Acyclic Stereoselection in the Reaction of Nucleophilic Reagents with Chiral *N*-Acyliminium Ions Generated from *N*-[1-(Phenylsulfonyl)alkyl]imidazolidin-2-ones†

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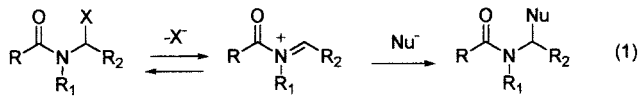
Optically active *N*-[1-(phenylsulfonyl)alkyl]imidazolidin-2-ones react at low temperature in the presence of tin tetrachloride to give acyclic *N*-acyliminium ions. These electrophilic substrates give addition products upon reaction with π-nucleophiles. Allyltrimethylsilane affords the corresponding allylated products in good yields and high diastereoselectivity. The stereochemical outcome of this process can be rationalized by taking into account the preference of the intermediate *N*-acyliminium ion for an *E* configuration that favors the attack of the nucleophile from the *si-si* face. Disappointing results are obtained using silyl ketene acetals; conversely trimethylsilyl enol ether of acetophenone gives the corresponding adducts in high diastereoselectivity. The utilization of trimethylsilyl enol ether of 2-acetylfuran is particularly interesting since the corresponding adducts are obtained with good diastereoselectivity and the furan ring could be amenable of further synthetic transformations.

Introduction

The addition of nucleophilic reagents to carbon−nitrogen double bonds is a well-recognized method to obtain interesting target molecules featured by the amino group.[1] Imines are usually poor electrophiles, and this dictates the use of powerful nucleophilic reagents for the addition reaction. Such carbanionic reagents in the presence of enolizable imines very often give deprotonation rather than addition products. These problems can be partially circumvented using nucleophiles with very low basicity as organocerium[2] or organocopper reagents,[3] but their application sometimes gives rather unexpected results.[4] Nitrogen derivatization of imines leads to a plethora of reactive substrates in which the electrophilic character may be suitably tuned by the appropriate choice of the N-substituent.[1,5] Reactive *N*-acylamino derivatives can also be generated in situ by reaction of α-substituted *N*-acylamines with excess of nucleophile, and this represents a viable method to obtain addition products from enolizable substrates.[6] A common item of the above cited imino derivatives is that they require rather strong nucleophiles to efficiently afford the corresponding addition products.A consistent increase in the electrophilic aptitude of carbon−nitrogen unsaturated substrates can be obtained moving to *N*-acyliminium ions that are able to react even with weak nucleophiles.[7] Such ions are also referred as α-amidoalkylating cations[8] and are generated according to eq 1. The equilibrium in which



(1)

1 **2** **3**

the *N*-acyliminium ion is involved is usually favored by acidic catalysts; the subsequent reaction with the nucleophile is an irreversible process and leads to the addition product. The nature of the acyl group contributes to the stability of the iminium ion as carbamates show a greater reactivity over simple amido groups. A suitable choice of the leaving group X is also essential for the success of this procedure. α-Oxygenated amides and carbamates are undoubtlely the most exploited precur-

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† Dedicated to Professor Goffredo Rosini on the occasion of his 60th birthday.

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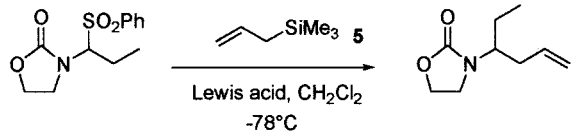
sors for *N*-acyliminium ions. These derivatives are mainly prepared by electrochemical oxidation of amides,[9] partial reduction of cyclic imides,[10] and suitable reactions of imino derivatives[11] and have been successfully used for the synthesis of biologically active compounds.[12] α-Haloamides have found only an occasional utilization as electrophilic substrates because of their insability.[13] Little attention has also been paid to the α-arylsulfide derivatives that need to be strongly activated before use, the sulfide moiety being a poor leaving group. These sulfur derivatives have found some application in the *β*-lactam chemistry.[7] Cyclic *N*-acyliminium ions can be readily formed by reaction of 2-phenylsulfonyl piperidines and pyrrolidines in the presence of Lewis acids.[14] The phenylsulfonyl group is known as a good leaving group, and furthermore, it has been revealed to be particularly beneficial in the synthesis of optically active benzenesulfonyl lactams that, being solid compounds, are easily purified by crystallization.[15] In connection with our interest in the utilization of α-amidoalkylphenyl sulfones as amidoalkylating agents,[6b,c] we began a study on the reactivity and stereoselectivity displayed by acyclic *N*-acyliminium ion intermediates prepared using optically active phenylsulfonylimidazolidin-2-ones.

Results and Discussion

Effect of the Lewis Acid in Allylation Reactions. The Lewis acid exerts a fundamental effect on the general equilibrium that leads to the formation of the *N*-acyliminium ion as depicted in eq 1. Both aluminum trichloride and boron trifluoride etherate have been shown to have a beneficial effect in reactions of allyltrimethylsilane with 2-phenylsulfonyl pyrrolidines[14] and benzenesulfonyl lactams.[15] Reaction of oxazolidinone **4** with silane **5** in the presence of various Lewis acids has revealed that tin tetrachloride is the most effective activator among the acids used (Scheme 1, Table 1). These trials have been made with the aim of using phenylsulfonyl derivatives of chiral oxazolidinones as substrates for allylation reaction;[16] however, despite various attempts we were unable to efficiently prepare such substrates.

Scheme 1



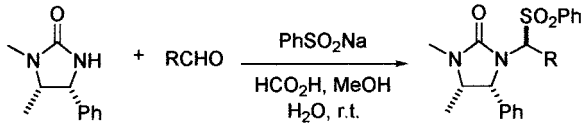
4 **6**

Table 1. Allylation of Oxazolidinone 4 Using Different Lewis Acids

entry	Lewis acid	time, h	yield,[a] %
1	$SnCl_4$	1	75
2	$TiCl_4$	4	10
3	$AlCl_3$	5	28
4	$EtAlCl_2$	5	40
5	BF_3Et_2O	24	0

[a] Yields of pure, isolated products.

Scheme 2



7 **8** **9**

Table 2. Synthesis of Phenylsulfonylimidazolidin-2-ones 9

entry		aldehyde	sulfone **9**	yield,[a] %
1	**8a**	EtCHO	**9a**	84
2	**8b**	$PhCH_2CH_2CHO$	**9b**	80
3	**8c**	$(CH_3)_2CHCH_2CHO$	**9c**	83
4	**8d**	n-$C_7H_{15}CHO$	**9d**	78
5	**8e**	$Cl(CH_2)_5CHO$	**9e**	75
6	**8f**	$BnOCH_2CH_2CH_2CH_2CHO$	**9f**	85
7	**8g**	$C_5H_{11}CH{=}CHCH_2CH_2CHO$	**9g**	88

[a] Yields of pure, isolated products.

(4*R*,5*S*)-1,5-Dimethyl-4-phenylimidazolidin-2-one as a Chiral Auxiliary. Several years ago, Pearson and co-workers[17] prepared some α-amidoalkyltolyl sulfones using an ephedrine-derived imidazolidin-2-one **7**.[18] These sulfones are formed as single diastereomers and have been used to produce optically active organolithium derivatives suitable for reaction with electrophiles. Compounds **9** have been prepared by reaction of imidazolidin-2-one **7** with an aldehyde and sodium benzenesulfinate following the procedure of Pearson (Scheme 2, Table 2). Reaction of imidazolidinones **9** with allyltrimethylsilane **5** in the presence of tin tetrachloride at −78 °C gives the corresponding allylated products **10** in good yields and with high diastereomeric ratios (Scheme 3, Table 3). The

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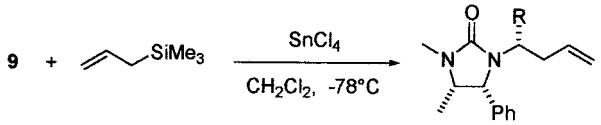
Scheme 3



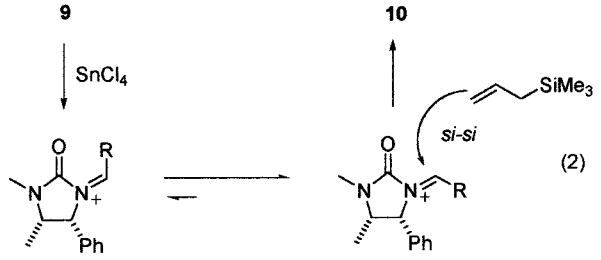
5 **10**

Table 3. Synthesis of Allylimidazolidin-2-ones 3

entry	sulfone **9**	allyl derivative **10**	dr[a]	yield,[b] %
1	**9a**	**10a**	95:5	74
2	**9b**	**10b**	95:5	70
3	**9c**	**10c**	94:6	75
4	**9d**	**10d**	95:5	68
5	**9e**	**10e**	93:7	70
6	**9f**	**10f**	95:5	80
7	**9g**	**10g**	97:3	72

[a] Diastereomeric ratio was evaluated by ^{1}H NMR analysis. [b] Yields of pure, isolated products.

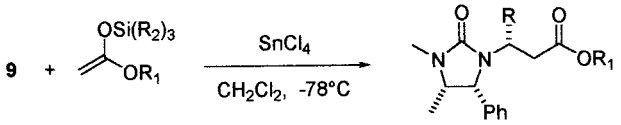
stereochemistry of the newly formed stereocenter in compound **10** has been inferred taking into account the relative stability between the intermediate *N*-acyliminium ions **11** (eq 2). Molecular mechanics calculations[17]



11-(*Z*) **11-(*E*)**

have shown for reactive ion **11-(*Z*)** derived from **9a** an energy level of 1.6 kcal/mol higher than **11-(*E*)**. This difference is mainly due to 1,3-allylic strain between the alkyl chain and the carbonyl oxygen in **11-(*Z*)**. The attack of allyltrimethylsilane from the less hindered upper side of **11-(*E*)** (*si-si* face) leads to the preferential formation of the allylated product **10**. This assumption has been confirmed by X-ray crystallographic analysis carried out for compound **10c**. The allylic moiety in compounds **10** is amenable to further synthetic transformations to give a carbonyl or a carboxylic group by oxidative procedures; however, the addition of ester derivatives to *N*-acyliminium ions would represent a direct route to the synthesis of *β*-aminoester analogues.[19] Silyl ketene acetals add to chiral cyclic *N*-acyliminium ions with modest diastereoselectivity,[20] and similar results have been observed for the reaction of imidazolidinones **9** with silyl ketene acetals **12** (Scheme 4, Table 4).The stereoselectivity and the chemical yields obtained by this procedure are invariably low, and the use of sterically hindered *tert*-butyldimethylsilyl acetal **12a** prevents any addition of the nucleophile to the iminium ion. Silyl enol ethers obtained from ketones have been exploited as reagents for addition reactions with *N*-acyliminium ions in a number of examples with better success.[12b,21] Particularly

Scheme 4



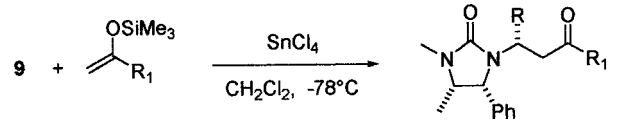
14 **15**

Table 4. Synthesis of Esters 15 by Reaction of Silyl Ketene Acetals 14 with Sulfones 9

		silyl ketene acetal **14**				
entry	sulfone **9**	R_1	R_2	ester **15**	dr[a]	yield,[b] %
1	**9a**	Et	*t*-BuMe$_2$			
2	**9b**	Et	Me	**15b**	60:40	30
3	**9c**	Et	Me	**15c**	70:30	57
4	**9d**	Ph	Me	**15d**	65:35	44

[a] Diastereomeric ratio was evaluated by ^{1}H NMR analysis. [b] Yields of pure, isolated products.

Scheme 5



16a-c **17-19**

16a: R_1 = Ph
16b: R_1 = Me
16c: R_1 = 2-furyl

Table 5. Synthesis of Ketones 17−19 by Reaction of Silyl Enol Ethers 16 with Sulfones 9

entry	sulfone **9**	silyl enol ether **16**	ketones **17−19**	dr[a]	yield,[c] %
1	**9b**	**16a**	**17b**	95:5	99
2	**9c**	**16a**	**17c**	>99:1[b]	97
3	**9d**	**16a**	**17d**	95:5	75
4	**9e**	**16a**	**17e**	98:2[b]	87
5	**9f**	**16a**	**17f**	>99:1[b]	98
6	**9c**	**16b**	**18**	70:30	58
7	**9a**	**16c**	**19a**	90:10	78
8	**9b**	**16c**	**19b**	>99:1[b]	91
9	**9c**	**16c**	**19c**	98:2[b]	85
10	**9d**	**16c**	**19d**	98:2[b]	70

[a] Diastereomeric ratio was evaluated by ^{1}H NMR analysis. [b] Diastereomeric ratio was evaluated by HPLC analysis. [c] Yields of pure, isolated products.

effective has been the trimethylsilyl enol ether of acetophenone **16a**, which is a largely planar molecule that is able to discriminate the less sterically demanding face of imidazolidinones **9** (Scheme 5, Table 5). This reflects on the high stereoselectivity observed for the efficient synthesis of ketones **17**. The importance of the phenyl group for the stereochemical outcome of this process is particularly evident by testing the behavior of the trimethylsilyl enol ether derived from acetone **16b** (Table

(19) *Enantioselective Synthesis of β-Amino Acids*; Juaristi, E., Ed.; Wiley-VCH: New York, 1997.

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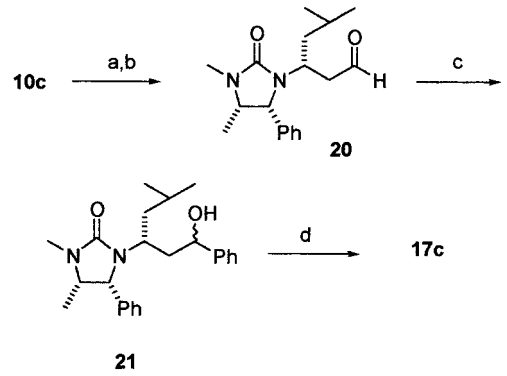
Scheme 6[a]



[a] Key: (a) OsO_4 (cat.), *N*-methylmorpholine *N*-oxide (NMO) *t*-BuOH−THF−H_2O, rt, 90%; (b) $NaIO_4$, MeOH−H_2O, rt, 81%; (c) PhMgBr, THF, −78 °C, 77%; (d) Pr_4NRuO_4 (cat.), NMO, CH_3CN, rt, 88%.

5, entry 6) that upon reaction with imidazolidinone **9c** fails to give the same excellent results in the synthesis of ketone **18**. The trimethylsilyl enol ether of 2-acetylfuran **16c** was tested in the reaction with imidazolidinones **9** (Scheme 5). As shown in Table 5, the diastereoselectivities obtained with enol ether **16c** are comparable with those observed using the phenyl analogue **16a**. The furan ring does not give any appreciable competitive side reaction with the intermediate *N*-acyliminium ion, and the corresponding ketones **19** are isolated in good yields. Since the furan nucleus can be easily cleaved under various conditions,[22] ketones **19** may become useful intermediates for the preparation of interesting building blocks in synthesis. Other simple enol ethers as ethyl vinyl ether and isopropenyl acetate have been used for this reaction but they gave only disappointing results with imidazolidinones **9** under the same conditions and using different Lewis acids.

Although it seems reasonable that the stereochemistry of the additional stereocenter in compounds **17**−**19** matches with that observed for the allylated products **10**, a chemical correlation between a representative compound **10c** and ketone **17c** was pursued (Scheme 6). Thus, allyl derivative **10c** was converted into aldehyde **20** by a two-step double-bond cleavage (OsO_4, *N*-methylmorpholine *N*-oxide (NMO); $NaIO_4$).[23] Reaction of aldehyde **20** with phenylmagnesium bromide in THF at −78 °C gave a diastereomeric mixture of alcohols **21** (85:15), which were oxidized using TPAP−NMO.[24] The resulting ketone was found to be identical to compound **17c** obtained by direct reaction of sulfone **9c** with silyl enol ether **16a**.

In summary, the *N*-acyliminium ions obtained from optically active imidazolidin-2-ones **9** are able to react with nucleophilic reagents affording the corresponding addition products. The most effective Lewis acid for the formation of the iminium ion is tin tetrachloride for all the unsaturated reagents tested. Reaction with allyltrimethylsilane is a very efficient process giving the corresponding allylated products in good yields and high diastereoselectivity. Poor results are obtained using silyl ketene acetals, while the trimethylsilyl enol ether of acetophenone reacts efficiently to give the corresponding ketones **17**. The phenyl group of acetophenone can be replaced by the furan ring mantaining the same efficacy in terms of chemical yield and diastereoselectivity. Unfortunately, deprotection of the imidazolidinone ring is not a trivial task since it is resistant to cleavage even under harsh conditions.[17] The utilization of this procedure for the synthesis of nitrogenous derivatives exploiting more practical chiral auxiliaries is currently under study in our laboratories.

Experimental Section

^1H NMR studies were performed at 300 MHz in $CDCl_3$ as solvent.^{13}C NMR studies were performed at 75 MHz in $CDCl_3$ as solvent. Dichloromethane was dried by refluxing it over calcium hydride and then distilled. All chemicals used are commercial. 6-Chlorohexanal,[25] 5-(benzyloxy)pentanal,[26] silyl ketene acetals **14**,[27] and silyl enol ethers **16**[28,29] were prepared following literature methods.

General Procedure for the Preparation of Phenylsulfonyl Derivatives 4 and 5. These compounds were prepared using the procedure described by Pearson.[17] Some imidazolidin-2-ones **9** were further purified by crystallization using hexanes−ethyl acetate.

3-[1-(Phenylsulfonyl)propyl]oxazolidin-2-one (4): yield 90%; mp 130 °C; IR (cm^{-1}, KBr) 1760, 1320, 1145; ^1H NMR δ ppm 1.02 (t, 3H, J = 7.4 Hz), 1.85−2.11 (m, 1H), 2.24−2.46 (m, 1H), 3.59 (q, 1H, J = 9.0 Hz), 3.97−4.09 (m, 1H), 4.25−4.45 (m, 2H), 4.89 (dd, 1H, J = 11.7, 3.5 Hz), 7.55−7.75 (m, 3H), 7.88−7.98 (m, 2H). Anal. Calcd for $C_{12}H_{15}NO_4S$ (269.31): C, 53.52; H, 5.61; N, 5.20. Found: C, 53.59; H, 5.57; N, 5.15.

(4*R*,5*S*,1′*S*)-1,5-Dimethyl-3-[1-(phenylsulfonyl)propyl]-4-phenylimidazolidin-2-one (9a): yield 84%; mp 119 °C; $[\alpha]^{20}_D = -88.1$ (*c* 1.9, $CHCl_3$); IR (cm^{-1}, KBr) 1690, 1380, 1140; ^1H NMR δ ppm 0.63 (t, 3H, J = 7.3 Hz), 0.72 (d, 3H, J = 6.6 Hz), 1.35−1.53 (m, 1H), 1.83−2.03 (m, 1H), 2.48 (s, 3H), 3.67 (dq, 1H, J = 8.6, 6.6 Hz), 5.09 (d, 1H, J = 8.7 Hz), 5.22 (dd, 1H, J = 9.9, 4.2 Hz), 7.20−7.38 (m, 5H), 7.52−7.68 (m, 3H), 7.95−8.01 (m, 2H). Anal. Calcd for $C_{20}H_{24}N_2O_3S$ (372.48): C, 64.49; H, 6.49; N, 7.52. Found: C, 64.56; H, 6.42; N, 7.57.

(4*R*,5*S*,1′*S*)-1,5-Dimethyl-3-[1-(phenylsulfonyl)-3-methylbutyl]-4-phenylimidazolidin-2-one (9c): yield 83%; mp 116 °C; $[\alpha]^{20}_D = -113.4$ (*c* 1.8, $CHCl_3$); IR (cm^{-1}, KBr) 1690, 1374, 1136; ^1H NMR δ ppm 0.22 (d, 3H, J = 6.6 Hz), 0.73 (d, 3H, J = 6.6 Hz), 0.76 (d, 3H, J = 6.6 Hz), 1.12−1.30 (m, 1H), 1.42−1.55 (m, 2H), 2.47 (s, 3H), 3.63 (dq, 1H, J = 8.5, 6.6 Hz), 5.11 (d, 1H, J = 8.5 Hz), 5.34 (dd, 1H, J = 10.1, 4.1 Hz), 7.20−7.35 (m, 5H), 7.55−7.80 (m, 3H), 7.95−8.00 (m, 2H); ^{13}C NMR δ ppm 15.1, 21.4, 22.9, 23.1, 24.8, 29.3, 33.6, 57.3, 59.2, 73.3, 126.6, 128.8, 128.9129.3, 129.4, 134.3, 138.0, 138.3, 161.8. Anal. Calcd for $C_{22}H_{28}N_2O_3S$ (400.53): C, 65.97; H, 7.05; N, 6.99. Found: C, 66.05; H, 7.00; N, 7.04.

General Procedure for the Preparation of Allyloxazolidin-2-one 6 and Allylimidazolidin-2-ones 10. Sulfone **4** or **9** (1 mmol) was dissolved in CH_2Cl_2 (10 mL), and the solution was cooled at −78 °C. $SnCl_4$(1.25 mmol) was then added dropwise over 10 min, and the temperature was kept at −78 °C for 30 min. Allyltrimethylsilane (1.25 mmol) dissolved in CH_2Cl_2 (5 mL) was then added dropwise, and after

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1 h at −78 °C the temperature was slowly warmed to room temperature. The reaction mixture was then diluted with CH_2Cl_2 (15 mL) and washed with brine (5 mL), and the organic phase was dried over $MgSO_4$. After removal of the solvent at reduced pressure, the allylation product **6** or **10** obtained was purified by column chromatography (hexanes−ethyl acetate (7:3)).

3-(1-Ethylbut-3-enyl)oxazolidin-2-one (6): yield 78%; oil; IR (cm^{-1}, neat) 1692; ^1H NMR δ ppm 0.88 (t, 3H, J = 7.4 Hz), 1.32, 1.70 (m, 2H), 2.10−2.40 (m, 2H), 3.35 (m, 2H), 3.70−3.85 (m, 1H), 4.21−4.33 (m, 2H), 4.97−5.12 (m, 2H), 5.61−5.85 (m, 1H). Anal. Calcd for $C_9H_{15}NO_2$ (169.22): C, 63.88; H, 8.93; N, 8.28. Found: C, 63.96; H, 8.88; N, 8.25.

(4*R*,5*S*,1′*R*)-1,5-Dimethyl-3-(1-ethylbut-3-enyl)-4-phenylimidazolidin-2-one (10a): yield 74%; mp 61 °C; $[\alpha]^{20}_D$ = +38.6 (*c* 3.4, $CHCl_3$); IR (cm^{-1}, KBr) 1692; ^1H NMR δ ppm 0.72 (d, 3H, J = 6.6 Hz), 0.73 (t, 3H, J = 7.3 Hz), 0.98−1.35 m, 2H), 2.18−2.48 (m, 2H), 2.68 (s, 3H), 3.62 (dq, 1H, J = 8.7, 6.6 Hz), 3.68−3.85 (m, 1H), 4.44 (d, 1H, J = 8.7 Hz), 4.98−5.11 (m, 2H), 5.63−5.84 (m, 1H), 7.28−7.21 (m, 5H). Anal. Calcd for $C_{17}H_{24}N_2O$ (272.39): C, 74.96; H, 8.88; N, 10.28. Found: C, 75.06; H, 8.81; N, 10.29.

(4*R*,5*S*,1′*R*)-1,5-Dimethyl-3-[1-(2-ethylpropyl)but-3-enyl]-4-phenylimidazolidin-2-one (10c): yield 75%; mp 117 °C; $[\alpha]^{20}_D$ = +48.8 (*c* 2.7, $CHCl_3$); IR (cm^{-1}, KBr) 1690; ^1H NMR δ ppm 0.48 (d, 3H, J = 6.7 Hz), 0.76 (d, 3H, J = 6.6 Hz), 0.77−0.83 (m, 1H), 0.84 (d, 3H, J = 6.5 Hz), 0.96−1.12 (m, 1H), 1.35−1.61 (m, 1H), 2.26−2.37 (m, 2H), 2.70 (s, 3H), 3.67 (dq, 1H, J = 8.7, 6.6 Hz), 3.95−4.10 (m, 1H), 4.43 (d, 1H, J = 8.7 Hz), 5.00−5.14 (m, 2H), 5.64−5.85 (m, 1H), 7.29−7.38 (m, 5H); ^{13}C NMR δ ppm 15.2, 22.6, 23.1, 25.1, 29.8, 38.4, 43.0, 51.7, 57.6, 60.2, 117.0, 128.6, 128.6, 128.9, 136.7, 139.1, 162.9. Anal. Calcd for $C_{19}H_{28}N_2O$ (300.44): C, 75.96; H, 9.39; N, 9.32. Found: C, 76.05; H, 9.44; N, 9.30.

General Procedure for the Preparation of Esters 15 and Ketones 17−19. Sulfone **9** (1 mmol) was dissolved in CH_2Cl_2 (10 mL), and the solution was cooled at −78 °C. $SnCl_4$ (1.25 mmol) was then added dropwise over 10 min, and the temperature was kept at −78 °C for 30 min. Enol derivative **16** (1.5 mmol) dissolved in CH_2Cl_2 (5 mL) was then added dropwise, and after 1,h at −78 °C, the temperature was warmed to −40 °C. After 30 min at −40 °C, the mixture was quenched with brine (5 mL) and diluted with CH_2Cl_2 (15 mL). The organic phase was separated and dried over $MgSO_4$. After evaporation of the solvent at reduced pressure, the crude carbonyl derivative was purified by column chromatography (hexanes−ethyl acetate (8:2)).

(4*R*,5*S*,1′*R*)-1,5-Dimethyl-3-[1-(2-methylpropyl)-3-oxo-3-phenylpropyl]-4-phenylimidazolidin-2-one (17c): yield 97%; mp 94 °C; $[\alpha]^{20}_D$ = +12.6 (*c* 3.4, $CHCl_3$); IR (cm^{-1}, KBr) 1692; ^1H NMR δ ppm 0.70 (d, 3H, J = 6.4 Hz), 0.74 (d, 3H, J = 6.6 Hz), 0.89 (d, 3H, J = 6.4 Hz), 1.05−1.24 (m, 1H), 1.45−1.68 (m, 2H), 2.71 (s, 3H), 3.20 (dd, 1H, J = 16.2, 6.1 Hz), 3.50 (dd, 1H, J = 16.2, 7.5 Hz), 3.71 (dq, 1H, J = 8.8, 6.6 Hz), 4.01−4.18 (m, 1H), 4.50 (d, 1H, J = 8.8 Hz), 7.18−7.31 (m, 5H), 735−7.55 (m, 3H), 7.82−7.97 (m, 2H); ^{13}C NMR δ ppm 14.6, 22.0, 22.9, 25.0, 28.9, 42.4, 42.7, 49.5, 56.7, 62.9, 128.1, 128.2, 128.3, 128.4, 128.6, 133.0, 136.1, 137.6, 161.0, 198.5. Anal. Calcd for $C_{24}H_{30}N_2O_2$ (378.51): C, 76.16; H, 7.99; N, 7.40. Found: C, 76.10; H, 8.01; N, 7.34.

(4*R*,5*S*,1′*R*)-1,5-Dimethyl-3-(1-heptyl-3-oxo-3-phenylpropyl)-4-phenylimidazolidin-2-one (17d): yield 75%; oil; $[\alpha]^{20}_D$ = +14.6 (*c* 2.8, $CHCl_3$); IR (cm^{-1}, neat) 1690; ^1H NMR δ ppm 0.74 (d, 3H, J = 6.6 Hz), 0.85 (t, 3H, J = 6.3 Hz), 1.08−1.45 (m, 10H), 1.53−1.75 (m, 2H), 2.71 (s, 3H), 3.20 (dd, 1H, J = 16.2, 6.1 Hz), 3.62 (dd,1H, 16.2, 7.5 Hz), 3.68 (dq, 1H, J = 8.7, 6.6 Hz), 3.82−4.04 (m, 1H), 4.58 (d, 1H, J = 8.7 Hz), 7.15−7.32 (m, 5H), 7.36−7.55 (m, 3H), 7.85−7.98 (m, 2H). Anal. Calcd for $C_{27}H_{36}N_2O_2$ (420.59): C, 77.10; H, 8.63; N, 6.66. Found: C, 77.18; H, 8.68; N, 6.70.

(4*R*,5*S*,1′*R*)-1,5-Dimethyl-3-(1-ethyl-3-oxo-3-furylpropyl)-4-phenylimidazolidin-2-one (19a): yield 78%; oil; $[\alpha]^{20}_D$ = +15.7 (*c* 1.2, $CHCl_3$); IR (cm^{-1}, neat) 1690; ^1H NMR δ ppm 0.72 (d, 3H, J = 6.6 Hz), 0.86 (t, 3H, J = 7.3 Hz), 1.25−1.40 (m, 1H), 1.55−1.78 (m, 1H), 2.68 (s, 3H), 3.06 (dd, 1H, J = 15.2, 7.4 Hz), 3.71 (dq, 1H, J = 8.7, 6.6 Hz), 3.81−3.98 (m, 1H), 4.60 (d, 1H, J = 8.7 Hz), 6.45−6.52 (m, 1H), 7.12−7.16 (m, 1H), 7.20−7.35 (m, 5H), 7.55−7.60 (m, 1H). Anal. Calcd for $C_{20}H_{24}N_2O_3$ (340.42): C, 70.57; H, 7.11; N, 8.23. Found: C, 70.65; H, 7.04; N, 8.28.

(4*R*,5*S*,1′*R*)-1,5-Dimethyl-3-[1-(2-methylpropyl)-3-oxo-3-furylpropyl]-4-phenylimidazolidin-2-one (19c): yield 85%; mp 132 °C; $[\alpha]^{20}_D$ = −2.2 (*c* 5.2, $CHCl_3$); IR (cm^{-1}, KBr) 1690; ^1H NMR δ ppm 0.66 (d, 3H, J = 6.4 Hz), 0.74 (d, 3H, J = 6.6 Hz), 0.88 (d, 3H, J = 6.4 Hz), 1.05−1.26 m, 1H), 1.38−1.62 (m, 2H), 2.70 (s, 3H), 3.05 (dd, 1H, J = 15.1, 7.4 Hz), 3.31 (dd, 1H, J = 15.1, 6.8 Hz), 3.71 (dq, 1H, J = 8.7, 6.6 Hz), 4.05−4.24 (m, 1H), 4.60 (d, 1H, J = 8.7 Hz), 6.50−6.52 (m, 1H), 7.12−7.15 (m, 1H), 7.18−7.33 (m, 5H), 7.56−7.58 (m, 1H); ^{13}C NMR δ ppm 15.0, 22.6, 23.2, 25.4, 29.4, 42.9, 50.0, 57.2, 62.6, 112.7, 118.1, 128.6, 128.8, 138.1, 146.9, 150.0, 153.1, 162.3, 187.8. Anal. Calcd for $C_{22}H_{28}N_2O_3$ (368.47): C, 71.71; H, 7.66; N, 7.60. Found: C, 71.80; H, 7.70; N, 7.65.

(3*R*)-3-[(4*R*,5*S*)-3,4-Dimethyl-2-oxo-5-phenylimidazolidin-1-yl]-5-methylhexanal (20). Allyl derivative **10c** (0.45 g, 1.5 mmol) was dissolved in a mixture of THF (6 mL), *tert*-butyl alcohol (6 mL), and water (1.2 mL), and then *N*-methylmorpholine *N*-oxide (0,195 g, 1.65 mmol) and OsO_4 (0.004 g, 0.015 mmol) were added at 0 °C. The mixture was stirred for 10 min at 0 °C and then for 6 h at room temperature before being quenched with saturated aqueous Na_2SO_3 (4 mL). The solution was stirred at room temperature for 1 h and then was diluted with water (10 mL) and extracted with $CHCl_3$ (3 × 20 mL). The organic phase was dried over $MgSO_4$, and after evaporation of the solvent the crude mixture of diols was purified by column chromatography (hexanes−ethyl acetate (6:4)) giving 0.45 g (90%) of a white solid. These diols (0.40 g, 1.2 mmol) were dissolved in a mixture of methanol (6 mL) and water (3 mL), and then, under vigorous stirring, $NaIO_4$ (1.54 g, 7.2 mmol) was added at 0 °C. Stirring was continued for 30 min at room temperature, and then water (10 mL) was added. The resulting solution was extracted with $CHCl_3$ (3 × 20 mL), and the organic phase was dried over $MgSO_4$. After the evaporation of the solvent at reduced pressure, the crude product was purified by column chromatography (hexanes−ethyl acetate (8:2)) affording 0.30 g (81%) of pure aldehyde **20**: mp 122 °C; $[\alpha]^{20}_D$ = +48.7 (*c* 3.8, $CHCl_3$); IR (cm^{-1}, KBr) 1715; ^1H NMR δ ppm 0.61 (d, 3H, J = 6.5 Hz), 0.76 (d, 3H, J = 6.5 Hz), 0.88 (d, 3H, J = 6.4 Hz), 0.95−1.04 (m, 1H), 1.21−1.34 (m, 1H), 1.38−1.62 (m, 1H), 2.70 (s, 3H), 2.72−2.80 (m, 2H), 3.61−3.64 (m, 1H), 4.15−4.31 (m, 1H), 4.15−4.31 (m. 1H), 4.47 (d, 1H, J = 8.6 Hz), 7.15−7.40 (m, 5H), 9.65 (t, 1H, J = 2.5 Hz); ^{13}C NMR δ ppm 15.0, 22.7, 22.9, 25.2, 29.4, 43.0, 47.8, 48.1, 57.2, 61.7, 128.8, 128.9, 129.1, 138.1, 162.3, 201.6. Anal. Calcd for $C_{18}H_{26}N_2O_2$ (302.41): C, 71.49; H, 8.67; N, 9.26. Found: C, 71.55; H, 8.64; N, 9.31.

(4*R*,5*S*)-1-[(1*R*)-1-(2-Hydroxy-2-phenylethyl)-3-methylbutyl]-3,4-dimethyl-5-phenylimidazolidin-2-one (21). Aldehyde **20** (0.28 g, 0.92 mmol) was dissolved in dry THF (10 mL) and then cooled at −78 °C. Phenylmagnesium bromide (2.3 M in ether, 0.44 mL, 1.0 mmol) was then added dropwise, and stirring was continued at the same temperature for 1 h. The mixture was quenched by addition of saturated aqueous NH_4Cl (5 mL), and the temperature was allowed to warm to room temperature. The resulting mixture was extracted with $CHCl_3$ (3 × 20 mL), and the organic phase was dried over $MgSO_4$. After the evaporation of the solvent at reduced pressure, the crude product was purified by column chromatography (hexanes−ethyl acetate (7:3)) giving 0.27 g (77%) of alcohol **21** as a 85:5 mixture of diastereomers: IR (cm^{-1}, KBr) 3400; ^1H NMR (major diastereomer) δ ppm 0.44 (d, 3H, J = 6.6 Hz), 0.78 (d, 3H, J = 6.4 Hz), 0.82 (d, 3H, J = 6.6 Hz), 0.88−0.98 (m, 1H), 1.06−1.18 (m, 1H), 1.24−1.48 (m, 1H), 1.68−1.85 (m, 1H), 1.92−1.05 (m, 1H), 2.75 (s, 3H), 3.58−3.80 (m, 2H), 4.18−4.39 (m, 1H), 4.45 (d, 1H, J = 8.8 Hz), 4.50−4.62 (m, 1H), 7.19−7.45 (m, 10H). Anal. Calcd for $C_{24}H_{32}N_2O_2$ (380.53): C, 75.75; H, 8.48; N, 7.36. Found: C, 75.71; H, 8.53; N, 7.40.

Oxidation of Alcohol 21. Alcohol **21** (0.25 g, 0.66 mmol) was dissolved in dry acetonitrile (3 mL), and then *N*-methyl-

morpholine *N*-oxide (0.12 g, 1.0 mmol), powdered 4 Å molecular sieves (0.30 g), and tetra-*n*-propylamonium perruthenate (0.01 g, 0.03 mmol) were added at room temperature. After being stirred for 1 h, the solvent was evaporated at reduced pressure and the black residue was suspended in CH_2Cl_2 (20 mL) and then filtered over a short pad of Florisil. The clear solution was evaporated at reduced pressure, and the residue was purified by column chromatography (hexanes−ethyl acetate (8:2)) affording 0.22 g (88%) of ketone **17c**.

Crystal Structure of Allyl Derivative 10c. Crystal Data: $C_{19}H_{28}N_2O$, M = 300.4, monoclinic, space group $P2_1$, a = 8.830(2) Å, b = 6.685(5) Å, c = 15.246(3) Å, β = 96.97 (3)°, U = 893.3(7) Å^3, Z = 2, D_c = 1.12 Mg m^{-3}, $F(000)$ = 328, λ = 0.710 69 Å, T = 293 K, (Mo Kα) μ = 0.069 mm^{-1}, crystal dimensions 0.70 × 0.30 × 0.20 mm. A total of 1829 reflections were collected (1716 unique, R_{int} =0.0191).

Data Collection and Processing. Intensity data were collected on an Enraf-Nonius CAD-4 diffractometer using graphite monochromated Mo Kα radiation, $\omega/2\theta$ scan mode, range 2.32° < θ < 24.98°. The unit cell parameters were determinated by least-squares refinement on diffractometer angles for 25 automatically centered reflections 3.78° < θ < 7.21°.

Structure Analysis and Refinement. The structure was solved by direct method and refined by full-matrix least-squares on F^2, using the SHELX program packages.[30] In the final refinement cycles 1407 reflections having $I > 2\sigma(I)$ were used, with 187 parameters varied. In refinements were used weights according to the scheme $w = 1/[\sigma^2(F_o^2) + (0.0794P)^2 + 0.0282P]$ where $P=(F_o^2 + 2F_c^2)/3$.

The hydrogen atoms were located by geometrical calculation and refined using a "riding" model. The final agreement indices were R_1 = 0.0457 and wR_2= 0.1079. Goodness of fit on F^2 = 1.15. Largest difference peak and hole was 0.136 and −0.222 e Å^{-3}.

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Supporting Information Available: Spectral and physical data for compounds not included in the Experimental Section. X-ray molecular structure and crystal data of compound **10c**. This material is available free of charge via the Internet at http://pubs.acs.org.

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