, 640. For $C_{14}H_{22}ClF_2NO_3$ (325.8) calculated: 51.61% C, 6.81% H, 4.30% N; found: 51.56% C, 6.89% H, 4.25% N.

Major diastereomer: ^{1}H NMR: 4.46 (dt, 1 H, $^{3}J_{HH}$ = 8.2, 4.0); 4.30 (t, 1 H, $^{2}J_{HH}$ = $^{3}J_{HH}$ = 7.5); 4.24 (dd, 1 H, $^{2}J_{HH}$ = 9.0, $^{3}J_{HH}$ = 3.3); 3.45 (dd, 1 H, $^{2}J_{HH}$ = 17.9, $^{3}J_{HH}$ = 5.9); 3.06 (m, 1 H); 2.94 (dd, 1 H, $^{2}J_{HH}$ = 18.2, $^{3}J_{HH}$ = 5.6); 2.37 (sepd, 1 H, $^{3}J_{HH}$ = 7.0, 3.8); 1.83–1.31 (m, 6 H); 0.94–0.87 (m, 9 H). ^{13}C NMR: 170.3, 153.8, 132.2 (t, $^{1}J_{CF}$ = 294.0); 63.3, 58.4, 44.6 (t, $^{2}J_{CF}$ = 22.3); 35.4 (t, $^{3}J_{CF}$ = 3.1); 29.4 (t, $^{3}J_{CF}$ = 2.5); 28.8, 28.1, 22.4, 17.6, 14.3, 13.6. ^{19}F NMR: –55.34 (d, $^{3}J_{HF}$ = 9.1).

Minor diastereomer: ^{1}H NMR: 3.31–3.02 (m, 3 H); 2.38 (sepd, 1 H, $^{3}J_{HH}$ = 7.0, 3.8). ^{13}C NMR: 170.2, 63.4, 58.5, 44.7 (t, $^{2}J_{CF}$ = 21.6); 29.6 (t, $^{3}J_{CF}$ = 2.5); 28.7, 28.2, 22.5, 17.7, 14.4. ^{19}F NMR: –55.14 (d, $^{3}J_{HF}$ = 9.1).

(S)-3-(4-Chloro-4,4-difluoro-3-isobutylbutanoyl)-4-isopropyloxazolidin-2-one (**2e**). IR (neat): 640, 676, 715, 754, 773, 814, 848, 890, 938, 973, 1000, 1027, 1060, 1079, 1113, 1206, 1260, 1305, 1331, 1373, 1389, 1469, 1488, 1704, 1784, 2874, 2963, 3546. For $C_{14}H_{22}ClF_2NO_3$ (325.8) calculated: 51.61% C, 6.81% H, 4.30% N; found: 51.50% C, 6.82% H, 4.25% N.

Major diastereomer: ^{1}H NMR: 4.46 (dt, 1 H, $^3J_{HH}$ = 8.1, 3.6); 4.30 (t, 1 H, $^2J_{HH}$ = $^3J_{HH}$ = 9.1); 4.23 (dd, 1 H, $^2J_{HH}$ = 9.3, $^3J_{HH}$ = 3.3); 3.51 (dd, 1 H, $^2J_{HH}$ = 18.3, $^3J_{HH}$ = 6.3); 3.19 (m, 1 H); 2.86 (dd, 1 H, $^2J_{HH}$ = 18.0, $^3J_{HH}$ = 4.8); 2.38 (sepd, 1 H, $^3J_{HH}$ = 6.9, 3.9); 1.63 (m, 1 H); 1.55 (dt, 1 H, $^2J_{HH}$ = 9.0, $^3J_{HH}$ = 4.5); 1.38 (dt, 1 H, $^2J_{HH}$ = 8.7, $^3J_{HH}$ = 4.8); 0.97 (d, 3 H, $^3J_{HH}$ = 6.3); 0.93 (d, 3 H, $^3J_{HH}$ = 6.3); 0.92 (t, 3 H, $^3J_{HH}$ = 6.9); 0.88 (d, 3 H, $^3J_{HH}$ = 6.9). ^{13}C NMR: 170.5, 153.9, 132.4 (t, $^1J_{CF}$ = 294.0); 63.4, 58.5, 42.7 (t, $^2J_{CF}$ = 22.3); 38.9, 35.8 (t, $^3J_{CF}$ = 3.1); 28.1, 25.3, 23.0, 21.8, 17.8, 14.4. ^{19}F NMR: –55.88 (dd, 1 F, $^2J_{FF}$ = 162.0, $^3J_{HF}$ = 9.0); –55.11 (dd, 1 F, $^2J_{FF}$ = 162.0, $^3J_{HF}$ = 9.0).

Minor diastereomer: ^{1}H NMR: 3.33 (dd, 1 H, $^2J_{HH}$ = 17.7, $^3J_{HH}$ = 6.0); 3.02 (dd, 1 H, $^2J_{HH}$ = 17.7, $^3J_{HH}$ = 4.8); 1.35 (dt, 1 H, $^2J_{HH}$ = 8.4, $^3J_{HH}$ = 5.1); 0.89 (d, 3 H, $^3J_{HH}$ = 6.9). ^{13}C NMR: 170.3, 63.5, 58.6, 42.9 (t, $^2J_{CF}$ = 21.7); 39.2, 35.9 (t, $^3J_{CF}$ = 3.1); 28.3, 23.1, 17.9, 14.5. ^{19}F NMR: –55.52 (dd, 1 F, $^2J_{FF}$ = 162.0, $^3J_{HF}$ = 9.6); –54.97 (dd, 1 F, $^2J_{FF}$ = 162.0, $^3J_{HF}$ = 9.6).

(S)-3-(4-Chloro-4,4-difluoro-3-phenylbutanoyl)-4-isopropyloxazolidin-2-one (**2f**).

Major diastereomer: M.p. 78.0–79.0 °C. $[\alpha]_D^{18}$ 46.5 (*c* 1.00, $CHCl_3$). ^{1}H NMR: 7.38–7.31 (m, 5 H); 4.35 (dt, 1 H, $^3J_{HH}$ = 8.1, 3.3); 4.24 (t, 1 H, $^2J_{HH}$ = $^3J_{HH}$ = 8.7); 4.15 (dd, 1 H, $^2J_{HH}$ = $^3J_{HH}$ = 9.0, 1.8); 4.26–4.10 (m, 1 H); 4.05 (dd, 1 H, $^2J_{HH}$ = 17.1, $^3J_{HH}$ = 10.2); 3.44 (dd, 1 H, $^2J_{HH}$ = 16.8, $^3J_{HH}$ = 3.9); 2.00 (sepd, 1 H, $^3J_{HH}$ = 6.9, 3.9); 0.74 (t, 3 H, $^3J_{HH}$ = 6.9); 0.54 (d, 3 H, $^3J_{HH}$ = 6.9). ^{13}C NMR: 169.4, 153.8, 134.5, 130.2 (t, $^1J_{CF}$ = 294.6); 129.4, 128.5, 128.4, 63.4, 58.3, 52.1 (t, $^2J_{CF}$ = 23.0); 35.5, 28.1, 17.5, 14.2. ^{19}F NMR: –55.31 (dd, 1 F, $^2J_{FF}$ = 162.0, $^3J_{HF}$ = 11.3); –56.43 (dd, 1 F, $^2J_{FF}$ = 162.0, $^3J_{HF}$ = 13.6). IR (neat): 3056, 2968, 2877, 2306, 1781, 1705, 1497, 1487, 1456, 1388, 1302, 1266, 1208, 1142, 1117, 1087, 1064, 1021, 1004, 975, 930, 89–8063, 740, 704, 668, 644, 629. For $C_{16}H_{18}ClF_2NO_3$ (345.8) calculated: 55.58% C, 5.25% H, 4.05% N; found: 55.63% C, 5.52% H, 4.04% N.

Minor diastereomer: ^{1}H NMR: 3.80 (dd, 1 H, $^2J_{HH}$ = 17.1, $^3J_{HH}$ = 9.6); 3.64 (dd, 1 H, $^2J_{HH}$ = 16.8, $^3J_{HH}$ = 3.9); 0.86 (d, 3 H, $^3J_{HH}$ = 6.9); 0.84 (d, 3 H, $^3J_{HH}$ = 6.9). ^{13}C NMR: 169.2, 134.1, 58.4, 51.6 (t, $^2J_{CF}$ = 23.0); 36.1, 28.2, 17.7, 14.5. ^{19}F NMR: –55.38 (dd, 1 F, $^2J_{FF}$ = 161.7, $^3J_{HF}$ = 11.6); –56.01 (dd, 1 F, $^2J_{FF}$ = 161.7, $^3J_{HF}$ = 11.6).

(S)-3-(4,4-Difluorobut-3-enoyl)-4-isopropyloxazolidin-2-one (**3**)[2]. ^{1}H NMR: 4.51 (dtd, 1 H, $^3J_{HF}$ = 24.9, $^3J_{HH}$ = 7.5, $^3J_{HF}$ = 1.8); 4.44 (dt, 1 H, $^3J_{HH}$ = 8.1, 3.6); 4.31 (t, 1 H, $^2J_{HH}$ = $^3J_{HH}$ = 9.0); 4.24 (dd, 1 H, $^2J_{HH}$ = 9.0, $^3J_{HH}$ = 3.3); 3.71 (ddt, 1 H, $^2J_{HH}$ = 18.6, $^3J_{HH}$ = 6.0, $^4J_{HF}$ = 1.5); 3.62 (ddt, 1 H, $^2J_{HH}$ = 18.6, $^3J_{HH}$ = 6.0, $^4J_{HF}$ = 1.5); 2.38 (sepd, 1 H, $^3J_{HH}$ = 6.9, 3.9); 0.93 (d, 3 H, $^3J_{HH}$ = 7.2); 0.89 (d, 3 H, $^3J_{HH}$ = 7.2). ^{13}C NMR: 169.7, 156.8 (dd, $^1J_{CF}$ = 289.0, 285.4); 154.0, 71.5 (dd, $^2J_{CF}$ = 28.9, 18.9); 63.6, 58.5, 29.9 (d, $^3J_{CF}$ = 5.6); 28.3, 17.8, 14.5. ^{19}F NMR: –87.16 (d, 1 F, $^2J_{FF}$ = 41.0); –89.47 (dd, 1 F, $^2J_{FF}$ = 43.4, $^3J_{HF}$ = 25.0).

(S)-3-(4-Chloro-4,4-difluorobutanoyl)-4-isopropyloxazolidin-2-one (**7**). ^{1}H NMR: 4.45 (dt, 1 H, $^3J_{HH}$ = 7.3, 3.3); 4.31 (t, 1 H, $^2J_{HH}$ = $^3J_{HH}$ = 9.2); 4.25 (dd, 1 H, $^2J_{HH}$ = 9.2, $^3J_{HH}$ = 3.3); 3.33 (ddd, 1 H, $^3J_{HF}$ = 18.3, $^3J_{HH}$ = 8.8, 6.7); 3.23 (ddd, 1 H, $^3J_{HF}$ = 18.3, $^3J_{HH}$ = 8.5, 6.5); 2.73 (m, 2 H); 2.37 (sepd, 1 H, $^3J_{HH}$ = 7.0, 3.8); 0.93 (d, 3 H, $^3J_{HH}$ = 7.0); 0.89 (d, 3 H, $^3J_{HH}$ = 7.0). ^{13}C NMR: 170.1, 153.9, 129.1 (t, $^1J_{CF}$ = 290.9); 63.5, 58.4, 36.3 (t, $^2J_{CF}$ = 25.4); 29.9 (t, $^3J_{CF}$ = 3.1); 28.2, 17.8, 14.5. ^{19}F NMR: –52.64 (t, $^3J_{HF}$ = 13.7). IR (neat): 3545, 2967, 2879, 2360, 1784, 1705, 1488, 1467, 1437, 1389, 1365, 1333, 1302, 1245, 1208, 1144, 1111, 1070, 1054, 1020, 997, 973, 935, 834, 773, 715, 696, 662, 639. For $C_{11}H_{18}ClF_2NO_3$ (285.7) calculated: 44.54% C, 5.23% H, 5.19% N; found: 45.01% C, 5.39% H, 5.18% N.

(*S*)-3-{3-[Bis(ethoxycarbonyl)methyl]-4-chloro-4,4-difluorobutanoyl}-4-isopropyloxazolidin-2-one (**8**)

To a suspension of NaH (3 mg, 0.1 mmol) in THF (2 ml), diethyl malonate (0.176 g, 1.1 mmol) in THF (2 ml) at 0 °C was added. After 30-min stirring, the acceptor **1b** (0.268 g, 1.0 mmol) in THF (2 ml) was added at the same temperature, and the whole mixture was stirred at 0 °C for 1.5 h and at room temperature for 0.5 h. The mixture was quenched with aqueous 1 M HCl and the usual work-up procedure afforded the crude materials which was purified by silica gel column chromatography (hexane–AcOEt, 6:1) to afford **8** (0.399 g, 0.933 mmol, 93%) as a colorless oil in a ratio of 60:40, the major isomer being more polar.

Major diastereomer: M.p. 46.0–47.0 °C. $[\alpha]_D^{18}$ 39.0 (*c* 1.00, $CHCl_3$). ^{1}H NMR: 4.47 (dt, 1 H, $^3J_{HH}$ = 8.1, 3.6); 4.31 (t, 1 H, $^2J_{HH}$ = $^3J_{HH}$ = 9.0); 4.22 (m, 5 H); 4.06 (tq, 1 H, $^3J_{HH}$ = 10.2, 5.7); 3.86 (d, 1 H, $^3J_{HH}$ = 5.7); 3.53 (dd, 1 H, $^2J_{HH}$ = 18.9, $^3J_{HH}$ = 5.4); 3.44 (dd, 1 H, $^2J_{HH}$ = 18.9, $^3J_{HH}$ = 6.0); 2.38 (sepd, 1 H, $^3J_{HH}$ = 6.9, 3.9); 1.28 (t, 6 H, $^3J_{HH}$ = 8.1); 0.91 (d, 3 H, $^3J_{HH}$ = 6.9); 0.88 (d, 3 H, $^3J_{HH}$ = 6.9). ^{13}C NMR: 169.8, 167.0, 166.7, 154.0, 130.3 (t, $^1J_{CF}$ = 294.6); 63.6, 62.2, 62.0, 58.6, 50.9, 44.6 (t, $^2J_{CF}$ = 22.9); 33.2 (t, $^3J_{CF}$ = 2.5); 28.3, 17.8, 13.9, 13.8, 13.0. ^{19}F NMR: –56.30 (dd, 1 F, $^2J_{FF}$ = 166.5, $^3J_{HF}$ = 11.3); –55.64 (dd, 1 F, $^2J_{FF}$ = 166.8, $^3J_{HF}$ = 11.6). IR (neat): 2967, 2878, 2360, 1785, 1738, 1706, 1467, 1456, 1447, 1389, 1372, 1340, 1303, 1273, 1251, 1209, 1098, 1059, 1024, 973, 953, 925, 894, 862, 773, 756, 715, 686, 667, 640. For $C_{17}H_{24}ClF_2NO_7$ (427.8) calculated: 47.73% C, 5.65% H, 3.27% N; found: 47.70% C, 5.78% H, 3.32% N.

Minor diastereomer: ^{1}H NMR: 4.45 (dt, 1 H, $^3J_{HH}$ = 7.8, 3.6); 4.30 (t, 1 H, $^2J_{HH}$ = $^3J_{HH}$ = 8.7); 4.23 (m, 5 H); 4.04 (tq, 1 H, $^3J_{HH}$ = 10.8, 5.7); 3.86 (d, 1 H, $^3J_{HH}$ = 5.7); 3.62 (dd, 1 H, $^2J_{HH}$ = 19.2, $^3J_{HH}$ = 5.1); 3.33 (dd, 1 H, $^2J_{HH}$ = 18.8, $^3J_{HH}$ = 5.6); 2.42 (sepd, 1 H, $^3J_{HH}$ = 6.9, 3.6); 1.28 (t, 6 H, $^3J_{HH}$ = 5.7); 0.93 (d, 3 H, $^3J_{HH}$ = 4.2); 0.91 (d, 3 H, $^3J_{HH}$ = 3.9). ^{13}C NMR: 169.8, 167.0, 166.7, 153.9, 130.3 (t, $^1J_{CF}$ = 294.6); 63.5, 62.2, 62.0, 58.7, 50.9, 44.6 (t, $^2J_{CF}$ = 22.9); 33.4 (t, $^3J_{CF}$ = 2.5); 28.2, 17.9, 14.5, 13.8. ^{19}F NMR: –56.18 (dd, 1 F, $^2J_{FF}$ = 166.4, $^3J_{HF}$ = 11.3); –55.51 (dd, 1 F, $^2J_{FF}$ = 164.2, $^3J_{HF}$ = 9.0). IR (neat): 3056, 2985, 2877, 2306, 1792, 1735, 1708, 1487, 1466, 1446, 1266, 1210, 1179, 1098, 1060, 1023, 973, 896, 862, 733, 705, 639. For $C_{17}H_{24}ClF_2NO_7$ (427.8) calculated: 47.73% C, 5.65% H, 3.27% N; found: 47.68% C, 5.71% H, 3.34% N.

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