SYNTHESIS OF THE β-KETOIMIDES AND THEIR CHEMICAL TRANSFORMATIONS.

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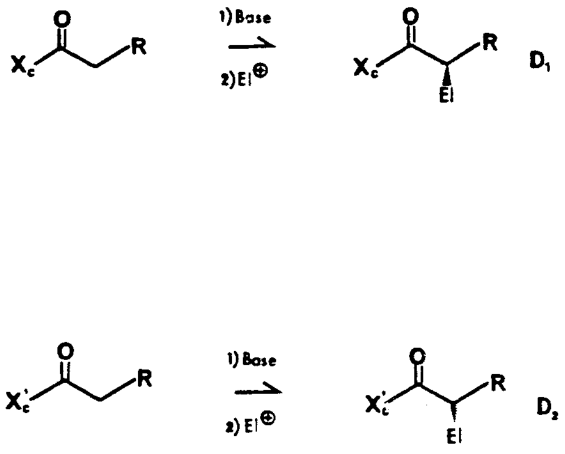
Introduction

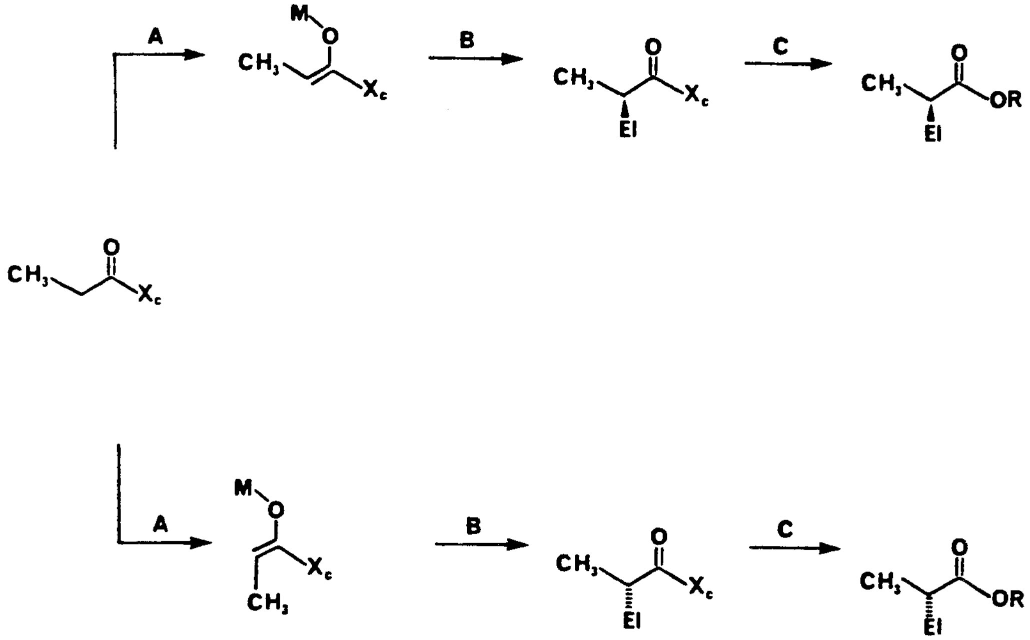
The development of general strategies for stereoselective bond construction has been one of the major objectives in organic synthesis.[1] The ability to control the stereochemical outcome of chemical reactions will allow the chemist to efficiently synthesize the more architecturally complex molecules exemplified by the polyether based ionophores and macrolide antibiotics. In the past, previous efforts in solving the stereochemical problems relied on one of three ways: (1) the "Woodwardian"[2] cyclic methodology which takes advantage of the stereochemical biases present in four, five and six-membered rings; (2) relative asymmetric induction whereby a resident chiral center dictates the generation of new stereocenters in close proximity; (3) by tapping nature's "chiral pool" for readily available chiral starting materials such as sugars. A conceptually different approach to the streochemical challenges presented by large ring or acyclic natural products involved the use of a chiral carboxylic acid enolate synthon. It could be described as an enolate species bearing a removable chiral auxiliary (X_C) which would bias the approaching electrophile in a stereoregular manner (eq. 1). In recent years, this strategy has been a primary focus of research efforts in our group to develop classes of carboxylic acid enolate synthons which perform effectively in both enantioselective alkylation and aldol condensations.[3]



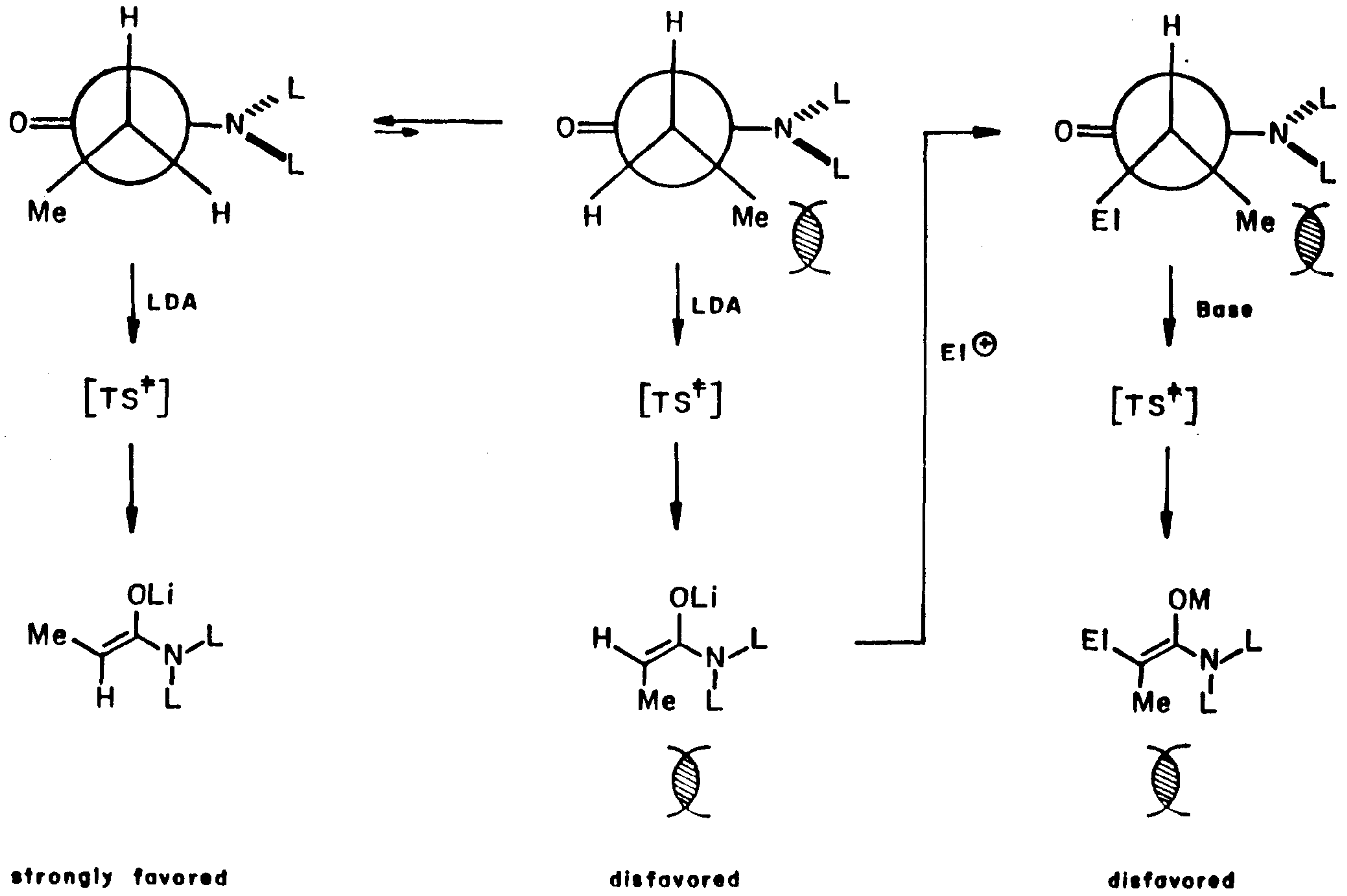
(1)

Chiral Enolate Design. There have been many publications on the subject of designing chiral enolates. To avoid redundancy, detailed discussions will be referred to the cited literature.[4] However, the three key problems of fundamental importance in the chiral enolate approach is summarized below and is depicted in Scheme I. In reaction A, one must achieve highly stereoselective enolization since enolate stereochemistry is directly transferred to product stereochemistry.[4] In reaction B, the enolate should efficiently biased the approaching electrophile with at least 98% diastereofacial discrimination. Finally, the removal of the chiral auxiliary must proceed with minimal racemization of the final product. With respect to the question of enolization

Scheme I



AMIDE DEPROTONATION
ALLYLIC STRAIN



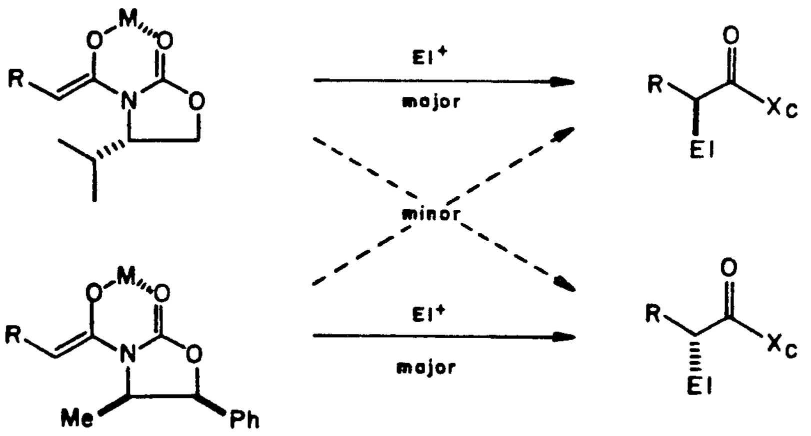
Scheme II

stereoselectivity, we reasoned that imide-derived, metal-chelated Z-enolates should be strongly preferred if one considers transition state allylic stain conformational control elements^4 (Scheme II). These same conformational control elements in the enolization process also assume an important role in preventing product racemization and β-ketoimide epimerization. The $A^{1,3}$-strain causes a higher energetic conformation when the C_2 proton is at a favorable position for enolization (vide infra).

Enantioselective Enolate Alkylations. Two highly efficient chiral enolate systems were developed from the S-valine-derived oxazolidone 1 (X_V) and the 1S,2R-norephedrine-derived oxazolidone 2 (X_N). The preparation of the derived imides and their respective alkylation results are summarized in Scheme III.^{5} In general, these reactions must be run

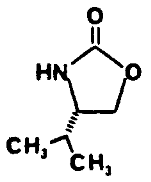
Enolate Diastereoselection

Scheme III



Alkyl Halides	Diastereoselection	Conditions
$ArCH_2Br$	50-100:1	M = Li, THF ≤0°C
CH_2=CH-CH_2Br	50:1	M = Na, THF -78 → 0°C
$BnOCH_2Br$	50:1	
Et-I	25:1	
MeI	13:1	

at temperatures $\leq 0°$ C to avoid enolate decomposition. The sense of asymmetric induction noted in these alkylation studies was that predicted from the more favored chelated *Z*-enolate 3.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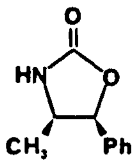
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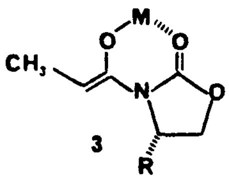
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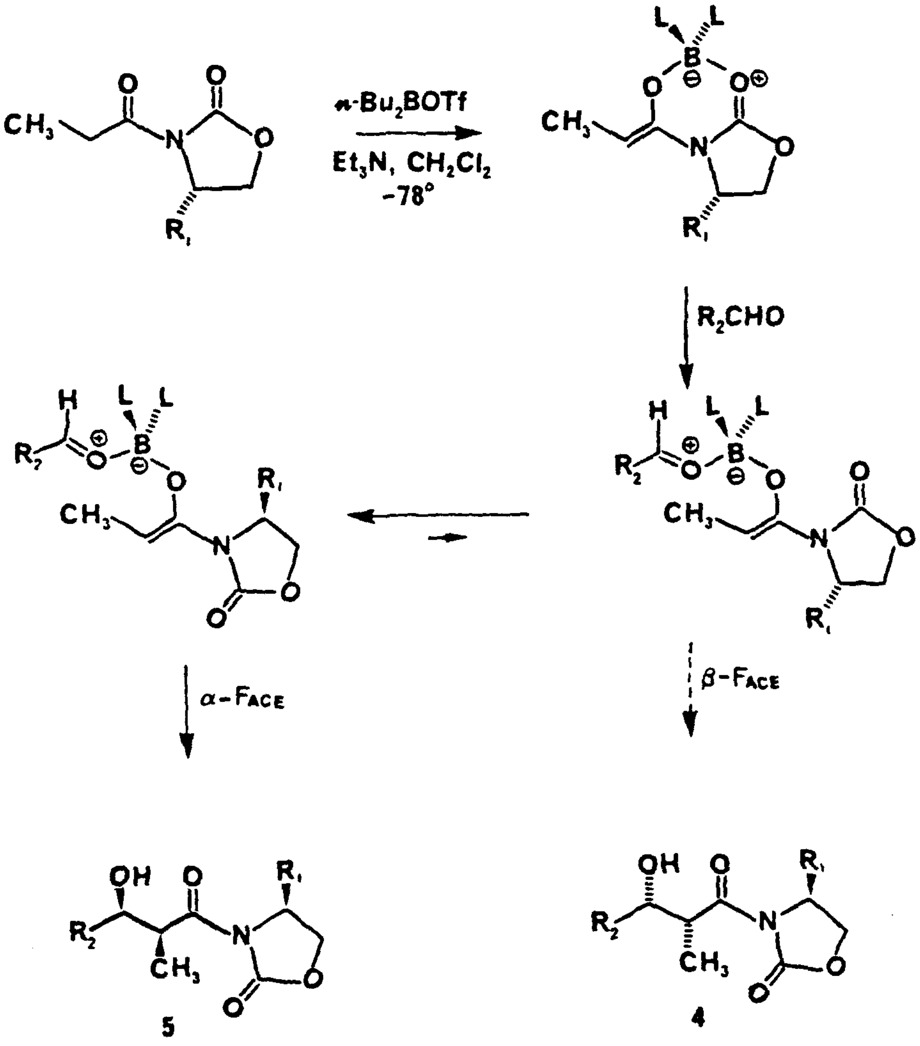
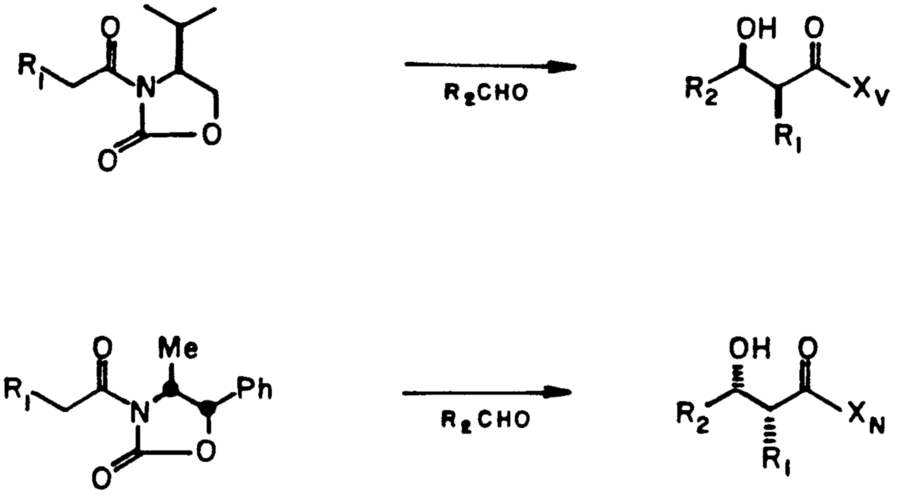
Enantioselective Aldol Condensations. Some recent experiments undertaken in our laboratory have addressed the use of chiral oxazolidone imides for the aldol process. These imides are readily transformed into their respective dibutylboryl enolates with dibutylboryl triflate (triethylamine, -78°C, methylene chloride) (Scheme IV). The projections on the sense of chirality transfer in this system were based upon transition state carbonyl-carbonyl dipole effects and would favor aldol diastereomer 5 in preference to 4. To date, a general survey of enatioselectived *erythro*-aldol condensations utilizing these propionate-derived auxiliaries showed that very high levels of selection can be achieved (Scheme V).[6]

Michael Ennis' Experiments. Throughout the coursed of the alkylation studies, it was observed that two minor by-products were routinely formed during the alkylation reactions and typically accounted for about 10% of all non-solvent peaks in the analytical GC traced. It was noted that these two by-products, formed in approximately equal amounts, were present in all reactions *independent* of which electrophile being used. These products could readily be purified by flash chromatography. The spectral data obtained from these compounds revealed that they were diastereomers, each possessing

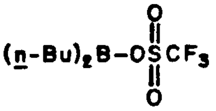
Scheme IV



Scheme V



Conditions



$(\underline{n}\text{-Bu})_2B-O\overset{O}{\underset{O}{\overset{\|}{\underset{\|}{S}}}}CF_3$

Et_3N or $EtN(\underline{i}\text{-}C_3H_7)_2$

CH_2Cl_2 $\leq 0°C$

Permutations on R_1

$-CH_3$ and $\underline{n}$-alkyl

$-CH_2CO_2Me$

$-CH{=}CH_2$

$-OMe$, OCH_2Ph

$-SMe$

Erythro Diastereoselection: >99%

three distinct C=O stretchings in the infrared spectrum. A tentative structural assignment was made from NMR and IR spectral data and they are shown in Figure 1.

6

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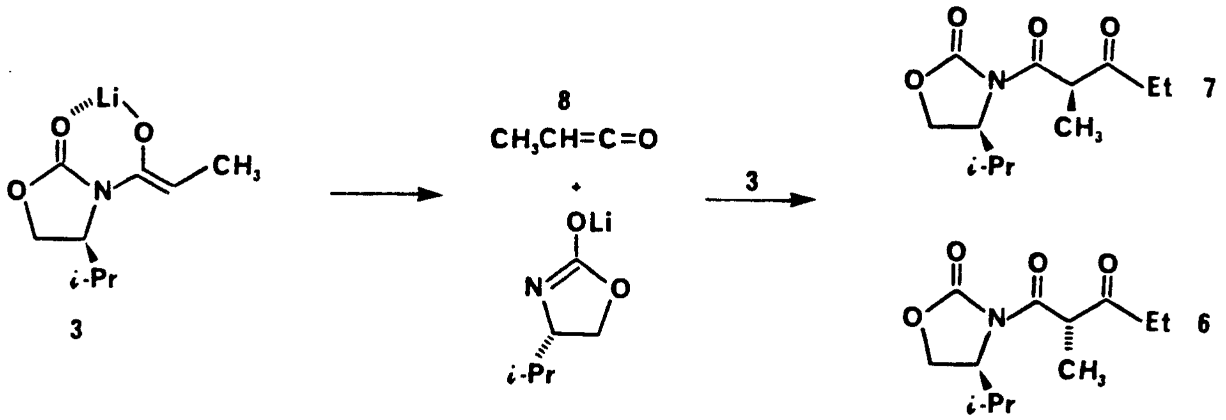
Figure 1. Tentative structural assignment for the β-ketoimide by-products.

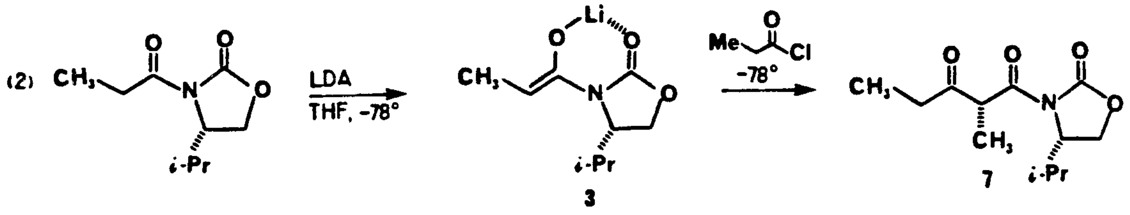
The formation of β-ketoimide by-products can be rationalized by the pathways outlined in Scheme VI. Thermal fragmentation of lithium enolate **3** occurs slowly at 0° C, affording the metallated valine oxazolidone and methyl ketene **8**. The highly electrophilic methyl ketene **8** would react immediately with the remaining enolate **3** to produce the β-ketoimides. This mechanism would require the generation of one equivalent of valine oxazolidone **1** for every equivalent of **6** and **7** formed. Reinspection of analytic al GC traces from past alkylation revealed that this was indeed the case. The resulting diastereomer ratio of 1:1 may have arisen from either poor diastereofacial selection during the acylation reaction or an epimerization of a stereoregular product under reaction conditions.

Structural Proof. Evidence for the proposed structure was obtained from an acylation experiment (eq. 2). Analysis of the unpurified reaction mixture by GC showed that the acylation reaction cleanly produced the same products as were seen from the thermal enolate decomposition experiments. However, equally interesting was the totally unexpected observation that this acylation proceeded with remarkable stereoselectivity,

Scheme VI

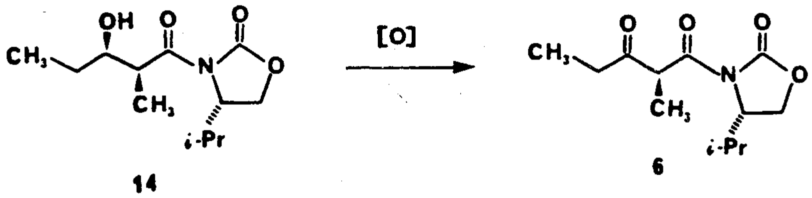


(2)



providing diastereomers of 7 in a ratio of 96:4. In addition, these systems exhibit a remarkable degree of stereochemical integrity (vide infra). It was desirable to determine whether the stereochemistry of the chiral center created during the acylation reaction was the same as that obtained from the alkylation experiments. An X-ray structure determination was carried out on the recrystallized product obtained from the quenching of lithium enolate 3 with propionyl chloride (eq. 2). Shown in Figure 2 is the calculated structure of the major diastereomer from this reaction. The absolute configuration at the C_2' center is R, consistent with the interpretation given for the alkylation reaction (vide supra). Thus, in analogy with alkyl halides, acid chlorides also react with imide-derived, metal-chelated, Z-enolates from the least hindered side. The correlation of the absolute stereochemistry at the C_2' center of the minor diastereomer from the acylation reaction (eq. 2) was carried out with the results of an oxidation of the corresponding aldol adducts[6] (eq. 3). The serendipitous discovery of the β-ketoimide system has opened a new area of

(3)



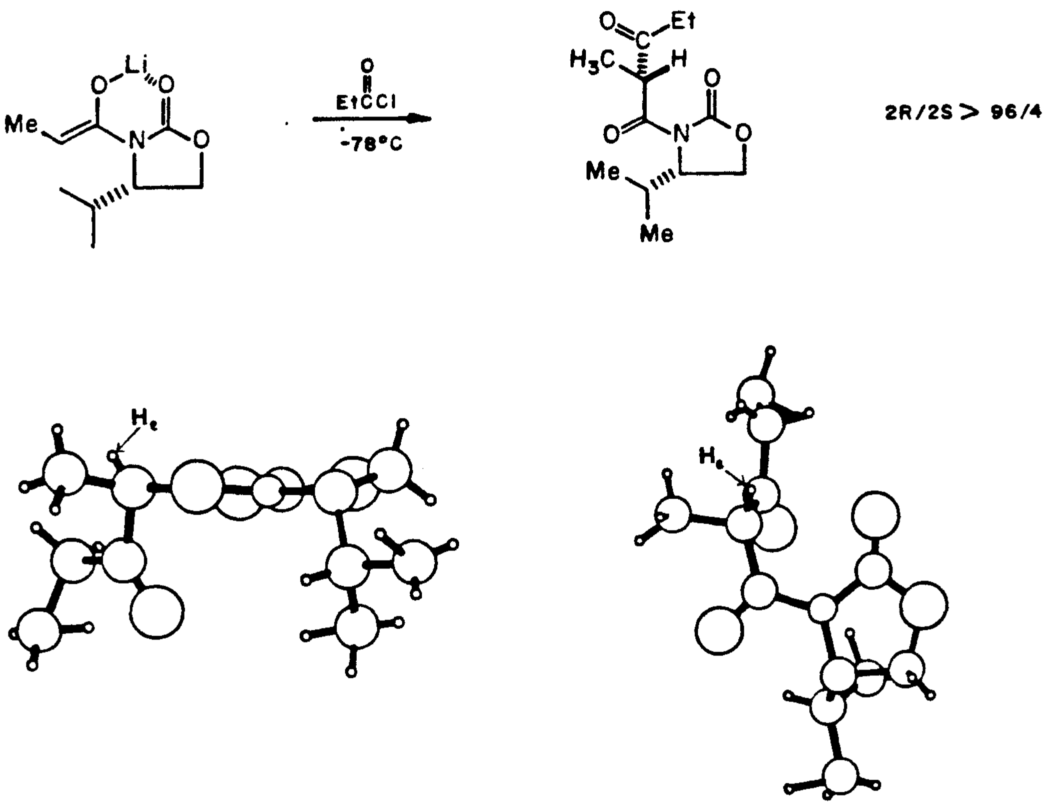
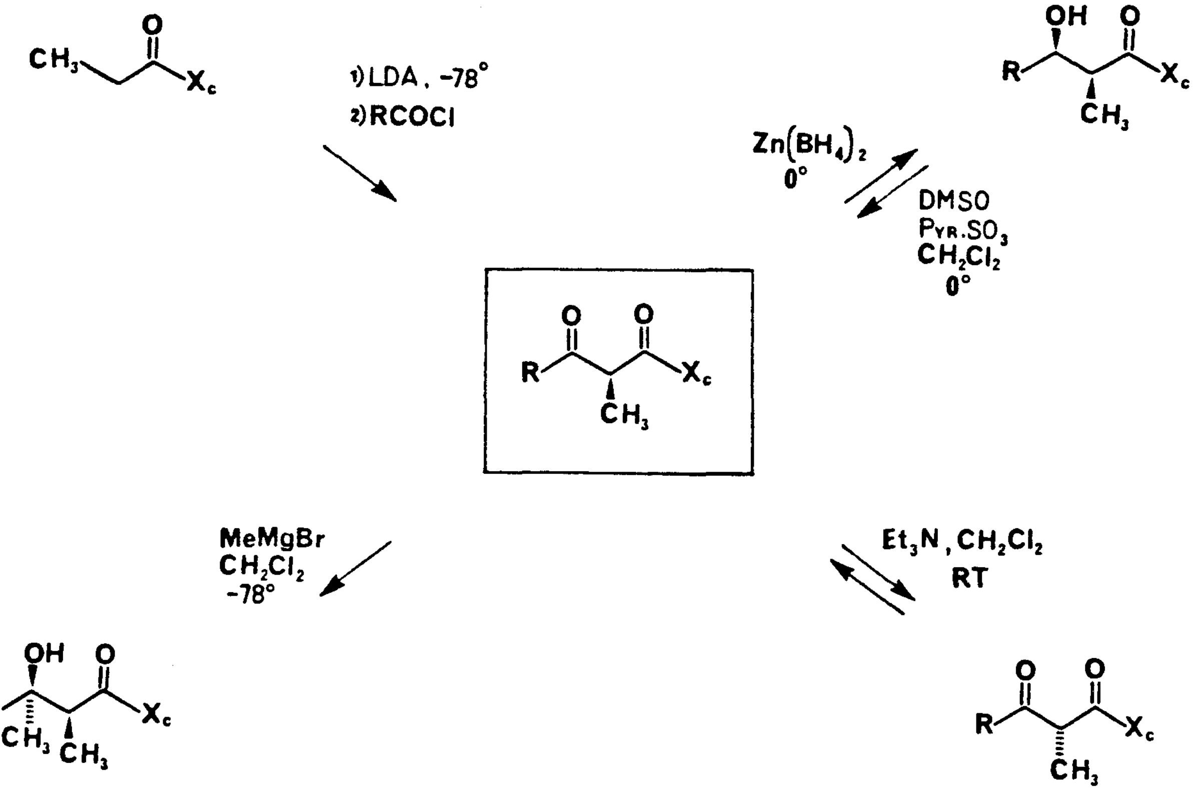


Figure 2

investigation in our studies of chiral enolates. The novelty and potential utility of this new class of compounds has prompted us to carry out the synthesis of a small family of β-ketoimides and to examine their further chemical transformations. Outlined in Scheme VII are some of the possible transformations available to this system.

Scheme VII


1) LDA, -78°
2) RCOCl
Zn(BH4)2
0°
DMSO
Pyr.SO3
CH2Cl2
0°
MeMgBr
CH2Cl2
-78°
Et3N, CH2Cl2
RT
CH3
O
Xc
OH
R

Results and Discussion

Starting Material Synthesis. The two chiral 2-oxazolidones chosen for study and their respective syntheses are shown in Scheme VIII. Both the *S*-valine-derived oxazolidone **1** (X_V) and the 1*S*,2*R*-norephedrine-derived oxazolidone **2** (X_N) are readily prepared from inexpensive commercially available chiral precursors whose optional purities exceed 99%.

Acylation Studies. In surveying conditions for optimizing the acylation process, we have found that cannulation of a cool lithium-chelated *Z*-enolate solution (-78°C) to the acid chlorides at -78°C is the method of choice. The reaction was quenched *immediately* and worked-up in the normal manner (see Experimental Section) to provide products in a kinetic diastereomer ratio exceeding 95:5. Simple addition of acid chlorides to the enolate solutions (-78°C) also gave satisfactory results in some cases such as the first Ennis acylation experiment (vide supra). The acylation studies are summarized in Table 1.

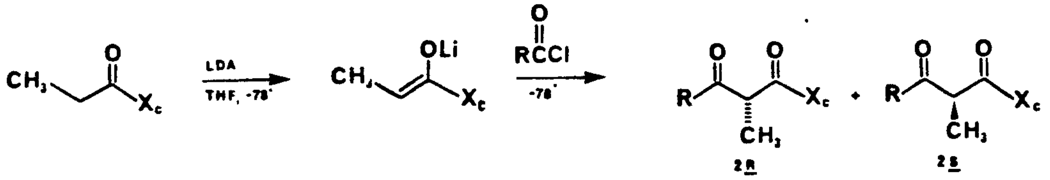
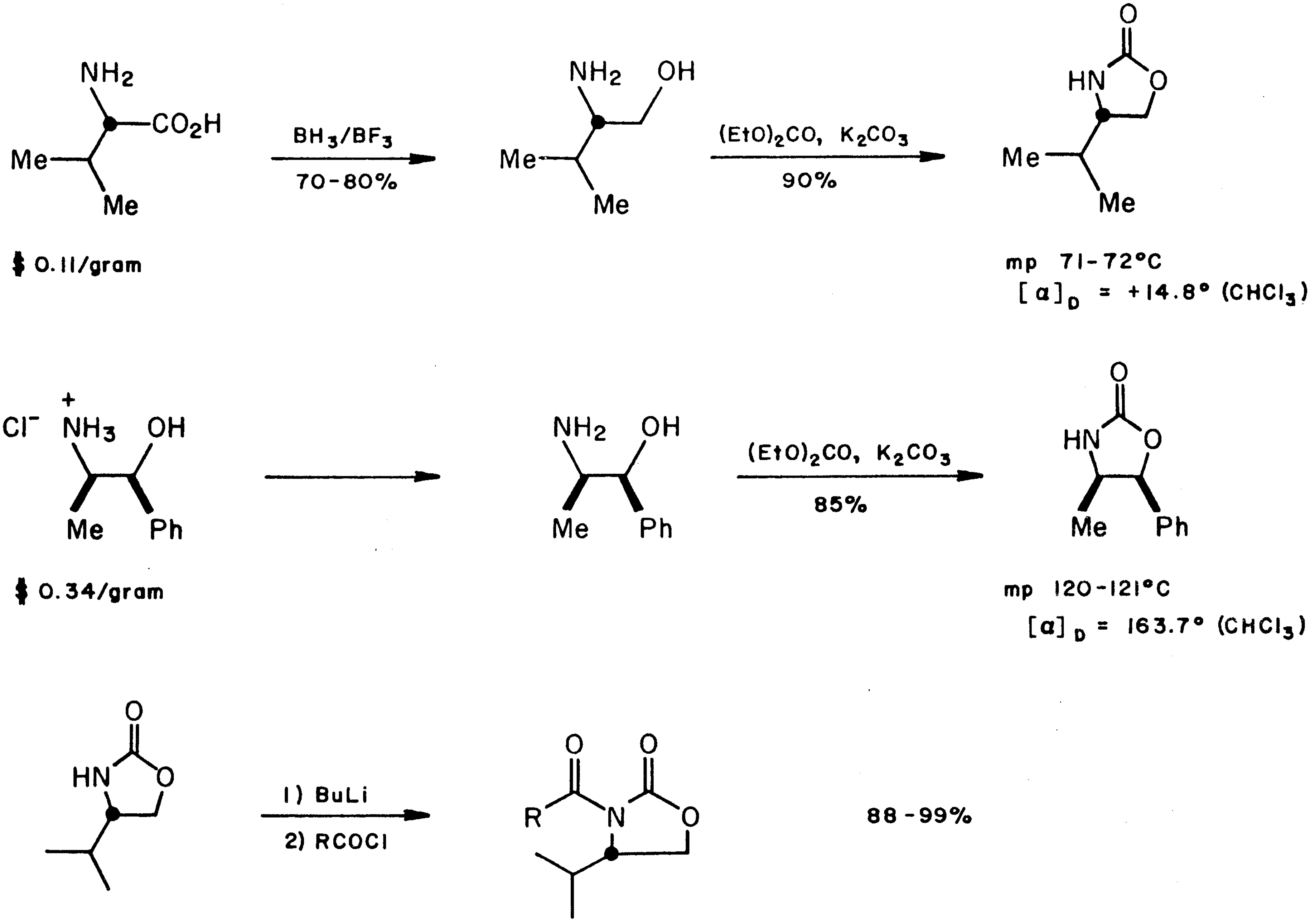


Table 1. Synthesis of β-Ketoimides *Via* Acylation.

X_C	Entry	#	R	Isolated Yield (%)	Kinetic Ratio *R*:*S*	mp
X_V	A	**8**	CH_3-	85-95	96:4	134-134.5°
X_V	B	**7**	CH_3CH_2-	89-95	96:4	131-132°
X_V	C	**9**	ϕ-	90-98	96.2:3.8	—
X_N	D	**10**	CH_3-	55	30:70	116.5-117.5°
X_N	E	**11**	CH_3CH_2-	83	5:95	123-124°
X_N	F	**12**	ϕ-	90:95	4.5:95.5	164.5-165°

CHIRAL AUXILIARY SYNTHESIS



$ 0.11/gram

mp 71-72°C
$[\alpha]_D$ = +14.8° ($CHCl_3$)

$ 0.34/gram

mp 120-121°C
$[\alpha]_D$ = 163.7° ($CHCl_3$)

Good selectivity was observed in all cases with the exception of the acetyl chloride acylation with the norephedrine-derived imide.

Aldol-Oxidation Studies. The complimentary (minor) diastereomers from the acylation studies were selectively prepared via an oxidation of the corresponding aldol adducts (Fig. 3).

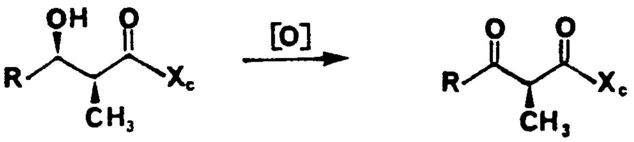
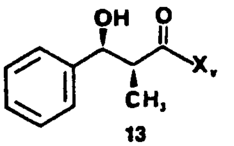


Figure 3.

The following aldol adducts (13-18) were synthesized according to the Bartroli procedure for the oxidation studies.[6]



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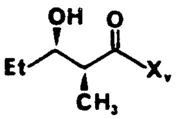

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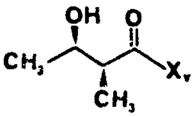

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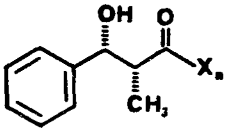
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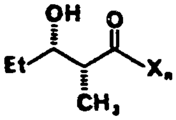
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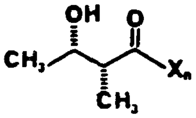
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Various oxidizing agents were surveyed and the results are tabulated in Table 2. The pyridine-SO_3 complex oxidation (Moffatt oxidation) at 0°C is found to be the method of choice. The oxidation studies are summarized in Table 3. Good selectivity was observed in all but one case. Since the absolute configuration of the C_2' center in the aldol

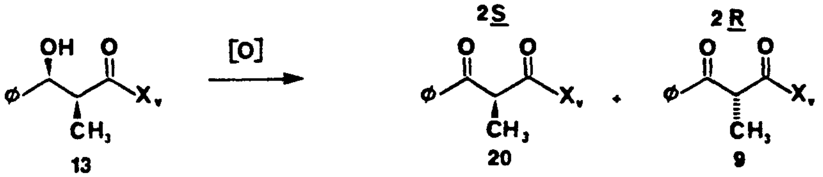


Table 2. Survey of Various Oxidizing Agents for the Preparation of β-Ketoimides.

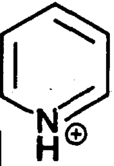
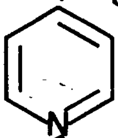
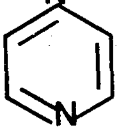
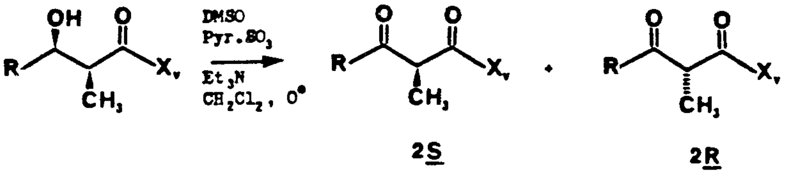
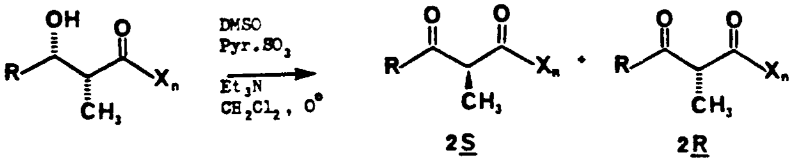
Oxidizing Agents	Ratio (20:9)	Yield (%)
CrO_3, pyridine, CH_2Cl_2, RT	73.5:26.5	85
$Na_2Cr_2O_7$, CH_2Cl_2, HOAc, H_2SO_4, $H_2\overset{O}{\wedge}$, 0° RT	78.5:21.5	80
PCC, CH_2Cl_2, 0°, 1-½ h	91.8:8.2	80
DDQ, CH_2Cl_2, RT, 10 min	94:6	85
PDC,  $CF_3CO_2^-$, CH_2Cl_2, RT, 3 h	97:3	65-80
 •SO_3, DMSO, Et_3N, RT, 30 min	92:8	80
 •SO_3, DMSO, CH_2Cl_2, Et_3N, 0°, 30 min	99:1	80-85

Table 3. Synthesis of the β-Ketoimides Via Oxidations of the Corresponding Aldol Adducts.



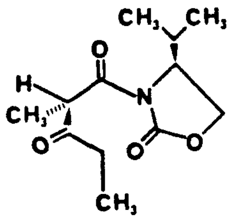
Entry	#	R	Isolated Yield (%)	Ratio R:S	mp
A	19	CH_3-	80	8:92	--
B	6	CH_3CH_2-	85	1:99	--
C	20	ϕ-	90	1:99	167-157.5°



Entry	#	R	Isolated Yield (%)	Ratio R:S	mp
D	21	CH_3-	55	65:35	--
E	22	CH_3CH_2-	85	99.7:0.3	--
F	23	ϕ-	85	99.9:0.1	--

adduct was well established,[6] and remained unchanged during the Moffatt oxidation, this correlation served as an additional structural proof of the stereochemistry of the C_2' center in the β-ketoimide systems.

Diastereomer Ratio Determination and Purification. Diastereomer ratio analysis was carried out by high performance liquid chromatography. Attempts to analyze the diastereomer ratio by capillary gas chromatography gave erroneous results because there is 5-10% epimerization at elevated temperatures (> 150° C). It is also feasible to obtain an accurate diastereomer ratio *via* high field ^1H NMR (500 MHz). For example, the methine proton ($OCC\underline{H}(CH_3)CO$) for **6** resonates at δ 4.63 ppm, while for **7** it resonates at δ 4.49 ppm. The diastereomer pair may readily be resolved by flash chromatography. For those compounds that are crystalline, a simple recrystallization was often sufficient to afford analytically pure products. Interestingly, the order of elution of the two diastereomers remains consistent throughout the family of β-ketoimides in this study. Tabled 4 serves to illustrate this point. The 2*R* diastereomers always eluted faster than the 2*S* diastereomers from silica gel. Model inspections of the two diastereomers revealed that 7 (2*S*) should have a tighter binding to silica gel than 6 (2*R*). This experimental observation supports



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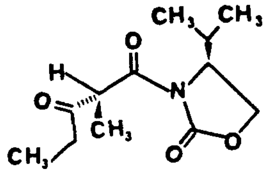

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the postulate that the β-ketoimides are conformationally regular. From these studies one can conclude that the reaction of imide-derived, lithium-chelated chiral enolates with electrophiles (primary alkyl halides and acid chlorides) is stereoregular.

Table 4.

Entry	2S #	2S R_f	2R #	2R R_f	ΔR_f	Solvent
A	**8**	0.19	**19**	0.27	0.08	15% EtOAc-hexane
B	**7**	0.19	**6**	0.27	0.08	30% EtOAc-hexane
C	**9**	0.25	**20**	0.40	0.15	20% EtOAc-hexane
D	**10**	0.18	**21**	0.25	0.07	30% EtOAc-hexane
E	**11**	0.25	**22**	0.44	0.19	40% EtOAc-hexane
F	**12**	0.22	**23**	0.31	0.09	15% EtOAc-hexane

Simple Chemical Transformations. The ketonic carbonyl functional group can be selectively reduced with zinc borohydride (CH_2Cl_2-ether, 0°C). Sodium borohydride worked poorly and afforded many side-products. The zinc borohydride reduction studies are summarized in Table 5. These data revealed that the stereochemical control in the reduction was dictated by the adjacent stereocenter and not affected by the chiral auxiliaries. These results may be best rationalized by the complexation of Zn^{2+} to the two carbonyl oxygens, and hydride reduction <u>via</u> the least hindered side (eq. 4).

(4)

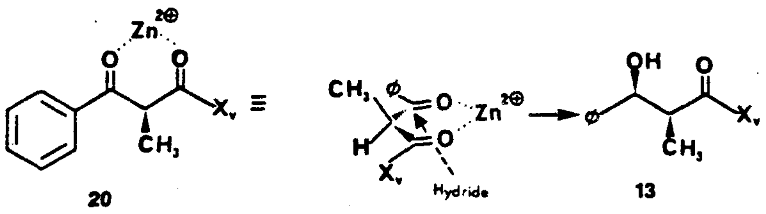
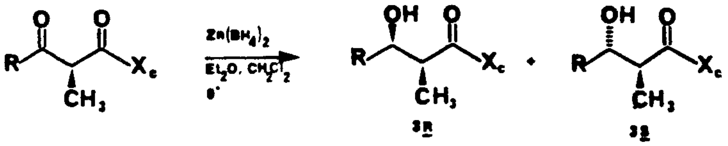
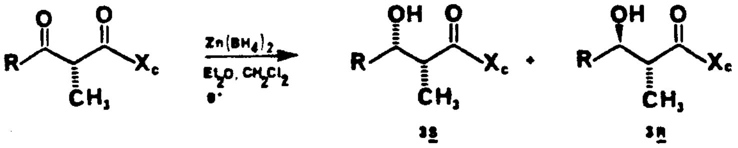


Table 5. $Zn(BH_4)_2$ Reduction Studies. Stereocontrol is dictated by the adjacent chiral center.



R	X_C	Ratio R:S
ϕ-	X_V	99:1
ϕ-	X_N	99:1
CH_3CH_2-	X_N	99:1
CH_3-	X_N	1:4



R	X_C	Ratio R:S
ϕ-	X_V	1:99
ϕ-	X_N	1:99
CH_3CH_2	X_N	1:99
CH_3	X_N	complex mixture

To unambiguously identify the newly created stereocenter, the two enantiomeric methyl esters, **25** and **26**, were prepared via methanolysis of the reduced adducts, **24** and **13** (Fig. 4).

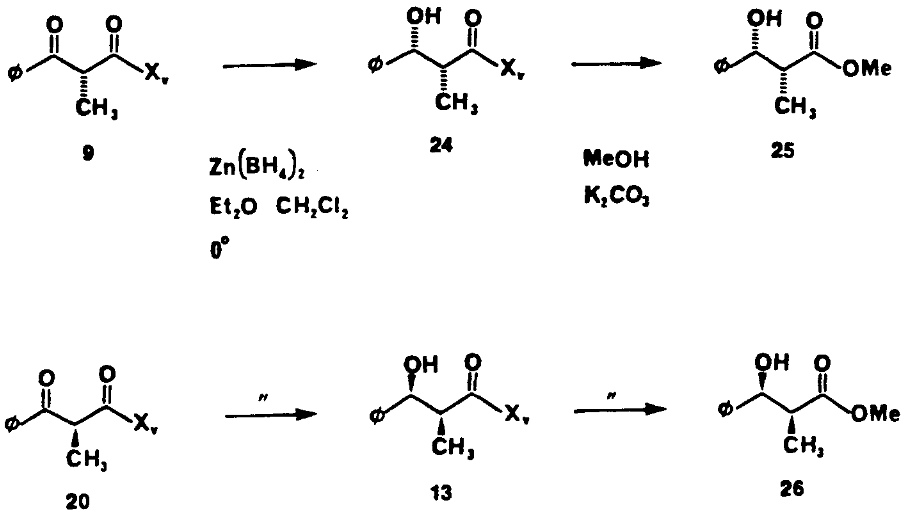


Figure 4

Correlation of **13** from zinc borohydride reduction to the known aldol adduct showed they are identical in all aspects (GC, IR, ^{1}H NMR, ^{13}C NMR and $[\alpha]_D^{25}$). On the basis of NMR comparison of **25** with **26** and their rotation being opposite and almost equal, [for **25**, $[\alpha]_D^{25}$ +18.95° (c 0.38, CH_2Cl_2), and for **26**, $[\alpha]_D^{25}$ -19.21° (c 0.38, CH_2Cl_2)], one can say that they are enantiomers. Consequently, the stereochemical relationship of **13** and **24** can be deduced. This set of experiments also served the purpose of reinforcing the then-proposed stereochemistry at the C$_2$' center of β-ketoimides.

Methyl Grignard also reacted cleanly with the ketonic functional group (MeMgBr, Et_2O, CH_2Cl_2, -78° C). Only one product was isolated. Immediate protection of the tertiary alcohol via silylation (R_3SiOTf, Et_3N, CH_2Cl_2, 0° C) was necessary to avoid

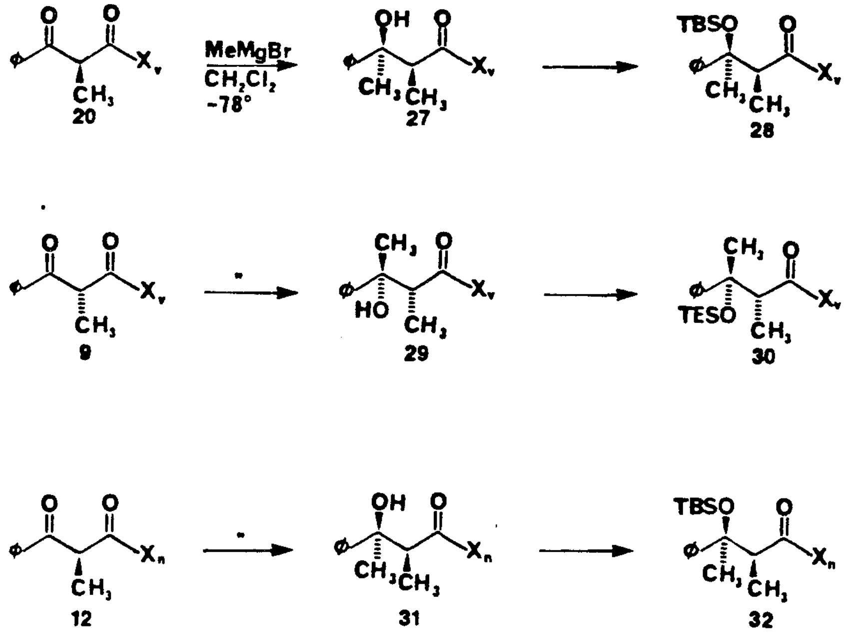
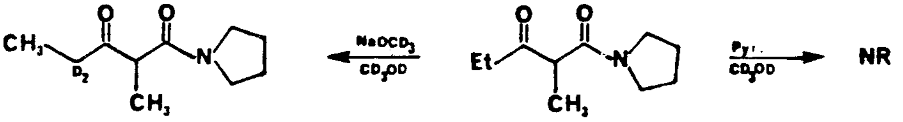


Figure 5

product decomposition (Fig. 5). Subsequent attempts to transform either protected or unprotected tertiary alcohols for structural proof purposes have failed.

The β-ketoimide systems exhibit a remarkable degree of stereochemical integrity. Racemization control experiments were carried out on purified diastereomers 6 and 7 in dichloromethane at room temperature in the presence of three equivalents of triethylamine. Under these conditions, it required over 18 h to reach an equilibrium value of *ca.* 3:2. The results of these studies are shown in Figures 6 and 7. An examination of the X-ray structure (Fig. 2) revealed a possible reason for the reluctance of these systems to undergo epimerization. The enolizable proton (labeled H_e in Fig. 2) is oriented in a configuration which places the C-H bond orthogonal to either of the two carbonyl

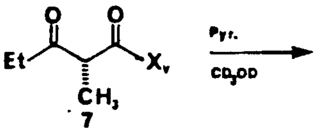
systems. Lack of σ-π orbital overlap may be responsible in part for the low kinetic acidity of the methine proton. Furthermore, the $A^{1,3}$-strain arguments given earlier to account for selective generation of the Z-enolate are also applicable here. This hypothesis is further supported by the observation of low enol content in the β-ketoimides and the parent compound 33 H-D exchange experiments in CD_3OD showed no deuterium



33

(5)

incorporation with pyridine (for three days), and complete exchange of both methine and methylene protons within 10 min with $NaOCD_3$ (eq. 5).



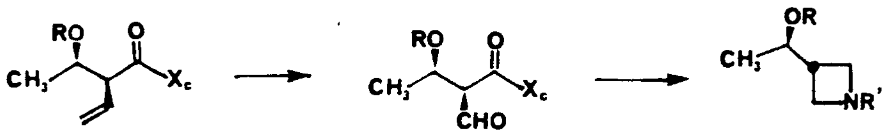
7

(6)

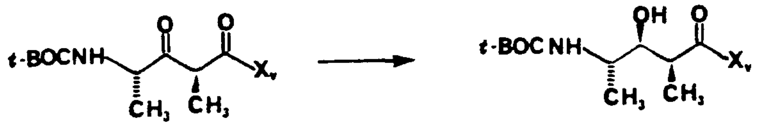
Similar observations were made for the H-D experiment for 7 (eq. 6).

Summary

The practical utility of N-acyl oxazolidones, derived from readily available chiral amine alcohols, as chiral enolate synthons has been demonstrated. The enolates derived from these systems exhibit high degrees of diastereoselectivity in reactions with alkyl halides and acid chlorides. These systems have already found applications in the total synthesis of natural products. They are exemplified by Sjogren's work in the β-lactam system (eq. 7) and DiPardo and Bock's work at Merck (eq. 8).



(7)



(8)

Experimental Section

General. Melting points were determined with a Buchi SMP-20 melting point apparatus and are uncorrected. Infrared spectra were recorded on a Beckman 4210 spectrometer. Proton magnetic resonance spectra were recorded on a Varian EM-390 (90 MHz) spectrometer or a Bruker WM-500 (500 MHz) spectrometer and are reported in ppm downfield from tetramethylsilane (internal standard). Data are reported as follows: chemical shift (multiplicity, integration, coupling constant in Hz, interpretation). Carbon-13 magnetic resonance spectra were recorded on a JEOL FX-90Q (22.5 MHz) spectrometer, and are reported in ppm downfield from tetramethylsilane (internal standard). GC analyses were performed on a HP-5880A series gas chromatograph with capillary columns: 25 x 0.25 mm carbowax (HP) or 25 M x 0.25 mm methyl silicon (HP). MPLC separations were performed using EM Laboratories LoBar silica gel 60 prepacked columns on a MPLC apparatus equipped with a Fluid Metering Inc. Model R.P. Lab Pump. HPLC analyses were performed on a Waters Associate chromatograph with a Radial-Pak B column (silica gel). Optical rotations were recorded on a JASCO DIP-181 polarimeter. Combustion analyses were performed by Spang Microanalytical Laboratory or Galbraith Laboratories, Inc.

When necessary, solvents and reagents were dried prior to use. THF and ether were distilled from sodium-benzophenone-ketyl. Triethylamine and diisopropylamine were distilled from CaH_2. Benzoyl chloride, propionyl chloride, and acetyl chloride were distilled immediately prior to use. Unless otherwise specified, all reactions were done under an argon atmosphere.

General Procedure for the Formation of Lithium Enolates from N-Propionyloxazolidones and Subsequent Acylation with Acid Chlorides. The indicated reactions were carried out under an argon atmosphere on a scale ranging from 1-200 mmol at enolate concentrations of _ca_ 0.25 _M_. All reagent additions were made _via_ hypodermic syringes.

Enolate Generation. To a dried, argon-filled, 25-mL one-necked flask equipped for magnetic stirring and sealed with a rubber septum was added 0.15 mL (1.05 mmol) of anhydrous diisopropylamine and 2 mL of anhydrous tetrahydrofuran (THF). After cooling to -78° C, 0.66 mL of *n*-butyllithium (1.6 *M* in hexane) was added and allowed to stir for 30 min. To this solution (-78° C) was added 1.0 mmol of the indicated *N*-propionyloxazolidone (37 and 38) over a 5-min period. After stirring for an additional 30-min period the desired lithium enolate was ready for acylation.

Enolate Acylation. To a dried, argon-filled, 25-mL, one-necked flask equipped for magnetic stirring and sealed with a rubber septum, was added 1.05 mmol of the indicated acid chloride (freshly distilled) in anhydrous THF (1 mL). After cooling the contents to -78° C, the enolate solution was cannulated *via* a cannula (stainless steel) into the acid chloride solution over a ½-min period. After the enolate transfer was completed, the reaction was *immediately* quenched with 5 mL of a saturated solution of ammonium chloride. The resulting solution was diluted with water and the desired product was isolated by methylene chloride extraction (2 x 5 mL). The combined organic layers were washed successively with aqueous bicarbonate (2 x 10 mL), brine (1 x 10 mL) and dried over anhydrous sodium sulfate. Solvent removal *in vacuo* afforded the desired β-ketoimides in a 85-100% mass balance. Purification of these substrates was then carried out *via* either recrystallization or chromatography on silica gel as indicated in the following specific cases.

β-Ketoimide 7.[9] The title compound 7 was prepared in accordance with the general procedure described above on a 27.4-mmol scale. *N*-Propionyloxazolidone **37** (5.073 gm, 27.4 mmol) in 20 mL THF was added to 28.8 mmol lithium diisopropylamide in 55 mL THF (-78° C), and was cannulated into 28.8 mmol propionyl chloride in 25 mL THF (-78° C). The desired product, 5.95 gm (90%), was isolated according to the provided procedure as a white crystalline solid. HPLC diastereomer analysis of the unpurified material (15% EtOAc-hexane, Radial-Pak B column; silica gel, 4 mL/min, retention time in min: **6** 3.60; **7** 6.60) indicated a kinetic ratio of 96:4 (**7**:**6**). A single recrystallization from ether-hexane (4:1) of the unpurified solid afforded 5.82 gm (88%) of analytically pure white crystals (HPLC diastereomer analysis: **7**:**6** > 99:1). mp 131-132° C; ^1H NMR (90 MHz, $CHCl_3$) δ 4.50-4.10 (m, 3H, $-\overset{|}{N}\overset{|}{C}\underline{H}C\underline{H}_2O-$), 4.48 [q, 1H, J = 7.5 Hz, $O\overset{|}{C}C\underline{H}(CH_3)\overset{|}{C}O$], 2.83-2.27 (m, 3H, $CH_3\overset{|}{C}\underline{H}CH_3$, $CH_3CH_2\overset{|}{C}O$), 1.35 [d, 3H, J = 7.5 Hz, $O\overset{|}{C}CH(C\underline{H}_3)\overset{|}{C}O$], 1.07 (t, 3H, J = 6.9 Hz, $C\underline{H}_3CH_2\overset{|}{C}O$), 0.92 (d, 6H, J = 6.9 Hz, $C\underline{H}_3\overset{|}{C}HC\underline{H}_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 4.49 [q, 1H, J = 7.5 Hz, $O\overset{|}{C}C\underline{H}(CH_3)\overset{|}{C}O$], 4.45 (dt, 1H, J = 8.8 Hz, 3.8 Hz, $-\overset{|}{N}\overset{|}{C}\underline{H}CH_2O-$), 4.28 [t, 1H, J = 8.5 Hz, $-\overset{|}{N}\overset{|}{C}HC\underline{H}(H)O-$], 4.23 [dd, 1H, J = 9.6 Hz, 3.8 Hz, $-\overset{|}{N}\overset{|}{C}HCH(\underline{H})O-$], 2.74 [dq, 1H, J = 18.8 Hz, 7.5 Hz, $CH_3C\underline{H}(H)\overset{|}{C}O$], 2.63 [dq, 1H, J = 18.8 Hz, 7.5 Hz, $CH_3CH(\underline{H})\overset{|}{C}O$], 2.52 (m, 1H, $CH_3\overset{|}{C}\underline{H}CH_3$), 1.37 [d, 3H, J = 7.5 Hz, $O\overset{|}{C}CH(C\underline{H}_3)\overset{|}{C}O$], 1.08 (t, 3H, J = 7.5 Hz, $C\underline{H}_3CH_2\overset{|}{C}O$), 0.93 (d, 6H, J = 7.5 Hz, $C\underline{H}_3\overset{|}{C}HC\underline{H}_3$); ^{13}C NMR (22.5 MHz, $CDCl_3$) δ 107.8, 170.0, 154.5, 63.8, 58.7, 52.4, 33.9, 28.5, 17.9, 14.7, 12.7, 7.6 ppm; IR ($CHCl_3$) 3030, 2982, 2952, 2890, 2408, 1776, 1722, 1705, 1487, 1459, 1390 cm^{-1}; $[\alpha]_D^{25}$ -17.2° (*c* 2.5, CH_2Cl_2).

Anal. calcd. for $C_{12}H_{19}NO_4$: C, 59.73; H, 7.94; N, 5.80. Found: C, 59.59; H, 7.91; N, 5.78.

β-Ketoimide 8. The title compound **8** was prepared in accordance with the general procedure described above on a 4.00-mmol scale. *N*-Propionyloxazolidone **37** (0.7414 gm, 4.00 mmol) in 5 mL THF was added to 4.80 mmol lithium diisopropylamide in 10 mL THF (-78° C), and was cannulated into 4.80 mmol acetyl chloride in 5 mL THF (-78° C). The desired product, 0.86 gm (98%) was isolated according to the provided procedure as a white crystalline solid. HPLC diastereomer analysis of the unpurified material (20% EtOAc-hexane, Radial-Pak B column; silica gel, 5 mL/min, retention time in min: **19** 3.50; **8** 10.8) indicated a kinetic ratio of 96:4 (**8**:**19**). A single recrystallization from ether-hexane (1:1) of the unpurified solid afforded 0.86 gm (95%) of analytically pure white crystals (HPLC diastereomer analysis: **8**:**19** > 99:1). mp 134-134.5 °C; ^{1}H NMR (90 MHz, CDCl$_3$) δ 4.49 (q, 1H, J = 7.5 Hz, $O\overset{|}{C}C\underline{H}(CH_3)\overset{|}{C}O$), 4.51-4.13 (m, 3H, $-\overset{|}{N}\overset{|}{C}\underline{H}C\underline{H}_2O-$), 2.70-2.27 (m, 1H, $CH_3\overset{|}{C}\underline{H}CH_3$), 2.30 (s, 3H, $C\underline{H}_3\overset{|}{C}O$), 1.37 (d, 3H, J = 7.5 Hz, $O\overset{|}{C}CH(C\underline{H}_3)\overset{|}{C}O$), 0.93 (d, 3H, 6H, J = 7 Hz, $C\underline{H}_3\overset{|}{C}HC\underline{H}_3$); ^{1}H NMR (500 MHz, CDCl$_3$) δ 4.49 (q, 1H, J = 7.5 Hz, $O\overset{|}{C}C\underline{H}(CH_3)\overset{|}{C}O$), 4.47-4.42 (m, 1H, $-\overset{|}{N}\overset{|}{C}\underline{H}CH_2O-$), 4.30-4.21 (m, 2H, $-\overset{|}{N}\overset{|}{C}HC\underline{H}_2O-$), 2.53-2.43 (m, 1H, $CH_3\overset{|}{C}\underline{H}CH_3$), 2.32 (s, 3H, $C\underline{H}_3\overset{|}{C}O$), 1.38 (d, 3H, J = 7.5 Hz, $O\overset{|}{C}CH(C\underline{H}_3)\overset{|}{C}O$), 0.93 (d, 3H, J = 4 Hz, $C\underline{H}_3\overset{|}{C}HCH_3$), 0.91 (d, 3H, J = 4 Hz, $CH_3\overset{|}{C}HC\underline{H}_3$); ^{13}C NMR (22.5 MHz, CDCl$_3$) δ 205.4, 169.7, 154.3, 63.7, 58.6, 53.2, 28.3, 17.9, 14.5, 12.3 ppm; IR (CHCl$_3$) 3029, 2980, 2408, 1778, 1723, 1704, 1487, 1457, 1390 cm^{-1}; (α)$_D^{25}$ -22.80° (c 1.4, CH$_2$Cl$_2$).

Anal. calcd. for $C_{11}H_{17}NO_4$: C, 58.13; H, 7.54. Found: C, 58.16; H, 7.50.

β-Ketoimide 9. The title compound **9** was prepared in accordance with the general procedure described above on a 3.95-mmol scale. N-Propionyloxazolidone **37** (0.7323 gm, 3.95 mmol) in 5 mL THF was added to 4.35 mmol lithium diisopropylamide in 10 mL THF (-78° C), and was cannulated into 4.35 mmol benzoyl chloride in 4 mL THF (-78° C). The desired product, 1.09 gm (95%) was isolated according to the provided procedure as a yellow liquid. HPLC diastereomer analysis of the unpurified material (20% EtOAc-hexane, Radial-Pak B column, silica gel, 4 mL/min, retention time in min: **20** 2.87; **9** 6.11) indicated a kinetic ratio of 96.2:3.8 (**9**:**20**). MPLC purification (20% EtOAc-hexane, C-column, 940 gm of silica gel) of the unpurified material afforded 1.07 gm (93%) of an analytically pure product as a colorless oil (HPLC diastereomer analysis: **9**:**20** > 99:1). For the diastereomeric compounds **9** and **20**; the R$_f$ values (20% EtOAc-hexane) were found to be 0.25 and 0.40, respectively. ^{1}H NMR (90 MHz, CDCl$_3$) δ 8.05-7.87, 7.67-7.30 (m, 5H, Ar$\underline{H}$), 5.34 (q, 1H, J = 8 Hz, $O\overset{|}{C}C\underline{H}(CH_3)\overset{|}{C}O$), 4.57-4.00 (m, 3H, $-\overset{|}{N}\overset{|}{C}\underline{H}C\underline{H}_2O-$), 2.68-2.30 (m, 1H, $CH_3\overset{|}{C}\underline{H}CH_3$), 1.43 (d, 3H, J = 8 Hz, $O\overset{|}{C}CH(C\underline{H}_3)\overset{|}{C}O$), 0.97 (d, 6H, J = 7 Hz, $C\underline{H}_3\overset{|}{C}HC\underline{H}_3$); ^{1}H NMR (500 MHz, C$_6D_6$) δ 8.04-8.00, 7.19-7.10 (m, 5H, Ar$\underline{H}$), 5.20 (q, 1H, J = 6.7 Hz, OCC$\underline{H}$(CH$_3$)CO), 4.07-4.02 (m, 1H, -NC$\underline{H}$CH$_2$O-), 3.48 (double doublet, 1H, J = 3.8 Hz, 9Hz, -NCHC$\underline{H}$(H)O-), 3.38 (t, 1H, J = 9 Hz, -NCHCH($\underline{H}$)O-), 2.46-2.38 (m, 1H, CH$_3$C$\underline{H}$CH$_3$), 1.37 (d, 3H, J = 6.7 Hz, OCCH(C$\underline{H}_3$)CO), 0.80 (d, 3H, J = 7.5 Hz, C$\underline{H}_3$CHCH$_3$), 0.50 (d, 3H, J = 7.5 Hz, CH$_3$CHC$\underline{H}_3$); ^{13}C NMR (22.5 MHz, CDCl$_3$) δ 197.8, 170.3, 154.2, 135.2, 133.2, 128.7, 63.7, 58.6, 48.6, 28.3, 17.9, 14.6, 13.6 ppm; IR (CHCl$_3$) 3029, 2982, 2408, 1776, 1715, 1683, 1600, 1577, 1485, 1450 cm^{-1}; $(\alpha)_D^{25}$ -62.3° (c 0.30, CH$_2$Cl$_2$).

Anal. calcd. for $C_{16}H_{19}NO_4$: C, 66.42; H, 6.62. Found: C, 66.41; H, 6.60.

β-Ketoimide 10. The title compound **10** was prepared in accordance with the general procedure described above on a 2.64-mmol scale. N-Propionyloxazolidone **38** (0.615 gm, 2.64 mmol) in 3 mL THF was added to 2.77 mmol lithium diisopropylamide in 6 mL THF (-78°C), and was cannulated into 3.16 mmol acetyl chloride in 3 mL THF (-78°C). The desired product, 0.71 gm (98%) was isolated according to the provided procedure as a viscous liquid. HPLC diastereomer analysis of the unpurified material (20% EtOAc-hexane, Radial-Pak B column; silica gel, 5 mL/min, retention time in min: **21** 0.85; 10 2.6) indicated a kinetic ratio of 70:340 (**10:21**). Double recrystallizations from pentane-ether (1:1) of the unpurified material afforded 0.39 gm (55%) of analytically pure crystals (HPLC diastereomer analysis: **10:21** > 99:1). mp 116.5-117.5°C; ^{1}H NMR (90 MHz, CHCl$_3$) δ 7.30-7.20 (m, 5H, Ar$\underline{H}$), 5.66 (d, 1H, J = 7.5 Hz, -NCH(CH$_3$)C$\underline{H}$(ϕ)O-), 4.80 (q, 1H, J = 6 Hz, OCC$\underline{H}$(CH$_3$)CO), 4.53 (quintet, 1H, J = 7.5 Hz, -NC$\underline{H}$(CH$_3$)CH(ϕ)O-), 2.30 (s, 3H, C$\underline{H}_3$CO), 1.39 (d, 3H, J = 6 Hz, OCCH(C$\underline{H}_3$)CO), 0.94 (d, 3H, J = 7.5 Hz, -NCH(C$\underline{H}_3$)CH(ϕ)O-); ^{1}H NMR (500 MHz, CHCl$_3$) δ 7.43-7.27 (m, 5H, Ar$\underline{H}$), 5.67(d, 1H, J = 6.9 Hz, -NCH(CH$_3$)C$\underline{H}$(ϕ)O-), 4.51 (q, 1H, J = 7.6 Hz, OCC$\underline{H}$(CH$_3$)CO), 4.30 (quintet, 1H, J = 7 Hz, -NC$\underline{H}$(CH$_3$)CH(ϕ)O-), 2.32 (s, 3H, C$\underline{H}_3$CO), 1.40 ((d, 3H, J = 7.6 Hz, OCCH(C$\underline{H}_3$)CO), 0.93 (d, 3H, J = 7.1 Hz, -NCH(CH$_3$)CH(ϕ)O-), ^{13}C NMR (22.5 MHz, CDCl$_3$) δ 204.9, 169.6, 153.2, 133.1, 128.7, 128.6, 125.6, 79.3, 54.8, 53.0, 28.1, 13.9, 12.3 ppm;

IR ($CHCl_3$) 3700, 3030, 2950, 2402, 1780, 1725, 1708, 1605, 1457, 1420 cm^{-1}; $(\alpha)_D^{25}$ +111.9° ($\underline{c}$ 1.20, CH_2Cl_2).

Anal. calcd. for $C_{15}H_{17}NO_4$: C, 65.44; H, 6.23. Found: C, 65.49; H, 6.20.

β-Ketoimide 11.[10] The title compound **11** was prepared in accordance with the general procedure described above on a 1.25-mmol scale. $\underline{N}$-Propionyloxazolidone **38** (0.295 gm, 1.25 mmol) in 1.25 mL THF was added to 1.38 mmol lithium diisopropylamide in 1.25 mL THF (-78°C) and was cannulated into 1.38 mmol propionyl chloride in 1 mL THF (-78°C). The desired product, 0.32 gm (89%) was isolated according to the provided procedure as a white crystalline solid. HPLC diastereomer analysis of the unpurified material (15% EtOAc-hexane, Radial Pak B column, silica gel, 4 mL/min, retention time in min: **22** 2.69; **11** 5.59) indicated a kinetic ratio of 95:5 (**11:22**). A single recrystallization of the unpurified material from EtOAc-hexane (1:4) afforded 0.30 gm (83%) of analytically pure needle-like crystals (HPLC diastereomer analysis, **11:22** > 99:1). mp 123-124°C; ^1H NMR (90 MHz, $CDCl_3$) δ 7.53-7.20 (m, 5H, Ar$\underline{H}$), 5.66 (d, 1H, J = 7 Hz, $-\overset{|}{N}\overset{|}{C}HC\underline{H}(\phi)O-$), 4.78 (quintet, 1H J = 7 Hz, $-\overset{|}{N}\overset{|}{C}\underline{H}CH(\phi)O-$), 4.53 (q, 1H, J = 7.2 Hz, $O\overset{|}{C}C\underline{H}(CH_3)\overset{|}{C}O$), 2.83-2.53 (m, 2H, $CH_3C\underline{H_2}\overset{|}{C}O$), 1.40 (d, 3H, J = 7.2 Hz, $O\overset{|}{C}CH(C\underline{H_3})\overset{|}{C}O$), 1.11 (t, 3H, J = 7.2 Hz, $C\underline{H_3}CH_2\overset{|}{C}O$), 0.97 (d, 3H, J = 7 Hz, $-\overset{|}{N}CH(C\underline{H_3})CH(\phi)O-$); ^{13}C NMR (22.5 MHz, $CDCl_3$) δ 207.9, 169.9, 153.2, 133.1, 128.7, 125.7, 79.3, 54.9, 52.4, 33.8, 14.0, 12.7, 7.5 ppm; IR ($CHCl_3$) 3022, 2990, 2946, 2910, 1775, 1720, 1702, 1604, 1494, 1452, 1410 cm^{-1}; $(\alpha)_D^{25}$ +108.3° ($\underline{c}$ 1.4, CH_2Cl_2).

Anal. calcd. for $C_{16}H_{19}NO_4$: C, 66.42; H, 6.62. Found: C, 66.63; H, 6.65.

β-Ketoimide 12.[10] The title compound 12 was prepared in accordance with the general procedure described above on a 0.394 mmol scale. $\underline{N}$-Propionyloxazolidone **38** (0.092 gm, 0.394 mmol) in 2 mL THF was added to 0.414 mmol lithium diisopropylamide in 4 mL THF (-78°C), and was cannulated into 0.414 mmol benzoyl chloride in 1 mL THF. The desired product, 0.13 gm (95%), was isolated according to the provided procedure as a white crystalline solid. HPLC diastereomer analysis of the unpurified material (10% EtOAc-hexane, Radial Pak B column, silica gel, 5 mL/min, retention time in min: **23** 3.78; **12** 11.26) indicated a kinetic ratio of 95.5:4.5 (**11**:**23**). A single recrystallization of the unpurified material from EtOAc-hexane (1:3) afforded 0.125 gm (92%) of analytically pure needle-like crystals (HPLC diastereomer analysis, **12**:**23** $>$ 99:1). mp 164.5-165°C; ^{1}H NMR (90 MHz, $CDCl_3$) δ 8.10-7.90, 7.67-7.15 (m, 10H, Ar$\underline{H}$) 5.68 (d, 1H, J = 7.2 Hz, $-\overset{|}{N}CH(CH_3)C\underline{H}(\phi)O-$), 5.41 (q, 1H, J = 6.9 Hz, $O\overset{|}{C}C\underline{H}(CH_3)\overset{|}{C}O$), 4.83 (quintet, 1H, J = 7.2 Hz, $-\overset{|}{N}C\underline{H}(CH_3)CH(\phi)O-$), 1.47 (d, 3H, J = 6.9 Hz, $O\overset{|}{C}CH(C\underline{H_3})\overset{|}{C}O$), 0.97 (d, 3H, J = 7.2 Hz, $-\overset{|}{N}CH(C\underline{H_3})CH(\phi)O-$); ^{13}C NMR (22.5 MHz, $CDCl_3$) δ 197.6, 170.2, 153.2, 135.2, 133.2, 128.7, 125.7, 79.4, 54.9, 48.6, 14.0, 13.6 ppm; IR ($CHCl_3$) 3032, 2440, 1780, 1717, 1684, 1601, 1580, 1452, 1372, 1362 cm^{-1}; $(\alpha)_D^{25}$ +154.5° (*c* 0.52, CH_2Cl_2).

Anal. calcd. for $C_{20}H_{19}NO_4$: C, 71.20; H, 5.68. Found: C, 71.55; H, 5.67.

General Procedures for the Formation of Boron Enolates from *N*-Propionyl Oxazolidones and Subsequent Condensation With Aldehydes.[6] The indicated reactions were carried out under an argon atmosphere on a scale ranging from 5-20 mmol of concentrations of starting oxazolidone of *ca* 0.25 *M*. All reagent additions were made *via* hypodermic syringes.

Enolate Generation. To a dried, argon-filled, 25-mL, one-necked flask, equipped with a rubber septum and for magnetic stirring, was added 1.0 mmol of the indicated *N*-propionyl oxazolidone (**5** or **6**) and 4 mL of anhydrous methylene chloride (CH_2Cl_2). After cooling to -78° C, 0.21 mL (1.1 mmol) of di-*n*-butylborontriflate (*n*-Bu_2BOTf) and 0.21 mL (1.2 mmol) of anhydrous triethylamine (Et_3N) were added successively. After stirring for an 1-h period the desired boron enolate was ready for condensation.

Enolate Aldolization. To the enolate solution (-78° C), was added one equivalent of non-enolizable aldehyde (or 1.2 equiv of enolizable aldehyde) in one portion. The solution was allowed to stir for 30 min at -78° C and then at 0° C for 1 h. The reaction was quenched with 1 mL of pH 7 phosphate buffer solution, followed with 4 mL MeOH. A cool solution of 1 mL of 30% H_2O_2 in 2 mL MeOH (0°C) was added dropwise over a 10 min period and the mixture was stirred for 1 h. The methanol was removed *in vacuo* and the remaining cloudy solution was extracted with methylene chloride (3 x 5 mL). The combined organic layers were washed successively with saturated aqueous bicarbonate (1 x 10 mL), brine (1 x 10 mL), and dried over anhydrous magnesium sulfate. Solvent removal *in vacuo* afforded the desired aldol adduct in a 85-99% mass balance. Purification of these substrates was then carried out *via* either recrystallization or chromatography on silica gel as indicated in the following specific cases.

Aldol Adduct 13.[6] The title compound **13** was prepared in accordance with the general procedure described above on a 10.0-mmol scale. *N*-Propionyl oxazolidone **37** (1.85 gm, 10.0 mmol) in 30 mL CH_2Cl_2, was treated with 11.0 mmol di-*n*-butylboron triflate, 12.0 mmol triethylamine (-78°C), and was subsequently condensed with 10.0 mmol benzaldehyde (-78° → 0°C). The desired product, 2.68 gm (96%), was isolated according to the provided procedure as a white crystalline solid. A single recrystallization of the unpurified material from other-petroleum ether (1:1) afforded 2.51 gm (90%) of analytically pure crystals. mp 97-98°C; ^1H NMR (90 MHz, $CDCl_3$) δ 7.32 (broad s, 5H, Ar$\underline{H}$), 5.00 (d, 1H, J = 4.5 Hz, $\phi\overset{|}{C}\underline{H}OH$), 4.4-3.9 (m, 4H, $-\overset{|}{N}\overset{|}{C}\underline{H}C\underline{H_2}O-$, $\overset{|}{O}\overset{|}{C}C\underline{H}CH_3$), 3.44 (s, 1H, -O$\underline{H}$), 0.92 (d, 3H, J = 3 Hz, $C\underline{H_3}\overset{|}{C}HCH_3$), 0.88 (d, 3H, J = 3 Hz, $CH_3\overset{|}{C}HC\underline{H_3}$); ^{13}C NMR (22.5 MHz, CCl_4) δ 176.0, 152.9, 141.9, 127.8, 127.0, 126.0, 73.2, 62.9, 58.1, 44.4, 28.3, 17.7, 14.7, 11.2 ppm; IR ($CHCl_3$) 3700, 3620, 3025, 2980, 2400, 1783, 1691, 1602, 1486, 1451, 1386, 1300 cm^{-1}; $(\alpha)_D^{25}$ +64.5° (*c* 8.4, CH_2Cl_2).

Aldol Adduct 14. The title compound **14** was prepared in accordance with the general procedure described above on a 7.34-mmol scale. *N*-Propionyl oxazolidone **37** (1.3586 gm, 7.34 mmol) in 25 mL CH_2Cl_2, was treated with 8.07 mmol di-*n*-butylboron triflate, 8.80 mmol triethylamine (-78°C), and was subsequently condensed with 8.80

mmol propionaldehyde (-78° → 0°C). The desired product, 1.75 gm (98%), was isolated according to the provided procedure as a yellow liquid. MPLC purification (40% EtOAc-hexane, C-column, 940 gm of silica gel, R_f for **20** 0.26) of the unpurified material yielded 1.63 gm (91%) of an analytically pure product as a colorless oil. ^{1}H NMR (90 MHz, $CDCl_3$) δ 4.62-4.21 (m, 3H, $\mathrm{-\overset{|}{N}\overset{|}{C}\underline{H}C\underline{H}_2O-}$), 4.00-3.73 (m, 2H, $\mathrm{CH_3CH_2\overset{|}{C}\underline{H}OH}$, $\mathrm{CH_3\overset{|}{C}\underline{H}\overset{|}{C}O}$), 3.05 (broad s, 2H, $\mathrm{-O\underline{H}}$), 2.61-2.57 (m, 1H, $\mathrm{CH_3\overset{|}{C}\underline{H}CH_3}$), 1.77-1.31 (m, 2H, $\mathrm{CH_3C\underline{H}_2\overset{|}{C}HOH}$), 1.31 (d, 3H, J = 6.6 Hz, $\mathrm{C\underline{H}_3\overset{|}{C}H\overset{|}{C}O}$), 1.11-1.01 (m, 6H, $\mathrm{C\underline{H}_3CH_2\overset{|}{C}HOH}$, $\mathrm{C\underline{H}_3\overset{|}{C}HCH_3}$), 0.94 (d, 3H, J = 3 Hz, $\mathrm{CH_3\overset{|}{C}HC\underline{H}_3}$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.52-4.48 (m, 1H, $\mathrm{-\overset{|}{N}\overset{|}{C}\underline{H}CH_2O-}$), 4.32 [t, 1H, J = 8.3 Hz, $\mathrm{-\overset{|}{N}\overset{|}{C}HC\underline{H}(H)O-}$], 4.25 [double d, 1H, J = 8.3 Hz, 3 Hz, $\mathrm{-\overset{|}{N}\overset{|}{C}HCH(\underline{H})O-}$], 3.90-3.86 (m, 1H, $\mathrm{CH_3CH_2\overset{|}{C}\underline{H}OH}$), 3.82 (double quartet, 1H, J = 7.5 Hz, 2.5 Hz, $\mathrm{CH_3\overset{|}{C}\underline{H}\overset{|}{C}O}$), 3.03 (d, 1H, J = 2.5 Hz, $\mathrm{-O\underline{H}}$), 2.42-2.35 (m, 1H, $\mathrm{CH_3\overset{|}{C}\underline{H}CH_3}$), 1.65-1.57 [m, 1H, $\mathrm{-\overset{|}{N}\overset{|}{C}HC\underline{H}(H)CHOH}$], 1.52-1.43 [m, 1H, $\mathrm{CH_3CH(\underline{H})\overset{|}{C}HOH}$],1.28 (d, 3H, J = 7 Hz, $\mathrm{C\underline{H}_3\overset{|}{C}H\overset{|}{C}O}$), 1.02 (t, 3H, J = 7.3 Hz, $\mathrm{C\underline{H}_3CH_2\overset{|}{C}HOH}$), 0.96 (d, 3H, J = 7 Hz, $\mathrm{C\underline{H}_3\overset{|}{C}HCH_3}$), 0.92 (d, 3H, J = 7 Hz, $\mathrm{CH_3\overset{|}{C}HC\underline{H}_3}$); ^{13}C NMR (22.5 MHz, $CDCl_3$) δ 177.7, 153.6, 72.7, 63.4, 58.2, 41.7, 28.4, 26.7, 17.9, 14.7, 10.7, 10.5 ppm; IR ($CHCl_3$) 3700, 3550, 3025, 2980, 2950, 2888, 2446, 1784, 1693, 1487, 1464, 1457, 1386, 1375, 1302, 1236, 1202 cm^{-1}; $(\alpha)_D^{25}$ +106.5° ($\underline{c}$ 5.5, CH_2Cl_2).

$\underline{\text{Anal.}}$ calcd. for $C_{12}H_{21}NO_4$: C, 59.24; H, 8.70. Found: C, 59.44; H, 8.83.

Aldol Adduct 15. The title compound 15 was prepared in accordance with the general procedure described above on a 14.87-mmol scale. $\underline{N}$-Propionyl oxazolidone 37 (2.7542 gm, 14.87 mmol) in 50 mL CH_2Cl_2, was treated with 16.36 mmol di-$\underline{n}$-butylboron triflate, 17.84 mmol triethylamine (-78°C), and was subsequently condensed with 29.74 mmol propionaldehyde (-78° → 0°C). The desired product, 3.34 gm (98%), was isolated according to the provided procedure as a clear liquid. MPLC purification (30% EtOAc-hexane, C-column, 940 gm of silica gel, R_f for **21** 0.17) of the unpurified material yielded 3.07 gm (90%) of an analytically pure product as a colorless oil. ^{1}H NMR (90 MHz,

$CDCl_3$) δ 4.57-3.98 (m, 4H, $CH_3\overset{|}{C}\underline{H}OH$, $-\overset{|}{N}\overset{|}{C}\underline{H}C\underline{H}_2O-$), 3.74 (double quartet, 1H, J = 7 Hz, 3 Hz, $CH_3\overset{|}{C}\underline{H}\overset{|}{C}O$), 3.03 (broad s, 1H, $-O\underline{H}$), 2.52-2.17 (m, 1H, $CH_3\overset{|}{C}\underline{H}CH_3$), 1.26 (d, 3H, J = 6.6 Hz, $C\underline{H}_3\overset{|}{C}HOH$), 1.18 (d, 3H, J = 7 Hz, $C\underline{H}_3\overset{|}{C}H\overset{|}{C}O$), 0.95 (d, 3H, J = 3 Hz, $C\underline{H}_3\overset{|}{C}HCH_3$), 0.87 (d, 3H, J = 3 Hz, $CH_3\overset{|}{C}HC\underline{H}_3$); ^{13}C NMR (22.5 MHz, $CDCl_3$) δ 177.5, 153.7, 67.4, 63.4, 58.3, 43.2, 28.4, 19.7, 17.9, 14.8, 10.9 ppm; IR ($CHCl_3$) 3560, 3025, 2980, 2400, 1784, 1689, 1488, 1460, 1387, 1375, 1369, 1302, 1287, 1237, 1202 cm^{-1}; $(\alpha)_D^{25}$ +80.1° (c 4.35, CH_2Cl_2).

Anal. calcd. for $C_{11}H_{19}NO_4$: C, 57.62; H, 8.35. Found: C, 57.43; H, 8.38.

Aldol Adduct 16.[6] The title compound 16 was prepared in accordance with the general procedure described above on a 5.28-mmol scale. N-Propionyl oxazolidone 38 (1.2308 gm, 5.28 mmol) in 25 mL CH_2Cl_2, was treated with 5.54 mmol di-n-butylboron triflate, 5.54 mmol triethylamine (-78°C), and was subsequently condensed with 5.54 mmol benzaldehyde. The desired product, 1.76 gm (98%), was isolated according to the provided procedure as a white crystalline solid. A single recrystallization of the unpurified material from ether-hexane (1:1) afforded 1.65 gm (92%) of analytically pure white needle-like crystals. mp 137-138°C; ^1H NMR (90 MHz, $CDCl_3$) δ 7.35 (m, 10H, Ar$\underline{H}$), 5.42 (d, J = 7.5 H, 1H, $-\overset{|}{N}CH(CH_3)C\underline{H}(\phi)O-$), 5.06 (d, J = 4.5 Hz, $\phi C\underline{H}OH$), 4.62 (quintet, 1H, J = 7 Hz, $-\overset{|}{N}C\underline{H}(CH_3)CH(\phi)O-$), 4.13 (m, 1H, $CH_3\overset{|}{C}\underline{H}\overset{|}{C}O$), 3.24 (broad s, 1H, $\phi\overset{|}{C}HO\underline{H}$), 1.23 (d, 3H, J = 7 Hz, $C\underline{H}_3\overset{|}{C}H\overset{|}{C}O$), 0.90 (d, 3H, J = 7.5 Hz, $-\overset{|}{N}CH(C\underline{H}_3)CH(\phi)O-$); ^{13}C NMR (90 MHz, $CDCl_3$) δ 176.4, 152.5, 141.4, 133.0, 128.7, 128.2, 127.6, 126.1, 125.6, 79.0, 74.1, 54.9, 44.7, 14.4, 10.9 ppm; IR ($CHCl_3$) 3700, 3630, 3032, 2405, 1784, 1693, 1687, 1605, 1454, 1381, 1370, 1345, 1220, 1201 cm^{-1}; $(\alpha)_D^{25}$ +5.5° (c 6, CH_2Cl_2).

Aldol Adduct 17. The title compound 17 was prepared in accordance with the general procedure described above on a 16.56-mmol scale. N-Propionyl oxazolidone 38 (3.8623 gm, 16.56 mmol) in 50 mL CH_2Cl_2, was treated with 18.22 mmol di-n-butylboron triflate, 19.87 mmol triethylamine (-78° C), and was subsequently condensed with 19.87

mmol propionaldehyde (-78° → 0°C). The desired product, 4.63 gm (96%), was isolated according to the provided procedure as a viscous oil. MPLC purification (40% EtOAc-hexane, C-column, 940 gm of silica gel, R_f for **23** 0.28) of the unpurified material yielded 4.53 gm (94%) of an analytically pure product as a very viscous oil. ^{1}H NMR (90 MHz, $CDCl_3$) δ 7.45-7.22 (m, 5H, Ar$\underline{H}$), 5.66 (d, 1H, J = 7.2 Hz, $-\overset{|}{N}CH(CH_3)C\underline{H}(\phi)O-$), 4.77 (quintet, 1H, J = 6.6 Hz, $-\overset{|}{N}C\underline{H}(CH_3)CH(\phi)O-$), 3.97-3.65 (m, 2H, $CH_3CH_2\overset{|}{C}\underline{H}OH$, $CH_3\overset{|}{C}\underline{H}\overset{|}{C}O$), 2.82 (d, 1H, J = 3 Hz, $-O\underline{H}$), 1.67-1.38 (m, 2H, $CH_3C\underline{H_2}\overset{|}{C}HOH$), 1.23 (d, 3H, J = 7.2 Hz, $C\underline{H_3}\overset{|}{C}H\overset{|}{C}O$), 0.98 (t, 3H, J = 7 Hz, $C\underline{H_3}CH_2\overset{|}{C}HOH$), 0.88 (d, 3H, J = 6 Hz, $-\overset{|}{N}CH(C\underline{H_3})CH(\phi)O-$); ^{13}C NMR (22.5 MHz, $CDCl_3$) δ 177.4, 152.6, 133.2, 128.7, 125.6, 78.9, 73.0, 54.8, 41.8, 267.8, 14.4, 10.5, 10.1 ppm; IR ($CHCl_3$) 3700, 3550, 3030, 2405, 1782, 1686, 1524, 1454, 1385, 1367, 1343, 1303, 1226 cm^{-1}; $(\alpha)_D^{25}$ +19.7° ($\underline{c}$ 0.50, CH_2Cl_2).

Anal. calcd. for $C_{16}H_{21}NO_4$: C, 65.96; H, 7.27. Found: C, 65.74; H, 7.21.

Aldol Adduct 18. The title compound **18** was prepared in accordance with the general procedure described above on a 8.906-mmol scale. $\underline{N}$-Propionyl oxazolidone **38** (2.0775 gm, 8.906 mmol) in 35 mL CH_2Cl_2, was treated with 9.80 mmol di-$\underline{n}$-butylboron triflate, 10.7 mmol triethylamine (-78°C), and was subsequently condensed with 20.0 mmol acetaldehyde (-78° →0°C). The desired product, 2.42 gm (98%), was isolated according to the provided procedure as a white crystalline solid. A single recrystallization from diisopropyl ether of the unpurified material afforded 2.17 gm (88%) of analytically pure white crystals. mp 114-115°C; ^{1}H NMR (90 MHz, $CDCl_3$) δ 7.50-7.17 (m, 5H, Ar$\underline{H}$), 5.66 (d, 1H, J = 7.5 Hz, $-\overset{|}{N}CH(CH_3)C\underline{H}(\phi)O-$), 4.76 (quintet, 1H, J = 7.4 Hz, $-\overset{|}{N}C\underline{H}(CH_3)CH(\phi)O-$), 4.16-4.11 (m, 1H, $CH_3\overset{|}{C}\underline{H}OH$), 3.71 (double quartet, 1H, J = 7.4 Hz, $CH_3\overset{|}{C}\underline{H}\overset{|}{C}O$), 2.86 (d, 1H, J = 3 Hz, $-O\underline{H}$), 1.25 (d, 3H, J = 6.6 Hz, $C\underline{H_3}\overset{|}{C}HOH$), 1.22 (d, 3H, J = 7.4 Hz, $C\underline{H_3}\overset{|}{C}H\overset{|}{C}O$), 0.90 (d, 3H, J = 7.2 Hz, $-\overset{|}{N}CH(C\underline{H_3})CH(\phi)O-$); ^{13}C NMR (22.5 MHz, $CDCl_3$) δ 177.1, 152.7, 133.2, 128.7, 125.6, 79.0, 67.7, 54.7, 43.2, 19.7, 14.4, 10.4 ppm; IR ($CHCl_3$) 3700, 3540, 3000, 1788, 1690, 1603, 1455, 1384, 1370, 1350, 1244 cm^{-1};

$(\alpha)_D^{25}$ +19.21° (c 1.01, CH_2Cl_2).

Anal. calcd. for $C_{15}H_{19}NO_4$: C, 64.96; H, 6.91. Found: C, 65.04; H, 7.10.

General Procedures for the Moffatt Oxidations of the Corresponding Aldol Adducts to β-Ketoimides. The indicated reactions were carried out under an argon atmosphere on a scaled ranging from 1-20 mmol at aldol adduct concentrations of ca 0.1 M. All reagent additions were made via hypodermic syringes. Into a dried, argon-filled, one-necked 50-mL flask, equipped for magnetic stirring and with a rubber septum, was added 1.0 mmol of the indicated aldol adduct. 5mL Methylene chloride (CH_2Cl_2) and 5 mL of anhydrous dimethylsulfoxide (DMSO) were introduced. After cooling to 0° C, 0.42 (3 mmol) of anhydrous triethylamine was added. Into another dried, argon-filled, one-necked 25-mL flask, equipped with rubber septum, was added 0.48 gm (3 mmol) of sulfur trioxide pyridine (pyr·SO_3) complex and 5 mL of anhydrous dimethylsulfoxide. After disconnecting the argon line to avoid Me_2S contamination, the pyridine·SO_3 solution was added in one portion, via syringe, into the aldol adduct solution and allowed to stir at 0° C for 30 min. The reaction was diluted with 15 mL of diethyl ether. The resulting solution was washed successively with saturated aqueous bicarbonate solution (2 x 15 mL), brine (1 x 15 mL), and dried over anhydrous sodium sulfate. Solvent removal in vacuo afforded the desired β-ketoimides in a 75-95% mass balance. Chromatography purification on silica gel of these substrates was carried out to eliminate the sulfur smelling compounds.

β-Ketoimide 6. The title compound 6 was prepared in accordance with the general procedure outlined above on a 2.02-mmol scale. The aldol adduct 14 (0.490 gm, 2.02 mmol), in 5 mL DMSO and 7 mL CH_2Cl_2, was treated successively with 6.05 mmol triethylamine and with 6.05 mmol pyridine·SO_3 complex in 5 mL DMSO (0° C). The desired product, 0.45 gm (92%) was isolated according to the provided procedure as a clear liquid. HPLC diastereomer analysis of the unpurified material (15% EtOAc-hexane, Radial-Pak B column, silica gel, 4 mL/min retention time in min: **6** 3.60; **7** 6.60) indicated a kinetic ratio of 99:1 (**6**:**7**). MPLC purification of the unpurified material afforded 0.41 gm (85%) of an analytically pure product as a colorless oil (HPLC diastereomer analysis **6**:**7**> 99:1). For the diastereomeric compounds **6** and **7**, the R_f values (30% EtOAc-hexane, C-column, 940 gm of silica gel) were found to be 0.27 and 0.19, respectively. ^1H NMR (90 MHz, $CDCl_3$) δ 4.61 (q, 1H, J = 7.5 Hz, $O\overset{|}{C}C\underline{H}(CH_3)\overset{|}{C}O$), 4.53-4.07 (m, 3H, $-\overset{|}{N}\overset{|}{C}\underline{H}C\underline{H}_2O-$), 2.80-2.47 (m, 2H, $CH_3C\underline{H}_2\overset{|}{C}O$), 2.57-2.17 (m, 1H, $CH_3\overset{|}{C}\underline{H}CH_3$), 1.39 (d, 3H, J = 7.5 Hz, $O\overset{|}{C}CH(C\underline{H}_3)\overset{|}{C}O$), 1.07 (t, 3H, J = 7.2 Hz, $C\underline{H}_3CH_2\overset{|}{C}O$), 0.93 (d, 3H, J = 4.5 Hz, $C\underline{H}_3\overset{|}{C}HCH_3$), 0.85 (d, 3H, J = 4.5 Hz, $CH_3\overset{|}{C}HC\underline{H}_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 4.63 (q, 1H, J = 7.3 Hz, $O\overset{|}{C}C\underline{H}(CH_3)\overset{|}{C}O$), 4.48 (double triplet, 1H, J = 8.1 Hz, 3.4 Hz, $-\overset{|}{N}\overset{|}{C}\underline{H}CH_2O-$), 4.30 (t, 1H, J = 8.4 Hz, $-\overset{|}{N}\overset{|}{C}HC\underline{H}(H)O-$), 4.20 (double doublet, 1H, J = 3.1 Hz, 9.1 Hz, $-\overset{|}{N}\overset{|}{C}HCH(\underline{H})O-$), 2.73-2.55 (m, 2H, $CH_3C\underline{H}_2\overset{|}{C}O$), 2.41-2.33 (m, 1H, $CH_3\overset{|}{C}\underline{H}CH_3$), 1.38 (d, 3H, J = 7.3 Hz, $O\overset{|}{C}CH(C\underline{H}_3)\overset{|}{C}O$), 1.05 (t, 3H, J = 8.3 Hz, $C\underline{H}_3CH_2\overset{|}{C}O$), 0.90 (d, 3H, J = 7.5 H, $C\underline{H}_3\overset{|}{C}HCH_3$), 0.85d, 3H, J = 7.5 Hz, $CH_3\overset{|}{C}HC\underline{H}_3$; ^{13}C NMR (22.5 MHz, $CDCl_3$) δ 208.1, 170.2, 154.5, 63.7, 58.7, 52.6, 34.0, 28.4, 17.9, 14.6, 13.0, 7.6 ppm; IR ($CHCl_3$) 3030, 2985, 2955, 2894, 1776, 1721, 1702, 1486, 1460 cm^{-1}; $(\alpha)_D^{25}$ +178.5° (c 2.84, CH_2Cl_2).

Anal. calcd. for $C_{12}H_{19}NO_4$: C, 59.73; H, 7.94. Found: C, 59.57; H, 7.78.

β-Ketoimide 19. The title compound **19** was prepared in accordance with the general procedure outlined above on a 5.08-mmol scale. The aldol adduct **15** (1.33 gm, 5.80 mmol), in 12 mL DMSO and 12 mL CH_2Cl_2, was treated successively with 17.4 mmol triethylamine and with 17.04 mmol pyridine·SO_3 complex in 12 mL DMSO (0°C). The desired product, 1.16 gm (87%) was isolated according to the provided procedure as a clear liquid. HPLC diastereomer analysis of the unpurified material (20% EtOAc-hexane, Radial-Pak B column, silica gel, 5 mL/min retention time in min: **19** 3.50; **8** 10.8) indicated a kinetic ratio of 92:8 (**19**:**8**). MPLC purification of the unpurified material afforded 1.05 gm (80%) of an analytically pure product as a colorless oil (HPLC diastereomer analysis **19:8** > 99:1). For the diastereomeric compounds **8** and **19**, the R_f values (15% EtOAc-hexane, C-column, 940 gm of silica gel) were found to be 0.19 and 0.27, respectively. ^{1}H NMR (90 MHz, $CDCl_3$) δ 4.61 [$O\overset{|}{C}C\underline{H}(CH_3)\overset{|}{C}O$], 4.53-4.07 (m, 3H, $-\overset{|}{N}\overset{|}{C}\underline{H}C\underline{H}_2O-$), 2.57- 2.13 (m, 1H, $CH_3\overset{|}{C}\underline{H}CH_3$), 2.27 (s, 3H, $C\underline{H}_3\overset{|}{C}O$), 1.39 [d, 3H, J = 7.5 Hz, $O\overset{|}{C}CH(C\underline{H}_3)\overset{|}{C}O$], 0.93 (d, 3H, J = 4.5 Hz, $C\underline{H}_3\overset{|}{C}HCH_3$), 0.84 (d, 3H, J = 4.5 Hz, $CH_3CHC\underline{H}_3$); ^{13}C NMR (22.5 MHz, $CDCl_3$) δ 205.4, 169.9, 154.5, 63.6, 58.6, 53.2, 28.3, 17.9, 14.6, 12.6 ppm; IR ($CHCl_3$) 3035, 2981, 2888, 2410, 1778, 1723, 1716, 1487, 1458 cm^{-1}; $[\alpha]_D^{25}$ +163.1° ($\underline{c}$ 2.5, CH_2Cl_2).

Anal. calcd. for $C_{11}H_{17}NO_4$: C, 58.13; H, 7.54. Found: C, 57.98; H, 7.55.

β-Ketoimide 20. The title compound **20** was prepared in accordance with the general procedure outlined above on a 17.6-mmol scale. The aldol adduct **13** (4.918 gm, 17.6 mmol), in 36 mL DMSO and 20 mL CH_2Cl_2, was treated successively with 52.8 mmol triethylamine and with 52.8 mmol pyridine·SO_3 complex in 36 mL DMSO (0° C). The desired product, 4.79 gm (94%) was isolated according to the provided procedure as a crystalline solid. HPLC diastereomer analysis of the unpurified material (15% EtOAc-hexane, Radial-Pak B column, silica gel, 4 mL/min retention time in min: **20** 5.06; **9** 12.46) indicated a kinetic ratio of >99:1 (**20:9**). A single recrystallization of the unpurified material from ether-hexane (1:1) afforded 4.59 gm (90%) of analytically pure crystals (HPLC diastereomer analysis, **20:9** > 99:1). ^{1}H NMR (90 MHz, $CDCl_3$) δ 8.05-7.88, 7.60-7.33 (m, 5H, Ar$\underline{H}$), 5.46 [q, 1H, J = 7.5 Hz, $O\overset{|}{C}C\underline{H}(CH_3)\overset{|}{C}O$], 4.63-4.07 (m, 3H, $-\overset{|}{N}\overset{|}{C}\underline{H}C\underline{H}_2O-$), 2.63-2.23 (m, 1H, $CH_3\overset{|}{C}\underline{H}CH_3$), 1.47 [d, 3H, J = 7.5 Hz, $O\overset{|}{C}CH(C\underline{H}_3)\overset{|}{C}O$], 0.95 (d, 3H, J = 3.3 Hz, $C\underline{H}_3\overset{|}{C}HCH_3$), 0.88 (d, 3H, J = 3.3 Hz, $CH_3\overset{|}{C}HC\underline{H}_3$; ^{1}H NMR (500 MHz, C_6D_6) δ 8.00-7.93, 7.13-7.03 (m, 5H, Ar$\underline{H}$), 5.43 [q, 1H, J = 7.4 Hz, $O\overset{|}{C}C\underline{H}(CH_3)\overset{|}{C}O$], 4.10-4.05 (m, 1H $-\overset{|}{N}\overset{|}{C}\underline{H}CH_2O-$), 3.33 [double doublet, 1H, J = 3.1 Hz, 9.3 Hz, $-\overset{|}{N}\overset{|}{C}HC\underline{H}(H)O-$], 3.24 [t, 1H, J = 9.3 Hz, $-\overset{|}{N}\overset{|}{C}HCH(\underline{H})O-$], 2.25-2.17 (m, 1H, $CH_3\overset{|}{C}\underline{H}CH_3$), 1.38 [d, 3H, J =

7.4 Hz, $OCCH(C\underline{H}_3)CO$), 0.56 (d, 3H, J = 7.7 Hz, $C\underline{H}_3CHCH_3$), 0.38 (d, 3H, $CH_3CHC\underline{H}_3$); ^{13}C NMR (22.5 MHz, $CDCl_3$) δ 197.8, 170.5, 154.4, 135.2, 133.3, 128.7, 128.6, 63.7, 58.7, 48.7, 28.3, 17.9, 14.6, 13.8 ppm; IR ($CHCl_3$) 3029, 2980, 2430, 2401, 1778, 1713, 1682, 1600, 1577, 1450, 1390 cm^{-1}; $(\alpha)_D^{25}$ +161.15° (c 1.22, CH_2Cl_2).

Anal. calcd. for $C_{16}H_{19}NO_4$: C, 66.42; H, 6.62. Found: C, 66.50; H, 6.60.

ß-Ketoimide 21. The title compound **21** was prepared in accordance with the general procedure outlined above on a 0.85-mmol scale. The aldol adduct **18** (0.236 gm, 0.85 mmol), in 4 mL DMSO and 4 mL CH_2Cl_2, was treated successively with 2.55 mmol triethylamine and with 2.55 mmol pyridine·SO_3 complex in 4 mL DMSO (0°C). The desired product was isolated according to the provided procedure, 0.20 gm (85%), as a viscous oil. HPLC diastereomer analysis of the unpurified material (20% EtOAc-hexane, Radial-Pak B column, silica gel, 5 mL/min retention time in min: **21** 0.85; **10** 2.6) indicated a kinetic ratio of 65:35 (**21:10**). MPLC purification of the unpurified material afforded 0.13 gm (55%) of an analytically pure product as a viscous oil (HPLC diastereomer analysis **21:10** > 99:1). For the diastereomeric compounds **10** and **21**, the R_f values (30% EtOAc-hexane, B-column, 50 gm of silica gel) were found to be 0.18 and 0.25, respectively. ^1H NMR (90 MHz, $CDCl_3$) δ 7.57-7.13 (m, 5H, Ar$\underline{H}$), 5.70 (d, 1H, J = 7.2 Hz, $-NCH(CH_3)C\underline{H}(\phi)O-$), 4.84 (q, 1H, J = 6.4 Hz, $OCC\underline{H}(CH_3)CO$), 4.63 (quintet, 1H, J = 7.2 Hz, $-NC\underline{H}(CH_3)CH(\phi)O-$), 2.31 (s, 3H, $C\underline{H}_3CO$), 1.42 (d, 3H, J = 6.4 Hz, $OCCH(C\underline{H}_3)CO$), 0.90 (d, 3H, J = 7.2 Hz, $-NCH(C\underline{H}_3)CH(\phi)O-$); ^{13}C NMR (22.5 MHz, $CDCl_3$) δ 205.5, 169.6, 153.4, 133.2, 128.7, 125.7, 79.3, 54.8, 53.5, 28.4, 14.7, 12.5 ppm; IR ($CHCl_3$) 3059, 2991, 2402, 2300, 1778, 1720, 1604, 1537, 1450 1416 cm^{-1}; $(\alpha)_D^{25}$ -48.6° (c 3.47, CH_2Cl_2).

Anal. calcd. for $C_{15}H_{17}NO_4$: C, 65.44; H, 6.23. Found: C, 65.10; H, 6.38.

ß-Ketoimide 22. The title compound **22** was prepared in accordance with the general procedure outlined above on a 12.9-mmol scale. The aldol adduct **17** (3.76 gm, 12.9 mmol), in 25 mL DMSO and 25 mL CH_2Cl_2, was treated successively with 38 mmol triethylamine and with 38 mmol pyridine•SO_3 complex in 25 mL DMSO (0 °C). The desired product, 3.44 gm (92%), was isolated according to the provided procedure as a clear liquid. HPLC diastereomer analysis of the unpurified material (15% EtOAc-hexane, Radial-Pak B column, silica gel, 4 mL/min retention time in min: **22** 2.69; **11** 5.59) indicated a kinetic ratio of 99.7:0.3 (**22**:**11**). MPLC purification of the unpurified material afforded 3.18 gm (85%) of an analytically pure product as a colorless oil (HPLC diastereomer analysis **22**:**11** > 99:1). For the diastereomeric compounds **11** and **22**, the R_f values (40% EtOAc-hexane, C-column, 90 gm of silica gel) were found to be 0.25 and 0.44, respectively. ^1H NMR (90 MHz, $CDCl_3$) δ 7.47-7.17 (m, 5H, Ar$\underline{H}$), 5.67 (d, 1H, J = 6.6 Hz, $-\overset{|}{N}CH(CH_3)C\underline{H}(\phi)O-$), 4.79 (quintet, 1H, J = 6.6 Hz, $-\overset{|}{N}C\underline{H}(CH_3)CH(\phi)O-$), 4.61 (q, 1H, J = 6.4 Hz, $O\overset{|}{C}C\underline{H}(CH_3)\overset{|}{C}O$), 2.83-2.53 (m, 2H, $CH_3C\underline{H}_2\overset{|}{C}O$, 1.41 (d, 3H, J = 6.4 H, $O\overset{|}{C}CH(C\underline{H}_3)\overset{|}{C}O$), 1.10 (t, 3H, J = 6.6 Hz, $C\underline{H}_3CH_2\overset{|}{C}O$), 0.91 (d, 3H, J = 6.6 Hz, $-\overset{|}{N}CH(C\underline{H}_3)CH(\phi)O-$); ^1H NMR 500 MHz, $CDCl_3$) δ 7.37-7.28 (m, 5H, Ar$\underline{H}$), 5.74 (d, 1H, J = 6.6 H, $-\overset{|}{N}CH(CH_3)C\underline{H}(\phi)O-$), 4.84 (quintet, 1H, J = 6.6 Hz, $-\overset{|}{N}C\underline{H}(CH_3)CH(\phi)O-$), 4.65 (q, 1H, J = 6.4 Hz, $O\overset{|}{C}C\underline{H}(CH_3)\overset{|}{C}O$), 2.80-2.62 (m, 2H, $CH_3C\underline{H}_2\overset{|}{C}O$), 1.35 (d, 3H, J = 6.4 Hz, $O\overset{|}{C}CH(C\underline{H}_3)\overset{|}{C}O$), 1.12 (t, 3H, J = 6.6 Hz, $C\underline{H}_3CH_2\overset{C}{\underset{\wedge}{O}}$), 0.92 (d, 3H, J = 6.6 Hz, $-\overset{|}{N}CH(C\underline{H}_3)CH(\phi)O-$); ^{13}C NMR (22.5 MHz, $CDCl_3$) δ 208.3, 169.8, 153.2, 133.2, 128.7, 125.6, 79.2, 54.8, 52.8, 34.1, 14.7, 12.8, 7.6 ppm; IR ($CHCl_3$) 3034, 3001, 2958, 2920, 2890, 2442, 1780, 1726, 1704, 1608, 1500, 1460, 1416 cm^{-1}; $(\alpha)_D^{25}$ -35.7° ($\underline{c}$ 0.5, CH_2Cl_2).

Anal. calcd. for $C_{16}H_{19}NO_4$: C, 66.42; H, 6.62. Found: C, 66.21; H, 6.66.

β-Ketoimide 23. The title compound **23** was prepared in accordance with the general procedure outlined above on a 0.95-mmol scale. The aldol adduct **16** (0.321 gm, 0.95 mmol), in 3 mL DMSO and 3 mL CH_2Cl_2, was treated successively with 2.84 mmol triethylamine and with 2.84 mmol pyridine•SO_3 complex in 3 mL DMSO (0 °C). The desired product, 0.29 gm (89%), was isolated according to the provided procedure as a clear liquid. HPLC diastereomer analysis of the unpurified material (10% EtOAc-hexane, Radial-Pak B column, silica gel, 5 mL/min retention time in min: **23** 4.70; **12** 11.10) indicated a kinetic ratio of 99.9:0.1 (**23**:**12**). MPLC purification of the unpurified material afforded 0.27 gm (85%) of an analytically pure product as a colorless oil (HPLC diastereomer analysis **23**:**12** > 99:1). For the diastereomeric compounds **12** and **23**, the R_f values were found to be 0.22 and 0.31 (15% EtOAc-hexane, B-column, 50 gm of silica gel) , respectively. ^1H NMR (90 MHz, $CDCl_3$) δ 8.12-7.92, 7.68-7.12 (m, 10H, Ar$\underline{H}$), 5.64 (d, 1H, J = 7.5 Hz, $-\overset{|}{N}CH(CH_3)C\underline{H}(\phi)O-$), 5.50 (q, 1H, J = 7 Hz, $O\overset{|}{C}C\underline{H}(CH_3)\overset{|}{C}O$), 4.85 (quintet, 1H, 7.5 Hz, $-\overset{|}{N}C\underline{H}(CH_3)CH(\phi)O-$), 1.47 (d, 3H, J = 7 Hz, $O\overset{|}{C}CH(C\underline{H_3})\overset{|}{C}O$), 0.91 (d, 3H, J = 7.5 Hz, $-\overset{|}{N}CH(C\underline{H_3})CH(\phi)O-$); ^{13}C NMR (22.5 MHz, $CDCl_3$) δ 197.9, 170.2, 153.2, 135.2, 133.3, 128.7, 125.7, 79.2, 54.8, 48.9, 14.6, 13.8 ppm; IR ($CHCl_3$) 3028, 2408, 1779, 1714, 1681, 1600, 1450, 1370 cm^{-1}; $(\alpha)_D^{25}$ -65.6° (c 6.07, CH_2Cl_2).

Anal. calcd. for $C_{20}H_{19}NO_4$: C, 71.20; H, 5.68. Found: C, 71.18; H, 5.80.

General Procedures for the $Zn(BH_4)_2$ Reduction of β-Ketoimides and Subsequent Silylation of Reduced Adducts. The indicated reactions were carried out under an argon atmosphere on a scale ranging from 0.1-0.5 mmol scale of oxazolidone concentrations of ca 0.02 M. All reagent additions were made via hypodermic syringes.

Into a dried, argon-filled, one-necked, 25-mL flask, equipped with a rubber septum, and for magnetic stirring was added 0.1 mmol of the indicated β-ketoimides. 5 mL of methylene chloride (CH_2Cl_2) was introduced. After cooling to 0°C, 0.42 mL of ethereal solution of 0.24 M zinc borohydride ($Zn(BH_4)_2$) was added in one portion. The solution was stirred for 30 min at 0°C. The reaction was quenched with 5 mL of saturated aqueous ammonium chloride solutions. It was diluted with 10 mL of ether. The separated organic layer was washed successively with saturated aqueous bicarbonate (2 x 10 mL), brine (1 x 10 mL) and dried over anhydrous magnesium sulfate. Solvent removal in vacuo afforded the desired reduced adducts in quantitative yields.

Silylation. Into a dried, argon-filled, one-necked 10-mL flask, equipped with a rubber septum, and for magnetic stirring was added the unpurified reduced adducts. 2 mL of anhydrous methylene chloride was introduced. 1.2 mg (0.01 mmol) of 4-dimethylaminopyridine (DMAP) and 0.19 mL (0.5 mmol) of trimethylsilyldimethylamine ($TMSNMe_2$) were successively added and the solution was allowed to stir for 8 h at room temperature. Solvent removal in vacuo afforded the desired silylated adducts. The threo-erythro ratios were analyzed on the capillary GC, in a methylene chloride solution (~1 mg/1mL).

Reduction of β-Ketoimide 20. The zinc borohydride reduction of β-ketoimide **20** was carried out in accordance with the general procedure described above on a 0.14-mmol scale. The title compound **20** (40 mg, 0.14 mmol) in 1 mL CH_2Cl_2 (0°C) was treated with 0.14 mmol $Zn(BH_4)_2$ (0.6 mL of 0.24 M in ether). The desired product was isolated in quantitative yields according to the provided procedure. The unpurified adduct was subsequently silylated with 0.70 mmol $TMSNMe_2$, 0.01 mmol DMAP in 1 mL CH_2Cl_2 (RT). GC diastereomer analysis (SE-54, 180°C, 5 psi, retention time in min: erythro 11.40; threo 13.59) indicated a kinetic ratio of >99:1 (erythro:threo).

Reduction of β-Ketoimide 12. The zinc borohydride reduction of β-ketoimide **12** was carried out in accordance with the general procedure outlined above, on a 0.12-mmol scale. The title compound **12** (31.3 mg, 0.12 mmol) in 1.5 mL CH_2Cl_2 (0°C) was treated with 0.37 mmol $Zn(BH_4)_2$ (1.5 mL of 0.24 M in ether). The desired product was isolated in quantitative yields according to the provided procedure. The unpurified adduct was subsequently silylated with 0.60 mmol $TMSNMe_2$ and 0.05 mmol DMAP in 2 mL CH_2Cl_2 (RT). GC diastereomer analysis (SE-54, 215°C, 10 psi, retention time in min: erythro 7.14; threo 7.71) indicated a kinetic ratio of >99:1 (erythro:threo).

Reduction of β-Ketoimide 11. The zinc borohydride reduction of β-ketoimide **11** was carried out in accordance with the general procedure outlined above on a 0.21-

mmol scale. The title compound **11** (50 mg, 0.21 mmol) in 2.5 mL CH_2Cl_2 (0° C) was treated with 0.4 mmol $Zn(BH_4)_2$ (1.7 mL of 0.24 *M* in ether). The desired product was isolated in quantitative yields according to the provided procedure. The unpurified adduct was subsequently silylated with 1.0 mmol $TMSNMe_2$ and 0.05 mmol DMAP in 2 mL CH_2Cl_2 (RT). GC diastereomer analysis (SE-54, 180° C, 10 psi, retention time in min: *erythro* 8.98; *threo* 9.70) indicated a kinetic ratio of >99:1 (*erythro*:*threo*).

Reduction of β-Ketoimide 10. The zinc borohydride reduction of β-ketoimide **10** was carried out in accordance with the general procedure described above on a 0.27-mmol scale. The title compound **10** (7.35 mg, 0.27 mmol) in 3 mL CH_2Cl_2 (0° C) was treated with 0.6 mmol $Zn(BH_4)_2$ (2.5 mL of 0.24 *M* in ether). The desired product was isolated in quantitative yields according to the provided procedure. The unpurified adduct was subsequently silylated with 1.0 mmol $TMSNMe_2$ and 0.05 mmol DMAP in 2 mL CH_2Cl_2 (RT). GC diastereomer analysis (SE-54, 175° C, 10 psi, retention time in min: *erythro* 8.42; *threo* 8.77) indicated a kinetic ratio of 21.8:78.2 (*erythro*:*threo*).

Reduction of β-Ketoimide 9. The zinc borohydride reduction of β-ketoimide **9** was carried out in accordance with the general procedure described above on a 0.276-mmol scale. The title compound **9** (80 mg, 0.276 mmol) in 1 mL CH_2Cl_2 (0° C) was treated with 0.276 mmol $Zn(BH_4)_2$ (1.15 mL of 0.24 *M* in ether). The desired product was isolated in quantitative yields according to the provided procedure. The unpurified adduct was subsequently silylated with 0.828 mmol $TMSNMe_2$ and 0.02 mmol DMAP in 2 mL CH_2Cl_2 (RT). GC diastereomer analysis (SE-54, 180° C, 5 psi retention time in min: *erythro* 11.25; *threo* 12.34) indicated a kinetic ratio of >99:1 (*erythro*:*threo*).

Reduction of β-Ketoimide 23. The zinc borohydride reduction of β-ketoimide **23** was carried out in accordance with the general procedure described above on a 0.36-mmol scale. The title compound **23** (121.4 mg, 0.36 mmol) in 1 mL CH_2Cl_2 (0° C) was treated with 0.72 mmol $Zn(BH_4)_2$ (3 mL of 0.24 *M* in ether). The desired product was isolated in quantitative yields according to the provided procedure. The unpurified adduct was subsequently silylated with 3.6 mmol $TMSNMe_2$ and 0.04 mmol DMAP in 2 mL CH_2Cl_2 (RT). GC diastereomer analysis (SE-54, 215° C, 10 psi, retention time in min: erythro 5.79; threo not found) indicated a kinetic ratio of >99:1 (erythro:threo).

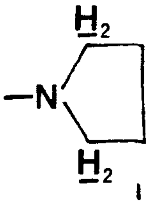
Reduction of β-Ketoimide 22. The zinc borohydride reduction of β-ketoimide **22** was carried out in accordance with the general procedure described above on a 0.10-mmol scaled. The title compound **22** (30 mg, 0.10 mmol) in 1.5 mL CH_2Cl_2 (0° C) was treated with 0.3 mmol $Zn(BH_4)_2$ (1.3 mL of 0.24 M in ether). The desired product was isolated in quantitative yields in accordance to the provided procedure. The unpurified adduct was subsequently silylated with 0.50 mmol $TMSNMe_2$ and 0.05 mmol DMAP in 2 mL CH_2Cl_2 (RT). GC diastereomer analysis (SE-54, 180° , 10 psi, retention time in min: erythro 8.05; threo not found) indicated a kinetic ratio of >99:1 (erythro:threo).

Reduction of β-Ketoimide 21. The zinc borohydride reduction of β-ketoimide **21** was carried out in accordance with the general procedure described above on a 0.1-mmol scale. The title compound **21** (24 mg, 0.1 mmol) in 1 mL CH_2Cl_2 (0° C) was treated with 0.26 mmol $Zn(BH_4)_2$ (1.1 mL of 0.24 M in ether). The desired product was isolated in quantitative yields according to the provided procedure. The unpurified adduct was subsequently silylated with 0.5 mmol $TMSNMe_2$ and 0.05 mmol DMAP in 1 mL CH_2Cl_2 (RT). GC diastereomer analysis (SE-54, 175° C, 10 psi) indicated a complex mixture of products was formed.

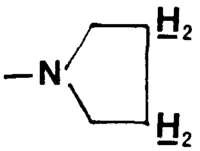
Methyl Ester 25.[6] To a dried, one-necked, 20-mL flask, equipped with a drying tube, an for magnetic stirring, was added the freshly reduced adduct **24** (30 mg, 0.10 mmol). 0.5 mL of methanol was introduced. After cooling to -10° C, potassium carbonate (3 mg, 0.01 mmol) was added, and the solution was allowed to stir for 1 h at -10° C. The reaction was quenched with 5 mL of pH 7 phosphate buffer, and partitioned with ethyl acetate (3 x 5 mL). The combined organic layers were washed with brine (1 x 5 mL) and dried over anhydrous sodium sulfate. Solvent removal *in vacuo* afforded the desired products in a 65% mass balance. Flash chromatography (20% EtOAc-hexane, 10 gm of silica gel, R_f for X_VH 0.06; **26**, 0.25) of the unpurified material yielded 7.6 mg (45%) of an analytically pure product as a clear liquid. ^1H NMR (90 MHz, $CDCl_3$) δ 7.37-7.17 (broad s, 5H, Ar$\underline{H}$), 5.03 (t, 1H, J = 4.2 Hz, $\phi\overset{|}{C}\underline{H}OH$), 3.62 (s, 3H, $\overset{|}{O}COC\underline{H}_3$), 2.93 (d, 1H, J = 3 H, $\phi\overset{|}{C}HO\underline{H}$), 2.77 [double quarter, 1H, J = 7.2 Hz, 4.5 Hz, $\phi\overset{|}{C}HC\underline{H}(CH_3)\overset{|}{C}O$), 1.11 [d, 3H, J = 7.2 Hz, $\phi\overset{|}{C}HCH(C\underline{H}_3)\overset{|}{C}O$); ^{13}C NMR (22.5 MHz, $CDCl_3$) δ 176.1, 141.5, 128.2, 127.4, 125.9, 73.7, 51.8, 46.5, 10.8 ppm; IR ($CHCl_3$) 3614, 3540, 3072, 2960, 2890, 2400, 1724, 1604, 1491, 1452, 1436 cm^{-1}; $(\alpha)_D^{25}$ +18.95° ($\underline{c}$ 3.38, CH_2Cl_2).

Methyl Ester 26.[6] To a dried, one-necked, 25-mL flask, equipped with a drying tube, and for magnetic stirring, was added the freshly reduced adduct **13** (0.49 gm, 1.75 mmol). Methanol (3.5 mL) was introduced. After cooling to -10°C, potassium carbonate (25 mg, 0.18 mmol) was added, and the solution was allowed to stir for 1 h at -10°C. The reaction was quenched with 10 mL of pH 7 phosphate buffer, and partitioned with ethyl acetate (3 x 30 mL). The combined organic layers were washed with brine (1 x 15 mL) and dried over anhydrous sodium sulfate. Solvent removal *in vacuo* afforded the desired products in a 90% mass balance. Flash chromatography (20% EtOAc-hexane, 50 gm of silica gel, R_f for S_VH 0.06; **25** 0.25) of the unpurified material yielded 0.235 gm (70%) of an analytically pure product as a clear liquid. ^1H NMR (90 MHz, $CDCl_3$) δ 7.37-7.17 (broad s, 5H, Ar$\underline{H}$), 5.03 (t, 1H, J = 4.2 Hz, $\phi\overset{|}{C}\underline{H}OH$), 3.62 (s, 3H, $\overset{|}{O}COC\underline{H}_3$), 3.02 (broad s, 1H, $\phi\overset{|}{C}HO\underline{H}$), 2.77 [double quarter, 1H, J = 7.2 Hz, 4.5 Hz, $\phi\overset{|}{C}HC\underline{H}(CH_3)\overset{|}{C}O$), 1.11 [d, 3H, J = 7.2 Hz, $\phi\overset{|}{C}HCH(C\underline{H}_3)\overset{|}{C}O$); ^{13}C NMR (22.5 MHz, $CDCl_3$) δ 176.1, 141.5, 128.2, 127.4, 125.9, 73.7, 51.8, 46.5, 10.8 ppm; IR ($CHCl_3$) 3614, 3540, 3072, 2960, 2890, 2400, 1724, 1604, 1491, 1452, 1436 cm^{-1}; $(\alpha)_D^{25}$ -19.21° ($\underline{c}$ 0.38, CH_2Cl_2).

β-Ketoimide 33. In a dried, argon-filled, one-necked, 200 mL flask, equipped with a rubber septum and for magnetic stirring, was added 5.5 mL (39 mmol) of anhydrous diisopropylamine and 80 mL of anhydrous tetrahydrofuran. After cooling to -78°C, 24.4 mL (39 mmol) of a 1.6 M solution of n-butyllithium in hexane was added. The solution was stirred at -78°C for 30 min. Into another dried, argon-filled, one-necked, 25-mL flask, equipped with a rubber septum, was weighed 4.72 gm (37.2 mmol) of N-propionylpyrrolidine. 5 mL of anhydrous tetrahydrofuran was introduced and this solution was added dropwise over a 10 min period, via syringe to th LDA solution. The reaction mixture was allowed to stir for 30 min at -78°C. 3.4 mL (39 mmol) of propionyl chloride was introduced neat in one portion. It was quenched after 10 sec, with 20 mL of saturated aqueous ammonium chloride solution, and warmed to room temperature. The desired product was obtained via methylene chloride extraction (3 x 50 mL). The combined organic layers were washed successively with saturated aqueous bicarbonate (1 x 75 mL), brine (1 x 75 mL) and dried over anhydrous magnesium sulfate. Solvent removal in vacuo afforded 6.5 gm (80%) of crude products. Flash chromatography (95% EtOAc-hexane, 600 gm of silica gel, R_f for **28** 0.24) of the unpurified material afforded 4.4 gm (62%) of analytically pure products as a colorless oil. ^{1}H NMR (90 MHz, $CDCl_3$) δ 3.53 [q, 1H, J = 6.8 Hz, $\overset{|}{O}CC\underline{H}(CH_3)\overset{|}{C}O$], 3.53-3.38 (m, 4H,



2.63-2.38 (m, 2H, $CH_3C\underline{H}_2\overset{|}{C}O$), 2.04-1.79 (m, 4H,



1.33 [d, 3H, J = 6.9 Hz, $\overset{|}{O}CCH(C\underline{H}_3)\overset{|}{C}O$], 1.02 (t, 3H, J = 7.2 Hz, $C\underline{H}_3CH_2CO$); ^{13}C NMR (22.5 MHz, $CDCl_3$) δ 207.8, 168.8, 52.9, 46.9, 46.1, 32.9, 26.2, 24.4, 13.4, 7.7 ppm; IR (CCl_4) 2982, 2948, 2886, 1714, 1645, 1457, 1420, 1379 cm^{-1}.

Anal. calcd. for $C_{10}H_{17}NO_2$: C, 65.54; H, 9.35. Found: C, 65.42; H, 9.36.

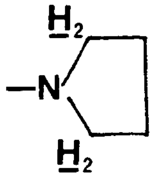
Equilibration Studies of β-Ketoimide 7. In a dried, one-necked, 10-mL flask, equipped with a glass stopper and for magnetic stirring, was added 0.093 mmol (22.5 mg) of the title compound **7** and 0.93 mL of anhydrous methylene chloride. An aliquot was drawn out and analyzed by GC (DB-1, 130° C, 10 psi, retention time in min: **6** 8.23; **7** 8.76). Anhydrous triethylamine (0.279 mmol, 39 µL) was added and the equilibration of **7** was followed over time at room temperature. The equilibrium value is approximately 3:2 (**7**:**6**).

Time	Ratio **7**:**6**	Time	Ratio **7**:**6**
0	125.6:1	2:00	9.0:1
5 min	96.7:1	2:30	7.3:1
15 min	48.9:1	3:00	6.1:1
30 min	29.6:1	13:00	2.03:1
45 min	21.3:1	15:00	1.93:1
1:00	17.7:1	16:00	1.87:1
1:30	11.7:1	18:00	1.76:1

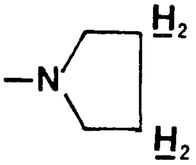
Equilibration Studies of β-Ketoimide 6. In a dried, one-necked, 10-mL flask, equipped with a glass stopper and for magnetic stirring, was added 0.11 mmol (25.6 mg) of the title compound **6** and 1.1 mL of anhydrous methylene chloride. An aliquot was drawn out and analyzed by HPLC (15% EtOAc-hexane, 4 mL/min, Radial Pak B column, silica gel, retention time in min: **6** 2.59; **7** 6.75). Anhydrous triethylamine (0.32 mmol, 44 µL) was added and the equilibration of **6** was followed over time at room temperature. The equilibration value is approximately 2:3 (**6**:**7**).

Time	Ratio **7**:**6**	Time	Ratio **7**:**6**
0	100:1	2:00	4.10:1
5 min	70.4:1	2:40	3.69:1
15 min	31.3:1	3:00	2.98:1
25 min	17.2:1	4:30	1.82:1
35 min	14.9:1	5:00	1.56:1
1:00	8.5:1	15:00	1.01:1
1:15	6.4:1	17:25	0.83:1
1:30	5.0:1	18:00	0.76:1
1:45	4.25:1	18:30	0.68:1

H-D Exchange Studies of β-Ketoamide 33 With NaOCD$_3$. In a dried 5-mm NMR tube was added 20 mg of the title compound **33** and 0.5 mL of CD$_3$OD. The NMR spectrum was recorded. ^{1}H NMR (90 MHz, CD$_3$OD) δ 3.76 (q, 1H, J = 7.2 Hz, $O\overset{|}{C}C\underline{H}(CH_3)\overset{|}{C}O$), 3.61-3.24 (m, 4H,



2.51 (q, 2H, J = 7.1 Hz, $CH_3C\underline{H}_2\overset{|}{C}O$), 2.05-1.81 (m, 4H,



1.28 (d, 3H, J = 7.2 H, $O\overset{|}{C}CH(C\underline{H}_3)\overset{|}{C}O$), 1.00 (t, 3H, J = 7.2 Hz, $C\underline{H}_3CH_2\overset{|}{C}O$). NaOCD$_3$ in CD$_3$OD (50 μL) was added. The disappearance rate for $O\overset{|}{C}C\underline{H}(CH_3)\overset{|}{C}O$ and $CH_3C\underline{H}_2\overset{|}{C}O$ was followed via NMR.

$OCC\underline{H}(CH_3)CO$		$CH_3C\underline{H}_2CO$	
Time (min)	% H-D Exchanged	Time (min)	% H-D Exchanged
1	50	1	30
3	100	3	60
		4	70
		5	75
		6	85
		8	95
		10	100

H-D Exchange Studies of βKetoamide 33 With Pyridine. In a dried 5-mm NMR tube was added 20 mg of the title compound **33** and 0.5 mL CD_3OD. The NMR spectrum was recorded (vide supra). Anhydrous pyridine (100 μL) was added and the H-D exchange rate was followed <u>via</u> NMR. Both the methine [$OCC\underline{H}(CH_3)CO$]) and methylene ($CH_3C\underline{H}_2CO$) proton's signals remained unchanged over a period of three days.

H-D Exchange Studies of β-Ketoimide 7 With Pyridine. In a dried 5-mm NMR tube was added 20 mg of the title compound **7** and 0.25 mL $CDCl_3$ and 0.5 mL CD_3OD. The NMR spectrum was recorded. ^1H NMR [90 MHz, $CDCl_3$ and CD_3OD (1:2)] δ 4.70-4.30 [m, 4H, $\overset{|}{O}C\underline{H}(CH_3)\overset{|}{C}O$, $-\overset{|}{N}\overset{|}{C}\underline{H}C\underline{H}_2O-$], 2.78 (q, 2H, J = 7.0 Hz, $CH_3C\underline{H}_2\overset{\backslash}{C}O$), 2.65-2.27 (m, 1H, $CH_3\overset{\backslash}{C}\underline{H}CH_3$), 1.44 [d, 3H, J = 7.5 Hz, $\overset{|}{O}CCH(C\underline{H}_3)\overset{|}{C}O$], 1.17 (t, 3H, J = 7.0 Hz, $\overset{|}{C}\underline{H}_3CH_2CO$), 1.05 (d, 3H, J = 2 Hz, $\overset{|}{C}\underline{H}_3CHCH_3$), 0.98 (d, 3H, J = 2 Hz, $CH_3\overset{\backslash}{C}HC\underline{H}_3$). 100 μL of anhydrous pyridine was added, and the H-D exchange rate for both the methine ($OCC\underline{H}C\underline{H}_2CH_3$) protons was followed <u>via</u> NMR. Both signals remained unchanged over a period of three days.

General Procedures for the Preparation of Methyl Grignard Adducts and their Subsequent Silylation. The indicated reactions were carried out under an argon atmosphere on a scale ranging from 0.5-5 mmol at β-ketoimide concentrations of <u>ca</u> 0.2 <u>M</u>. All reagent additions were made <u>via</u> hypodermic syringes.

Preparation of Methyl Grignard Adducts. To a dried, argon-filled, one-necked, 10-mL flask equipped with a rubber septum and for magnetic stirring, was added 1.0 mmol of the indicated βketoimide and 2.0 mL of anhydrous methylene chloride (CH_2Cl_2). To a second dried, argon-filled, one-necked, 25-mL flask equipped as described above, was charged with 3.0 mmol of methyl magnesium bromide (MeMgBr) ethereal solution (1.06 mL, 2.84 M) and 2.0 mL of anhydrous CH_2Cl_2. After cooling to -78°C, the βketoimide solution was transferred via syringe, dropwise over a period of 5 min, into the methyl Grignard reagent, and was allowed to stir for 4 h. The reaction was quenched with 5 mL of pH 7 phosphate buffer solution and partitioned with CH_2Cl_2 (2 x 50 mL). The combined organic portions were washed with brine (1 x 50 mL) and dried over anhydrous sodium sulfate (Na_2SO_4). Solvent removal in vacuo afforded an unpurified adduct with a 96-98% mass balanced. Immediate protection of this material was necessary to avoid product decomposition.

Silylation of the Methyl Grignard Adduct. To a dried, argon-filled, one-necked, 25-mL flask, equipped as described above, was added the unpurified Grignard adduct and 2.0 mL of anhydrous CH_2Cl_2. After cooling to 0°C, 2.5 mmol of anhydrous triethylamine and 1.5 mmol of either t-butyldimethylsilyltriflate (TBSOTf) or triethylsilyltriflate (TESOTf) were introduced in succession, and the reaction was allowed to stir for 2 h and then 4 h at room temperature. It was diluted with 50 mL CH_2Cl_2 and washed successively with saturated aqueous carbonate (1 x 25 mL), and brine (1 x 25 mL), and dried over anhydrous Na_2SO_4. Solvent removal in vacuo afforded the silylated adduct with a 92-96% mass balance. Purification of these substrates was then carried out via either recrystallization or chromatography on silica gel as indicated in the following specific cases.

Methyl Grignard Adduct 28. The title compound **28** was prepared in accordance with the general procedure described above on a 0.569-mmol scale. β-ketoimide **20** (0.1646 gm, 0.569 mmol) in 1.2 mL CH_2Cl_2 (-78°C) was added to 1.7 mmol (0.6 mL of 2.84

$\underline{M}$ in ether, -78°C) methyl magnesium bromide. The desired product was isolated according to the provided procedure and was subsequently silylated with 0.85 mmol TBSOTf and 1.42 mmol Et_3N in 1.2 mL CH_2Cl_2 (0°C). The protected adduct, 0.240 gm (101%) was isolated according to the provided procedure as a white crystalline product. A single recyrstallization from ether-hexane (1:1) of the unpurified solid afforded 0.220 gm (92%) of analytically pure white crystals. mp 120-121°C; ^1H NMR (90 MHz, $CDCl_3$) δ 7.10 (m, 5H, Ar$\underline{H}$), 4.12-3.92 (m, 3H, $-\overset{|}{N}\overset{|}{C}\underline{H}C\underline{H}_2O-$), 3.19 (q, 1H, J = 6.6 Hz, $-\overset{|}{C}\underline{H}(CH_3)\overset{|}{C}O$), 2.30-2.02 (m, 1H, $CH_3\overset{|}{C}\underline{H}CH_3$), 1.85 (s, 3H, $\phi\overset{|}{C}(C\underline{H}_3)OTBS$), 1.00-0.93 (m, 18H, $-SiC(C\underline{H}_3)_3$, $C\underline{H}_3\overset{|}{C}HC\underline{H}_3$, $-CH(C\underline{H}(C\underline{H}_3)\overset{|}{C}O$), 0.29 (s, 3H, $C\underline{H}_3\overset{|}{\underset{|}{Si}}CH_3$), 0.26 (s, 3H, $CH_3\overset{|}{\underset{|}{Si}}C\underline{H}_3$); ^{13}C NMR (22.5 MHz, $CDCl_3$) δ 169.3, 142.1, 128.0, 127.4, 125.9, 81.0, 66.7, 60.90, 43.8, 30.7, 27.6, 25.9, 19.0, 18.1, 17.8, 10.6 ppm; IR ($CHCl_3$) 3024, 2970, 2948, 2908, 2872, 2402, 1683, 1464, 1422 cm^{-1}; $(\alpha)_D^{25}$ +51.5° ($\underline{c}$ 0.08, $CHCl_3$).

Anal. calcd. for $C_{23}H_{37}SiNO_4$: C, 65.83; H, 8.89; N, 3.34. Found: C, 65.92; H, 8.80; N, 3.32.

Methyl Grignard Adduct 30. The title compound **30** was prepared in accordance with the general procedure described above on a 0.77-mmol scale. β-Ketoimide **9** (0.29 gm, 0.77 mmol) in 10 mL CH_2Cl_2 (-78°C) was added to 1.92 mmol (0.68 mL of 2.84 $\underline{M}$ in ether, -78°C) methyl magnesium bromide. The desired product was isolated according to the provided procedure and was subsequently silylated with 1.16 mmol TESOTf and 1.92 mmol Et_3N in 2 mL CH_2Cl_2 (0°C). The protected adduct, 0.31 gm (96%) was isolated according to the provided procedure as a clear oil. MPLC purification (10% EtOAc-hexane, B column, silica gel, R_f for **30** 0.16) of the unpurified material afforded 0.30 gm (93%) of an analytically pure product as a colorless oil. ^1H NMR (90 MHz, C_6D_6) δ 7.97-7.82, 7.47-7.22 (m, 5H, Ar$\underline{H}$), 5.18 (q, 1H, J = 7.5 Hz, $-C\underline{H}(CH_3)\overset{|}{C}O$), 4.17 (dt, 1H, J = 7.5 Hz, 3Hz, $-\overset{|}{N}\overset{|}{C}\underline{H}CH_2O-$), 3.73-3.39 (m, 2H, $-\overset{|}{N}\overset{|}{C}HC\underline{H}_2O-$), 2.30 (s, 3H, $\phi\overset{|}{C}(C\underline{H}_3)OTES$), 2.28-2.00 (m, 1H, $CH_3\overset{|}{C}\underline{H}CH_3$), 1.75 (d, 3H, J = 6.6 Hz, $-CH(C\underline{H}_3)\overset{|}{C}O$), 1.40-0.55 (m, 21H, $(C\underline{H}_3C\underline{H}_2)_3Si$-, $C\underline{H}_3CHC\underline{H}_3$) ; ^{13}C NMR (22.5 MHz, C_6D_6)δ 174.4, 153.6, 14.7, 78.2, 61.9, 58.2, 49.1, 28.5, 24.4, 17.7, 14.2, 13.5, 7.3, 7.1, 6.9 ppm; IR ($CHCl_3$) 3024, 2970, 2946, 2872, 2402, 1686, 1460 cm^{-1}; $(\alpha)_D^{25}$ -42.5° ($\underline{c}$ 0.12, $CHCl_3$).

Anal. calcd. for $C_{23}H_{37}SiNO_4$: C, 65.83; H, 8.89. Found: C, 65.75; H, 8.82.

Methyl Grignard Adduct 32. The title compound **32** was prepared in accordance with the general procedure described above on a 2.09-mmol scale. β-Ketoimide **12** (0.7060 gm, 2.09 mmol) in 4.2 mL CH_2Cl_2 (-78° C) was added to 6.3 mmol (2.2 mL of 2.84 $\underline{M}$ in ether, -78° C) methyl magnesium bromide. The desired product was isolated according to the provided procedure and was subsequently silylated with 3.14 mmol TBSOTf and 5.23 mmol Et_3N in 4.2 mL CH_2Cl_2 (0° C). The protected adduct, 1.02 gm (96%) was isolated according to the provided procedure as a clear oil. MPLC purification (10% EtOAc-hexane, B column, silica gel, R_f for **32** 0.12) of the unpurified material afforded 1.01 gm (96%) of an analytically pure product as a colorless oil. ^1H NMR (90 MHz, $CDCl_3$) δ 7.55-7.08 (m, 10H, Ar$\underline{H}$), 5.48 (d, 1H, J = 7.5 Hz, -$\overset{|}{N}\overset{|}{C}HC\underline{H}(\phi)O$-), 4.59 (quintet, 1H, J = 7.2 Hz, -$\overset{|}{N}C\underline{H}(CH_3)CHO$-), 4.55 (q, 1H, J = 7.2 Hz, -$C\underline{H}(CH_3)\overset{|}{C}O$), 1.81 (s, 3H, $\phi\overset{|}{C}(C\underline{H}_3)OTBS$), 1.22 (d, 3H, J = 7.2 H, -$CH(C\underline{H}_3)\overset{|}{C}O$), 0.96 (s, 9H, -$SiC(C\underline{H}_3)_3$), 0.39 (d, 3H, J = 7.5 Hz, -$\overset{|}{N}CH(C\underline{H}_3)\overset{|}{C}HO$-), 0.00 (s, 3H, $C\underline{H}_3\overset{|}{\underset{|}{Si}}CH_3$), -0.23 (s, 3H, $CH_3\overset{|}{\underset{|}{Si}}C\underline{H}_3$); ^{13}C NMR (22.5 MHz, $CDCl_3$) δ 174.5, 152.7, 146.6, 133.5, 128.6, 127.6, 126.9, 126.4, 125.7, 78.2, 54.8, 54.3, 48.8, 26.1, 24.2, 18.6, 14.2, 13.0, -1.8, -2.7 ppm; IR ($CHCl_3$) 3024, 2968, 2942, 2890, 2877, 2404, 1776, 1697, 1460 cm^{-1}; $(\alpha)_D^{25}$ +29.5° ($\underline{c}$ 1.2, $CHCl_3$).

Anal. calcd. for $C_{27}H_{37}SiNO_4$: C, 69.34; H, 7.98; N, 3.00. Found: C, 69.16; H, 7.90; N, 3.03.

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