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New Bis-Lactam Chiral Auxiliaries for Nitrile Oxide Cycloadditions

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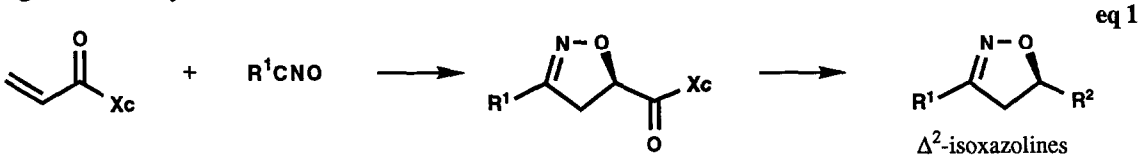
Summary: *Two "pseudoenantiomeric" bis lactam chiral auxiliaries are introduced for use in asymmetric nitrile oxide cycloaddition reactions with derived acrylimides. Outstanding selectivities in the nitrile oxide cycloadditions (99/1) are not duplicated in other related reactions.*

Cycloaddition reactions of nitrile oxides with alkenes are an important, representative class of 1,3-dipolar cycloadditions,[3] and the development of chiral auxiliaries to effect asymmetric nitrile oxide/alkene cycloadditions has progressed rapidly in recent years (eq 1).[4,5] This development has provided access to optically active Δ^2-isoxazolines, which are especially versatile synthetic intermediates.[6,7] More generally, it has increased the level of understanding about what features are required for chiral auxiliaries to provide high levels of asymmetric induction in thermal reactions where metals are not involved.[8]

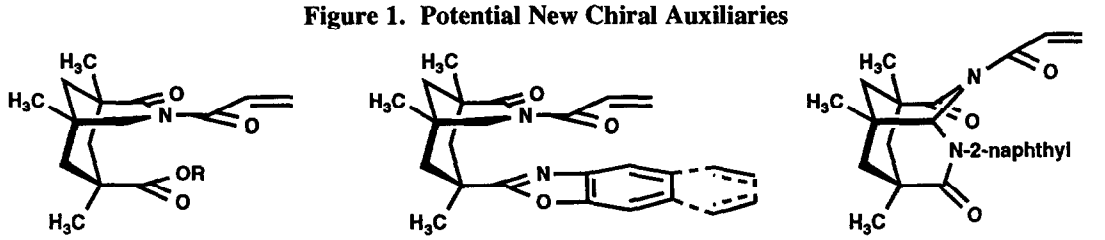
eq 1



Δ^2-isoxazolines
useful synthetic intermediates

Several years ago, K.-S. Jeong, P. Ballester, and J. Rebek, Jr. prepared for us a series of racemic compounds for testing as potential chiral auxiliaries.[9] These compounds have a new structural motif based on Kemp's triacid,[10] as shown in Figure 1. We conducted cycloadditions of each of the racemic acrylates shown in Figure 1 with benzonitrile oxide (25 °C), and the indicated ratios of diastereomers were observed. In only one case (**2**)[9e] was the stereostructure of the cycloadduct actually proven. For this preliminary survey, we did not prepare authentic samples of minor products, nor did we attempt to remove the Δ^2-isoxazolines from the racemic auxiliaries. Ratios listed as >95/<5 indicate that resonances attributable to the minor diastereomers could not be located in the ^{1}H NMR spectrum of the crude reaction medium.

Figure 1. Potential New Chiral Auxiliaries



1 R = 2-phenylethyl (87/13)
2 R = 2-naphthyl (>95/<5)
3 benzoxazole (96/4)
4 naphthoxazole (98/2)
5 (>95/<5)

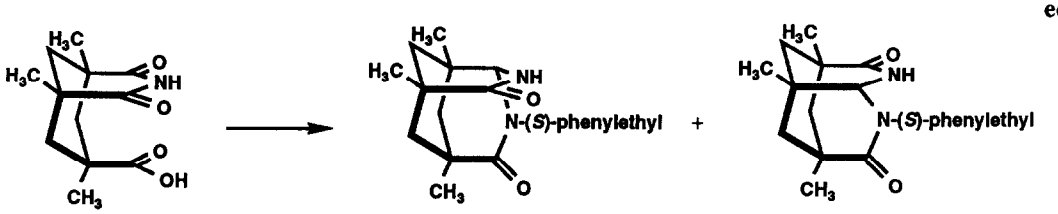
Compounds **1-5** are racemic; only one enantiomer is shown
Numbers in parentheses are diastereomer ratios on cycloaddition with PhCNO

Diastereoselectivities in several of these reactions far exceeded the best level of selectivity in nitrile oxide cycloadditions at that time. Among the candidates for development as a chiral auxiliary, we selected the bis-lactam structure represented by **5**. This compound does not have the "U-turn" shape of the rest of the molecules in Figure 1, and indeed it was not prepared intentionally. However, it gave one of the highest diastereoselectivities with benzonitrile oxide, and it was very easy to prepare. Furthermore, we expected that the bis-lactam group would be more robust than esters like **2**—a clear asset for projected cleavage reactions. Bis-lactam **5** is rendered chiral only by its differing nitrogen substituents. The parent bis-lactam (with two N–H groups) has a plane of symmetry passing through the cyclohexyl ring at the carbon bearing the two nitrogens.

We now report the complete details of the development of a new pair of chiral auxiliaries based on the bis-lactam structure **5**.[11] These auxiliaries provide exceptional levels of stereocontrol (~99/1) in nitrile oxide cycloadditions, and they can be cleaved and recycled. However, this high stereocontrol in nitrile oxide cycloadditions does not translate to high stereocontrol in a variety of other (apparently related) thermal addition and cycloaddition reactions. Based on crystal structures and other factors, we speculate about why these chiral auxiliaries are successful in nitrile oxide cycloadditions.

Results: To synthesize a resolvable bis-lactam chiral auxiliary, we selected (*S*)-phenylethylamine for acylation. The synthesis of the auxiliaries **7** and **8** has already been described,[12] and it is summarized in eq 2. Full details are provided in the experimental section. Imide acid **6**[10] was coupled with (*S*)-phenylethylamine. The resulting amide was reduced with $NaBH_4$ to give a mixture of lactols. Brief exposure of this mixture to *p*TsOH provided a mixture of **7** and **8** in a ratio of 3/2 (indicating a small group selectivity in the $NaBH_4$ reduction). Diastereomers **7** and **8** were easily separable by flash chromatography, and were nicely crystalline. The x-ray crystal structure of each isomer was solved (see below). Though bis-lactams **7** and **8** are diastereomers, it was our hope that they would behave like enantiomers with stereochemistry being dictated by the bis-lactam ring and not the (*S*)-phenylethyl group. In this way, either enantiomeric isoxazoline would be available from a single enantiomer of the chiral amine.

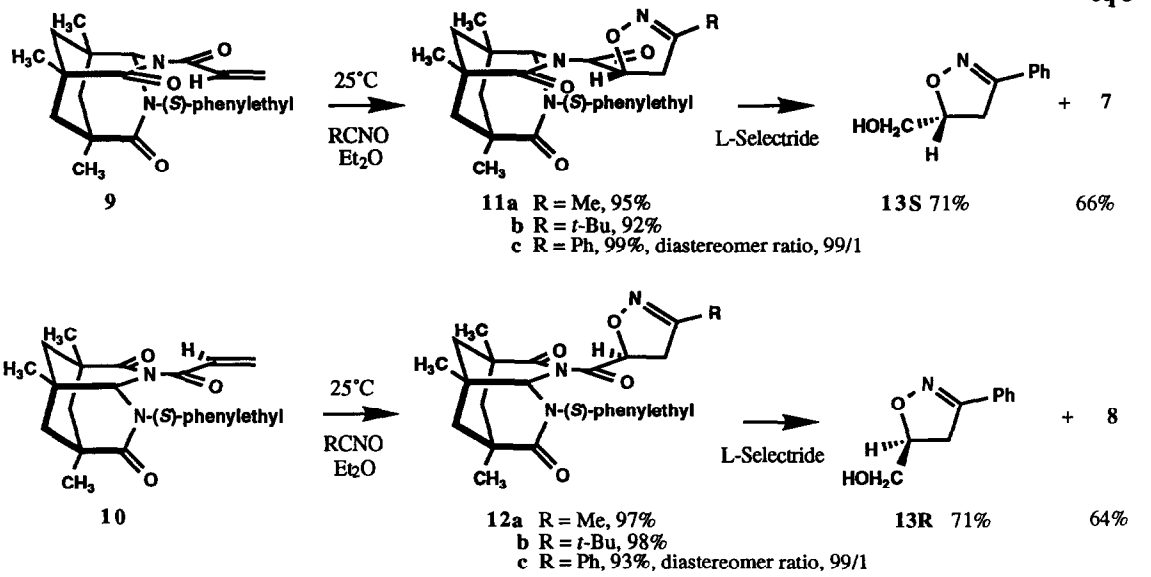
eq 2



Steps: a) $SOCl_2$, (*S*)-phenylethylamine; b) $NaBH_4$, EtOH; c) *p*TsOH, CH_2Cl_2

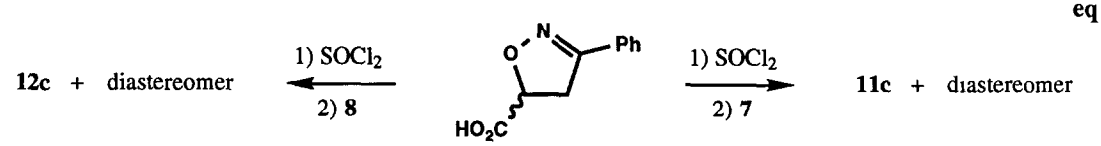
Equation 3 summarizes the results of the nitrile oxide cycloaddition. Bis-lactams **7** and **8** were converted to acryloyl derivatives **9** and **10** by the procedure of Evans (MeMgBr, acryloyl chloride, 45-66%).[13] Other standard acylation procedures gave very poor yields with acryloyl chloride. Nitrile oxide cycloadditions were conducted by standard procedures at 25°C. Each isomer **9** and **10** was subjected to cycloadditions with ethane nitrile oxide, 2,2-dimethylpropane nitrile oxide, and benzonitrile oxide. After flash chromatography, a single product (**11a-c** or **12a-c**) was isolated from each reaction in >90% yield. Configurations were rigorously assigned only in the case of the benzonitrile oxide adducts **11c** and **12c**; other structures were assigned by analogy. Reduction of **11c** with L-Selectride™ provided known, optically pure Δ^2-isoxazoline **13S** and recovered bis-lactam **7**. Similar reduction of **12c** provided optically pure **13R** and recovered **8**. Yields in the cleavage reactions were respectable (64-71%), and we made no effort to improve them. 5-Hydroxymethyl -Δ^2-isoxazolines like **13** are very useful synthetic intermediates.[7]

eq 3



We carried out a careful product analysis by preparing authentic samples of both possible products from the reactions of **9** and **10** with benzonitrile oxide (see eq 4). Each pair of diastereomeric 2-isoxazolines was separable by HPLC. Analysis of the crude cycloaddition products by HPLC then revealed that both **11c** and **12c** formed along with their respective diastereomers in a ratio of 99/1. With authentic minor isomers of the **c** series in hand, we looked back at the crude ^{1}H NMR spectra of the **a** and **b** series, and located very small peaks that are undoubtedly due to minor isomers. Based on proton integrations, we estimate that all six cycloadditions in eq 3 proceeded with a selectivity of about 99/1.

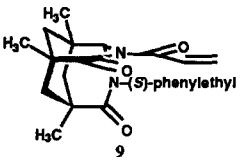
eq 4



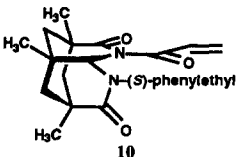
"Pseudoenantiomers" **7** and **8** have all the earmarks of outstanding chiral auxiliaries for asymmetric nitrile oxide cycloadditions. Only recently have the selectivity levels exhibited by acrylates **9** and **10** been matched by Oppolzer's new toluene sultam auxiliaries.[5e]

In the past, good levels of asymmetric induction in asymmetric nitrile oxide cycloadditions have often been a harbinger of equally good results in other thermal addition and cycloaddition reactions.[8] Unfortunately, this was not the case for **7** and **8**. Table 1 summarizes the results of reactions of several derivatives of this pair of auxiliaries. Diastereoselection was typically assessed by integration of the ^{1}H NMR spectrum of the crude reaction mixture. The proton bonded to the carbon bearing the two nitrogens was especially useful because it is a downfield singlet whose chemical shift is sensitive to the product stereochemistry. Though good selectivities were observed in some reactions, the outstanding levels of the nitrile oxide cycloadditions were never equaled. We presume that the configurations of major diastereomers from each reaction can be anticipated from the nitrile oxide results, though this could be verified for only one pair of products (entries 1, 2).

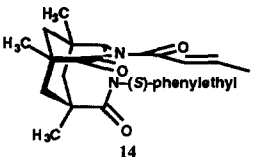
Table I. Thermal Reactions of Compounds **9**, **10**, and **14–17**



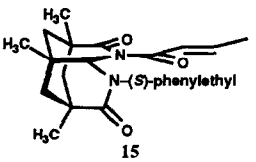
9



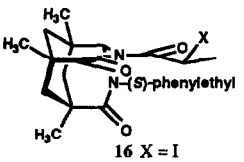
10



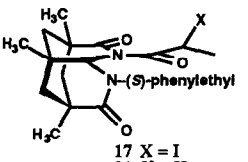
14



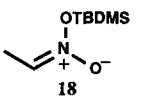
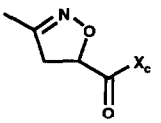
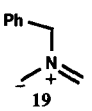
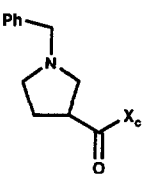
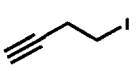
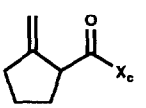
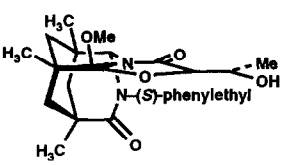
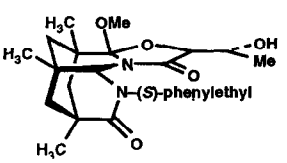
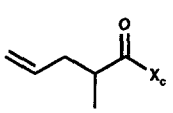
15



16 X = I
30 X = H



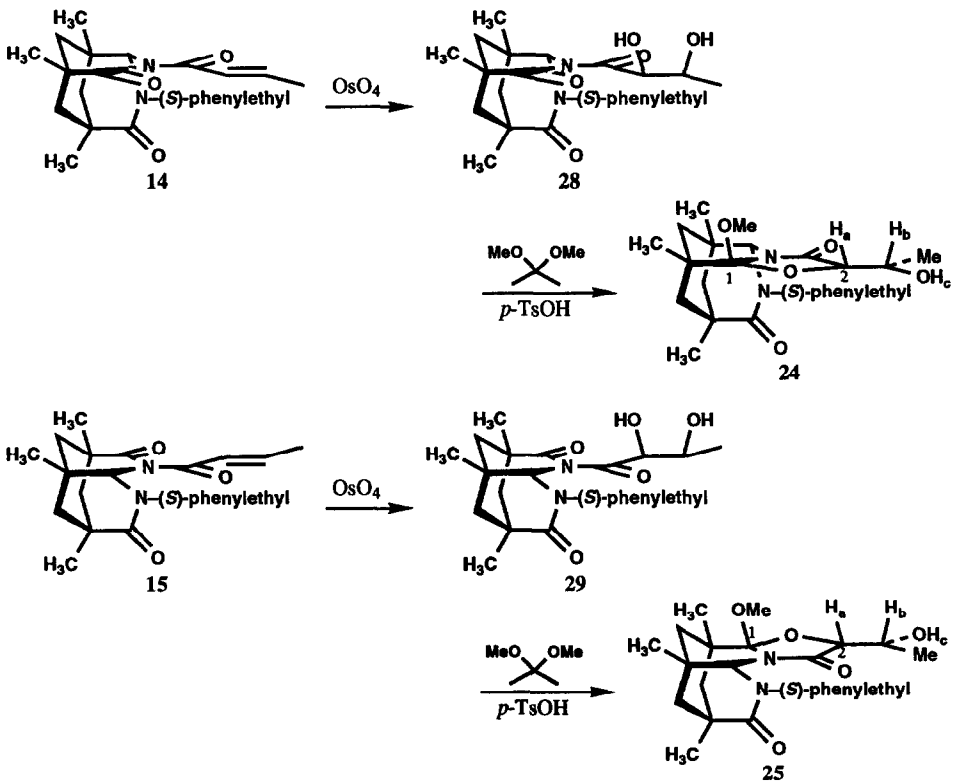
17 X = I
31 X = H

Entry	Cmpd	Reactant	Product		Temp (°C)	Ratio	% Yield
1	**9**			**11a**	25	93:7	70
2	**10**	**18**		**12a**	25	93:7	61
3	**9**			**20**	25	83:17	92
4	**10**	**19**		**21**	25	76:24	86
5	**9**	1.  2. Bu_3SnH		**22**	80	83:17	37
6	**10**			**23**	80	63:37	31
7	**14**	OsO_4; *p*-TsOH, $(MeO)_2CMe_2$		**24**	25	94:6	67
8	**15**	OsO_4; *p*-TsOH, $(MeO)_2CMe_2$		**25**	25	93:7	74
9	**16**			**26**	80	78:22	64
10	**17**			**27**	80	63:37	69

Condensation of **9** or **10** with the silyl nitronate **18** (entries 1,2),[14] followed by acidic hydrolysis gives, only one regioisomeric isoxazoline (**11a** and **12a**) with good stereoselectivity (93:7) for both of the acrylimides. *N*-benzyl 3-substituted pyrrolidines are formed in high yield by the reaction of **9** or **10** with the unsubstituted azomethine ylide **19** (generated in situ by treatment of *N*-benzyl-*N*-(methoxymethyl)-*N*-[(trimethylsilyl)methyl]amine[15] with catalytic trifluoroacetic acid in CH_2Cl_2[16]); however, stereoselectivities for this 1,3-dipole are lower than those observed for the silyl nitronate or nitrile oxide cycloadditions (entries 3,4). Radical annulations[17] of **9** and **10** with 4-iodo-1-butyne and 10 mol% hexabutylditin in C_6H_6, followed by Bu_3SnH reduction, afford the methylenecyclopentanes **22** or **23** with moderate (**9**; 83:17) to poor (**10**; 63:37) diastereoselectivity (entries 5, 6).

Treatment of **7** and **8** with *n*-BuLi at –78 °C followed by crotonyl chloride[13] gives the crotonylimides **14** and **15** in 61–79% yield. Osmylation of **14** and **15** in acetone with 1 mol% OsO_4 affords the diols **28** and **29**, which were not isolated (eq 5). During an attempt to convert **28** and **29** to their corresponding acetonides, an acid-catalyzed cyclization instead occurred to give the monoalcohols **24** and **25** (eq 5). The proposed structure of these compounds is supported by spectroscopic evidence. The ^1H NMR spectra of these compounds exhibit a singlet for the methoxy group, doublets for the methyl group, H_a and H_c, and a multiplet for H_b. Additionally, exchange with D_2O results in the disappearance of only one doublet, consistent with the presence of only one hydroxyl group. Only two carbonyl signals are observed in the ^{13}C NMR spectra, as well as distinct signals for the triheteroatom-substituted carbon C1 (112 ppm) and carbon C2 (80 ppm). The molecular composition is also confirmed by mass spectrometry. The ^1H NMR spectra of the crude products also indicate very good stereoselection (86–88% de). Flash chromatography gives single diastereomers **24** and **25** in 64 and 70% yield, respectively (entries 7, 8).

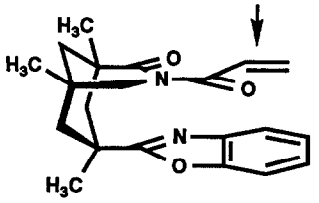
eq 5



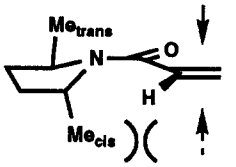
Radical allylation reactions of α-iodopropionimides have also been investigated. Formation of the enolate of **30** with LDA and treatment with I_2 at –78 °C affords the iodide **16** in 67% yield. The identical protocol with **31** gives the iodide **17** and its diastereomer in 82% overall yield. Reaction of **16** or **17** (0.3 M) with 2 equiv of allyltributyltin and 15 mol% of AIBN in C_6H_6 at 80 °C[18] affords the allylated products **26** or **27** with poor selectivities (entries 9, 10).

Discussion: Chiral auxiliaries for asymmetric thermal addition and cycloaddition reactions often possess either a "U-turn" shape or have an sp^3 atom oriented "cis 1,4" to the attacking reagent (Figure 2). Benzoxazole **3** is a nice example of the "U-turn" class while 2,5-dimethylpyrrolidine **32** is a good example of the "cis 1,4" class.[19] We have also proposed that Oppolzer's camphor sultam **33** is an example of the "cis 1,4" class by virtue of the different orientations of its two S–O bonds with respect to the acrylate plane.[8] Bis-lactams **9** and **10** do not appear to fit into either class.

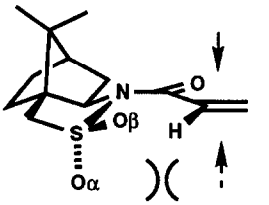
Figure 2. Structural Motifs for Chiral Auxiliaries in Thermal Additions and Cycloadditions



3 "U turn"



32 2,5-dimethylpyrrolidine
")(" signifies cis 1,4-interaction



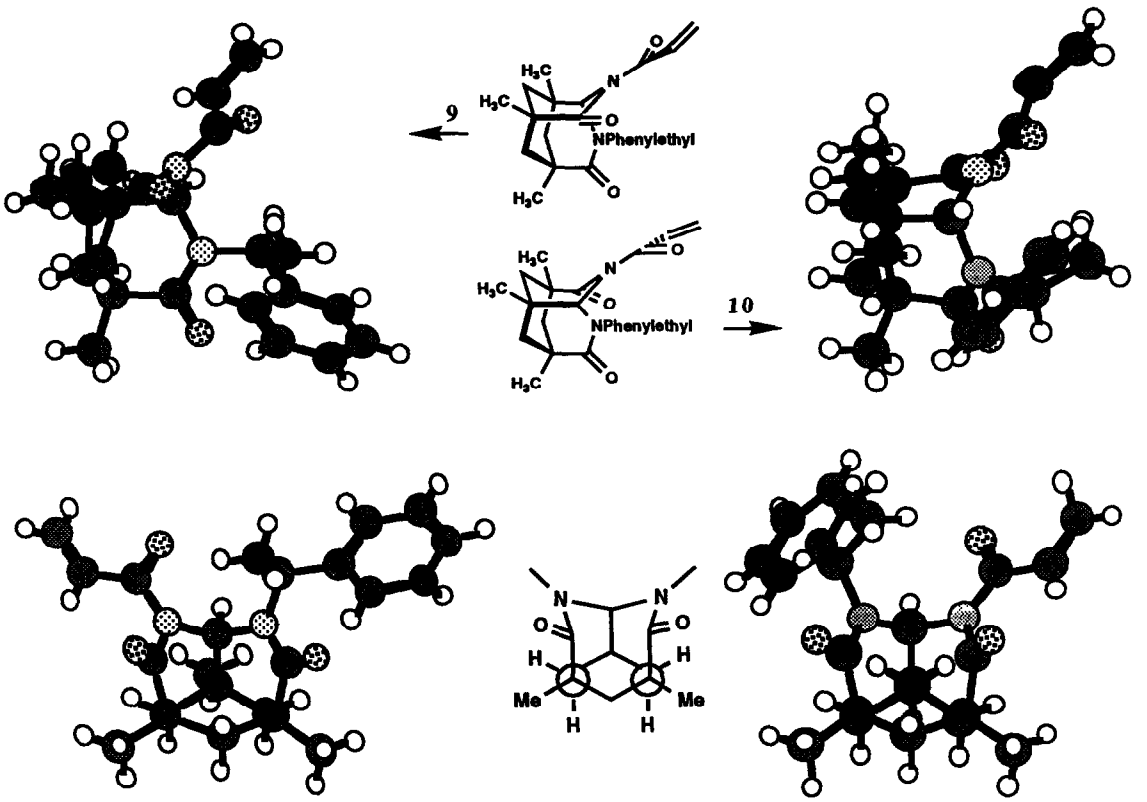
33 non-chelate model

To aid in interpreting our results, we solved the x-ray crystal structures of both **9** and **10**, and Figure 3 shows two views of each structure. At first glance, these structures provide little insight into the origins of asymmetric induction. Indeed, it appears that both faces of the acrylate are wide open to attack, and it is astonishing that any induction is observed at all.

These two molecules have interesting structural features. As expected from dipole considerations, the two carbonyl groups of the imide are roughly opposed. This puts the sp^2 imide carbonyl carbon in the "cis 1,4" position, and appears to eliminate this class of induction. The overall shape of both bis-lactams resembles a "bowl", not a "U-turn". The bowl is made up of a "chair-like" cyclohexane ring and two "boat-like" lactam rings (see lower structures in Figure 3). That the shapes of the bis-lactam portions of the two isomers are very similar is not surprising given the inflexibility of the ring system. The phenylethyl group is oriented differently in each isomer, but in neither isomer is it well positioned to influence reactions at the acrylate double bond. This is because the rigid ring fusion forces the two lactam rings into flattened boats, thus directing the two nitrogen substituents out and away from each other.

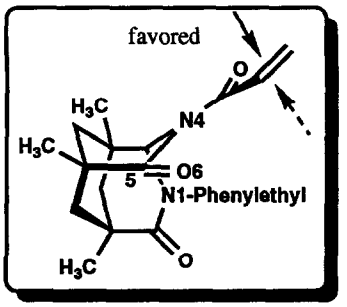
Based on these structures, we can confidently propose a model for asymmetric induction; however, it is more difficult to explain both the reason for the face selectivity and the trends in selectivity as a function of attacking reagent. The stereochemical model shown in Figure 4 proposes that the transition state (TS) closely resembles the favored ground state (GS) rotamer. The x-ray structures confirm expectations that the imides carbonyls are roughly opposed, and that the acryloyl group is planar, *s*-*cis*. We have argued

Figure 3. Two Views of the Crystal Structures of Acrylimides 9 (left) and 10 (right)

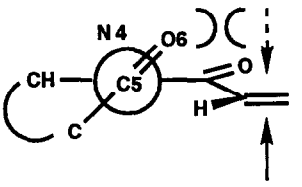


elsewhere that the geometry of the acryloyl group in the TS is similar to that of the GS in these types of reactions.[8] Accepting this assumption, then a model is defined simply by the stereochemical outcome of the reaction; reagents attack the "top face" of **9**.

Figure 4. Stereochemical Models Illustrated with 9



Model with **9** (imide carbonyls anti)



Newman projection
down the C5–N4 bond
shows proposed "cis 1,4" interaction
between O6 and incoming reagent

We have good confidence in this model. But just what controls the facial selectivity, and why are some reagents more selective than others? Our answers to these questions are more speculative, and they come from a more careful look at the x-ray structures. The acrylimide nitrogens in **9** and **10** are effectively planar, so arguments based on *N*-pyramidalization cannot be made. However, one can see even from the drawings in Figure 3 that the two imide carbonyls are not in the same plane. The dihedral angle about C5/N4 defines a degree of twisting of the ring carbonyl out of the acryloyl plane, as shown in the Newman projection in Figure 4. This angle is significant (29° for **9**, -29° for **10**, and the direction of the twist is enforced by the bis-lactam ring. In other words, the ring imide carbonyl is always held to one side of the acrylate plane. We then suggest that a "cis 1,4" interaction between an incoming reagent and the ring imide oxygen may be responsible for the observed stereoselectivity. The selectivities are not uniformly excellent because this oxygen is not in the best position to shield one face. Judging from other auxiliaries (Figure 2), it should be even further out of the amide plane for better selection. At this time, we can offer no explanation for why some types of reactions give significantly better selectivities than others or why the diastereomeric auxiliaries sometimes give different levels of induction (this is especially true for the radical allylations); from our model it is not evident how the configuration of the phenylethyl group can effect the selectivity.

Conclusions: We have introduced two new bis-lactam chiral auxiliaries that are readily available from Kemp's triacid. They provide outstanding levels of stereoselection in dipolar cycloaddition reactions of nitrile oxides and good levels of stereoselection in silyl nitronate cycloadditions and osmylations. We have put forth a stereochemical model for these reactions and proposed an unprecedented explanation of the face selectivity. This explanation, based on the enforced twisting of an imide carbonyl, is admittedly speculative. However, it suggests new possibilities for designing auxiliaries with improved selectivity. Finally, auxiliaries based on imides are very popular, and we wonder if this kind of interaction might also be involved in the thermal reactions of any existing classes of imides.

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Experimental Section.

Synthesis of Chiral Auxiliaries 7 and 8. To a flask containing $SOCl_2$ (60 mL) was added **6** (4.06 g, 17.0 mmol) in portions as a solid. The flask was filled with a condenser that was topped with a gas trap (vacuum adapter connected to aspirator and a drying tube filled with $CaCl_2$. The aspirator was just turned on enough to give a slight flow across the top of the system). The mixture was heated at reflux for 3 h, during which time the heterogeneous mixture turned to a clear, yellow solution. The mixture was concentrated by distillation (760 mm) to a few mL and the remainding $SOCl_2$ was removed under reduced pressure (aspirator) for 2 h. To a stirred solution of the crude product (4.38 g) and DMAP (104 mg) in CH_2Cl_2 (85 mL) was added pyridine (4.5 mL) and (*S*)-phenylethyl amine (2.67 mL) sequentially. The nearly clear, colorless solution turned pale yellow upon addition of the amine. The reaction mixture was allowed to stand for 16 h. The mixture was transferred to a separating funnel and was washed with 3 x 20 mL of 1 M HCl (until the aqueous layer was acidic to Congo red), and 20 mL each of H_2O, $NaHCO_3$, and brine, dried over Na_2SO_4 and evaporated to give 4.96 g (85%) of cream colored solid. To a stirred suspension of the above imide amide (5.53 g) in 100% EtOH (135 mL) at 0°C was added $NaBH_4$ (6.5 g) in several portions over 3 h. The mixture was stirred a total of 6 h and then poured into 1 L of ice water, and the aqueous layer was extracted with 5 x 200 mL of $CHCl_3$. The combined $CHCl_3$ extracts were washed with 200 mL each of H_2O and brine and dried over Na_2SO_4. Evaporation of the solvent gave 4.80 g (86%) of white solid. To a stirred solution of the above alcohol (4.80 g) in CH_2Cl_2 (75 mL) was added TsOH (132 mg). The mixture was stirred for 12 h at 25° C. More TsOH (132 mg) was added along with a few 4Å molecular sieves. The mixture was then heated at reflux for 6 h. The reaction mixture was cooled, washed with 50 mL each of aqueous $NaHCO_3$, H_2O, and brine, dried over Na_2SO_4 and evaporated to give 4.7 g of off-white, viscous oil. Purification of the oil by flash chromatography (silica gel; 7.5 in; 100 mL 5:1 CH_2Cl_2; EtOAc, followed by 500 mL 1:1 CH_2Cl_2:EtOAc) gave 2.57 g of **7** (polar diastereomer) and 1.17 g of **8** more polar diastereomer): **7** mp 107-109 °C; IR, 3376, 3291, 2928, 1690, 1657, 1471, 1450, 1381, 1267, 1207, 1156 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.45-7.34 (m, 5H), 5.99 (q, 1H, J = 7.0 Hz), 4.42 (d, 1H, J = 3.4 Hz), 4.17 (s, 1H, NH), 1.94 (d,

1H, J = 14.6 Hz), 1.75 (d, 1H, J = 11.0 Hz), 1.72 (d, 1H, J = 11.0 Hz), 1.48 (d, 3H, J = 7.0 Hz), 1.32-1.07 (m, 12H, including 1.25 [s, 3H], 1.24 [s, 3H], and 1.07 [s, 3H]); HRMS calcd for $C_{20}H_{26}N_2O_2$ calcd 326.1994, found 326.1994. **8:** mp 187-188 °C; IR, 3227, 2969, 2928, 1682, 1655, 1453, 1271, 1205, 1159 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.41-7.24 (m, 5H), 5.68 (m, 1H), 5.59 (s, 1H, NJ), 4.16 (d, 1H, J = 3.6 Hz), 1.98 (d, 1H, J - 14.7 Hz), 1.78 (d, 1H, J = 12.5 Hz), 1.71 (d, 1H, J = 14.0 Hz), 1.63 (d, 3H, J = 7.1 Hz), 1.29-1.24 (m, 6H), 1.17 (s, 3H), 0.80 (s, 3H); HRMS calcd for $C_{20}H_{26}N_2O_2$ calcd 326.1994, found 326.1994.

Acrylimide 9. To a stirred solution of **7** (489 mg; 1.50 mmol) and hydroquinone (<1 mg) in THF (10 mL) at 0 °C was added MeMgBr in Et_2O (0.55 mL of 2.85 M; 1.57 mmol). After 15 min, freshly distilled acryloyl chloride (135 μL, 150 mg; 1.66 mmol) was added by syringe and the mixture was stirred an additional 15 min at 0 °C. The reaction was then diluted with Et_2O (15 mL, peroxide free!) and the turbid mixture was transferred to a separatory funnel. The organic layer was washed with aq NH_4Cl and brine (10 mL each), dried over $MgSO_4$, and evaporated to give a white solid (592 mg). Purification of this material by flash chromatography (silicam gel; 1:1 hexanes Et_2O) gave a white, crystalline solid (365 mg; 64%): ^1H NMR ($CDCl_3$) δ 1.16 (3H, s), 1.25 (s, 3H), 1.29-1.44 (m, 3H), 1.34 (s, 3H), 1.65 (d, 3H, J = 7.0 Hz), 1.71 (d, 1H, J = 13.1 Hz), 1.88 (d, 1H, J = 12.9 Hz), 2.07 (d, 1H, J = 14.4 Hz), 5.32 (q, 1H, J = 7.0 Hz), 5.59 (dd, 1H, J = 10.2, 1.9 Hz), 6.18 (dd, 1H, J = 16.6, 1.9 Hz), 6.21 (s, 1H), 6.41 (dd, 1H, J = 16.6, 10.2 Hz), 7.14 (m, 1H), 7.25 (m, 4H). ^{13}C NMR ($CDCl_3$) δ 181.8, 176.6, 165.1, 140.8, 130.0, 128.5, 128.0, 126.9, 126.8, 69.6, 54.5, 46.0, 45.9, 43.9, 42.6, 40.3, 34.8, 29.3, 27.2, 26.3, 15.8; IR ($CDCl_3$) 3021, 2977, 2932, 1727, 1673, 1522, 1476, 1426, 1381, 1310, 1219, 1098, 1048, 930, 878, 851, 756, 671, 627 cm^{-1}; $[\alpha]_D^{21}$ = +175° (c = 1.3, $CHCl_3$); MS (*m/z*) 380 (M^+), 365, 325, 289, 262, 253, 233, 220, 205, 178, 150, 120, 105, 91, 79, 69; HRMS Calcd for $C_{23}H_{28}N_2O_3$: 380.2100; Found: 380.2101.

Acrylimide 10. Following the foregoing procedure for the preparation of **9**, reaction of **8** (244 mg; 0.75 mmol) afforded a white, semi-solid residue (300 mg). Purification of this residue by flash chromatography (1:1 hexanes/Et_2O) yielded a white, crystalline solid (129 mg; 45%): ^1H NMR ($CDCl_3$) δ 0.91 (s, 3H), 1.20-1.40 (m, 2H), 1.26 (s, 3H), 1.27 (s, 3H), 1.44 (d, 3H, J = 7.2 Hz), 1.61 (m, 2H), 1.78 (d, 1H, J = 12.8 Hz), 2.09 (d, 1H, J = 14.3 Hz), 5.63 (q, 1H, J = 7.2 Hz), 5.68 (s, 1H), 5.77 (dd, 1H, J = 10.4, 1.7 Hz), 6.44 (dd, 1H, J = 16.9, 1.7 Hz), 6.69 (dd, 1H, J = 16.9, 10.4 Hz), 7.26-7.41 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 182.7, 177.1, 164.6, 139.8, 130.8, 128.6, 128.3, 128.1, 127.6, 67.0, 53.5, 46.4, 45.7, 44.1, 42.7, 40.5, 34.9, 28.1, 27.1, 26.7, 15.8; IR (thin film) 3021, 2977, 2932, 1727, 1673, 1522, 1476, 1426, 1381, 1310, 1219, 1098, 1048, 930, 878, 851, 756, 671, 627 cm^{-1}; $[\alpha]_D^{21}$ = –222° (c = 7.0, $CHCl_3$); MS (*m/z*) 380 (M^+), 365, 325, 289, 262, 253, 233, 220, 205, 178, 150, 120, 105, 91, 79, 69; HRMS Calcd for $C_{23}H_{28}N_2O_3$: 380.2100; Found, 380.2101.

General procedure for preparation of cycloadducts 11a-c and 12a-c by nitrile oxide cycloaddition. To a solution of acrylate (1.0 equiv), hydroximic chloride (1.1 equiv), and ether (1 mL per 0.01 mmol acrylate) was added Et_3N (1.1 equiv). After 16 h at 25 °C, the reaction mixture was filtered and the filtrate was concentrated under reduced pressure. The residue was purified by chromatography to give the individual cycloadducts.

Cycloadduct 11a: Purified by chromatography (25:75, EtOAc/hexanes) to give a film (97%): ^1H NMR ($CDCl_3$) δ 1.21 (s, 3H), 1.26 (d, 1H, J = 13.3 Hz), 1.27 (s, 3H), 1.31 (s, 3H), 1.37 (d, 1H, J = 14.4 Hz), 1.42 (d, 1H, J = 12.7 Hz), 1.66 (d, 3H, J = 7.1 Hz), 1.80 (d, 1H, J = 13.3 Hz), 1.83 (d, 1H, J = 13.1 Hz), 1.92 (s, 3H), 2.08 (d, 1H, J = 14.4 Hz), 2.77 (dd, 1H, J = 17.4, 11.0 Hz), 2.95 (dd, 1H, J = 17.4, 5.4 Hz), 4.99 (dd, 1H, J = 11.0, 5.4 Hz), 5.54 (q, 1H, J = 7.1 Hz), 5.96 (s, 1H), 7.16 (m, 1H), 7.23 (m, 4H). ^{13}C NMR ($CDCl_3$) δ 182.1, 177.0, 168.5, 155.9, 140.7, 127.8, 127.5, 126.7, 76.9, 68.3, 52.5, 46.0, 45.0, 43.8, 42.9, 40.4, 39.9, 35.1, 29.1, 26.9, 26.4, 15.8, 12.7. IR (thin film) cm^{-1}: 3021, 2977, 2932, 1738, 1657, 1522, 1476, 1429, 1381, 1327, 1217, 1098, 1045, 930, 876, 851, 741, 671; $[\alpha]_D^{21}$ = –38° (c = 2.8, $CHCl_3$); MS (*m/z*) 437 (M^+), 422, 353, 319, 221, 208, 178, 151, 135, 120, 105, 96, 84, 69, 56. HRMS Calcd for $C_{25}H_{31}N_3O_4$: 437.2315; Found: 437.2315.

Cycloadduct 11b: Purified by chromatography (20:80, EtOAc/hexanes) to give a film (98%): ^1H NMR ($CDCl_3$) δ 1.16 (s, 9H), 1.20 (s, 3H), 1.25 (d, 1H, J = 13.5 Hz), 1.27 (s, 3H), 1.32 (s, 3H), 1.36 (d, 1H, J = 14.4 Hz), 1.41 (d, 1H, J = 13.0 Hz), 1.66 (d, 3H, J = 7.1Hz), 1.83 (d, 1H, J = 12.5 Hz), 1.85 (d, 1H, J = 13.0 Hz), 2.08 (d, 1H, J = 14.4 Hz), 2.76 (dd, 1H, J = 16.9, 10.8 Hz), 3.20 (dd, 1H, J = 16.9, 5.6 Hz), 5.01 (dd, 1H, J = 10.8, 5.6 Hz), 5.53 (q, 1H, J = 7.1 Hz), 5.95 (s, 1H), 7.10-7.30 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 182.1, 177.0, 168.4, 166.8, 140.6, 127.8, 127.4, 126.7, 77.0, 68.5, 52.7, 45.9, 44.9, 43.9, 42.9, 40.4, 35.5, 35.1, 33.0, 29.2, 28.1, 26.9, 26.4, 15.8; IR (thin film) 3021, 2977, 2247, 1738, 1655, 1522, 1478, 1426, 1381, 1335, 1217, 1048, 930, 876, 851, 741, 671 cm^{-1}; $[\alpha]_D^{21}$ = –36° (c = 2.5, $CHCl_3$); MS (*m/z*) 479 (M^+), 464, 422, 353, 325, 305, 287, 221, 208, 178, 151, 120, 105, 96, 79, 69, 57; HRMS Calcd for $C_{28}H_{37}N_3O_4$: 479.2784; Found: 479.2784.

Cycloadduct 11c: Purified by chromatography (25:75, EtOAc/hexanes) to give a film (93%): ^1H NMR ($CDCl_3$) δ 1.12-1.45 (m, 3H), 1.22 (s, 3H), 1.27 (s, 3H), 1.35 (s, 3H), 1.67 (d, 3H, J = 7.2 Hz), 1.84 (d, 2H, J = 12.5 Hz), 2.12 (d, 1H, J = 14.4 Hz), 3.14 (dd, 1H, J = 17.1, 11.2 Hz), 3.42 (dd, 1H, J = 17.1, 5.9 Hz), 5.16 (dd, 1H, J = 11.2, 5.9 Hz), 5.58 (q, 1H, J = 7.1 Hz), 5.98 (s, 1H), 7.10-7.27 (m, 5H), 7.35-7.42 (m, 3H), 7.63 (m, 2H); ^{13}C

NMR ($CDCl_3$) δ 182.2, 177.2, 168.1, 157.0, 140.7, 130.5, 128.8, 127.8, 127.6, 127.0, 126.8, 77.9, 68.1, 52.3, 46.0, 45.1, 43.9, 42.9, 40.4, 36.4, 35.1, 29.1, 27.0, 26.5, 15.8; IR (thin film) 3021, 2977, 2934, 1738, 1657, 1522, 1476, 1426, 1381, 1356, 1217, 1098, 1048, 930, 878, 851, 747 cm^{-1}; $[\alpha]_D^{21} = -72°$ (c = 1.2, $CHCl_3$); MS (*m/z*) 499 (M^+), 484, 396, 381, 363, 353, 325, 311, 249, 221, 208, 178, 146, 133, 120, 105, 91, 77, 69, 55; HRMS Calcd for $C_{30}H_{33}N_3O_4$: 499.2471; Found: 499.2471.

Diastereomer of Cycloadduct 11c: Purified by chromatography (25:75, EtOAc/hexanes) to give a film: ^1H NMR ($CDCl_3$) δ 1.22 (s, 3H), 1.27 (s, 3H), 1.31 (s, 3H), 1.32 (d, 1H, *J* = 13.1 Hz), 1.36 (d, 1H, *J* = 14.5 Hz), 1.43 (d, 1H, *J* = 12.9 Hz), 1.69 (d, 3H, *J* = 7.1 Hz), 1.76 (d, 1H, *J* = 13.1 Hz), 1.87 (d, 1H, *J* = 12.9 Hz), 2.07 (d, 1H, *J* = 14.5 Hz), 2.79 (dd, 1H, *J* = 16.6, 8.8 Hz), 3.33 (dd, 1H, *J* = 16.6, 12.3 Hz), 4.86 (dd, 1H, *J* = 12.3, 8.8 Hz), 5.67 (q, 1H, *J* = 7.1 Hz), 6.08 (s, 1H), 7.23-7.42 (m, 8H), 7.54 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 181.2, 177.0, 169.7, 155.5, 140.6, 130.4, 128.8, 128.1, 127.6, 126.9, 80.0, 68.1, 51.8, 45.9, 45.7, 43.9, 42.8, 40.3, 35.1, 29.1, 27.0, 26.4, 15.5; IR (thin film) 3021, 2977, 2934, 1738, 1657, 1522, 1476, 1426, 1381, 1356, 1217, 1098, 1048, 930, 878, 851, 747 cm^{-1}; $[\alpha]_D^{21} = +120°$ (c = 0.5, $CHCl_3$); MS (*m/z*) 499 (M^+), 484, 396, 381, 363, 353, 325, 311, 249, 221, 208, 178, 146, 133, 120, 105, 91, 77, 69, 55; HRMS Calcd for $C_{30}H_{33}N_3O_4$: 499.2471; Found: 499.2471.

Cycloadduct 12a: Purified by chromatography (24:76, EtOAc/hexanes) to give a film (95%): ^1H NMR ($CDCl_3$) δ 0.86 (3H, s), 1.19 (d, 1H, *J* = 13.1 Hz), 1.26 (s, 3H), 1.35 (d, 1H, *J* = 12.8 Hz), 1.36 (s, 3H), 1.36 (d, 1H, *J* = 14.2 Hz), 1.46 (d, 3H, *J* = 7.2 Hz), 1.75 (d, 2H, *J* = 12.8 Hz), 1.96 (s, 3H), 2.09 (d, 1H, *J* = 14.2 Hz), 3.03 (1H, dd, *J* = 17.3, 11.0 Hz), 3.40 (dd, 1H, *J* = 17.3, 4.9 Hz), 5.42 (dd, 1H, *J* = 11.0, 4.9 Hz), 5.44 (s, 1H), 5.62 (q, 1H, *J* = 7.2 Hz), 7.27-7.40 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 183.3, 177.2, 168.9, 156.2, 139.9, 128.3, 128.0, 127.7, 77.5, 67.6, 53.6, 46.4, 44.6, 43.9, 43.0, 40.5, 40.0, 35.4, 28.2, 26.8, 26.7, 16.0, 12.8. IR (thin film) 3021, 2977, 2932, 1738, 1657, 1522, 1476, 1429, 1381, 1327, 1217, 1098, 1045, 930, 876, 851, 741, 671 cm^{-1}; $[\alpha]_D^{21} = -21°$ (c = 2.6, $CHCl_3$); MS (*m/z*) 437 (M^+), 422, 353, 319, 221, 208, 178, 151, 135, 120, 105, 96, 84, 69, 56; HRMS Calcd for $C_{25}H_{31}N_3O_4$: 437.2309; Found: 437.2309.

Cycloadduct 12b: Purified by chromatography (18:82, EtOAc/hexanes) to give a film (92%): ^1H NMR ($CDCl_3$) δ 0.85 (s, 3H), 1.18 (s, 9H), 1.19-1.38 (m, 3H), 1.26 (s, 3H), 1.36 (s, 3H), 1.45 (d, 3H, *J* = 7.2 Hz), 1.73 (d, 1H, *J* = 13.0 Hz), 1.78 (d, 1H, *J* = 13.3 Hz), 2.08 (d, 1H, *J* = 14.3 Hz), 3.07 (dd, 1H, *J* = 17.1, 10.9 Hz), 3.47 (dd, 1H, *J* = 17.1, 5.7 Hz), 5.40 (dd, 1H, *J* = 10.9, 5.7 Hz), 5.47 (s, 1H), 5.63 (q, 1H, *J* = 7.2 Hz), 7.27-7.40 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 183.3, 177.2, 168.7, 166.8, 139.8, 128.4, 128.0, 127.7, 77.7, 67.5, 53.5, 46.4, 44.7, 43.9, 42.9, 40.5, 36.4, 35.3, 33.1, 28.2, 28.1, 26.9, 26.7, 16.0; IR (thin film) 3021, 2977, 2247, 1738, 1655, 1522, 1478, 1426, 1381, 1335, 1217, 1048, 930, 876, 851, 741, 671 cm^{-1}; $[\alpha]_D^{21} = -37°$ (c = 2.4, $CHCl_3$); MS (*m/z*) 479 (M^+), 464, 422, 353, 325, 305, 287, 221, 208, 178, 151, 120, 105, 96, 79, 69, 57; HRMS Calcd for $C_{28}H_{37}N_3O_4$: 479.2789; Found: 479.2789.

Cycloadduct 12c: Purified by chromatography (20:80, EtOAc/hexanes) to give a film (99%): ^1H NMR ($CDCl_3$) δ 0.86 (s, 3H), 1.23 (d, 1H, *J* = 13.0 Hz), 1.28 (s, 3H), 1.36 (d, 1H, *J* = 12.6 Hz), 1.38 (d, 1H, *J* = 14.0 Hz), 1.41 (s, 3H), 1.48 (d, 3H, *J* = 7.2 Hz), 1.76 (d, 1H, *J* = 14.0), 1.81 (d, 1H, *J* = 14.9 Hz), 2.11 (d, 1H, *J* = 14.3 Hz), 3.42 (dd, 1H, *J* = 17.0, 11.3 Hz), 3.86 (dd, 1H, *J* = 17.0, 5.3 Hz), 5.47 (s, 1H), 5.57-5.65 (m, 2H), 7.26-7.42 (m, 8H), 7.64 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 183.3, 177.2, 168.5, 157.3, 139.8, 130.6, 128.8, 128.6, 128.3, 128.0, 127.7, 127.0, 78.5, 67.8, 53.8, 46.4, 44.7, 44.0, 43.0, 40.6, 36.7, 35.4, 28.2, 26.9, 26.7, 16.2; IR (thin film): 3021, 2977, 2934, 1738, 1657, 1522, 1476, 1426, 1381, 1356, 1217, 1098, 1048, 930, 878, 851, 747 cm^{-1}; $[[\alpha]_D^{21} = +48°$ (c = 2.5, $CHCl_3$); MS (*m/z*) 499 (M^+), 484, 396, 381, 363, 353, 325, 311, 249, 221, 208, 178, 146, 133, 120, 105, 91, 77, 69, 55; HRMS Calcd for $C_{30}H_{33}N_3O_4$: 499.2471; Found: 499.2471.

Diastereomer of Cycloadduct 12c: Purified by chromatography (20:80, EtOAc/hexanes) to give a film: ^1H NMR ($CDCl_3$) δ 0.93 (s, 3H), 1.26 (s, 3H), 1.26 (d, 1H, *J* = 12.9 Hz), 1.31 (s, 3H), 1.34 (d, 1H, *J* = 14.2 Hz), 1.36 (d, 1H, *J* = 12.6 Hz), 1.52 (d, 3H, *J* = 7.2 Hz), 1.74 (d, 1H, *J* = 12.9 Hz), 1.78 (d, 1H, *J* = 12.6 Hz), 2.06 (d, 1H, *J* = 14.2 Hz), 3.45 (dd, 1H, *J* = 16.5, 9.5 Hz), 3.58 (dd, 1H, *J* = 16.5, 12.0 Hz), 5.37 (dd, 1H, *J* = 12.0, 9.5 Hz), 5.54 (s, 1H), 5.57 (q, 1H, *J* = 7.2 Hz), 7.27-7.42 (m, 8H), 7.63 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 181.9, 177.1, 169.1, 155.9, 139.9, 130.5, 128.8, 128.7, 128.3, 128.2, 127.7, 127.0, 80.4, 68.2, 54.2, 46.3, 45.4, 43.9, 43.1, 40.5, 40.1, 35.3, 28.2, 26.8, 26.6, 16.4; IR (thin film) 3021, 2977, 2934, 1738, 1657, 1522, 1476, 1426, 1381, 1356, 1217, 1098, 1048, 930, 878, 851, 747 cm^{-1}; $[\alpha]_D^{21} = -181°$ (c = 2.9, $CHCl_3$); MS (*m/z*) 499 (M^+), 484, 396, 381, 363, 353, 325, 311, 249, 221, 208, 178, 146, 133, 120, 105, 91, 77, 69, 55; HRMS Calcd for $C_{30}H_{33}N_3O_4$: 499.2471; Found: 499.2471.

Isoxazoline 11a. A solution of acrylimide **9** (76 mg; 0.20 mmol) and *tert*-butyldimethylsilyl ethylnitronate **18** (95 mg; 0.50 mmol) in C_6H_6 (1 mL) was stirred at ambient temperature for 18 h. Analysis of the reaction mixture by TLC (2/1, hexanes/EtOAc) indicated consumption of **9** and the formation of one major product (R_f = 0.52). Two small crystals of *p*-toluenesulfonic acid were added and the mixture was allowed to stand for 1 h. TLC indicated the disappearance of the intermediate product (R_f = 0.52) and the appearance of a new product (R_f = 0.25). The yellow-

green reaction mixture was diluted with EtOAc (10 mL), washed with satd aq $NaHCO_3$ and brine (5 mL each), dried over $MgSO_4$, and evaporated to give a yellow oil (139 mg). Analysis of the crude reaction mixture by ^1H NMR spectroscopy indicated a 93:7 ratio of diastereomers. Purification of this oil by flash chromatography (2/1 hexanes/EtOAc) afforded a white solid (62 mg; 70%) that was identical by ^1H NMR spectroscopy to that prepared by nitrile oxide cycloaddition.

Isoxazoline 12a. Following the general procedure for **11a**, reaction of acrylimide **10** (50 mg; 0.13 mmol) gave a brown residue (65 mg). Analysis of the crude reaction mixture by ^1H NMR spectroscopy indicated a 93:7 ratio of diastereomers. Flash chromatography (60/40, EtOAc/hexanes) yielded an off-white semi-solid (35 mg; 61%) that was identical by ^1H NMR spectroscopy to that prepared by nitrile oxide cycloaddition.

Pyrrolidine 20. To a stirred solution of acrylimide **9** (74 mg; 0.20 mmol) and *N*-benzyl-*N*-(methoxymethyl)-*N*-[(trimethylsilyl)methyl]amine[15] (54 mg; 0.24 mmol) in CH_2Cl_2 (0.5 mL) at 0 °C was added 1 M trifluoroacetic acid in CH_2Cl_2 (20 μL; 0.02 mmol). The ice bath was removed and the solution was stirred at ambient temperature for 3 h. The reaction mixture was diluted with CH_2Cl_2 (10 mL) and was washed with satd aq $NaHCO_3$ and brine (5 mL each), dried over $MgSO_4$, and evaporated to give a clear oil that crystallized upon standing (101 mg). Analysis of the crude reaction mixture by ^1H NMR spectroscopy indicated a 83:17 ratio of diastereomers. Purification of this mixture by flash chromatography (97/3, CH_2Cl_2/MeOH) afforded a white, crystalline solid (95 mg; 92%), mp 154–56 °C. $[\alpha]_D^{21}$ = +82.0° (*c* = 1.7, $CHCl_3$); IR (thin film): 2961, 1710, 1694, 1684, 1370, 1210, 1149 cm^{-1}; ^1H NMR (major diastereomer) δ 1.08 (s, 3H), 1.15–1.39 (m, 4H), 1.17 (s, 3H), 1.28 (s, 3H), 1.66 (d, 3H, *J* = 7.1 Hz), 1.68–1.80 (m, 1H), 1.83 (d, 1H, *J* = 13.6 Hz), 1.92–2.00 (m, 1H), 2.02 (d, 1H, *J* = 14.1 Hz), 2.20 (dd, 1H, *J* = 9.2, 6.0 Hz), 2.48–2.57 (m, 3H), 3.04–3.16 (m, 1H), 3.52 (AB, 2H, J_{AB} = 12.7 Hz, ν_{AB} = 61.7), 5.42 (q, 1H, *J* = 7.1 Hz), 6.15 (s, 1H), 7.15–7.32 (m, 10H); ^{13}C NMR (major diastereomer) δ 15.73, 26.21, 26.89, 27.04, 29.09, 34.66, 40.09, 42.19, 42.55, 43.71, 45.43, 45.85, 53.03, 53.71, 57.23, 59.85, 68.28, 126.56, 126.88, 127.05, 127.73, 128.18, 138.98, 140.69, 173.89, 176.67, 181.78; HRMS calcd for $C_{32}H_{39}N_3O_3$: 513.2990; Found: 513.2991.

Pyrrolidine 21. Following the foregoing procedure for **20**, acrylimide **10** (75 mg; 0.20 mmol) gave a glassy residue that crystallized upon standing (110 mg). Analysis of the crude residue by ^1H NMR spectroscopy indicated a 76:24 ratio of diastereomers. Flash chromatography (1/1, CH_2Cl_2/Et_2O) yielded a white, semi-solid residue (89 mg; 86%). $[\alpha]_D^{21}$ = −163.5°, (*c* = 1.9, $CHCl_3$); IR (thin film): 2963, 2928, 1725, 1661, 1375, 1211, 1169, 1150 cm^{-1}; ^1H NMR (major diastereomer) δ 0.85 (s, 3H), 1.23 (s, 3H), 1.23–1.40 (m, 4H), 1.44 (d, 3H, *J* = 7.1 Hz), 1.71 (d, 1H, *J* = 12.8 Hz), 2.01 (d, 1H, *J* = −14.4 Hz), 2.00–2.21 (m, 2H), 2.46 (dd, 1H, *J* = 9.1, 6.6 Hz), 2.56–2.68 (m, 3H), 3.35–3.44 (m, 1H), 3.57 (AB, 2H, J_{AB} = 12.7 Hz, ν_{AB} = 43.1), 5.57 (q, 1H, *J* = 7.1 Hz), 5.65 (s, 1H), 7.19–7.40 (m, 10H); ^{13}C NMR δ 16.06, 26.48, 26.89, 27.67, 27.99, 34.65, 40.19, 42.42, 42.51, 43.68, 45.17, 46.15, 53.59, 53.64, 57.04, 59.89, 66.93, 126.82, 127.37, 127.79, 128.09, 128.66, 138.89, 139.79, 173.25, 176.83, 182.53; HRMS calcd for $C_{32}H_{39}N_3O_3$: 513.2991; Found: 513.2991.

Radical annulation product 22. A solution of acrylimide **9** (152 mg; 0.40 mmol), hexabutylditin (20 μL, 23 mg; 0.04 mmol), and 4-iodo-1-butyne (105 μL, 180 mg; 1.00 mmol) in C_6H_6 (1.5 mL) was heated in an oil bath maintained at 80 °C and irradiated with a sunlamp for 2.5 h. Two additional portions of hexabutylditin (20 μL, 23 mg; 0.04 mmol) were added after 2 h and 4.5 h of irradiation. The mixture was irradiated for a total of 8 h, then was concentrated under reduced pressure to give a yellow, semi-solid residue (321 mg). This residue was dissolved in C_6H_6 (4.0 mL) and tributyltin hydride (215 μL, 233 mg; 0.80 mmol) and a catalytic amount of AIBN were added. The mixture was heated at 80 °C for 4 h, allowed to cool to ambient temperature, and diluted with Et_2O (30 mL). The solution was transferred to a separatory funnel, treated with 0.1 M I_2 in Et_2O until the color persisted, and washed with half-saturated aq KF (4 × 5 mL), satd aq $Na_2S_2O_3$ (5 mL), and brine (5 mL), dried over $MgSO_4$, and evaporated to give a yellow oil (475 mg). The oil was dissolved in EtOAc and was passed through a column (15 × 50 mm) of silica gel and the eluent evaporated. Analysis of the crude residue by ^1H NMR spectroscopy indicated a 83:17 ratio of diastereomers. Purification of the crude reaction mixture by flash chromatography (1/1 hexanes/Et_2O) afforded a pale yellow, semi-solid residue (64 mg; 37%). $[\alpha]_D^{21}$ = +126.7° (*c* = 2.1, $CHCl_3$); IR (thin film) 2928, 1719, 1671, 1165 cm^{-1}; ^1H NMR (major diastereomer) δ 1.15 (s, 3H), 1.25–1.43 (m, 3H), 1.28 (s, 3H), 1.31 (s, 3H), 1.46–1.87 (m, 6H), 1.67 (d, 3H, *J* = 7.1 Hz), 2.08 (d, 1H, *J* = 14.4 Hz), 2.25–2.37 (m, 2H), 3.70–3.77 (m, 1H), 4.61 (d, 1H, *J* = 1.8 Hz), 4.89 (d, 1H, *J* = 1.7 Hz), 5.26 (q, 1H, *J* = 7.1 Hz), 6.16 (s, 1H), 7.13–7.27 (m, 5H); ^{13}C NMR δ 15.83, 24.66, 26.14, 27.12, 29.29, 30.96, 33.42, 40.09, 42.61, 43.71, 45.49, 45.85, 48.37, 54.29, 69.27, 106.73, 126.50, 126.62, 127.76, 140.96, 153.18, 174.83, 176.54, 182.18; HRMS calcd for $C_{27}H_{35}N_2O_3$ [M+H]: 435.2648; Found: 435.2648.

Radical annulation product 23. Reaction of acrylimide **10** (76 mg; 0.20 mmol) following the general procedure for the preparation of **22** gave a clear oil (66 mg). Analysis of the crude residue by ^1H NMR spectroscopy indicated a 63:37 ratio of diastereomers. Flash chromatography yielded a white, semi-solid residue (27 mg; 31%). $[\alpha]_D^{21}$ = −173.3° (*c* = 2.7, $CHCl_3$); IR (thin film) 2961, 2928, 1725, 1661, 1364, 1208, 1165 cm^{-1}; ^1H NMR (major diastereomer) δ 1.24–1.36 (m, 3H), 1.25 (s, 6H), 1.27 (s, 3H), 1.44 (dd, 3,H *J* = 7.1, 1.8 Hz), 1.51–2.11 (m, 7H), 2.34–2.47 (m, 2H), 3.81–3.87 (m, 1H), 4.61 (br s, 1H), 4.94 (br s, 1H), 5.60 (q, 1H, *J* = 7.1 Hz), 5.71 (s, 1H),

7.25–7.36 (m, 5H); ^{13}C NMR (diastereomeric mixture) δ 15.89, 15.99, 25.05, 25.43, 26.44, 26.58, 27.11, 28.05, 28.15, 31.58, 32.39, 33.67, 34.07, 34.69, 34.85, 40.32, 40.86, 42.71, 43.98, 45.44, 45.58, 46.26, 48.11, 48.73, 53.04, 53.52, 53.64, 66.48, 66.68, 66.93, 107.00, 109.35, 127.44, 127.50, 127.87, 127.98, 128.20, 139.79, 152.93, 173.63, 174.11, 176.97, 183.06; HRMS calcd for $C_{27}H_{34}N_2O_3$: 434.2569; Found: 434.2569.

Crotonylimide 14. To a stirred solution of auxiliary **7** (151 mg; 0.46 mmol) in THF (3 mL) at –78 °C was added *n*-BuLi (0.20 mL, 1.6 M in hexanes; 0.48 mmol) by syringe dropwise. After 15 min, freshly distilled crotonyl chloride (50 μL, 55 mg; 0.53 mmol) was added by syringe in one portion. The mixture was maintained at –78 °C for 0.5 h and at 0 °C for 15 min. The reaction was quenched with satd aq NH_4Cl (0.1 mL), concentrated in vacuo, and the residue was extracted with Et_2O (3 × 5 mL). The combined ether extracts were washed with satd aq $NaHCO_3$ and brine (5 mL each), dried over Na_2SO_4, and evaporated to give a white-yellow solid (181 mg). Purification of this material by flash chromatography (1/1 hexanes/Et_2O) afforded a white, crystalline solid (116 mg; 64%), mp 168–69 °C. $[\alpha]_D^{21}$ = +182.6° (*c* = 1.9, $CHCl_3$); IR (thin film) 2928, 1729, 1674, 1640, 1372, 1211, 1175, 1150 cm^{-1}; ^{1}H NMR δ 1.14 (s, 3H), 1.26 (s, 3H), 1.29 (d, 1H, *J* = 13.1 Hz), 1.31 (d, 1H, *J* = 14.3 Hz), 1.33 (s, 3H), 1.40 (d, 1H, *J* = 12.8 Hz), 1.64 (d, 3H, *J* = 7.1 Hz), 1.71 (d, 1 H, *J* = 13.1 Hz), 1.81 (dd, 3H, *J* = 6.8, 1.6 Hz), 1.87 (d, 1H, *J* = 13.0 Hz), 2.06 (d, 1H, *J* = 14.4 Hz), 5.22 (q, 1H, *J* = 7.1 Hz), 6.21 (s, 1H), 6.21 (dd, 1H, *J* = 15.2, 1.6 Hz), 6.84 (dq, 1H *J* = 15.2, 6.8 Hz), 7.10–7.17 (m, 1H), 7.20–7.26 (m, 4H); ^{13}C NMR δ 15.75, 18.21, 26.12, 27.12, 29.21, 34.69, 40.15, 42.47, 43.77, 45.73, 45.88, 54.94, 69.85, 122.71, 126.40, 126.69, 127.85, 140.87, 145.00, 165.19, 176.36, 181.78; HRMS calcd for $C_{24}H_{30}N_2O_3$: 394.2256; Found: 394.2256.

Crotonylimide 15. Following the foregoing general procedure for the preparation of **14**, reaction of auxiliary **8** (151 mg; 0.46 mmol) gave an off-white solid (179 mg). Flash chromatography (1/1, hexanes/Et_2O) yielded a white, crystalline solid (124 mg; 69%), mp 87–89 °C. $[\alpha]_D^{21}$ = –200.5° (*c* = 1.8, $CHCl_3$); IR (thin film) 2928, 1722, 1661, 1636, 1211, 1173, 1150 cm^{-1}; ^{1}H NMR δ 0.89 (s, 3H), 1.21 (d, 1H, *J* = 13.2 Hz), 1.26 (s, 6H), 1.32 (d, 1H, *J* = 14.3 Hz), 1.34 (d, 1H, *J* = 12.8 Hz), 1.43 (d, 3H, *J* = 7.2 Hz), 1.57 (d, 1H, *J* = 13.0 Hz), 1.76 (d, 1H, *J* = 12.9 Hz), 1.89 (dd, 3H, *J* = 7.0, 1.4 Hz), 2.08 (d, 1H, *J* = 14.1 Hz), 5.64 (q, 1H, *J* = 7.2 Hz), 5.69 (s, 3H), 6.45 (dd, 1, *J* = 15.2, 1.4 Hz), 7.07 (dq, 1H, *J* = 15.0, 7.0 Hz), 7.26–7.41 (m, 5H); ^{13}C NMR δ 15.57, 18.35, 26.57, 27.04, 27.96, 34.69, 40.28, 42.55, 43.97, 45.57, 46.28, 53.09, 66.58, 122.58, 127.47, 127.95, 128.13, 139.73, 145.78, 164.44, 176.96, 182.72; HRMS calcd for $C_{24}H_{30}N_2O_3$: 394.2256; Found: 394.2256.

Alcohol 24. To a stirred solution of **14** (79 mg; 0.20 mmol) in acetone (1 mL) was added *N*-morpholine-*N*-oxide (60 wt %, 0.68 M in H_2O, 0.35 mL; 0.24 mmol) and osmium tetroxide (2.5 wt %, 0.08 M in *tert*-butyl alcohol, 25 μL; 0.002 mmol) sequentially. The mixture was stirred for 18 h at room temperature and 10% aq $NaHSO_3$ (5 mL) was added. The reaction mixture was extracted with EtOAc (4 × 5 mL) and the combined organics were washed with brine (5 mL), dried over $MgSO_4$, and concentrated to give an off-white solid (86 mg). The residue was dissolved in acetone (1 mL) and 2,2-dimethoxypropane (1 mL) and a catalytic amount (a few small crystals) of *p*-TsOH was added. The solution was stirred at ambient temperature for 2 h; TLC (2/1, hexanes/acetone) indicated consumption of the diol. The reaction mixture was transferred to a separatory funnel and diluted with CH_2Cl_2 (10 mL). The organic layer was washed with satd aq $NaHCO_3$ (5 mL) and the layers separated. The aqueous layer was extracted with CH_2Cl_2 (2 × 5 mL) and the combined organic layers were washed with brine (5 mL), dried over $MgSO_4$, and evaporated to give a foamy residue (81 mg). Analysis of this crude mixture by ^{1}H NMR spectroscopy indicated a 94:6 ratio of diastereomers. Purification of this material by flash chromatography (3/1, hexanes/acetone) gave the major diastereomer as a white, semi-solid (60 mg; 67%). $[\alpha]_D^{21}$ = –41.7° (*c* = 2.0, $CHCl_3$); IR (thin film) 3445, 2973, 1719, 1652, 1394, 1379, 1139, 1081, 755 cm^{-1}; ^{1}H NMR: δ 0.91 (d, 1H, *J* = 13.4 Hz), 0.99–1.04 (m, 1H), 1.04 (s, 3H), 1.17 (s, 3H), 1.18 (s, 3H), 1.22 (d, 1H, *J* = 12.6 Hz), 1.30 (d, 3H, *J* = 6.5 Hz), 1.53 (d, 1H, *J* = 13.3 Hz), 1.59–1.64 (m, 1H), 1.64 (d, 1H, *J* = 7.2 Hz), 1.98 (d, 1H, *J* = 6.2 Hz), 2.11 (s, 3H), 2.35 (d, 1, *J* = 14.2 Hz), 3.97 (d, 1H, *J* = 3.2 Hz), 4.12 (ddq, 1H, *J* = 6.5, 6.2, 3.2 Hz), 5.53 (q, 1H, *J* = 7.3 Hz), 5.61 (s, 1H), 7.13–7.27 (m, 3H), 7.62 (d, 2H, *J* = 7.7 Hz); ^{13}C NMR δ 17.99, 18.89, 24.43, 27.27, 29.05, 35.62, 40.96, 41.28, 43.10, 43.39, 47.25, 47.89, 52.61, 64.09, 66.42, 80.23, 112.13, 127.59, 128.01, 128.70, 140.76, 169.88, 179.06.

Alcohol 25. Reaction of **15** (79 mg; 0.20 mmol) using the foregoing general procedure for **24** gave a white solid (93 mg). Analysis of this crude reaction mixture by ^{1}H NMR spectroscopy indicated a 93:7 diastereomeric ratio. Flash chromatography (85/15, CH_2Cl_2/Et_2O) yielded the major diastereomer as a white foam (66 mg; 74%). $[\alpha]_D^{21}$ = –29.1° (*c* = 1.7, $CHCl_3$); IR (thin film) 3430, 2971, 1719, 1647, 1399, 1379, 1159, 1086, 754 cm^{-1}; ^{1}H NMR δ 0.53 (s, 3H), 0.80 (d, 1H, *J* = –13.5 Hz), 1.02 (d, 1H, *J* = –14.1 Hz), 1.04–1.09 (m, 1H), 1.09 (s, 3H), 1.17 (s, 3H), 1.32 (d, 3H, *J* = 6.6 Hz), 1.40 (d, 1H, *J* = 12.6 Hz), 1.47–1.52 (m, 1H), 1.53 (d, 3H, *J* = 7.2 Hz), 2.41 (d, 1H, *J* = 5.9 Hz), 2.40–2.44 (m, 1H), 3.17 (s, 3H), 4.12 (ddq, 1H, *J* = 6.6, 5.9, 3.3 Hz), 4.31 (d, 1H, *J* = 3.3 Hz), 4.95 (s, 1H), 5.69 (q, 1H, *J* = 7.2 Hz), 7.25–7.37 (m, 5H); ^{13}C NMR δ 16.12, 18.87, 24.43, 27.38, 28.05, 35.11, 40.70, 41.09, 43.13, 43.29, 47.33, 49.21, 51.93, 64.09, 66.62, 80.66, 112.36, 127.65, 127.88, 128.37, 140.70, 169.88, 178.32.

Iodide 16. A solution of LDA was generated by stirring diisopropylamine (90 μL, 65 mg; 0.64 mmol) in THF (1 mL) with *n*-BuLi (0.38 mL, 1.6 M in hexanes; 0.61 mmol) for 0.5 h at 0 °C. The flask was then cooled to –78 °C and a

solution of propionimide **30**[12b] (191 mg; 0.50 mmol) in THF (3.0 mL) was added dropwise by syringe. After 2 h at –78 °C, the solution was transferred by cannula to a flask containing a solution of I_2 (203 mg; 0.80 mmol) in THF (5 mL), also at –78 °C. The dark red mixture was maintained at –78 °C for 0.5 h and at 0 °C for 0.5 h, then was quenched by the addition of 1 M HCl (several drops). The reaction mixture was diluted with Et_2O (50 mL) and was washed with 1 M HCl (10 mL), satd aq $Na_2S_2O_3$ (3 × 10 mL), satd aq $NaHCO_3$ (10 mL), and brine (10 mL), dried over $MgSO_4$, and evaporated to give a yellow oil (265 mg). Purification of this material by flash chromatography (55/45, hexanes/Et_2O) afforded a white solid (171 mg; 67%), mp 115–18 °C (dec), that was a single diastereomer. $[\alpha]_D^{21}$ = –15.8° (*c* = 2.3, $CHCl_3$); IR (thin film) 2971, 2928, 1725, 1684, 1372, 1215, 1144 cm^{-1}; ^1H NMR δ 1.22–1.27 (m, 1H), 1.23 (s, 3H), 1.32 (s, 3H), 1.38 (s, 3H), 1.38–1.43 (m, 1H), 1.50–1.56 (m, 1H), 1.52 (d, 3H, *J* = 6.8 Hz), 1.66 (d, 3H, *J* = 7.2 Hz), 1.84 (d, 1H, *J* = 12.9 Hz), 1.97 (d, 1H, *J* = 13.1 Hz), 2.10 (d, 1H, *J* = 14.5 Hz), 4.92 (q, 1H, *J* = 6.7 Hz), 5.65 (q, 1H, *J* = 7.2 Hz), 6.12 (s, 1H), 7.13–7.26 (m, 5H); ^{13}C NMR δ 15.34, 15.54, 22.26, 26.37, 27.32, 29.18, 35.37, 40.12, 43.07, 43.94, 44.05, 46.17, 51.18, 66.94, 126.59, 127.14, 127.66, 140.43, 170.78, 177.29, 181.92; HRMS calcd for $C_{23}H_{29}IN_2O_3$: 508.1223; Found: 508.1223. Another fraction (16 mg) was obtained that contained a mixture of two diastereomers.

Iodide 17. Following the foregoing general procedure for the preparation of **16**, reaction of propionimide **31**[12b] (191 mg; 0.50 mmol) gave a yellow oil (244 mg). Flash chromatography (85/65, hexanes/Et_2O) yielded a major diastereomer as a white, foamy residue (125 mg; 49%). $[\alpha]_D^{21}$ = –54.6° (*c* = 2.3, $CHCl_3$); IR (thin film) 2971, 2928, 1727, 1667, 1370, 1215, 1144 cm^{-1}; ^1H NMR δ 0.95 (s, 3H), 1.19 (d, 1H, *J* = 13.2 Hz), 1.25 (s, 3H), 1.25–1.34 (m, 2H), 1.39 (s, 3H), 1.41 (d, 3H, *J* = 7.4 Hz), 1.76 (d, 1H, *J* = 12.9 Hz), 1.88 (d, 3H, *J* = 6.8 Hz), 1.94 (d, 1H, *J* = 13.3 Hz), 2.06 (d, 1H, *J* = 14.3 Hz), 5.44 (q, 1H, *J* = 6.8 Hz), 5.49 (q, 1H, *J* = 7.4 Hz), 5.66 (s, 1H), 7.22–7.39 (m, 5H); ^{13}C NMR δ 14.61, 16.47, 22.46, 26.54, 27.29, 28.37, 35.50, 40.35, 43.13, 44.00, 46.48, 54.39, 67.80, 127.53, 127.85, 128.18, 139.79, 171.06, 177.06, 182.85; MS calcd for $C_{23}H_{29}IN_2O_3$: 508.1223. Found: 508.1223. Further elution gave a minor diastereomer as a white, crystalline solid (85 mg; 33%, 82% overall), dec >82 °C. $[\alpha]_D^{21}$ = –208.6° (*c* = 2.0, $CHCl_3$); IR (thin film): 2967, 2928, 1728, 1655, 1366, 1213, 1150 cm^{-1}; ^1H NMR δ 0.79 (s, 3H), 1.23 (d, 1H, *J* = 13.2 Hz), 1.26 (s, 6H), 1.31 (d, 1H, *J* = 12.8 Hz), 1.34 (d, 1H, *J* = 14.2 Hz), 1.46 (d, 1H, *J* = 13.2 Hz), 1.53 (d, 3H, *J* = 7.3 Hz), 1.70 (d, 1H, *J* = 12.9 Hz), 1.96 (d, 3H, *J* = 6.9 Hz), 2.08 (d, 1H, *J* = 14.2 Hz), 4.85 (q, 1H, *J* = 6.9 Hz), 5.64 (s, 1H), 5.65 (q, 1H, *J* = 7.3 Hz), 7.30–7.41 (m, 5H); ^{13}C NMR δ 14.70, 16.90, 24.43, 26.70, 27.31, 27.83, 34.69, 40.32, 42.24, 44.23, 45.52, 46.33, 52.64, 66.91, 127.76, 128.11, 128.28, 139.53, 169.40, 176.96, 182.34; HRMS calcd for $C_{23}H_{29}IN_2O_3$: 508.1223; Found: 508.1223.

Radical allylation product 26. A solution of **16** (102 mg; 0.20 mmol), allyltributylstannane (125 μL, 134 mg; 0.41 mmol), and AIBN (5 mg; 0.03 mmol) in C_6D_6 (0.6 mL; 0.3 M) was placed in a 5 mm NMR tube and purged with Ar for 1 min. The tube was capped, wrapped with Parafilm, and heated at 80 °C for 4 h. ^1H NMR spectroscopy confirmed the consumption of **16** and indicated a 78:22 ratio of diastereomers. The solvent was concentrated and the residue was dissolved in Et_2O (0.5 mL) then stirred with satd aq KF (0.3 mL) for 3 h. The heterogeneous mixture was diluted with Et_2O (10 mL) and the layers were separated. The ethereal layer was washed with brine (2 mL), dried over $MgSO_4$, and evaporated to give a semi-solid residue (131 mg). Purification of this material by flash chromatography (1.25/1, hexanes/Et_2O) afforded a white solid (54 mg; 64%), mp 127–33 °C. $[\alpha]_D^{21}$ = +183.2° (*c* = 2.0, $CHCl_3$); IR (thin film) 2973, 2930, 1723, 1684, 1374, 1173, 1150 cm^{-1}; ^1H NMR (major diastereomer) δ 0.89 (d, 3H, *J* = 6.7 Hz), 1.13 (s, 3H), 1.25 (s, 3H), 1.26–1.33 (m, 2H), 1.27 (s, 3H), 1.38 (d, 1H, *J* = 12.8 Hz), 1.66 (d, 3H, *J* = 7.0 Hz), 1.69–1.73 (m, 1H), 1.83 (d, 1H, *J* = 12.8 Hz), 1.90–2.07 (m, 1H), 2.03 (d, 1H, *J* = 15.3 Hz), 2.17–2.29 (m, 1H), 2.82–2.91 (m, 1H), 4.99 (d, 2H, *J* = 12.0 Hz), 5.16 (q, 1H, *J* = 6.9 Hz), 5.53–5.66 (m, 1H), 6.10 (s, 1H), 7.14–7.25 (m, 5H); ^{13}C NMR δ 15.92, 16.99, 26.08, 27.02, 29.02, 34.69, 38.86, 38.99, 40.09, 42.38, 43.55, 45.46, 45.74, 54.78, 69.53, 117.11, 126.55, 126.62, 127.79, 135.46, 141.05, 176.15, 176.37, 182.33; HRMS calcd for $C_{26}H_{34}N_2O_3$: 422.2569; Found: 422.2569.

Radical allylation product 27. Following the foregoing general procedure for the preparation of **20**, reaction of **17** (102 mg; 0.20 mmol) gave a clear oil (134 mg). Analysis of the crude reaction mixture by ^1H NMR spectroscopy indicated a 63:37 diastereomeric ratio. Flash chromatography (1.25/1, hexanes/Et_2O) yielded a clear oil (59 mg; 69%). $[\alpha]_D^{21}$ = –206.8° (*c* = 2.95, $CHCl_3$); IR (thin film): 2970, 2930, 1726, 1659, 1377, 1210, 1175, 1150 cm^{-1}; ^1H NMR (major diastereomer) δ 0.84 (s, 3H), 1.18 (d, 3H, *J* = 6.8 Hz), 1.18–1.23 (m, 1H), 1.23 (s, 3H), 1.24 (s, 3H), 1.30 (d, 1H, *J* = 14.3 Hz), 1.31 (d, 1H, *J* = 13.1 Hz), 1.42 (d, 3H, *J* = 7.3 Hz), 1.58 (d, 1H, *J* = 13.2 Hz), 1.72 (d, 1H, *J* = 12.8 Hz), 1.97–2.08 (m, 1H), 2.05 (d, 1H, *J* = 14.2 Hz), 2.31–2.41 (m, 1H), 2.90–3.00 (m, 1H), 4.92–5.00 (m, 2H), 5.51–5.65 (m, 2H), 5.64 (s, 1H), 7.22–7.38 (m, 5H); ^{13}C NMR: δ 15.84, 15.92, 17.38, 26.51, 26.89, 27.18, 27.83, 27.99, 34.56, 34.75, 37.18, 37.34, 38.37, 39.02, 40.23, 42.55, 43.81, 43.94, 45.27, 43.36, 46.11, 46.20, 53.09, 53.22, 66.32, 66.45, 117.04, 127.41, 127.50, 127.76, 127.89, 128.14, 135.57, 135.72, 139.65, 139.76, 174.89, 175.28, 176.90, 182.88, 183.04; HRMS calcd for $C_{26}H_{34}N_2O_3$: 422.2569; Found: 422.2569.

References and Notes

1. Director, University of Pittsburgh X-Ray Crystallography Laboratory.
2. National Institutes of Health Research Career Development Awardee, 1987-92.
3. (a) Grundmann, C.; Grünhanger, P. "The Nitrile Oxides," Springer-Verlag: NY, 1971. (b) Caramella, P.; Grünhanger, P. "1,3-Dipolar Cycloaddition Chemistry," Padwa, A., Ed., Wiley: NY, 1984.
4. Review of stereochemical aspects: Annunziata, R.; Cinquini, M.; Cozzi, F.; Raimondi, L. *Gazz. Chim. Ital.* **1989**, *119*, 253.
5. (a) Curran, D. P.; Kim, B. H.; Piyasena, H. P.; Loncharich, R. J.; Houk, K. N. *J. Org. Chem.* **1987**, *52*, 2137; (b) Olsson, T.; Stern, K.; Sundell, S. *J. Org. Chem.* **1988**, *53*, 2468. (c) Kanemasa, S.; Hayashi, T.; Yamamoto, H.; Wada, E.; Sakurai, T. *Bull. Chem. Soc. Jpn.* **1991**, *64*, 3274. (d) Kanemasa, S.; Onimura, K.; Wada, E.; Tanaka, J. *Tetrahedron-Asymmetry* **1991**, *2*, 1185. (e) Oppolzer, W.; Kingma, A. J.; Pillai, S. K. *Tetrahedron Lett.* **1991**, *32*, 4893. (f) deLange, B.; Feringa, B. *Tetrahedron Lett.* **1988**, *29*, 5317.
6. (a) Curran, D. P. "Advances in Cycloaddition", JAI: Greenwich, CN, 1988, p129. (b) Jäger, V.; Grund, H.; Franz, R.; Ehrler, R. *Lect. Heterocyc. Chem.* **1985**, *8*, 79. (c) Kozikowski, A. P. *Acc. Chem. Res.* **1984**, *17*, 410. (d) Torssell, K. B. G. "Nitrile Oxides, Nitrones and Nitronates in Organic Synthesis", VCH: New York, 1988.
7. (a) Zhang, J. C.; Curran, D. P. *J. Chem. Soc., Perkin Trans. I* **1991**, 2627. (b) Curran, D. P.; Zhang, J. C *Ibid.* **1991**, 2613. (c) Curran, D. P.; Heffner, T. A. *J. Org. Chem.* **1990**, *55*, 4585.
8. Kim, B. H.; Curran, D. P. *Tetrahedron* **1993**, *49*, 293.
9. (a) Curran, D. P.; Jeong, K. S.; Heffner, T. A.; Rebek, J. J. *J. Am. Chem. Soc.* **1989**, *111*, 9238. (b) Stack, J. G.; Curran, D. P.; Rebek, J.; Ballester, P. *J. Am. Chem. Soc.* **1991**, *113*, 5918. (c) K. S. Jeong, unpublished results, University of Pittsburgh. (d) P. Ballester, unpublished results, University of Pittsburgh. (e) T. A. Heffner, Master's Thesis, University of Pittsburgh, 1990.
10. Askew, B.; Ballester, P.; Buhr, C.; Jeong, K. S.; Jones, S.; Paris, K.; Williams, K.; Rebek, J., Jr. *J. Am. Chem. Soc.* **1989**, *111*, 1082.
11. Some of these results have been communicated in reference 9a.
12. (a) Potin, D.; Williams, K.; Rebek, J., Jr. *Angew. Chem., Int. Ed. Eng.* **1990**, *29*, 1420. (b) Jeong, K.-S.; Parris, K.; Ballester, P.; Rebek, J., Jr. *Angew. Chem., Int. Ed. Eng.* **1990**, *29*, 555.
13. Evans, D. A.; Chapman, K. T.; Bisaka, J. *J. Am. Chem. Soc.* **1988**, *110*, 1238.
14. Colvin, E. W.; Beck, A. K.; Bastani, B.; Seebach, D.; Kai, Y.; Dunitz, J. D. *Helv. Chim. Acta.* **1980**, *63*, 697.
15. Padwa, A.; Dent, W. *J. Org. Chem.* **1987**, *52*, 235.
16. Terao, Y.; Kotaki, H.; Imai, N.; Achiwa, K. *Chem. Pharm. Bull.* **1985**, *33*, 2762.
17. Curran, D. P.; Chen, M.-H. *J. Am. Chem. Soc.* **1987**, *109*, 6558.
18. Keck, G. E.; Enholm, E. J.; Yates, J. B.; Wiley, M. R. *Tetrahedron* **1985**, *41*, 4079.
19. Whitesell, J. K. *Chem. Rev.* **1989**, *89*, 1581.