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Diastereoselective perfluoroalkylation of chiral imide enolates with perfluoroalkyl iodides mediated by triethylborane

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Abstract

The perfluoroalkylation of lithium enolates of chiral *N*-acyloxazolidinones with perfluoroalkyl iodides mediated by triethylborane proceeds with good diastereomeric excess (55%–93% de).

Keywords: Diastereoselective perfluoroalkylation; Chiral imide enolates; Perfluoroalkyl iodides; Triethylborane

1. Introduction

The synthesis of selectively fluorinated homochiral molecules is now an important aspect of organofluorine chemistry in relation to analytical and medicinal chemistry and optoelectric substances such as liquid crystals [1]. This paper presents for the first time the diastereoselective perfluoroalkylation of lithium enolates of *N*-acyloxazolidinones **1** to α-perfluoroalkyl carboximides **2** in 55%–93% de using a perfluoroalkyl iodide and triethylborane.

Triethylborane is an effective radical initiator for perfluoroalkyl iodides and induces the trifluoromethylation of acetylenes, olefins, silyl enol ethers and ketene silyl acetals, as previously reported by Oshima, Utimoto and coworkers [2]. The present authors recently conducted the diastereoselective trifluoromethylation (CF_3) [3] and ethoxycarbonyldifluoromethylation (EtO_2CCF_2) [4] of **1** with iodotrifluoromethane and ethyl difluoroiodoacetate, respectively, mediated by triethylborane. Taguchi et al. have successfully carried out the stereoselective synthesis of *gem*-difluorocyclopropanes using triethylborane-mediated intramolecular reactions [5].

2. Experimental details

In the present work, chiral imide enolates were generated at −78 °C in tetrahydrofuran by treatment of 2.0 mmol of **1** with 1.1 equiv. of lithium diisopropylamide (LDA) for 60 min. Perfluoroalkylation was accomplished by the addition of 1.5 equiv. of a perfluoroalkyl iodide and then 0.2–1.0 equiv. of triethylborane to the enolate, with stirring −78 °C for 2 h, and warming to −20 °C for 1 h prior to quenching with saturated aqueous NH_4Cl. α-Perfluoroalkyl carboximides **2** and their diastereomers **3** were isolated by flash chromatography (n-hexane/CH_2Cl_2). These results are summarized in Table 1.

3. Results and discussion

The perfluoro-n-hexylation of **1a** with 1.0 equiv. of triethylborane proceeded with good diastereomeric excess and in good chemical yield (entry 1) [1]. The new asymmetric center of the major isomer **2a** was shown to have the (*S*)-configuration by X-ray crystallography. Entry 2 shows the decrease in triethylborane to have had virtually no effect on diastereoselectivity or chemical yield. However, the perfluoroalkylation of **1a** was inhibited not only with the radical scavenger, galvinoxyl, but also in the absence of triethylborane (entries 3 and 5). With perfluoroethyl and perfluoroisopentyl iodides, good diastereomeric excess and good chemical yield were obtained (entries 4 and 6). The perfluoroalkylation of **1a** with 2-iodoheptafluoropropane was unsuccessful and the α-iodocarboximide **4a** was obtained in 22% yield (entry 7). With 2-iodoheptafluoropropane in the absence of triethylborane, **4a** was obtained in 81% yield (entry 8).

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[1] The starting imide **1a** was recovered in 10% yield.

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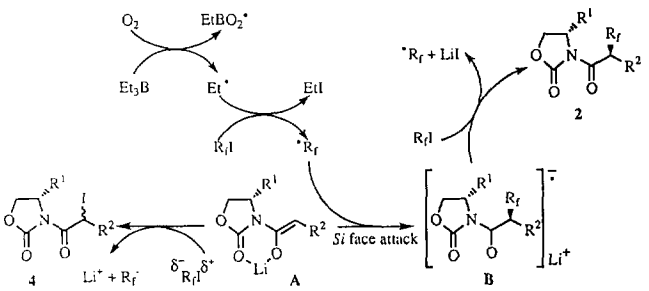
Results of the diastereoselective perfluoroalkylation of various *N*-acyloxazolidinones **1** with perfluoro-n-hexyl iodide are presented in entries 9–15 (Table 1). Good diastereoselectivity was achieved with **1b** (R^1 = Bn, R^2 = Me), **1c** (R^1 = ^{i}Pr, R^2 = Bn) and **1d** (R_1 = ^{i}Pr, R^2 = ^{n}Bu). Stereochemical assignment of the major isomer **2b** was made based on X-ray crystallography. Reaction of **1e** (R^1 = ^{i}Pr, R^2 = ^{t}Bu) with perfluoro-n-hexyl iodide gave the highest diastereomeric excess (93% de, entry 12). The reaction of **1e** in the absence of triethylborane afforded the α-iodocarboximide **4e** in 52% yield (entry 13). With **1f** (R^1 = ^{i}Pr, R^2 = Ph) and **1g** (R^1 = ^{i}Pr, R^2 = OBn), moderate diastereoselectivity was obtained (entries 14 and 15). In all cases, the starting imide **1** was partially recovered at 12%–35%.

It is the opinion of the authors that the present diastereoselective perfluoroalkylation of *N*-acyloxazolidinones **1** proceeds *via a radical mechanism involving perfluoroalkyl radicals*. The mechanism proposed for this is shown in Scheme 1 and is supported by the following observations: (1) triethylborane promotes perfluoroalkylation and (2) the radical scavenger, galvinoxyl, suppresses perfluoroalkylation. Attack of the perfluoroalkyl radical must thus proceed via an *Si-face* process involving the C(α) atom in preference

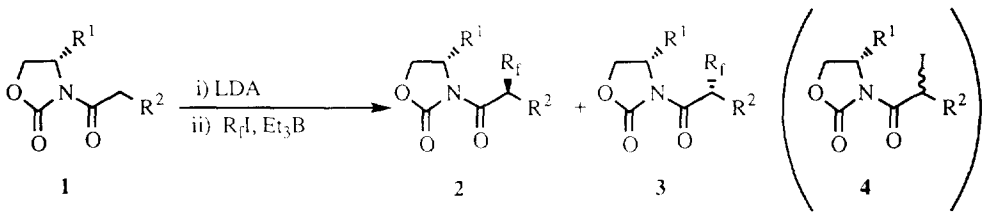


Scheme 1.

to a Li-chelated intermediate **A**. The by-product **4** is obtained via an ionic mechanism involving the iodo cation of **A**.

In conclusion, this paper presents the first examples of the diastereoselective perfluoroalkylation of *N*-acyloxazolidinones **1** with perfluoroalkyl iodides mediated by triethylborane to produce α-perfluoroalkyl carboximides **2** in 55%–93% de. Reduction of α-perfluoroalkyl carboximides **2** with lithium borohydride gave homochiral β-perfluoroalkyl alcohols in good yield without racemization. Application of the present process to the synthesis of important chiral fluoroorganic compounds is now being made.

Table 1
Diastereoselective perfluoroalkylation of chiral imide enolates **1**



Entry No.	Imide **1**		R_fI	Et_3B (equiv.)	Product (**2**, **3**)		Yield of by-product **4** [a] (%)
	R^1	R^2			de (%) [b]	Yield (**2**+**3**) (%) [c]	
1	^{i}Pr	Me (**1a**)	n-$C_6F_{13}I$	1.0	71 (*S*) [e]	79 (87)	0
2	^{i}Pr	Me (**1a**)	n-$C_6F_{13}I$	0.2	68 (*S*) [e]	83 (88)	0
3 [d]	^{i}Pr	Me (**1a**)	n-$C_6F_{13}I$	1.0	61 (*S*) [e]	11 (16)	0
4	^{i}Pr	Me (**1a**)	CF_3CF_2I	1.0	74 (*S*) [e]	74 (85)	0
5	^{i}Pr	Me (**1a**)	CF_3CF_2I	0.0	–	0	2
6	^{i}Pr	Me (**1a**)	$(CF_3)_2CF(CF_2)_2I$	1.0	79	75 (84)	0
7	^{i}Pr	Me (**1a**)	$(CF_3)_2CFI$	1.0	–	0	22
8	^{i}Pr	Me(**1a**)	$(CF_3)_2CFI$	0.0	–	0	81
9	Bn	Me (**1b**)	n-$C_6F_{13}I$	1.0	83 (*S*) [e]	81 (93)	0
10	^{i}Pr	Bn (**1c**)	n-$C_6F_{13}I$	1.0	81	70 (79)	0
11	^{i}Pr	^{n}Bu (**1d**)	n-$C_6F_{13}I$	1.0	83	73 (89)	0
12	^{i}Pr	^{t}Bu (**1e**)	n-$C_6F_{13}I$	1.0	93	57 (87)	0
13	^{i}Pr	^{t}Bu (**1e**)	n-$C_6F_{13}I$	0.0	–	0	52
14	^{i}Pr	Ph (**1f**)	n-$C_6F_{13}I$	1.0	57	63 (89)	0
15	^{i}Pr	OBn (**1g**)	n-$C_6F_{13}I$	1.0	55	59 (82)	0

[a] Diastereomeric excess ranged from 22% to 30%.
[b] Values determined by capillary GLC.
[c] All yields are of isolated compounds. Values in parentheses are those of conversion yields.
[d] The reaction was carried out in the presence of 1.0 equiv. of galvinoxyl.
[e] Configuration of the new asymmetric center of the major isomer. All products had satisfactory analyses, and spectroscopic parameters.

References

[1] P. Bravo and G. Resnati, *Tetrahedron: Asymm., 1* (1990) 661, and references cited therein.

[2] (a) Y. Takeyama, Y. Ichinose, K. Oshima and K. Utimoto, *Tetrahedron Lett., 30* (1989) 3159; (b) K. Miura, Y. Takeyama, K. Oshima and K. Utimoto, *Bull. Chem. Soc. Jpn., 64* (1991) 1542.

[3] (a) K. Iseki, T. Nagai and Y. Kobayashi, *Tetrahedron Lett., 34* (1993) 2169; (b) K. Iseki, T. Nagai and Y. Kobayashi, *Tetrahedron: Asymm., 5* (1994) 961.

[4] K. Iseki, D. Asada, M. Takahashi, T. Nagai and Y. Kobayashi, *Tetrahedron Lett., 35* (1994) 7399.

[5] (a) T. Taguchi, H. Sasaki, A. Shibuya and T. Morikawa, *Tetrahedron Lett., 35* (1989) 913; (b) T. Taguchi, A. Shibuya, H. Sakai, J. Endo, T. Morikawa and M. Shiro, *Tetrahedron: Asymm., 5* (1994) 1423.