Diastereoselective α-alkoxylation of lactamide *N*-alkyl groups *via* intramolecular formation of oxonium ions as the key intermediate

Tohru Kamada and Akira Oku*

Department of Chemistry, Faculty of Engineering and Design, Kyoto Institute of Technology, Matsugasaki, Sakyo-ku, Kyoto 606-8585, Japan

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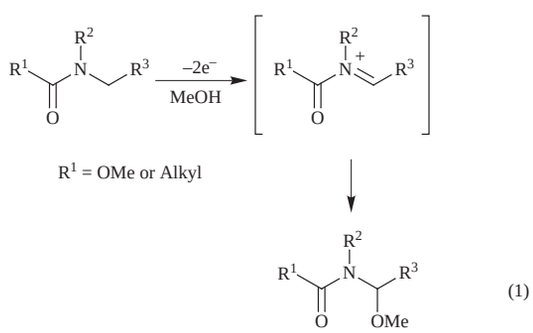
Stereoselective introduction of an alkoxy group to the amine unit of lactamide derivatives, under electrochemical oxidation conditions, was investigated based upon the assumption that a cyclic oxonium ion can be formed between the alkoxy substituent on the chiral center and a carbocation generated at the α-position of *N*-alkyl substituents. With *N*-monosubstituted lactamides, diastereoselectivity in the *N*-α-alkoxylated product was not observed. With *N*,*N*-disubstituted lactamides, however, the selectivity appeared though in low ratios (~2.2). Requisite factors that govern the stereoselectivity, *i.e.* nucleophilicity of both internal and external nucleophiles and substitution on amine units, were also examined.

Introduction

Recently, for the protection of the environment as well as energy efficiency, new synthetic methods with high yields, reduced by-products and reduced energy consumption are needed. For this purpose, electro-organic reactions seem to be suitable because they can take place at ambient temperatures, in heavy metal-free media and with high product selectivity.[1] In the course of extending their domain toward highly-selective reactions, a number of stereoselective reactions were developed by the use of, for example, asymmetrically modified electrodes,[2] chiral mediators[3] and substrates possessing chiral substituents.[4] In the study of substrates possessing chiral substituents, some stereoselective intramolecular reactions were reported[5] whereas few satisfactory results were reported for intermolecular reactions. This may be attributable to weaker interaction between reaction centers and chiral substituents because electro-organic reactions are ordinarily carried out under highly polar conditions.[6]

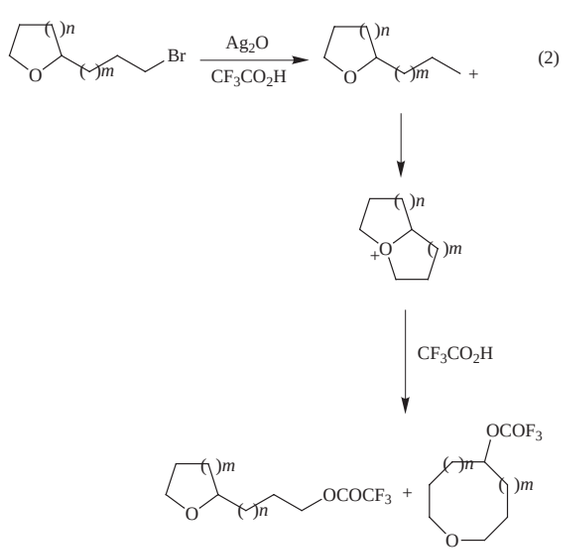
Matsumura and Shono developed many electo-organic reactions of amines utilizable for the synthesis of biologically active compounds.[7] Among them, methoxylation at the position α to the nitrogen atom of carbamates and amides is a useful method for introducing a functional group to the α position of amines [eqn. (1)].[8] Since α-methoxyamine derivatives can be activated



(1)

by Lewis acids, stereoselective introduction of a nucleophile seems possible by the use of asymmetric Lewis acid catalysts. Although some stereoselective electro-organic reactions of chiral amines were reported, the selectivity was attributed to the non-bonded repulsion between substituents on the asymmetric center and the species to be introduced.[4]

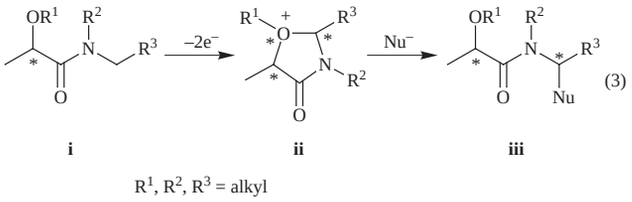
Lactic acid is a naturally occurring inexpensive chiral compound.[9] However, there are few reports on stereoselective electro-organic reactions using lactic acid.[10] This is because the highly polar conditions of the reactions disfavor the electrostatic interaction of the hydroxy group of lactic acid, which is necessary for stereocontrol. In this regard, the authors recently have found that under highly polar conditions, such as in trifluoroacetic acid solution, the oxygen atom of a cyclic ether forms a bicyclic oxonium ion with an intramolecularly generated carbocation, and the oxonium ion underwent either a ring-expansion or ring-switching reaction [eqn. (2)].[11] In this



(2)

bicyclooxonium ion formation, one of the key factors that governs the chemoselectivity is the nucleophilicity of the ethereal oxygen atom.

Based on this finding, we expected that an alkoxy derivative of lactic acid may form an oxonium ion with a carbocation intramolecularly generated by anodic oxidation and result in a stereoselective reaction. To verify this possibility, the authors chose the methoxylation reported by Matsumura and Shono[8a] as a prototype reaction and applied it to lactamides **i** [eqn. (3)]. In this anodic methoxylation, the alkoxy-substituted carbon of lactamides is expected to play a stereogenic role; the alkoxy group functions as an internal nucleophile to attack the



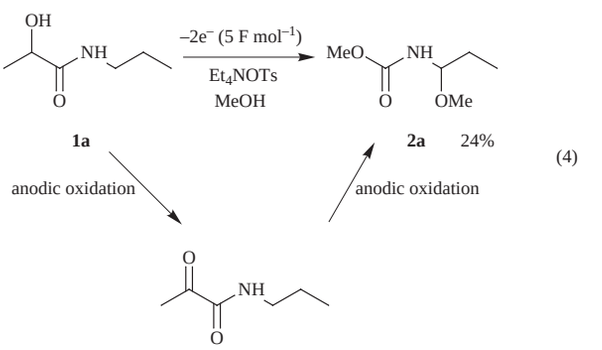
carbocation on the amine unit, thus forming a cyclic oxonium ion **ii**. Then, **ii** will be attacked by an external nucleophile more or less in a stereoselective way to give lactamide derivative **iii**.

In this paper, we report evidence that the alkoxy substituent of lactamide derivatives can form a cyclic oxonium ion with an electrochemically generated internal carbocation and, thence, a stereoselective substitution on the amine unit can be realized.

Results and discussions

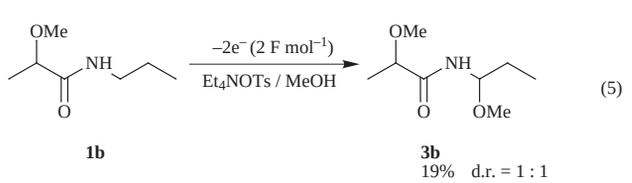
Stabilization of the lactic acid unit as a chiral source

First of all, to make it clear why lactic acid has not been used widely in electro-organic reactions despite it being an inexpensive chiral source, anodic methoxylation of *N*-propyllactamide **1a** was examined according to Shono's method[12] [eqn. (4)].

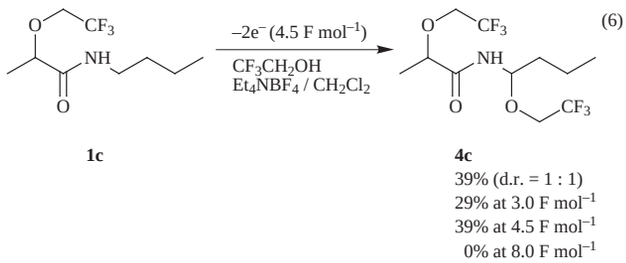


Instead of the expected product *N*-α-methoxypropyllactamide, methyl *N*-α-methoxypropylcarbamate **2a** was obtained. It is known that under electrochemical conditions alcohols are oxidized to carbonyl compounds[13] and diketones are cleaved.[14] This means that in the oxidation of lactamides, the hydroxy group of the lactic acid unit is first oxidized to a carbonyl group and the diketone, thus formed, is cleaved oxidatively to give methyl *N*-α-methoxypropylcarbamate **2a**. As a consequence, lactamide **1a** is not suitable as a chiral source in electro-organic reactions.

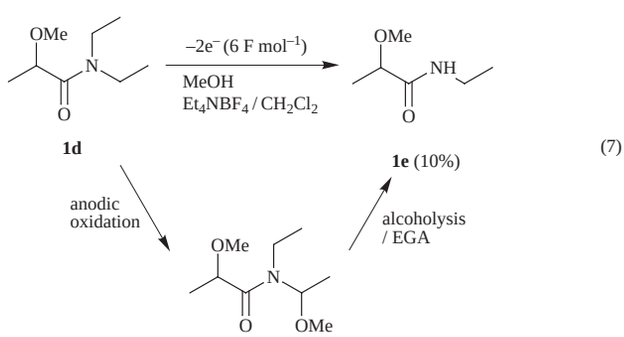
To protect the acid unit from oxidative decomposition, increasing the oxidation potential of the α oxygenic substituent might prove effective. In this regard, substrate **1b** possessing an α methoxy group instead of the hydroxy group was examined [eqn. (5)]. However, electrolysis of **1b** gave the expected methoxylation product **3b** in only 19% yield. Ethers are known to be oxidized electrochemically to carbonyl compounds, which are further decomposed.[15] The low product yield of **3b** can be attributed to the electrochemical oxidation of the methoxy group of the acid unit.



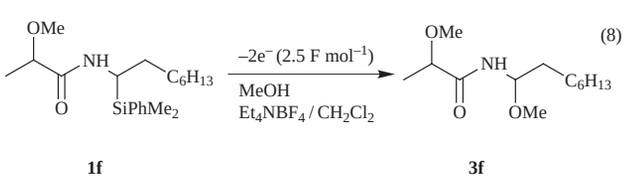
Therefore, an alkoxy group on the acid unit possessing a higher oxidation potential than that of the amine unit seems essential for both protecting the acid unit from electrochemical decomposition and producing the expected α-methoxyamine derivative in high yields. Matsumura reported that α-(trifluoroethoxy)carbamates were obtained when trifluoroethanol, possessing a higher oxidation potential than methanol, was used as a nucleophile in a similar reaction.[16] Thus, we carried out the electrochemical oxidation of trifluoroethoxy-substituted lactamide **1c** and obtained α-trifluoroethoxylation product **4c** in 39% yield [eqn. (6)]. However, an excess amount of electricity (8 F mol^{-1}) caused its decomposition.



Although oxidation of the acid unit was suppressed by protecting the hydroxy group with a trifluoroethyl group, the yield of **4c** was still low. We suspected that oxidative decomposition of the amine unit may be the reason for such a low yield. In fact, when we carried out the electrochemical oxidation of *N*,*N*-diethyllactamide derivative **1d**, *N*-ethyllactamide derivative **1e** was obtained [eqn. (7)]. This means that the initially formed α-methoxylation product was decomposed by the electrochemically generated acid (EGA).



Now, we have found that having the oxidation potential of the acid unit higher than that of the amine unit is not appropriate because it may not always prevent the oxidation of *N*-alkyl groups in the product. Instead, it seems more promising to reduce the oxidation potential of the amine unit of the starting amide relative to the acid unit. This method can also suppress the generation of EGA. Based on the report that a silyl or stannyl group on the α-position of an *N*-alkyl chain can reduce the oxidation potential of the amine unit,[17] we carried out electrochemical oxidation of α-silyl-substituted *N*-alkyllactamide **1f**, finding improvement in both the current efficiency and product yield [eqn. (8)].

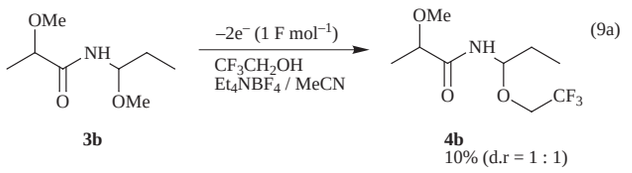


Internal *vs.* external nucleophilic attack

So far, appropriate modification of substrate structures had enabled lactic acid to be used in electro-organic reactions, albeit that the acid still did not function as a stereogenic unit. In the ring-expansion reaction,[11] when the nucleophilicity of the internal nucleophile was lower than that of an external one, the latter attacked the cationic center to disfavor the ring-

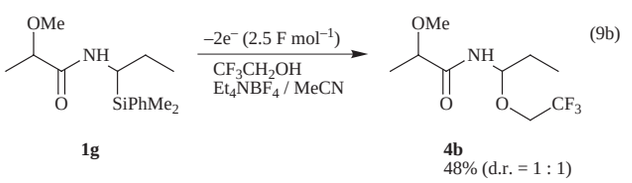
expansion. In the present electrochemical reactions thus far examined, external alcohols are more nucleophilic than the internal alkoxy groups because both have the same alkoxy groups. Therefore, when a carbocation is electrochemically generated on the amine unit, attack by the external nucleophile can predominate over the internal one and disfavors intramolecular oxonium ion formation, which is essential for the stereoselective reaction we designed.

On this assumption, external nucleophiles which are less nucleophilic than the internal alkoxy substituents were examined [eqn. (9)]. First, anodic oxidation of *N*-(α-methoxypropyl)-



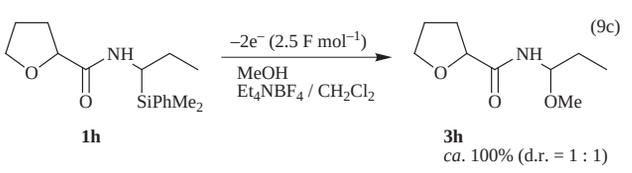
(9a)

3b **4b**
10% (d.r = 1 : 1)



(9b)

1g **4b**
48% (d.r. = 1 : 1)

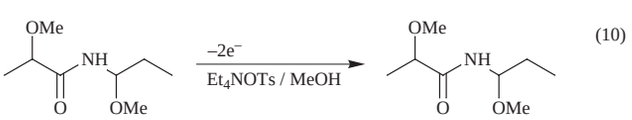


(9c)

1h **3h**
ca. 100% (d.r. = 1 : 1)

O-methyllactamide **3b** was examined in the presence of CF_3CH_2OH to discover if the exchange of α-CH_3O group on the *N*-alkyl substituent for a trifluoroethoxyl group can produce any diastereoselectivity. However, exchanged product **4b** was obtained in low yield without selectivity [eqn. (9a)]. Second, the similar oxidation of *N*-(α-silylalkyl)carboxylic amides **1g** and **1h** was examined in the presence of CF_3CH_2OH for **1g** and methanol for **1h**. However, again, the expected diastereoselectivity was not observed in products **4b** and **3h** [eqns. (9b) and (9c)].

The starting amides used in the reactions shown in eqn. (9) were composed of equal amounts of the diastereomers. If the external nucleophilic attack proceeded directly *via* an S_N2-like mechanism with these substrates, not *via* the cyclic oxonium intermediate, the products would also show diastereomer ratios of 1 : 1. To examine this possibility, the exchange reaction of the α-CH_3O group of **3b** possessing a diastereomer ratio of 2.38 : 1 was examined in MeOH under the catalysis of EGA [eqn. (10)].



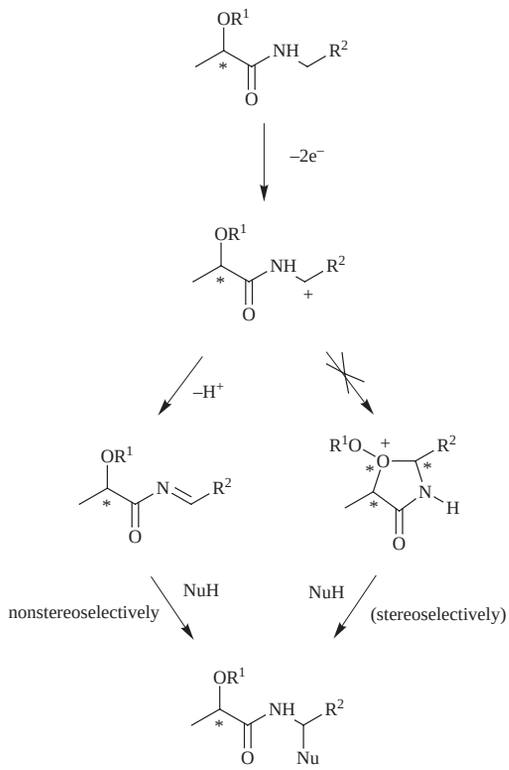
(10)

3b **3b**
0 F mol^{-1} d.r. = 2.38 : 1
1 F mol^{-1} d.r. = 1.23 : 1
2 F mol^{-1} d.r. = 1.18 : 1

The ratio was decreased to 1 after the passage of electricity. This indicates that the stereoselectivity of the external nucleophilic attack on **3b** or on the corresponding oxonium ion intermediate is low, or the reaction proceeds *via* a different mechanism.

N-Methyl-*N*-(α-silylalkyl)-*O*-alkyllactamide derivatives

The amide cation, in which the cation center is located on the α-position of the *N*-alkyl group, tends to release the proton on the nitrogen to generate a stable imine. The substrates we have examined thus far were *N*-monosubstituted amides and, therefore, the corresponding amide cations probably underwent deprotonation to form imines rather than cyclic oxonium ions (Scheme 1). Therefore, the reaction of *N*,*N*-disubstituted

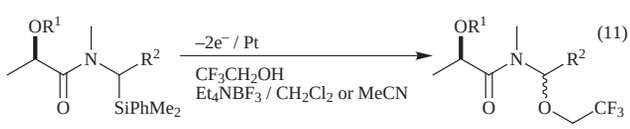


Scheme 1

amides **5**, with which the intermediacy of cyclic oxonium ions is more likely than with monosubstituted amides, seems more appropriate for the generation of the expected stereoselectivity.

In advance of the reaction, the relative stability of each stereoisomer of the oxonium ion was calculated by molecular mechanics calculation: the oxonium atom was replaced by a nitrogen atom for these approximate calculations (Table 1). The calculation predicts that the stereoisomer **ii**(**f**) is the most stable.

Based upon this prediction, electrochemical alkoxylation of *N*-methyl-*N*-(α-silylalkyl)-*O*-alkyllactamides **5a**–**e** was examined [eqn. (11)] (Table 2). When an external nucleophile possess-

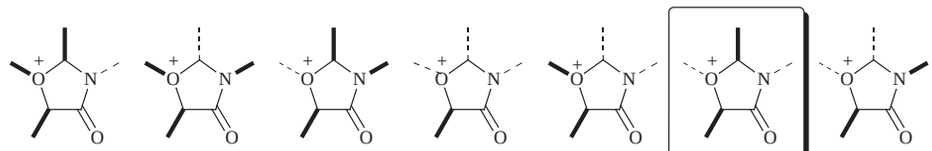


(11)

5a–e **7a–e**
d. r. = 1.2 - 2.2 : 1

ing the same alkoxy group as that of the internal nucleophile was used, the diastereomer ratio was 1.2 : 1 (runs 1 and 5, Table 2). When the external nucleophile was less nucleophilic than the internal one, the ratio was improved to 1.7 : 1 (run 3). When no internal nucleophile existed, the selectivity was not observed (run 6), probably because intramolecular formation of the oxonium ion did not take place. This implies that simple steric hindrance in an acyclic intermediate does not produce diastereoselectivity. Hence, for the diastereogenesis, internal oxonium ion formation seems essential, as was indicated by the

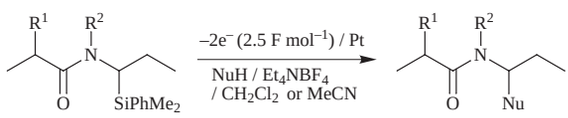
Table 1 Relative stability of cyclic oxonium ions estimated by MM2 calculation[a]



ii	a	b	c	d	e	f	g
ΔE/kcal mol^{-1}	12.44	7.91	5.72	8.03	7.91	0	8.36

[a] Substituents are methyl groups. Oxonium ion replaced with a nitrogen atom for the purpose of the calculations.

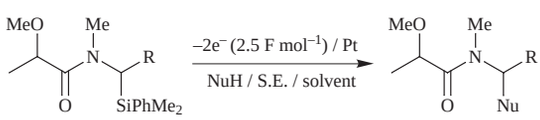
Table 2 Electrochemical α-alkoxylation of *N*,*N*,*O*-trisubstituted lactamide derivatives



Run	Substrate	R^1	R^2	NuH	Product	Diastereomer ratio	Yield (%)[a]
1	**5a**	MeO	Me	MeOH	**6a**	1.2 : 1	18 (20)
2	**1g**	MeO	H	MeOH	**3b**	1.0 : 1	33 (48)
3	**5a**	MeO	Me	CF_3CH_2OH	**7a**	1.7 : 1	43 (77)
4	**5b**	CF_3CH_2O	Me	MeOH	**6b**	1.0 : 1	65 (73)
5	**5b**	CF_3CH_2O	Me	CF_3CH_2OH	**7b**	1.2 : 1	28 (30)
6	**8a**	Et	Me	MeOH	**9a**	1.0 : 1	50 (50)

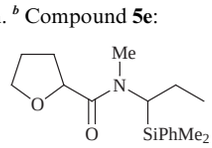
[a] Yields in parentheses are based on the substrate conversion.

Table 3 Electrochemical α-alkoxylation of *N*,*N*,*O*-trisubstituted lactamide derivatives



Run	Substrate	R	NuH	Solvent	S.E.	Product	Diastereomer ratio (% yield)[a]
1	**5a**	Et	CF_3CH_2OH	MeCN	Et_4NBF_4	**7a**	1.7 : 1 (77)
2	**5a**	Et	CF_3CH_2OH	CH_2Cl_2	Bu_4NBF_4	**7a**	1.5 : 1 (47)
3	**5a**	Et	CF_3CH_2OH	CH_2Cl_2	Et_4NClO_4	**7a**	1.5 : 1 (52)
4	**5a**	Et	CF_3CH_2OH	CH_2Cl_2	Bu_4NClO_4	**7a**	1.5 : 1 (59)
5	**5a**	Et	CF_3CH_2OH	CF_3CH_2OH	Et_4NBF_4	**7a**	1.4 : 1 (70)
6	**5a**	Et	CF_3CO_2H	CH_2Cl_2	Et_4NBF_4	none	decomposed
7	**5a**	Et	CH_3CO_2H	CH_2Cl_2	Et_4NBF_4	none	no reaction
8	**5c**	Pr	CF_3CH_2OH	MeCN	Et_4NBF_4	**7c**	1.5 : 1 (52)
9	**5c**	Pr	CF_3CH_2OH	CH_2Cl_2	Et_4NBF_4	**7c**	1.6 : 1 (52)
10	**5d**	heptyl	CF_3CH_2OH	MeCN	Et_4NBF_4	**7d**	2.2 : 1 (53)
11	**5d**	heptyl	CF_3CH_2OH	CH_2Cl_2	Et_4NBF_4	**7d**	1.6 : 1 (34)
12	**5e**	Et (THF)[b]	CF_3CH_2OH	MeCN	Et_4NBF_4	**7e**	1.7 : 1 (50)
13	**5e**	Et (THF)[b]	MeOH	MeCN	Et_4NBF_4	**6e**	1.1 : 1 (64)

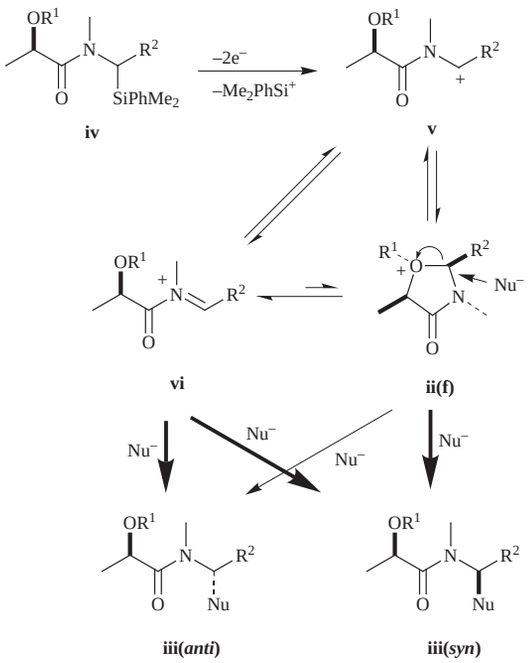
[a] Yields in parentheses are based on the substrate conversion. [b] Compound **5e**:



observation that the diastereoselectivity appeared only when the external nucleophile was less nucleophilic than the internal one.

Results for the other reactions are shown in Table 3. Again, the use of external nucleophiles with low nucleophilicity also leads to the appearance of diastereoselectivity. When acetonitrile was used as the solvent, it gave a better result than dichloromethane (compare runs 1 with 2, and 10 with 11, Table 3). It was also presumed that the properties of the supporting electrolytes is important for the stabilization of intramolecular oxonium ion **ii**, but the diastereoselectivity was not influenced by the electrolytes examined (runs 2, 3 and 4, Table 3).

The appearance of the diastereoselectivity shown in Tables 2 and 3 can be explained as follows (Scheme 2). Electrochemically generated carbocation **v** first forms oxonium ion **ii** as a result of internal nucleophilic attack by the alkoxy group. The stereochemistry of the oxonium ion is controlled by the relative stability difference (Table 1) to favor isomer **f**, upon which



Scheme 2

consecutive attack by an external nucleophile takes place on the α position of amine unit, namely, an external nucleophile approaches from the backside of the oxonium atom to give predominantly diastereomer **iii**(***syn***), as shown in Scheme 2. On the other hand, if carbocation **v** cannot form **ii** efficiently, it can be stabilized in the form of iminium ion **vi** to which external nucleophile attack takes place nonstereoselectively. However, in general, intermediates **ii**(**f**) and **vi** are in equilibrium and, therefore, the diastereoselectivity in products **iii** is attenuated.[18]

Conclusion

After a large number of discouraging results, we finally obtained evidence to conclude that the electrochemical alkoxylation of lactamide derivatives can proceed stereoselectively *via* the formation of a cyclic oxonium ion as the key intermediate. To generate the selectivity, the following factors must be taken into consideration: (i) the internal nucleophiles, *i.e.* alkoxy substituents, must be more nucleophilic than the external ones for the intramolecular oxonium ion formation, (ii) the secondary amine unit is essential, not only for oxonium ion formation, but also for stereocontrol of the consecutive substitution, and (iii) the combination of an alkoxy group on the lactic acid unit, which is stable under the oxidation conditions, and a readily oxidizable substituent on the amine unit must be assembled in the starting substrate.

Experimental

Tetrahydrofuran, dichloromethane, acetonitrile and triethylamine were purified by the usual methods[19] and other commercially available chemicals were used without further purification. ^{1}H NMR and ^{13}C NMR spectra were measured on a GE QE-300 spectrometer in $CDCl_3$ solutions using $CHCl_3$ (δ_H 7.26) and $CDCl_3$ (δ_C 77.0) as internal standards. Chemical shifts (δ) are given in ppm and the coupling constants (J) are given in Hz. IR spectra were recorded on a JASCO IR-810 spectrometer. High resolution mass spectra were measured on a Hitachi M-80 spectrometer or a JEOL MS Station JMD-700. Elemental analyses were performed on a Yanaco MT-5 analyzer. Molecular mechanics calculation was conducted by the use of HyperChemTM, Hypercube, Inc. Ether refers to diethyl ether.

Materials

N-Propyllactamide **1a**,[20] *N*,*N*-diethyl-2-methoxypropanamide **1d**[21] and methyl *N*-(1-methoxypropyl)carbamate **2a**[8a] are known compounds.

N-Propyl-2-methoxypropanamide 1b

N-Propyl-2-bromopropanamide[22] (13.3 g, 68.6 mmol) and sodium methoxide in methanol (28 wt%, 41.2 g, 214 mmol) were mixed in dry methanol (43 cm^3) and the mixture was refluxed for 1 h. After the solvent was removed, water (50 cm^3) was added to the residue,[23] acidified to pH 4 with conc. hydrochloric acid, the aqueous solution was extracted with ether (5 × 50 cm^3), organic extracts were combined and dried over $MgSO_4$. After removing ether, the residue was distilled to afford **1b** (4.4 g, 45%): bp 108 °C/18 mmHg; δ_H 0.90 (3 H, t, *J* 7.5), 1.34 (3 H, d, *J* 6.6), 1.52 (2 H, qd, *J* 7.5 and 6.9), 3.21 (2 H, td, *J* 6.9 and 6.9), 3.36 (3 H, s), 3.71 (1 H, q, *J* 6.6) and 6.57 (1 H, br s); δ_C 11.17, 18.01, 22.72, 40.34, 57.29, 78.16 and 172.89; ν_{max}/cm^{-1} (liq. film) 3300, 2960, 2940, 2870, 1660, 1540, 1460 and 1120; *m*/*z* (EI) (Found: M$^+$, 145.1104. $C_7H_{15}NO_2$ requires *M*, 145.1104).

N-Butyl-2-(2,2,2-trifluoroethoxy)propanamide 1c

To a solution of *N*-butyl-2-bromopropanamide[24] (3.0 g, 14.4 mmol) in 2,2,2-trifluoroethanol (9 cm^3) was added 60% sodium hydride in oil (1.02 g, 25.5 mmol) at ambient temperature under an Ar atmosphere and the solution was refluxed for 2 h. Water (20 cm^3) was added to the solution. The solution was extracted with ether (3 × 30 cm^3) and the organic extracts were dried over $MgSO_4$ and evaporated to give a residue, which was subjected to flash column chromatography (eluent: 10 to 80% ethyl acetate–hexane) to afford **1c** (2.53 g, 77%); δ_H 0.92 (3 H, t, *J* 7.2), 1.34 (2 H, dt, *J* 7.5 and 7.2), 1.43 (3 H, d, *J* 6.6), 1.49 (2 H, tt, *J* 7.5 and 7.2), 3.27 (2 H, m, contains t, *J* 6.9), 3.87 (2 H, m, contains q, *J* 8.3), 3.99 (1 H, q, *J* 6.6) and 6.40 (1 H, br s); δ_C 13.58, 18.14, 19.89, 31.50, 38.69, 67.07 (q, *J* 34.4), 78.41, 123.40 (q, *J* 278.8) and 171.22; ν_{max}/cm^{-1} (liq. film) 3300, 2960, 2940, 1660, 1540, 1280, 1160, 1130 and 960.

N-[1-(Dimethylphenylsilyl)octyl]-2-methoxypropanamide 1f

A general procedure for the preparation of *N*-(silylalkyl) substituted lactamides **1g**, **1h**, **5a**–**e** and **8a**.

To a solution of 1-(dimethylphenylsilyl)octanol[25] (4.0 g, 15.2 mmol) and dry triethylamine (3.2 cm^3, 22.7 mmol) in dichloromethane (74 cm^3), methanesulfonyl chloride (1.3 cm^3, 16.7 mmol) was added at 0 °C under an Ar atmosphere.[26] After stirring for 15 min, water (80 cm^3) was added to the solution, and the organic layer was separated. The organic layer was dried over $MgSO_4$ and evaporated to give a residue. The residue was dissolved in methanol (150 cm^3), through which NH_3 gas was bubbled for 3 h at 0 °C. After stirring overnight at ambient temperature, the solution was concentrated to afford a residue. 1 M aq. NaOH (100 cm^3) was added to the residue and extracted with ether (4 × 50 cm^3). The organic extracts were combined, dried over $MgSO_4$ and evaporated to give a residue, which was subjected to flash column chromatography (eluent: 10–100% ethyl acetate–hexane) to afford 1-(dimethylphenylsilyl)octylamine (1.35 g, 34%).

At 0 °C under an Ar atmosphere, a solution of 2-methoxypropanoic acid[27] (0.41 g, 3.89 mmol) in dichloromethane (1.7 cm^3) was added into a solution of DCC (0.79 g, 3.82 mmol) in dichloromethane (2.5 cm^3) and stirred for 15 min.[28] To this solution, a solution of 1-(dimethylphenylsilyl)octylamine (1.0 g, 3.83 mmol) in dichloromethane (1.7 cm^3) was added, and the mixture was gradually warmed to ambient temperature under stirring overnight. The white precipitate was filtered off and washed with dichloromethane (30 cm^3). The filtrate was washed with water (30 cm^3). The organic layer was dried over $MgSO_4$

and evaporated to give a residue, which was subjected to flash column chromatography (eluent: 5 to 20% ethyl acetate–hexane) to afford a 1:1 diastereomeric mixture of **1f** (1.08 g, 81%): δ_H 0.32 (1.5 H, s), 0.33 (3 H, s), 0.34 (1.5 H, s), 0.84 (3 H, t, *J* 6.6), 1.27 (1.5 H, d, *J* 6.6), 1.30–1.60 (12 H, m), 1.32 (1.5 H, d, *J* 6.6), 3.31 (1.5 H, s), 3.27 (1.5 H, s), 3.68 (0.5 H, q, *J* 6.6), 3.70 (0.5 H, q, *J* 6.6), 3.73 (1 H, m), 6.12 (0.5 H, d, *J* 9.6), 6.15 (0.5 H, d, *J* 9.6), 7.36 (3 H, m) and 7.50 (2 H, m); δ_C −5.18, −4.99, −4.84, −4.74, 13.98, 18.60, 22.52, 27.05, 27.30, 29.04, 29.29, 30.79, 30.99, 31.70, 38.54, 38.75, 57.46, 57.58, 78.59, 127.83, 129.35, 133.95, 136.06 and 172.38; ν_{max}/cm^{-1} (liq. film) 3300, 2960, 2930, 2850, 1660, 1520, 1250, 1120, 840, 820 and 700; *m*/*z* (EI) (Found: M$^+$, 349.2436. $C_{20}H_{35}NO_2Si$ requires *M*, 349.2439).

***N*-[1-(Dimethylphenylsilyl)propyl]-2-methoxypropanamide 1g.** Prepared from 1-(dimethylphenylsilyl)propanol;[29] δ_H 0.32 (1.5 H, s), 0.33 (3 H, s), 0.35 (1.5 H, s), 0.86 (1.5 H, t, *J* 7.2), 0.88 (1.5 H, t, *J* 7.2), 1.28 (1.5 H, d, *J* 6.6), 1.31 (1 H, m, containing *J* 14.4 and 7.2), 1.33 (1.5 H, d, *J* 6.6), 1.62 (0.5 H, dq, *J* 14.4 and 7.2), 1.63 (0.5 H, dq, *J* 14.4 and 7.2), 3.27 (1.5 H, s), 3.32 (1.5 H, s), 3.63 (1 H, m), 3.69 (0.5 H, q, *J* 6.6), 3.71 (0.5 H, q, *J* 6.6), 6.12 (0.5 H, br s), 6.15 (0.5 H, br s), 7.37 (3 H, m), 7.50 (2 H, m); δ_C −5.16, −4.96, −4.83, −4.72, 11.84, 12.17, 18.70, 23.95, 24.18, 40.29, 40.58, 57.55, 57.63, 78.60, 127.87, 129.37, 129.45, 133.96, 136.02, 172.61, 172.75; ν_{max}/cm^{-1} (liq. film) 3400, 3290, 2960, 2930, 1660, 1520, 1250, 1120, 840, 820; *m*/*z* (EI) (Found: M$^+$, 279.1649. $C_{15}H_{25}NO_2Si$ requires *M*, 279.1656).

***N*-[1-(Dimethylphenylsilyl)propyl]tetrahydro-2-furamide 1h.** δ_H 0.30 (1.5 H, s), 0.32 (3 H, s), 0.33 (1.5 H, s), 0.83 (1.5 H, t, *J* 7.2), 0.87 (1.5 H, t, *J* 7.2), 1.6–2.2 (6 H, m), 3.62 (0.5 H, td, *J* 21.3 and 11.1), 3.64 (0.5 H, td, *J* 21.6 and 10.5), 3.81 (2 H, dd, *J* 13.8 and 6.9), 4.33 (1 H, dd, *J* 8.4 and 5.4), 6.30 (0.5 H, d, *J* 10.2), 6.37 (0.5 H, d, *J* 11.1), 7.36 (3 H, m), 7.49 (2 H, m); δ_C −5.25, −5.00, −4.90, −4.76, 11.98, 23.93, 24.08, 25.38, 30.34, 40.41, 40.73, 69.28, 78.42, 127.84, 129.39, 133.88, 136.00, 172.68, 172.81; ν_{max}/cm^{-1} (liq. film) 3400, 3300, 2950, 2930, 2870, 1660, 1520, 1250, 1070, 840; *m*/*z* (EI) (Found: M$^+$, 291.1647. $C_{16}H_{25}NO_2Si$ requires *M*, 292.1656).

***N*-[1-(Dimethylphenylsilyl)propyl]-*N*-methyl-2-methoxypropanamide 5a.** δ_H 0.34 (3 H, s), 0.35 (3 H, s), 0.84 (1.5 H, t, *J* 7.2), 0.85 (1.5 H, t, *J* 7.2), 1.17 (1.5 H, d, *J* 6.6), 1.20 (1.5 H, d, *J* 6.6), 1.65 (2 H, m, containing *J* 7.2), 2.85 (1.5 H, s), 2.87 (1.5 H, s), 3.17 (1.5 H, s), 3.19 (1.5 H, s), 3.90 (1 H, m), 4.03 (0.5 H, q, *J* 6.6), 4.04 (0.5 H, q, *J* 6.6), 7.32 (3 H, m), 7.50 (2 H, m); δ_C −3.77, −3.28, 12.18, 12.29, 17.37, 17.41, 20.39, 20.56, 33.08, 33.38, 49.97, 50.13, 56.43, 56.57, 76.20, 76.59, 127.71, 129.33, 133.89, 137.66, 171.43; ν_{max}/cm^{-1} (liq. film) 2950, 2930, 1810, 1640, 1460, 1430, 1400, 1250, 1120, 840, 820, 730, 700; *m*/*z* (EI) (Found: M$^+$, 293.1812. $C_{16}H_{27}NO_2Si$ requires *M*, 293.1812) (Found: C, 65.16; H, 9.26; N, 4.73; $C_{16}H_{27}NO_2Si$ requires C, 65.48; H, 9.27; N, 4.77%).

***N*-[1-(Dimethylphenylsilyl)propyl]-*N*-methyl-2-(2,2,2-trifluoroethoxy)propanamide 5b.** 2,2,2-Trifluoroethanol (16.4 g, 0.163 mol) and 2-bromopropanoic acid (12.5 g, 81.7 mmol) were added dropwise into a suspended solution of sodium hydride (60% in oil, 6.5 g, 0.164 mol) in tetrahydrofuran (50 cm^3) at 0 °C under an Ar atmosphere and the solution was refluxed for 2 h. The solvent was removed, water (30 cm^3) was added to the residue, the mixture was acidified to pH 3 with conc. hydrochloric acid, the aqueous solution was extracted with ether (3 × 30 cm^3), the organic extracts were combined and dried over $MgSO_4$. After removing ether, the residue was distilled to afford 2-(2,2,2-trifluoroethoxy)propanoic acid; bp 103 °C/15 mmHg; δ_H 1.35 (3 H, d, *J* 6.9), 3.80 (1 H, dd, *J* 12.3 and 8.4), 4.09 (1 H, dd, *J* 12.3 and 8.4), 4.21 (1 H, q, *J* 6.9), 11.45 (1 H, br s); δ_C 17.98, 67.34 (q, *J* 34.4), 75.47, 123.50 (q, *J* 276.8), 177.86; ν_{max}/cm^{-1} (liq. film) 3000, 2950, 1730, 1280, 1170, 1140, 970.

According to the general procedure, 2-(2,2,2-trifluoroethoxy)propanoic acid was converted to **5b**; δ_H 0.33 (1.5 H, s), 0.35 (1.5 H, s), 0.38 (3 H, s), 0.84 (1.5 H, t, *J* 7.2), 0.86 (1.5 H, t, *J* 7.2), 1.23 (1.5 H, d, *J* 6.6), 1.27 (1.5 H, d, *J* 6.6), 1.60–1.80 (2 H, m), 2.83 (1.5 H, s), 2.84 (1.5 H, s), 3.31 (0.5 H, q, *J* 8.4), 3.35 (0.5 H, q, *J* 8.7), 3.67 (0.5 H, q, *J* 8.7), 3.71 (0.5 H, q, *J* 9.0), 3.92 (1 H, m), 4.30 (0.5 H, q, *J* 6.6), 4.31 (0.5 H, q, *J* 6.6), 7.33 (3 H, m), 7.51 (2 H, m); δ_C −4.16, −4.05, −3.22, −3.00, 12.12, 16.83, 17.23, 20.36, 20.49, 33.19, 33.42, 50.26, 50.39, 65.67 (q, *J* 34.4), 75.22, 75.42, 123.75 (q, *J* 274.4), 127.74, 129.23, 133.90, 137.17, 170.04; ν_{max}/cm^{-1} (liq. film) 2960, 2940, 1640, 1280, 1160, 1140, 970, 840; *m*/*z* (EI) (Found: M$^+$, 361.1679. $C_{17}H_{26}NO_2F_3Si$ requires *M*, 361.1686).

***N*-[1-(Dimethylphenylsilyl)butyl]-*N*-methyl-2-methoxypropanamide 5c.** According to the reported method,[25] butanal was converted to 1-(dimethylphenylsilyl)butanol; δ_H 0.34 (3 H, s), 0.35 (3 H, s), 0.91 (3 H, t, *J* 7.2), 1.30 (2 H, m, containing *J* 7.2), 1.52 (3 H, m, containing *J* 9.6 and 4.2), 3.53 (1 H, dd, *J* 9.6 and 4.2), 7.39 (3 H, m), 7.57 (2 H, m); δ_C −5.71, −5.42, 13.83, 19.87, 35.48, 65.15, 127.85, 129.25, 134.09, 136.74; ν_{max}/cm^{-1} (liq. film) 3400, 2950, 2940, 1430, 1250, 1110, 830, 820, 780, 730, 700; *m*/*z* (CI) (Found: M$^+$, 209.1383. $C_{12}H_{20}OSi$ + H requires *M*, 209.1362) (Found: C, 69.06; H, 9.71; $C_{12}H_{20}OSi$ requires C, 69.17; H, 9.67%).

According to the general procedure, 1-(dimethylphenylsilyl)-butanol was converted to **5c**; δ_H 0.34 (3 H, s), 0.35 (3 H, s), 0.86 (1.5 H, t, *J* 7.2), 0.87 (1.5 H, t, *J* 7.2), 1.16 (1.5 H, d, *J* 6.6), 1.19 (1.5 H, d, *J* 6.6), 1.46 (2 H, m, containing *J* 7.2), 1.73 (2 H, m), 2.84 (1.5 H, s), 2.86 (1.5 H, s), 3.17 (1.5 H, s), 3.19 (1.5 H, s), 4.02 (0.5 H, q, *J* 6.6), 4.03 (0.5 H, q, *J* 6.6), 4.09 (1 H, m), 7.33 (3 H, m), 7.53 (2 H, m); δ_C −4.27, −3.93, −3.81, −3.55, 13.70, 17.23, 20.57, 20.62, 29.47, 29.59, 33.10, 33.35, 47.59, 48.06, 56.28, 56.39, 76.05, 76.44, 127.65, 128.97, 133.85, 133.88, 137.45, 137.54, 171.20; ν_{max}/cm^{-1} (liq. film) 2950, 2930, 1640, 1400, 1250, 1120, 840, 820, 740, 700; *m*/*z* (EI) (Found: M$^+$, 307.1964. $C_{17}H_{29}NO_2Si$ requires *M*, 307.1969) (Found: C, 66.75; H, 9.54; N, 4.51; $C_{17}H_{29}NO_2Si$ requires C, 66.40; H, 9.51; N, 4.55%).

***N*-[1-(Dimethylphenylsilyl)octyl]-*N*-methyl-2-methoxypropanamide 5d.** δ_H 0.34 (4.5 H, s), 0.35 (1.5 H, s), 0.84 (3 H, t, *J* 7.2), 1.16 (3 H, d, *J* 6.9), 1.20 (10 H, br), 1.51 (1 H, m), 1.69 (1 H, m), 2.84 (1.5 H, s), 2.86 (1.5 H, s), 3.17 (1.5 H, s), 3.19 (1.5 H, s), 4.00 (1 H, m), 4.02 (0.5 H, q, *J* 6.9), 4.03 (0.5 H, q, *J* 6.9), 7.33 (3 H, m), 7.53 (2 H, m); δ_C −3.90, −3.76, −3.35, −3.27, 13.99, 17.30, 17.35, 22.53, 27.24, 27.40, 29.13, 29.20, 31.71, 33.38, 35.96, 47.86, 56.34, 56.51, 76.52, 127.68, 129.02, 133.93, 137.61, 171.19; ν_{max}/cm^{-1} (liq. film) 2920, 2850, 1640, 1460, 1400, 1250, 1120, 840, 820, 740, 700; *m*/*z* (EI) (Found: M$^+$, 363.2593. $C_{21}H_{37}NO_2Si$ requires *M*, 363.2595) (Found: C, 69.05; H, 10.19; N, 3.73; $C_{21}H_{37}NO_2Si$ requires C, 69.37; H, 10.26; N, 3.85%).

***N*-[1-(Dimethylphenylsilyl)propyl]-*N*-methyltetrahydro-2-furamide 5e.** δ_H 0.32 (1.5 H, s), 0.33 (1.5 H, s), 0.35 (3 H, s), 0.82 (1.5 H, t, *J* 7.2), 0.84 (1.5 H, t, *J* 7.2), 1.50–1.73 (3 H, m), 1.76–2.05 (4 H, m), 2.81 (1.5 H, s), 2.85 (1.5 H, s), 3.83 (2 H, m, containing *J* 5.7), 3.93 (0.5 H, dd, *J* 12.9 and 6.6), 4.06 (0.5 H, dd, *J* 11.4 and 4.5), 4.57 (1 H, dd, *J* 7.8 and 3.9), 7.34 (3 H, m), 7.51 (2 H, m); δ_C −3.96, −3.80, −3.62, 12.13, 12.30, 20.45, 20.62, 25.43, 25.59, 28.67, 28.77, 33.05, 33.81, 48.94, 50.18, 50.35, 68.53, 68.89, 75.71, 75.95, 127.62, 127.71, 128.95, 129.09, 133.86, 133.93, 134.00, 171.50; ν_{max}/cm^{-1} (liq. film) 2950, 2930, 2860, 1640, 1430, 1300, 1250, 1110, 1060, 830, 700; *m*/*z* (EI) (Found: M$^+$, 305.1814. $C_{17}H_{27}NO_2Si$ requires *M*, 305.1812).

***N*-[1-(Dimethylphenylsilyl)propyl]-*N*,2-dimethylbutanamide 8a.** δ_H 0.31 (1 H, s), 0.32 (1 H, s), 0.33 (1 H, s), 0.34 (1 H, s), 0.35 (1 H, s), 0.36 (1 H, s), 0.82 (3 H, t, *J* 7.2), 0.99 (1.5 H, t, *J* 5.4), 1.00 (1.5 H, t, *J* 4.8), 1.32 (1 H, m, containing *J* 7.2), 1.49–1.72 (3 H, m, containing *J* 7.2), 2.52 (1 H, m, containing *J* 7.2), 2.80 (1.5 H, s), 2.84 (1.5 H, s), 3.91 (0.5 H, dd, *J* 11.1 and 3.6), 4.16 (0.5 H, dd, *J* 11.1 and 4.5), 7.34 (3 H, m), 7.52 (2 H, m); δ_C −5.57, −5.38, −3.76, −3.66, −3.52, −3.41, 12.09, 12.21, 17.26, 17.42, 20.57, 20.57, 26.46, 27.03, 27.22, 36.63, 36.79, 67.21, 127.69, 129.00, 133.92, 136.87, 176.12; ν_{max}/cm^{-1} (liq. film) 2950, 2930, 2860, 1630, 1460, 1400, 1250, 1110, 830, 770, 730, 700; *m*/*z* (CI) (Found: M$^+$, 292.2090. $C_{17}H_{29}NOSi$ + H requires *M*, 292.2098).

Electrolysis of lactamide derivatives: typical procedures

Method (a).[12] In methanol. A solution of lactamide derivative (0.7 mmol) and the supporting electrolyte (0.2 mmol) in methanol (4 cm^3) was placed in an undivided cell equipped with a carbon rod anode (i.d. 0.5 cm) and a platinum plate cathode (2 × 1 cm^2). Constant current (20 mA) was passed at room temperature. After the electricity shown in the equations or Tables was consumed, the reaction mixture was partitioned between brine and ether. The ether layer was separated and dried over $MgSO_4$. After evaporation of the solvent, the crude product was purified *via* flash column chromatography (eluent: ethyl acetate–hexane) to obtain the product.

Method (b).[17a] In dichloromethane or acetonitrile. A solution of lactamide derivative (0.7 mmol), alcohol (7.0 mmol) and the supporting electrolyte (0.2 mmol) in dichloromethane or acetonitrile (4 cm^3) was placed in an undivided cell equipped with a platinum plate anode (2 × 1 cm^2) and a platinum plate cathode (2 × 1 cm^2). Electrolysis and work-up were carried out in a similar way to that for Method (a). Yields and diastereomer ratios of the products are shown in the equations or Tables.

***N*-Ethyl-2-methoxypropanamide 1e.** δ_H 1.13 (1.5 H, t, *J* 7.4), 1.13 (1.5 H, t, *J* 7.4), 1.33 (1.5 H, d, *J* 6.6), 1.34 (1.5 H, d, *J* 6.6), 3.28 (1 H, q, *J* 7.4), 3.28 (1 H, q, *J* 7.4), 3.35 (1.5 H, s), 3.36 (1.5 H, s), 3.69 (0.5 H, q, *J* 6.6), 3.70 (0.5 H, q, *J* 6.6), 6.52 (1 H, br s); δ_C 14.74, 17.93, 33.62, 57.32, 78.15, 172.85; ν_{max}/cm^{-1} (liq. film) 3300, 2980, 2940, 1660, 1530, 1450, 1120.

***N*-(1-Methoxypropyl)-2-methoxypropanamide 3b.** δ_H 0.90 (1.5 H, t, *J* 6.9), 0.92 (1.5 H, t, *J* 6.9), 1.35 (1.5 H, d, *J* 6.6), 1.40 (1.5 H, d, *J* 6.6), 1.54 (1 H, m, containing *J* 6.9 and 6.0), 1.69 (1 H, m, containing *J* 6.9 and 6.0), 3.29 (1.5 H, s), 3.32 (1.5 H, s), 3.37 (1.5 H, s), 3.39 (1.5 H, s), 3.74 (0.5 H, q, *J* 6.6), 3.76 (0.5 H, q, *J* 6.6), 5.01 (1 H, td, *J* 10.5 and 6.0), 6.64 (1 H, br d, *J* 6.0); δ_C 8.91, 18.15, 18.24, 28.45, 55.56, 55.83, 57.35, 57.53, 77.93, 78.07, 81.62, 81.88, 173.76; ν_{max}/cm^{-1} (liq. film) 3300, 2970, 2940, 2830, 1670, 1520, 1460, 1370, 1200, 1120, 1030; *m*/*z* (CI) (Found: M$^+$, 176.1270. $C_8H_{17}NO_3$ + H requires *M*, 176.1287).

***N*-(1-Methoxyoctyl)-2-methoxypropanamide 3f.** δ_H 0.86 (3 H, t, *J* 6.3), 1.36 (3 H, d, *J* 6.9), 1.20–1.44 (10 H, br), 1.52 (1 H, m), 1.68 (1 H, m), 3.29 (1.5 H, s), 3.33 (1.5 H, s), 3.37 (1.5 H, s), 3.40 (1.5 H, s), 3.74 (0.5 H, q, *J* 6.9), 3.78 (0.5 H, q, *J* 6.9), 5.07 (1 H, dt, *J* 9.3 and 6.3), 6.67 (1 H, br t, *J* 9.3); δ_C 13.70, 18.13, 22.52, 24.70, 29.06, 29.14, 31.63, 35.44, 55.83, 57.58, 78.09, 80.75, 173.55; ν_{max}/cm^{-1} (liq. film) 3300, 2930, 2850, 1680, 1520, 1460, 1120, 1060; *m*/*z* (EI) (Found: M$^+$, 230.1753. $C_{13}H_{27}NO_3 - CH_3$ requires *M*, 230.1757).

***N*-(1-Methoxypropyl)tetrahydro-2-furamide 3h.** δ_H 0.87 (1.5 H, t, *J* 7.2), 0.90 (1.5 H, t, *J* 7.2), 1.5–2.2 (6 H, m), 3.27 (1.5 H, s), 3.29 (1.5 H, s), 3.89 (2 H, m), 4.32 (0.5 H, dd, *J* 8.3 and 5.7), 4.37 (0.5 H, dd, *J* 8.4 and 5.7), 4.96 (0.5 H, t, *J* 6.0), 4.99 (0.5 H, t, *J* 6.0), 6.79 (1 H, br s); δ_C 8.94, 25.40, 28.37, 28.53, 30.19, 30.42, 55.60, 55.73, 69.37, 78.13, 78.27, 81.72, 173.81; ν_{max}/cm^{-1} (liq. film) 3400, 3300, 2960, 2930, 2870, 1670, 1510, 1080.

***N*-[1-(2,2,2-Trifluoroethoxy)propyl]-2-methoxypropanamide 4b.** δ_H 0.95 (1.5 H, t, *J* 7.5), 0.97 (1.5 H, t, *J* 7.5), 1.36 (1.5 H, d, *J* 6.3), 1.37 (1.5 H, *J* 6.6), 1.62 (1 H, qd, *J* 7.5 and 6.6), 1.78 (1 H, qd, *J* 7.5 and 6.6), 3.38 (1.5 H, s), 3.40 (1.5 H, s), 3.79 (1 H, q, *J* 6.6), 3.95 (2 H, m), 5.18 (0.5 H, t, *J* 6.6), 5.22 (0.5 H, t, *J* 6.6), 6.90 (1 H, br s); δ_C 8.93, 17.67, 17.84, 28.19, 57.27, 57.38, 65.89 (q, *J* 35.5), 66.09 (q, *J* 33.9), 77.87, 81.40, 81.67, 123.73 (q, *J* 275.7), 174.03; ν_{max}/cm^{-1} (liq. film) 3400, 3300, 2980, 2940, 2830, 1680, 1510, 1460, 1280, 1160, 1120, 1100, 980.

***N*-[1-(2,2,2-Trifluoroethoxy)butyl]-2-(2,2,2-trifluoroethoxy)-propanamide 4c.** δ_H 0.93 (3 H, t, *J* 7.4), 1.44 (1.5 H, d, *J* 6.9), 1.47 (1.5 H, d, *J* 6.9), 1.3–1.8 (4 H, m), 3.8–4.3 (5 H, m), 5.28 (0.5 H, td, *J* 9.9 and 3.0), 5.29 (0.5 H, td, *J* 9.9 and 3.0), 6.81 (0.5 H, br d, *J* 9.9), 6.84 (0.5 H, br d, *J* 9.9); δ_C 13.41, 17.43, 18.09, 36.96, 66.10 (q, *J* 34.6), 67.17 (q, *J* 34.4), 78.13, 80.32, 80.56, 123.32 (q, *J* 279.9), 123.70 (q, *J* 276.7), 172.18, 172.34; ν_{max}/cm^{-1} (liq. film) 3300, 2960, 2940, 2880, 1680, 1520, 1280, 1170, 970; *m*/*z* (EI) (Found: M$^+$, 324.0956. $C_{11}H_{17}NO_3F_6$ − H requires *M*, 324.1035).

***N*-(1-Methoxypropyl)-*N*-methyl-2-methoxypropanamide 6a.** δ_H 0.85 (1.4 H, t, *J* 7.5), 0.85 (1.6 H, t, *J* 7.5), 1.38 (1.6 H, d, *J* 6.6), 1.40 (1.4 H, d, *J* 6.6), 1.45–1.60 (1 H, m), 1.60–1.80 (1 H, m), 2.86 (3 H, s), 3.21 (1.4 H, s), 3.22 (1.6 H, s), 4.15 (q, *J* 6.6) and 4.17 (q, *J* 6.6)(1 H), 4.90 (0.2 H, t, *J* 5.4), 4.92 (0.2 H, t, *J* 5.7), 5.57 (0.3 H, t, *J* 6.6), 5.59 (0.3 H, t, *J* 6.6); δ_C 8.98, 9.58, 17.03, 17.21, 25.07, 55.36, 56.47, 75.14, 75.45, 77.01, 77.44, 85.35, 85.56, 88.21, 88.56, 173.08; ν_{max}/cm^{-1} (liq. film) 2880, 2840, 1660, 1460, 1120, 1090, 1060; *m*/*z* (EI) (Found: M$^+$, 189.1373. $C_9H_{19}NO_3$ requires *M*, 189.1365).

***N*-(1-Methoxypropyl)-*N*-methyl-2-(2,2,2-trifluoroethoxy)-propanamide 6b.** δ_H 0.84 (1.5 H, t, *J* 7.2), 0.86 (1.5 H, t, *J* 7.5), 1.45 (1.5 H, d, *J* 6.6), 1.47 (1.5 H, *J* 6.6), 1.51 (1 H, m), 1.68 (1 H, m), 2.84 (3 H, s), 3.20 (1.5 H, s), 3.22 (1.5 H, s), 3.71 (2 H, m), 3.94 (2 H, m), 4.48 (1 H, q, *J* 6.6), 5.54 (0.5 H, t, *J* 6.9), 5.56 (0.5 H, t, *J* 6.6); δ_C 8.82, 16.78, 17.01, 25.02, 26.19, 26.59, 54.83, 55.34, 65.66 (q, *J* 32.7), 74.08, 74.81, 85.53, 85.72, 88.52, 123.70 (q, *J* 274.2), 171.61; ν_{max}/cm^{-1} (liq. film) 2970, 2940, 2880, 2830, 1660, 1460, 1410, 1280, 1160, 1140, 1060, 960; *m*/*z* (EI) (Found: M$^+$, 257.1244. $C_{10}H_{18}NO_3F_3$ requires *M*, 257.1239).

***N*-(1-Methoxypropyl)-*N*-methyltetrahydro-2-furamide 6e.** δ_H 0.83 (1.4 H, t, *J* 7.2), 0.84 (1.6 H, t, *J* 7.5), 1.40–1.80 (2 H, m), 1.80–2.20 (4 H, m) 2.84 (1.6 H, s), 2.85 (1.4 H, s), 3.19 (1.6 H, s), 3.20 (1.4 H, s), 3.89 (2 H, m), 4.65 (1 H, m), 5.03 (0.2 H, t, *J* 6.6), 5.04 (0.2 H, t, *J* 6.6), 5.53 (0.3 H, t, *J* 6.9), 5.54 (0.3 H, *J* 6.9); δ_C 8.96, 9.03, 9.35, 9.49, 25.14, 25.19, 25.56, 25.79, 26.51, 26.64, 28.12, 28.67, 28.90, 54.88, 55.40, 68.72, 68.92, 69.07, 75.61, 75.95, 76.04, 85.29, 85.49, 88.26, 88.90, 171.76, 173.31; ν_{max}/cm^{-1} (liq. film) 2970, 2940, 2880, 1650, 1450, 1410, 1300, 1140, 1080, 1060, 920; *m*/*z* (EI) (Found: M$^+$, 201.1369. $C_{10}H_{19}NO_3$ requires *M*, 201.1366).

***N*-Methyl-*N*-[1-(2,2,2-trifluoroethoxy)propyl]-2-methoxy-propanamide 7a.** δ_H 0.87 (t, *J* 7.2) and 0.88 (t, *J* 7.5)(3 H), 1.37 (1.1 H, d, *J* 6.6), 1.39 (1.9 H, d, *J* 6.6), 1.56 (1 H, m, containing *J* 7.5 and 7.2), 1.77 (1 H, m, containing *J* 7.5 and 7.2), 2.89 (1.1 H, s), 2.90 (1.9 H, s), 3.31 (1.9 H, s), 3.33 (1.1 H, s), 3.77 (2 H, m), 4.14 (0.4 H, d, *J* 6.6), 4.15 (0.6 H, d, *J* 6.6), 5.78 (0.6 H, t, *J* 6.9), 5.79 (0.4 H, t, *J* 6.9); δ_C 8.92, 16.79, 16.89, 24.94, 26.47, 26.72, 56.36, 56.56, 65.58 (q, *J* 33.8), 75.99, 76.12, 85.23, 85.36, 129.52 (q, *J* 273.7), 173.51; ν_{max}/cm^{-1} (liq. film) 2980, 2950, 2830, 1660, 1460, 1410, 1380, 1280, 1210, 1160, 1110, 980; *m*/*z* (CI) (Found: M$^+$, 258.1306. $C_{10}H_{18}NO_3F_3$ + H requires *M*, 258.1312).

***N*-Methyl-*N*-[1-(2,2,2-trifluoroethoxy)propyl]-2-(2,2,2-trifluoroethoxy)propanamide 7b.** δ_H 0.87 (1.6 H, t, *J* 7.2), 0.89 (1.4 H, t, *J* 7.5), 1.45 (1.6 H, d, *J* 6.9), 1.46 (1.4 H, d, *J* 6.9), 1.50–1.70 (1 H, m), 1.75–1.90 (1 H, m), 2.90 (3 H, s), 3.60–4.00 (4 H, m), 4.48 (1 H, q, *J* 6.9), 5.76 (0.6 H, t, *J* 6.9), 5.77 (0.4 H, t, *J* 6.9); δ_C 8.86, 16.70, 16.85, 24.96, 26.76, 65.68 (q, *J* 35.6), 65.92 (q, *J* 36.8), 74.81, 75.10, 85.49, 123.62 (q, *J* 275.9), 127.35 (q, *J* 285.1), 172.22; ν_{max}/cm^{-1} (liq. film) 2970, 2940, 1660, 1460, 1410, 1280, 1160, 970; *m*/*z* (EI) (Found: M$^+$, 325.1092. $C_{11}H_{17}NO_3F_6$ requires *M*, 325.1113).

***N*-Methyl-*N*-[1-(2,2,2-trifluoroethoxy)butyl]-2-methoxypropanamide 7c.** δ_H 0.91 (t, *J* 6.9) and 0.92 (t, *J* 6.9)(3 H), 1.37 (d, *J* 6.6) and 1.38 (d, *J* 6.6)(3 H), 1.52 (2 H, m), 1.74 (2 H, m), 2.90 (s) and 2.91 (s)(3 H), 3.31 (1.8 H, s), 3.33 (1.2 H, s), 3.77 (2 H, m), 4.14 (q, *J* 6.6) and 4.15 (q, *J* 6.6)(1 H), 5.87 (1 H, *J* 6.9); δ_C 13.55, 16.83, 17.96, 18.06, 26.79, 33.81, 56.34, 56.57, 65.47 (q, *J* 33.9), 75.93, 76.06, 83.92, 127.25 (q, *J* 265.2), 173.33, 173.53; ν_{max}/cm^{-1} (liq. film) 2960, 2940, 2880, 2820, 1660, 1460, 1410, 1380, 1280, 1210, 1160, 1110, 1080, 980; *m*/*z* (CI) (Found: M$^+$, 272.1468. $C_{11}H_{20}NO_3F_3$ + H requires *M*, 272.1474).

***N*-Methyl-*N*-[1-(2,2,2-trifluoroethoxy)octyl]-2-methoxypropanamide 7d.** δ_H 0.85 (3 H, t, *J* 6.3), 1.15–1.30 (10 H, br), 1.37 (0.9 H, d, *J* 6.6), 1.38 (2.1 H, d, *J* 6.6), 1.54 (1 H, m), 1.77 (1 H, m), 2.90 (2.1 H, s) and 2.91 (0.9 H, s), 3.31 (2.1 H, s), 3.33 (0.9 H, s), 3.76 (2 H, m), 4.14 (0.3 H, q, *J* 6.6), 4.15 (0.7 H, q, *J* 6.6), 5.85 (1 H, t, *J* 6.9); δ_C 13.94, 16.79, 16.91, 22.50, 24.61, 24.69, 26.80, 29.01, 29.13, 31.60, 31.79, 56.36, 56.57, 65.52 (q, *J* 33.5), 76.02, 76.13, 84.09, 84.21, 123.63 (q, *J* 276.5), 173.35, 173.52; ν_{max}/cm^{-1} (liq. film) 2930, 2900, 1660, 1460, 1410, 1370, 1280, 1160, 1110, 1080, 980; *m*/*z* (EI) (Found: M$^+$, 327.1988. $C_{15}H_{28}NO_3F_3$ requires *M*, 327.2022).

***N*-Methyl-*N*-[1-(2,2,2-trifluoroethoxy)propyl]tetrahydro-2-furamide 7e.** δ_H 0.87 (1.9 H, t, *J* 7.5), 0.88 (1.1 H, t, *J* 7.5), 1.50–2.20 (6 H, m), 2.76 (0.6 H, s), 2.77 (0.4 H, s), 2.89 (0.7 H, s), 2.90 (1.3 H, s), 3.65–3.84 (2 H, m), 3.84–4.05 (2 H, m), 4.48 (0.4 H, dd, *J* 6.3 and 6.0), 4.53 (0.6 H, dd, *J* 6.6 and 6.0), 4.64 (0.7 H, dd, *J* 8.1 and 6.0), 4.66 (1.3 H, dd, *J* 8.8 and 5.7), 5.36 (0.4 H, t, *J* 6.9), 5.38 (0.6 H, t, *J* 6.9), 5.74 (0.7 H, t, *J* 6.9), 5.75 (1.3 H, t, *J* 6.9); δ_C 8.97, 8.91, 9.23, 24.97, 25.56, 26.27, 26.91, 28.63, 65.28 (q, *J* 33.75), 68.73, 68.85, 69.08, 69.16, 75.86, 76.09, 84.95, 85.30, 123.73 (q, *J* 277.05), 173.63; ν_{max}/cm^{-1} 2960, 2880, 1660, 1440, 1410, 1280, 1150, 1090, 1060, 970; *m*/*z* (EI) (Found: M$^+$. 269.1248. $C_{11}H_{18}NO_3F_3$ requires *M*, 269.1239).

***N*-[(1-Methoxy)propyl]-*N*,2-dimethylbutanamide 9a.** δ_H 0.83 (1.5 H, t *J* 7.5), 0.87 (1.5 H, t, *J* 7.2), 0.88 (1.5 H, t, *J* 7.5), 0.90 (1.5 H, t, *J* 7.2), 1.09 (0.5 H, d, *J* 6.9), 1.10 (1 H, d, *J* 12.0), 1.13 (1 H, d, *J* 12.3), 1.15 (0.5 H, d, *J* 6.6), 1.30–1.60 (2 H, m), 1.60–1.80 (2 H, m), 2.63 (1 H, m), 2.74 (1 H, s), 2.81 (1 H, s), 2.81 (1 H, s), 3.19 (1 H, s), 3.19 (1 H, s), 3.21 (0.5 H, s), 3.22 (0.5 H, s), 4.83 (0.3 H, dd, *J* 12.0 and 6.6), 5.61 (0.7 H, dd, *J* 13.2 and 6.2); δ_C 9.06, 11.93, 12.06, 17.27, 17.40, 25.33, 25.40, 26.82, 26.94, 38.30, 38.41, 55.24, 55.30, 84.91, 85.11, 88.84, 89.11, 178.04; ν_{max}/cm^{-1} (liq. film) 2960, 2930, 2870, 2820, 1640, 1460, 1400, 1300, 1140, 1110, 1080, 1060, 940; *m*/*z* (EI) (Found: M$^+$. 187.1567. $C_{10}H_{21}NO_2$ requires *M*, 187.1573).

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