dideuteriocyclohexane (based on $AlCl_2$).

Reaction of Bromobenzene with Aluminum and Aluminum Trichloride. Bromobenzene (22 mmol) was added to a slurry of aluminum dichloride (74 mmol obtained by $AlCl_3$ + K) in xylene. After the solution was stirred for 10 h at 100 °C, the solvent was removed by vacuum and the slurry was quenched with 10% HCl. The GC analysis of the products showed benzene (55%) and unreacted bromobenzene (40%).

Reaction of Dimethyl Ether with Aluminum and Aluminum Trichloride. Into a 200-mL Monel autoclave was charged the reaction product of aluminum trichloride (110 mmol) and aluminum (60 mmol) in 30 mL of xylene under argon. A total of 10 mL of dimethyl ether was then added at −30 °C; the vessel was closed and heated from 70 to 190 °C for 3 h. The autoclave was then cooled, and the product (obtained by hydrolysis) was analyzed by GC–MS showing methane (31%), methyl chloride (29%), and unreacted dimethyl ether (39%) with traces of ethane and butane.

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Registry No. 8 (X = Cl), 59534-55-3; 9 (X = Cl), 95465-40-0; 9 (X = Br), 113749-58-9; $AlCl_3$, 7446-70-0; $AlBr_3$, 7727-15-3; Cl_2, 7782-50-5; Al_2Cl_4, 12330-29-9; $AlCl_2$, 16603-84-2; $CH_2{=}CH_2$, 74-85-1; CH_3CH_3, 74-84-0; $CH_3CH(HgCl)_2$, 32823-01-1; $EtAlCl_2$, 563-43-9; CH_3Cl, 74-87-3; CH_3AlCl_2, 917-65-7; CO_2, 124-38-9; Et_3Al, 97-93-8; C_6H_5Br, 108-86-1; CH_3OCH_3, 115-10-6; CH_4, 74-82-8; $HgCl_2$, 7487-94-7; HCl, 7647-01-0; $Al_2(i\text{-}Bu)_4$, 60253-71-6; AlCl, 13595-81-8; Et_2AlCl, 93-10-6; Al, 7429-90-5; K, 7440-09-7; methylmalonic acid, 516-05-2; cyclohexene, 110-83-8; cyclohexane, 110-82-7; sodium acetate, 127-09-3.

4-Oxazoline Route to Stabilized Azomethine Ylides. Controlled Reduction of Oxazolium Salts

E. Vedejs* and J. W. Grissom

Contribution from S. M. McElvain Laboratory of Organic Chemistry, Department of Chemistry, University of Wisconsin, Madison, Wisconsin 53706. *Received September 3, 1987*

Abstract: Treatment of oxazolium salts with phenylsilane/CsF generates 4-oxazolines **14** in situ. Provided that R_4 = H or alkoxy, ring opening to azomethine ylides **15** occurs spontaneously and [2 + 3] cycloadducts are obtained in the presence of acrylate, *N*-phenylmaleimide, propiolate, or dimethyl acetylenedicarboxylate (DMAD) dipolarophiles. If R_5 = alkyl or aryl, the initially formed 4-oxazoline resists ring opening, probably due to steric interactions in the dipole, and affords products **30** derived from 2 + 2 trapping with DMAD. In typical cases, the [2 + 3] cycloadducts are formed with geometry corresponding to the trapping of the S-dipole **15** to the exclusion of other dipole isomers. Pyrolysis of analogous *N*-methylaziridines results in an equilibrated dipole, although the major adduct also corresponds to the trapping of **15**. Dipole trapping with phenyl vinyl sulfone is also possible, and reductive desulfonylation with sodium amalgam affords the adduct **41**, which corresponds to the adduct of the stabilized azomethine ylide with ethylene. Overall, the oxazolium salt reduction provides access to a large variety of azomethine ylides stabilized by acyl, ester, benzoyl, and formyl substituents. The dipoles can be generated and trapped at room temperature or below.

Azomethine ylides have been extensively studied since the 1965 discovery that they can be generated by pyrolysis of aziridines. The reaction of 1,2,3-triphenylaziridine with electron-deficient olefins or acetylenes to yield five-membered nitrogen rings was reported by Heine and Peavey,[1a] and similar independent findings were described by Padwa and Hamilton[1b] and by Huisgen, Scheer, Szeimies, and Huber.[1c] Due to the systematic investigations by Huisgen et al., it is now well known that thermolysis of 1-phenyl-2,3-dicarbomethoxyaziridine involves conrotatory ring opening to the carbonyl-stabilized ylides **3** or **4**.[2] Trapping products of the S-dipole **3** are obtained from the cis aziridine **1**, while adducts of the isomeric W-dipole **4** result from the trans aziridine **2**. The S-dipole **3** is trapped by several dipolarophiles without loss of dipole geometry. In contrast, the W-dipole **4** reacts cleanly only with the most reactive of traps such as dimethyl acetylenedicarboxylate (DMAD). With less reactive dipolarophiles (fumarate and norbornene), products derived from the S-dipole **3** are also observed due to dipole interconversion. These topics have been extensively reviewed, and the concepts have been extended to nonstabilized azomethine ylides.[3-9]

Many other examples of aziridine thermolysis have been reported in the literature.[10-18] The mechanism of dipole trapping

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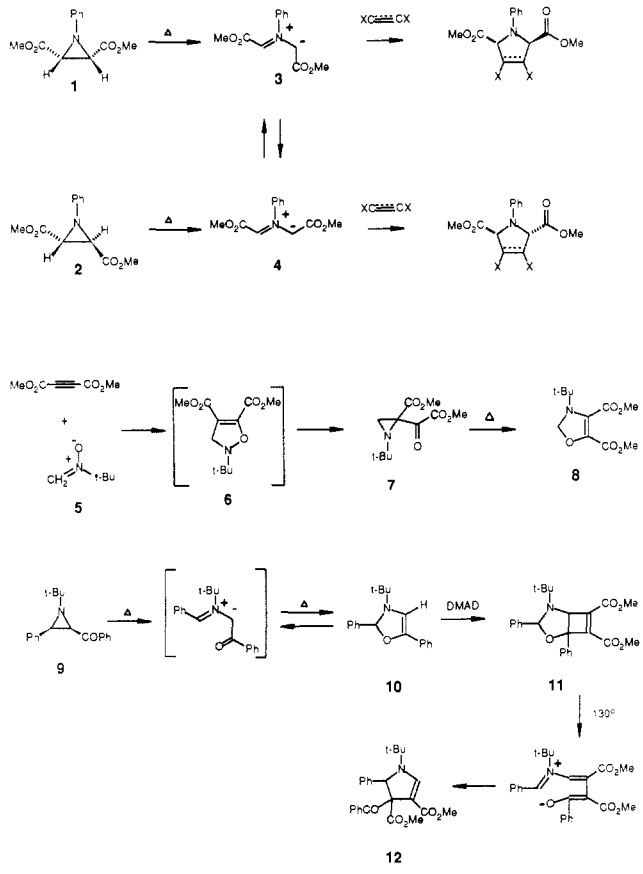


Figure 1.

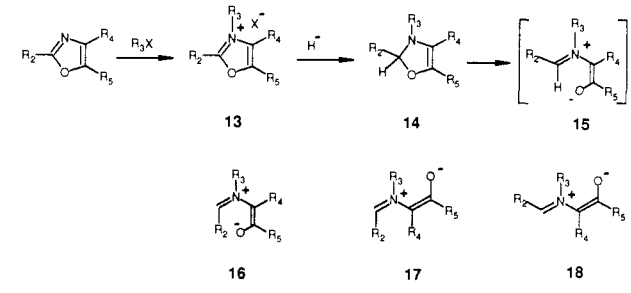
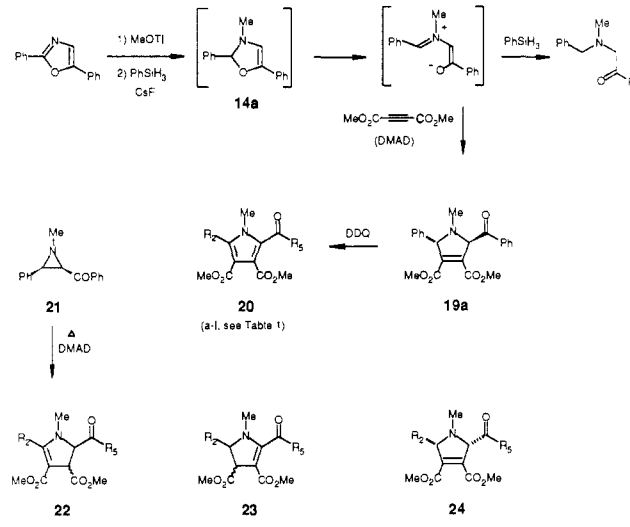


Figure 2.

Scheme I



is generally described as an asynchronous cycloaddition,[3b,20] although alternative interpretations have been proposed.[19] The *N*-arylaziridines have been investigated most intensively,[12-14] but *N*-alkyl,[15-18] *N*-H,[10] and *N*-acyl[11] derivatives have also been encountered. Other routes to stabilized azomethines include the thermolysis of benzaldimines,[21] the related method of thermal *N*-alkylamino ester/aldehyde condensation,[22,23] iminium salt deprotonation or desilylation,[24,25] or carbene insertion into an imine nitrogen lone pair.[26]

While many of these techniques are synthetically useful, most suffer from some limitations. In particular, stabilized ylides that are substituted by an "enolizable" alkyl group can be troublesome. They have been generated from the thermolysis of aziridines, but the resulting ylides undergo proton transfer and intramolecular cyclization at the elevated temperatures required for their formation.[27-29]

A possible low-temperature alternative to the methods outlined above could involve the generation of an acyl-stabilized azomethine ylide from the valence bond tautomer 4-oxazoline. An example of the reverse reaction has been encountered in a study by Baldwin et al. (Figure 1).[30] The aziridine **7** (formed from the cycloadduct **6** between nitrone **5** and DMAD) is converted into the stable 4-oxazoline **8** upon further heating. Presumably, the rearrangement involves an intermediate azomethine ylide. There is also a realted example where the formation of 4-oxazoline **10** from the pyrolysis of aziridine **9** is indicated by the isolation of the [2 + 2] DMAD adduct **11** and its thermal rearrangement product **12**.[16c] The intermediate azomethine ylide in this case does not react by [2 + 3] cycloaddition with DMAD. In an earlier study, Texier et al. have obtained a 4-oxazoline from the thermolysis of a 5-acyltriazoline.[14a] Further heating of the oxazoline in the presence of DMAD affords a pyrroline via the azomethine ylide. This is the only prior example where a 4-oxazoline has been shown to give azomethine ylide trapping products, although 4-oxazolines have been isolated in other studies.[31,32]

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The relatively few stable 4-oxazolines cited in the literature are heavily substituted by electron-withdrawing groups, which stabilize the enamine double bond. It seemed likely that increasing the basicity of nitrogen by replacement of the stabilizing substituents by alkyl, phenyl, etc., would promote ring opening to the ylide. To test this proposition, a general method for synthesis of 4-oxazolines was required. This long-standing problem has been solved by the controlled reduction of oxazolium salts[33] with the $PhSiH_3/CsF$ reagent,[34] and the behavior of the resulting 4-oxazolines is the subject of this report.

Results

Several factors influenced the ultimate choice of the reducing agent for conversion of oxazolium salts into 4-oxazolines. A nucleophilic hydride donor was required that would not affect the 4-oxazoline or the iminium portion of the azomethine ylide **15** or its isomers **16–18** (Figure 2). These limitations rule out protic conditions and reducing agents having Lewis acid character. In order for this approach to succeed, either the oxazoline **14** must be stable under the reaction conditions or the azomethine ylide generated must undergo [2 + 3] cycloaddition faster than it can be reduced. If the product oxazoline is stable, the dipolarophile need not be present during the reduction step and could be added later. However, if the oxazoline spontaneously opens to the ylide, the dipolarophile would have to be present throughout. In this case, the reducing agent would have to reduce the oxazolium salt **13** selectively while leaving the dipolarophile intact. All of these conditions are satisfied by the silane/CsF reagent.

Treatment of *N*-methyl-2,5-diphenyloxazolium salt with sodium borohydride or with sodium cyanoborohydride under a variety of conditions produced *N*-methyl-*N*-phenacylbenzylamine as the major product. A similar experiment at room temperature with phenylsilane/cesium fluoride led to the same amine overreduction product (Scheme I) as before, indicating that ring opening of the 4-oxazoline **14a** was rapid in all cases. However, when the reduction was carried out in the presence of DMAD in deuteriated acetonitrile, NMR analysis of the crude product revealed the presence of the trans 3-pyrroline **19a**. The structure is clear from the large value (J = 7.5 Hz) observed for the long-range H_2–H_5 coupling that is characteristic of this ring system.[14c,15a] The issue of adduct stereochemistry will be discussed in the section dealing with dipole geometry.

Attempts to purify the 3-pyrroline **19a** were complicated by epimerization, double-bond isomerization, and aromatization, resulting in a mixture of 3-pyrrolines, 2-pyrrolines, and the pyrrole **20a**. Therefore, treatment of the crude reaction mixture with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) was performed to convert all of the cycloadduct-derived structures into the pyrrole **20a**. To obtain supporting evidence for the structural assignments, the same pyrrole was also made by the aziridine method. Thus, thermolysis of 1-methyl-*cis*-2-benzoyl-3-phenylaziridine (**21**)[35] at 100 °C in the presence of DMAD yielded the 2-pyrrolines **22a** (53%) and the pyrrole **20a** (47%). All of these products had been observed in the attempted purification of **19a** obtained via the oxazoline route. However, the sensitive 3-pyrroline **19a** did not survive the high-temperature conditions for azomethine ylide formation from the aziridine.

Due to the sensitivity of the initial adduct **19a**, the DDQ aromatization procedure was used routinely in optimization experiments. Despite some gas evolution from the silane/CsF reagent in acetonitrile, this solvent proved to be superior to ethers or halocarbons. Of the various silane reducing agents that were tried, phenylsilane gave the cleanest reactions and the highest yields of pyrrole **20a** (95%), although diphenylsilane (93%) and phenyldimethylsilane (60%) also led to the desired cycloadduct. No reduction was seen with tributyltin hydride in the absence of a catalyst, but both tributyltin hydride and triethoxysilane could act as marginally useful hydride donors in the presence of a fluoride source (<20% yield). Cesium fluoride was the anhydrous fluoride source of choice. The use of tris(dimethylamino)sulfonium difluorotrimethylsilicate (TASF) or tetrabutylammonium fluoride resulted in destruction of the silane. Further studies were therefore restricted to the $PhSiH_3/CsF$–CH_3CN conditions.

An attempt was made to observe the 4-oxazoline **14a** at low temperature (−40 °C) by NMR. The reduction of *N*-methyl-2,5-diphenyloxazolium salt in the presence of DMAD was carried out at −40 °C in deuteriated acetonitrile, but the spectrum (−35 °C probe) showed only the azomethine ylide derived adduct. Therefore, the 4-oxazoline opens to the dipole spontaneously even at this temperature. For preparative purposes, room-temperature reduction and trapping proved satisfactory, and these conditions were used without further optimization.

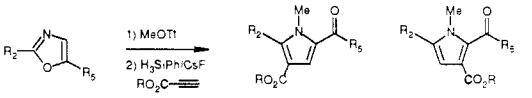
The standard conditions were applied to a variety of *N*-methyloxazolium salts. Cycloadducts with DMAD were routinely obtained in good to excellent yield after DDQ-induced aromatization to pyrroles. In several cases, reactions were run in deuteriated solvent, and the initially formed trans 3-pyrroline **19** was observed by NMR. However, **19** was usually not sufficiently stable for isolation, and exposure to air, or to silica gel, resulted in a complex mixture of the pyrrole **20** and epimerized or isomerized products **22–24**, all of which were converted into **20** by DDQ.

Examples of ylide trapping by propiolate or acrylate dipolarophiles are summarized in Table II and III. The sensitive propiolate adducts were converted directly into pyrroles by using the DDQ method, but the acrylate adducts were stable and could be isolated. In both the propiolate and acrylate series, mixtures

Table I. Dimethyl Acetylenedicarboxylate Trapping of **14**

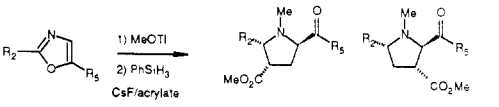
entry	R_2	R_5	yield of **20**, %
a	Ph	Ph	95
b	Ph	OEt	90
c	Ph	Me	93
d	Me	Ph	85
e	Me	OEt	64
f	H	Ph	74

Table II. Propionate Trapping of **14**



entry	R_2	R_5	R	isolated yields, %	
a	Ph	Ph	Et	40	10
b	Ph	OEt	Et	48	13
c	Ph	Me	Et	16	3
d	Me	Ph	Me	14	0
e	Me	OEt	Et	35	9
f	H	Ph	Et	6	21
g	H	OEt	Me	20	9

Table III. Acrylate Trapping of **14**



entry	R_2	R_5	isolated yield, %	
a	Ph	Ph	55	9
b	Ph	OEt	63	10
c	Ph	Me	87	0
d	Me	Ph	40	20
e	Me	OEt	61	0
f	H	Ph	0	67
g	H	OEt	47[a]	0
h	Ph	H	57	0

[a] 1.35:1 mixture of stereoisomers.

(33) Turchi, I. J. In *Oxazoles*; Turchi, I. J., Ed.; Wiley: New York, 1986; Chapter 1.
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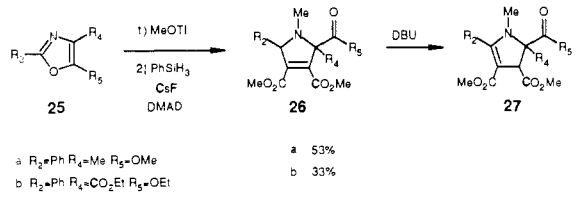
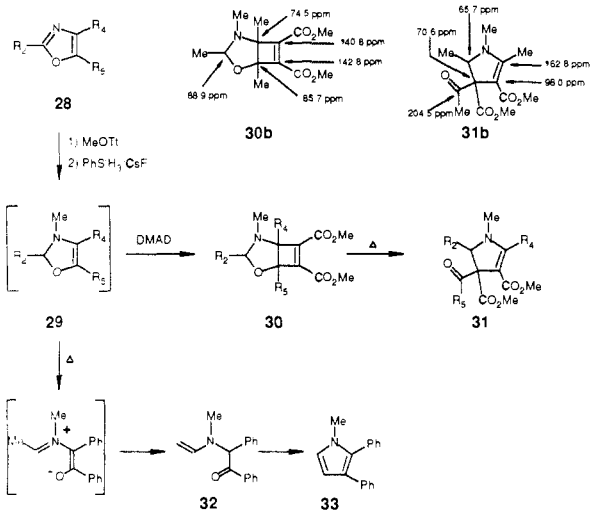
Scheme II



Scheme III



of regioisomers were obtained. Usually, there was a preference for the product having "meta" acyl or carboxyl groups, but this trend was lowest for the benzoyl-stabilized dipoles and in the exceptional case of entry f, the opposite orientation was observed. We have no explanation for this unusual regiochemistry. However, the other entries are consistent with the FMO approximation, assuming that the reactions are dipole HOMO controlled and that the largest dipole HOMO coefficient is at the acceptor-substituted carbon.[20] The regiochemical assignments are based on extensive NMR decoupling studies, and are confirmed for entry c, Table III, by an X-ray structure determination.

Inspection of Tables I–III indicates that benzoyl-, acetyl-, ester-, and even formyl-stabilized ylides can be successfully generated from the oxazolines. In the case of Table entries d and f, the alkylation/reduction procedure leads to azomethine ylides that have not been generated by any other method. Entry d demonstrates access to an alkyl-substituted dipole, which is sensitive to proton transfer as mentioned previously and which generally cannot be trapped from the aziridine method.[27-29] Other permissible dipole substituents on the iminium subunit include hydrogen or phenyl.

The oxazolium salt technique could also be applied to certain 2,4,5-trisubstituted oxazoles to generate a rare class of azomethine ylides that contain an alkyl substituent at the acyl-bearing dipole terminus. Methylation and reduction of 2-phenyl-4-methyl-5-methoxyoxazole (**25a**) in the presence of DMAD gave the stable 3-pyrroline **26a** in 53% yield as an inseparable 2:1 mixture of isomers, presumed to differ in stereochemistry (Scheme II). Subsequent treatment of **26a** with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) led to isomerization to yield the 2-pyrroline **27a** as a 1:1 mixture of diastereomers. The same procedure applied to 2-phenyl-4-carbethoxy-5-ethoxyoxazole (**25b**) yielded 3-pyrroline **26b** (33%), which could also be converted to the 2-pyrroline **27b** by DBU treatment. When less reactive dipolarophiles such as acrylate or maleimide were used, no [2 + 3] products were observed in either case.

The 2,4,5-trisubstituted oxazoles that contain an alkyl or aryl group at C_5 behaved differently than their C_5 alkoxy counterparts (Scheme III). Alkylation and reduction of oxazole **28b** in the presence of DMAD afforded a single product in good yield. This compound proved to be analogous to **11** (Figure 1) and is assigned the bicyclic structure **30b** on the basis of the ^{13}C NMR data.

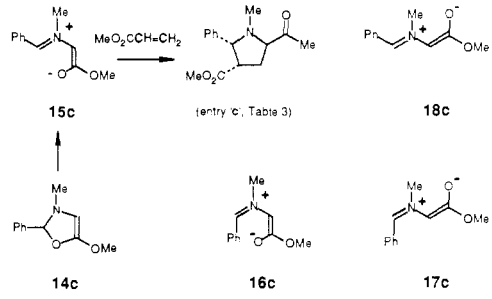


Figure 3.

Table IV

entry	R_2	R_4	R_5	yield of **30**, %	yield of **31**, %
a	Me	Ph	Ph	70	33
b	Me	Me	Me	82	63
c	Ph	Me	Ph	81	51

Although the proton NMR spectrum does not distinguish between bicyclic oxazolidine **30b** and the [2 + 3] adduct 3-pyrroline, the ^{13}C NMR data rules out the 3-pyrroline due to the obvious lack of a ketone (no signals below 167 ppm). The bicyclic **30b** results from the enamine [2 + 2] addition[36-38] between the initially formed oxazoline and DMAD. Upon heating to 130 °C, **30b** rearranged to a 2-pyrroline **31b**, presumably by the same process illustrated from **11** to **12** (Figure 1).[16c] Oxazoles **28a** and **28c** gave analogous [2 + 2] adducts, which also rearranged at 130 °C (Table IV).

Apparently, oxazolines **29** derived from the 2,4,5-trisubstituted oxazoles (where C_5 is not substituted by an alkoxy group) are resistant to ring opening. This fact suggests that **29** might be stable. When reductions were done without DMAD present, the oxazoline **29a** derived from 2-methyl-4,5-diphenyloxazole could indeed be observed in solution (^1H NMR, CD_3CN, CH_3CH, 5.02 ppm, q, J = 5.5 Hz), but the oxazolines **29b** and **29c** decomposed. No other observable 4-oxazolines were encountered in this study.

Upon being heated in methanol or toluene, **29a** was converted into the pyrrole **33a**. This transformation is a well-known reaction of azomethine ylides containing an "enolizable" α-hydrogen and involves proton transfer in the initially formed azomethine ylide followed by cyclization of the resulting enamine **32a** to the pyrrole.[27-29] Thermolysis of **29a** in a sealed tube in the presence of methyl acrylate also led to the pyrrole **33a**. Furthermore, methyl acrylate did not intercept azomethine ylides from **29b** or **29c** under the standard conditions for oxazoline formation nor did it afford recognizable adducts of the oxazolines. All of these observations indicate that those 4-oxazolines that can be trapped by DMAD in [2 + 2] additions correspond to short-lived azomethine ylide intermediates that are difficult to trap by intermolecular means.

We had expected that low-temperature generation of azomethine ylide intermediates from oxazolines would have major stereochemical advantages over the aziridine method. Although the familiar *N*-phenylaziridines can often produce cycloadducts derived from the conrotatory ring opening pathway, analogous *N*-alkylaziridines are far more sensitive to dipole equilibration. This fact has not always been recognized, but there are several examples of loss of aziridine stereochemistry at the adduct stage,[15,16] including a close analogue of entry e, Table III.[39,40] The results from the oxazoline method are highly significant in this context because the acrylate additions typically occur with high stereospecificity, and the geometry in the case of entry c, Table III, has been proven by X-ray analysis.[39] Similarities in the NMR spectra of the other entries in Table III argue for the same ste-

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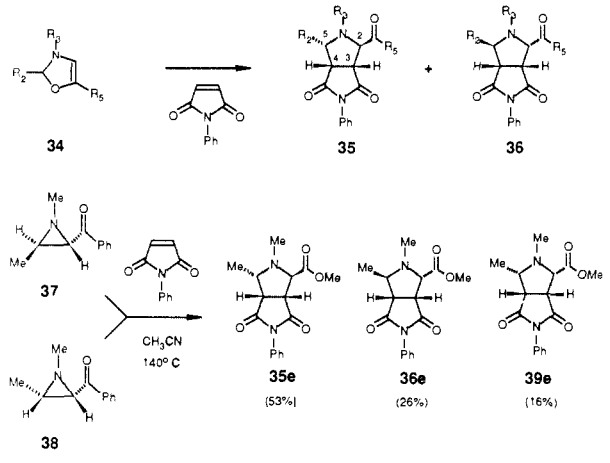
Table V

entry[a]	R_2	R_5	R_3	yield of 35,[b] %	yield of 36,[b] %	ratio 35/36[c]
a	Ph	Ph	Me	55	20	2.7:1
b[d]	Ph	Ph	Me	87	0	>50:1[d]
c	Ph	Ph	*i*-Pr	8	60	1:7.5
d	Ph	OEt	Me	27	36	1:1.3
e	Me	OMe	Me	42	36	1.2:1
f	H	Ph	Me	22	50	1:2.3
g	H	OEt	Me	40	16	2.5:1
h	CO_2Et	OEt	Me	43	0	>50:1

[a] All reactions were run in CH_3CN (except b) at 0.03 M concentration. [b] Isolated yields. [c] Ratios based on NMR analysis of crude reaction mixture. [d] Reaction in chloroform.

Scheme IV



reochemical preference in all cases, with the exception of entry g where a mixture was produced. The important question is whether or not the initial dipoles have been trapped prior to equilibration.

As shown below, a dipole substituted with a group at each terminus can exist in four possible geometries, neglecting enolate *E,Z* isomers, as in Figure 3. Assuming that formation of the U-dipole **16** is highly unfavorable on steric grounds,[41] an azomethine ylide derived from a 4-oxazoline must open to give the S-dipole **15**. The detailed adduct structure of entry c, Table III (X-ray), has trans C_2,C_5 stereochemistry, as expected from the kinetically controlled trapping of **15c** without equilibration. Furthermore, the geometry corresponds to approach of dipole and dipolarophile in an endo transition state.[34,15a]

There is a literature consensus that the azomethine S-dipoles are more likely to participate in [2 + 3] cycloadditions than either the U- or W-dipoles.[2a,15,16] Therefore, it is possible that the high stereoselectivity seen in Table III is the coincidental result of catalyzed interconversion of dipole isomers with selective formation of the product derived from the most reactive dipole. This subtlety cannot be resolved in the case of the acrylate adducts, but a comparison of oxazoline and aziridine *N*-phenylmaleimide dipole trapping experiments discussed below provides some evidence that the oxazoline method does indeed allow the stereospecific trapping of the initially formed dipole isomer.

The oxazolines **34** were generated as usual in the presence of *N*-phenylmaleimide to yield a mixture of the bicyclic pyrrolidines **35** and **36** (Scheme IV, Table V). In pyrrolidine **35** the $J_{H\text{-}3,H\text{-}4}$ and $J_{H\text{-}4,H\text{-}5}$ values are large (8–10 Hz) and are indicative of a cis arrangement. In contrast, the $J_{H\text{-}2,H\text{-}3}$ value is 0 Hz, which strongly suggests a trans configuration between C_2 and C_3. Pyrrolidine **36** contains H_2, H_3, and H_4 in a cis arrangement ($J_{H\text{-}2,H\text{-}3}$ and $J_{H\text{-}3,H\text{-}4}$ = 8–10 Hz) while the smaller $J_{H\text{-}4,H\text{-}5}$ value (4–5 Hz) suggests a trans configuration at C_4 and C_5.[13b,15,17] In general, all of the results are in accord with trapping of the initially formed S-dipole **15**, although the exo/endo ratios are variable.

The aziridine method for azomethine ylide generation has been used to study the reaction corresponding to entry e, Table V.[42]

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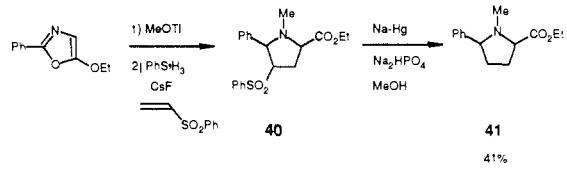

Figure 4.

The thermolysis of *cis*- or *trans*-1,3-dimethyl-2-carbomethoxyaziridine **37** or **38** in the presence of *N*-phenylmaleimide in acetonitrile affords a mixture of pyrrolidine products consisting of **35e**, **36e**, and **39e** (3.6:1.8:1) from either isomer. Since the aziridine experiment must be done at a different temperature compared to the oxazoline route, an unambiguous comparison of product ratios is not possible. However, the formation of the same product mixture from both aziridine isomers indicates dipole equilibration due to the elevated temperatures and high dielectric solvent. Since the aziridine thermolysis provides product **39e** (from cycloaddition of the W-dipole) while the oxazoline method does not, the difference can be attributed to dipole equilibration in the aziridine reaction. Provided that the relative rates of trapping of S- and W-dipoles do not change drastically with temperature, the absence of **39e** in the oxazoline experiment indicates that equilibration of the initially formed S-dipole **15** has not occurred. It should be noted that the aziridine-derived **35e** and **36e** could arise from a different S-dipole **17** than in the oxazoline reaction, but our evidence does not allow a distinction to be made.

Replacement of the *N*-methyl group by an *N*-isopropyl group was readily accomplished by alkylation of the oxazole with in situ generated isopropyl triflate. Reduction of *N*-isopropyl-2,5-diphenyloxazolium salt in the presence of *N*-phenylmaleimide gave a reversed pyrrolidine ratio compared to the *N*-methyl case (Table V, entry c, **35c/36c** = 1:7.5). A likely source for this product reversal is the steric bulk of the isopropyl group, which could interfere with the endo transition state. The tendency for an *N*-isopropyl ylide to prefer the exo transition state has been noted in the literature.[15] The other entries in Table V indicate that a delicate balance between exo and endo pathways is the rule, depending on steric factors.

In practice, stabilized azomethine ylide additions are restricted to electron-deficient dipolarophiles. However, synthetic applications often require the incorporation of simpler alkene fragments. In this connection (Figure 4), we have briefly examined trapping with the ethylene equivalent phenyl vinyl sulfone.[22b] Application of the typical reaction conditions to 2-phenyl-5-ethoxyoxazole in the presence of phenyl vinyl sulfone yielded the pyrrolidine sulfone adduct **40** as a mixture of stereoisomers, which was immediately subjected to sodium amalgam reduction conditions to yield the pyrrolidine **41**. The overall yield is modest (41%), but the procedure is not difficult, and synthetic applications should be feasible.

Conclusions

A comparison of the 4-oxazolines reported in the literature and encountered in this study allows some generalizations to be made regarding the effect of substitution on oxazoline ring opening to

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azomethine ylides. When R_4 = H, oxazoline ring cleavage to the azomethine ylide is usually rapid as evidenced by the formation of cycloadducts in the presence of suitable dipolarophiles. One known exception is the stable 2,2-bis(trifluoromethyl)-4-oxazoline.[32c] All of the other stable, *observable* oxazolines contain substituents at both the C_4 and C_5 positions. The Baldwin[30] and Texier[14a] oxazolines are also stabilized by electron-withdrawing groups while the only observable 4-oxazoline (**29a**) seen in the present study has $R_4 = R_5$ = Ph. These substituents favor the oxazoline because they reduce enamine nitrogen basicity and destabilize the dipole iminium subunit.

The 4-oxazolines that contain an alkyl and/or aryl group at both C_4 and C_5 are reluctant to undergo ring opening, and the corresponding azomethine ylides cannot be trapped. This is probably due to an unfavorable steric interaction between R_3, R_4, and R_5 in the more nearly planar ylide geometry and in the transition state for cycloaddition. In the presence of DMAD, the 4,5-disubstituted 4-oxazolines react as enamines to form cyclobutene adducts. The steric effects that destabilize the dipole can also be encountered in the aziridine method of azomethine ylide generation.[30,16c] The striking example of Figure 1 shows that aziridine pyrolysis in the presence of DMAD can result in [2 + 2] trapping of the 4-oxazoline isomer, even when the C_4 substituent is hydrogen.[16c] The steric effect of a *tert*-butyl group at nitrogen probably inhibits the conrotatory ring opening of aziridine **9** to the S-dipole **17**. The alternative conrotatory opening to S-dipole **15** provides a direct avenue to the 4-oxazoline **10**, and the formation of [2 + 2] products with DMAD is the result.

The 4-oxazolines which contain an alkoxy group at C_5 as well as a substituent at C_4 do not afford products of enamine [2 + 2] addition with DMAD. The examples where R_5 = OR and R_4 = Me or CO_2R readily open to azomethine ylides and react normally by [2 + 3] cycloaddition. Apparently, the alkoxy group is sufficiently compact that it does not inhibit ring opening of the oxazoline to the azomethine ylide.

With respect to synthetic potential, the major advantage of the oxazoline method is its ability to generate a wide variety of acyl-stabilized azomethine ylides at room temperature. Ylide stabilizing groups such as benzoyl, acetyl, carboalkoxy, and even formyl are all feasible. The other dipole terminus can have a variety of substituents, including hydrogen or alkyl groups, substituents that often interfere with thermal azomethine ylide generation. The method also allows generation and trapping of the S-dipole **15** with high stereospecificity in several examples, in contrast to high-temperature techniques where dipole equilibration in the *N*-alkyl series is the rule.

An oxazole is a relatively inert group that can be carried through a lengthy synthetic sequence and can subsequently be unleashed as an azomethine ylide by alkylation and reduction. Applications of this technique to more complex problems will be described in future publications.

Experimental Section

Proton nuclear magnetic resonance (NMR) spectra were obtained on a Bruker WP200 (200 MHz), WP270 (270 MHz), or AM500 (500 MHz) spectrometer. Chemical shifts are reported in parts per million (ppm) relative to solvent peak ($CDCl_3$ 7.24 ppm, CD_3CN 1.93 ppm and acetone-d_6 2.09). Infrared spectra (IR) were recorded with a Beckman Acculab 7 or a Mattson FT IR spectrometer and calibrated with a polystyrene peak (1601.8 cm^{-1}). Mass spectra were obtained on an MS-80 high-resolution mass spectrometer. Melting points were obtained on a hot stage microscope apparatus and are not corrected.

Column chromatography was performed with Kieselgel 60 flash silica gel. Solvents were dried as follows: diethyl ether (Et_2O), dioxane, tetrahydrofuran (THF), and glyme (dimethoxyethane) were distilled from sodium/benzophenone; halocarbons and hydrocarbons were distilled from calcium hydride; hexane and EtOAc for silica gel chromatography were flash distilled prior to use; acetonitrile was distilled first from CaH_2 then from P_2O_5. All reagents that are not referenced were obtained from Aldrich with the exception of phenylsilane, which was obtained from Petrarch. All 2-substituted 5-alkoxyoxazoles were made by the method of Cornforth.[43] Other oxazoles were made by the following literature procedures: 2-methyl-5-phenyloxazole,[44] 2-phenyl-5-methyloxazole,[44] 5-phenyloxazole,[45] 5-ethoxyoxazole,[46] 2,5-diphenyl-4-methyloxazole,[47] and 2-phenyloxazole.[48]

Anhydrous reactions were carried out under a N_2 atmosphere. Anhydrous cesium fluoride was prepared by flame drying under vacuum, taking care not to fuse the salt.

Alkylation and Reduction of 2,5-Disubstituted Oxazoles in the Presence of DMAD and Subsequent DDQ Oxidation: Scheme I and Table I Results. Methyl triflate (0.028 mL, 0.249 mmol) was added to a solution of the oxazole (0.226 mmol) in 2 mL of acetonitrile. After the mixture was stirred for 2 h at room temperature, phenylsilane (distilled from CaH_2; 0.049 mL, 0.339 mmol) and dimethyl acetylenedicarboxylate (DMAD; 0.083 mL, 0.678 mmol) were added, and the mixture was transferred by cannula to anhydrous cesium fluoride (0.069 g, 0.452 mmol) in acetonitrile (4 mL). After the mixture was stirred vigorously for 2 h at ambient temperature, the solvent was removed (rotary evaporator) to leave a residue, which was purified by passage through a plug of silica gel (5:4 hexane/EtOAc). The resultant oil was dissolved in 5 mL of dioxane, 2,3-dichloro-5,6-dicyano-1,4-benzophenone (DDQ; 0.056 g, 0.249 mmol) was added, and the reaction was refluxed for 12 h. The reaction mixture was poured into ethyl acetate (20 mL) and extracted with 1 M KOH (3 × 20 mL). The organic layer was dried (MgSO4), and the solvent was removed (rotary evaporator) to leave the pyrrole, which was purified on a silica gel column. The products from the alkylation and reduction of 2,5-diphenyloxazole were observed in solution and isolated by silica gel chromatography prior to DDQ oxidation.

1. Entry a. Product analysis prior to chromatography indicated the presence of 3-pyrroline **19a**: sample observed by NMR without isolation; formula $C_{22}H_{21}O_5N$; IR ($CDCl_3$, cm^{-1}) 1680 (C=O), 1722 (C=O), 1735 (C=O); 270-MHz NMR (CD_3CN) δ 8.09–7.24 (10 H, m), 5.89 (1 H, d, J = 5.7 Hz), 5.22 (1 H, d, J = 5.7 Hz), 3.55 (3 H, s), 3.54 (3 H, s), 2.14 (3 H, s); after exposure to silica gel, 3-pyrroline **24a** could be detected, but this also decomposed upon attempted purification. **24a**: IR ($CDCl_3$, cm^{-1}) 1735 (C=O), 1722 (C=O), 1680 (C=O); 270-MHz NMR ($CDCl_3$) δ 8.09–7.24 (10 H, m), 4.91 (1 H, d, J = 4.9 Hz), 4.84 (1 H, d, J = 4.9 Hz), 3.55 (3 H, s), 3.54 (3 H, s), 2.12 (3 H, s). Chromtography as described above gave the following isolable products. 2-Pyrroline **22a**: oil; separated on flash silica gel Kieselgel 60, 5:4 hexane/EtOAC, R_f 0.40; IR ($CDCl_3$, cm^{-1}) 1730 (C=O), 1689 (C=O), 1674 (C=O); 270-MHz NMR ($CDCl_3$) δ 7.82–7.53 (2 H, m), 7.65–7.31 (8 H, m), 4.82 (1 H, d, J = 7.5 Hz), 3.95 (1 H, d, J = 7.5 Hz), 3.79 (3 H, s), 3.39 (3 H, s), 2.54 (3 H, s). 2-Pyrroline **22a'**: oil; separated on flash silica gel Kieselgel 60, 5:4 hexane/EtOAc, R_f 0.47; IR ($CDCl_3$, cm^{-1}) 1721 (C=O), 1719 (C=O), 1680 (C=O); 270-MHz NMR ($CDCl_3$) δ 7.82–7.78 (2 H, m), 7.51–7.3 (8 H, m), 4.93 (1 H, d, J = 12.1 Hz), 4.24 (1 H, d, J = 12.1 Hz), 3.42 (3 H, s), 3.17 (3 H, s), 2.48 (3 H, s). Prolonged manipulation of the mixture resulted in the accumulation of pyrrole **20a**, which was stable. Treatment of the mixture with DDQ as described above gave pyrrole **20a** (0.081 g, 0.215 mmol, 95%): oil; separated on flash silica gel Kieselgel 60, 5:2 hexane/EtOAc, R_f 0.24; exact mass calcd for $C_{22}H_{19}O_5N$ 377.1258, found 377.1258, error 0 ppm; IR ($CDCl_3$, cm^{-1}) 1710 (C=O), 1730 (C=O), 1740 (C=O); 200-MHz NMR (acetone-d_6) δ 7.8–7.45 (10 H, m), 3.57 (3 H, s), 3.53 (3 H, s), 3.23 (3 H, s).

2. Entry b. Pyrrole **20b** (0.048 g, 0.165 mmol, 73%): oil; separated on flash silica gel Kieselgel 60, 5:2 hexane/EtOAc, R_f 0.24; exact mass calcd for $C_{18}H_{19}O_6N$ 345.1207, found 345.1179, error 8.1 ppm; IR ($CDCl_3$, cm^{-1}) 1738 (C=O), 1720 (C=O), 1700 (C=O); 270-MHz NMR ($CDCl_3$) δ 7.49–7.4 (3 H, m), 7.3–7.22 (2 H, m), 4.29 (2 H, q, J = 6.7 Hz), 3.92 (3 H, s), 3.63 (3 H, s), 3.57 (3 H, s), 1.33 (3 H, d, J = 6.7 Hz).

3. Entry c. Pyrrole **20c** (0.064 g, 0.203 mmol, 90%): oil; separated on flash silica gel Kieselgel 60, 5:2 hexane/EtOAc, R_f 0.37; exact mass calcd for $C_{17}H_{17}O_5N$ 315.1102, found 315.1112, error 3.1 ppm; IR ($CDCl_3$, cm^{-1}) 1740 (C=O), 1732 (C=O), 1710 (C=O); 200-MHz NMR ($CDCl_3$) δ 7.69–7.17 (5 H, m), 3.77 (3 H, s), 3.59 (3 H, s), 3.56 (3 H, s), 2.43 (3 H, s).

4. Entry d. Pyrrole **20d** (0.0605 g, 0.192 mmol, 85%): oil; separated on flash silica gel Kieselgel 60, 5:2 hexane/EtOAc, R_f 0.16; exact mass calcd for $C_{17}H_{17}O_5N$ 315.1102, found 315.1098, error 1.4 ppm; IR ($CDCl_3$, cm^{-1}) 1740 (C=O), 1700 (C=O); 270-MHz NMR ($CDCl_3$)

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δ 7.74–7.36 (5 H, m), 3.75 (3 H, s), 3.72 (3 H, s), 3.15 (3 H, s), 2.54 (3 H, s).

5. Entry e. Pyrrole **20e** (0.041 g, 0.145 mmol, 64%): oil; separated on flash silica gel Kieselgel 60, 5:4 hexane/EtOAc, R_f 0.22; exact mass calcd for $C_{13}H_{17}O_6N$ 283.1051, found 283.1057, error 2.2 ppm; IR ($CDCl_3$, cm^{-1}) 1730 (C=O), 1718 (C=O), 1690 (C=O); 200-MHz NMR ($CDCl_3$) δ 4.24 (2 H, q, J = 7.2 Hz), 3.87 (3 H, s), 3.82 (3 H, s), 3.76 (3 H, s), 2.52 (3 H, s), 1.29 (3 H, t, J = 7.2 Hz).

6. Entry f. Pyrrole **20f** (0.050 g, 0.167 mmol, 74%): oil; separated on flash silica gel Kieselgel 60, 5:2 hexane/EtOAc, R_f 0.08; exact mass calcd for $C_{16}H_{15}O_5N$ 301.0946, found 301.0951, error 1.6 ppm; IR ($CDCl_3$, cm^{-1}) 1735 (C=O), 1719 (C=O), 1710 (C=O); 270-MHz NMR ($CDCl_3$) δ 7.75–7.7 (2 H, m), 7.58–7.37 (4 H, m), 3.85 (3 H, s), 3.79 (3 H, s), 3.2 (3 H, s).

Alkylation and Reduction of Oxazoles in the Presence of Propiolate and Subsequent DDQ Oxidation. Table II Results. The procedure was repeated as described above except that propiolate (methyl or ethyl, 0.678 mmol) was used as the dipolarophile.

1. Entry a. Major pyrrole (0.030 g, 0.090 mmol, 40%): oil; analytical TLC (silica gel F254), 5:4 hexane/EtOAc, R_f 0.50; exact mass calcd for $C_{21}H_{19}O_3N$ 333.130, found 333.136, error 18 ppm; IR ($CDCl_3$ cm^{-1}) 1710 (C=O), 1695 (C=O); 270-MHz NMR ($CDCl_3$) δ 7.91–7.84 (2 H, m), 7.62–7.36 (8 H, m), 7.26 (1 H, s), 4.10 (2 H, q, J = 7.1 Hz), 3.79 (3 H, s), 1.15 (3 H, t, J = 7.1 Hz).

Minor pyrrole (0.008 g, 0.023 mmol, 10%): oil; analytical TLC (silica gel F254), 5:4 hexane/EtOAc, R_f 0.5; exact mass calcd for $C_{21}H_{19}O_3N$ 333.136, found 333.13, error 18 ppm; IR ($CDCl_3$, cm^{-1}) 1710 (C=O), 1695 (C=O); 270-MHz NMR ($CDCl_3$) δ 7.91–7.84 (2 H, m), 7.62–7.36 (8 H, m), 6.67 (1 H, s), 3.87 (2 H, q, J = 7.1 Hz), 3.66 (3 H, s), 0.86 (3 H, t, J = 7.1 Hz).

2. Entry b. Major pyrrole (0.033 g, 0.108 mmol, 48%): solid; mp 76–77 °C (crystallized from hexane); exact mass calcd for $C_{17}H_{19}O_4N$ 301.1309, found 301.1322, error 4.3 ppm; IR (CH_2Cl_2, cm^{-1}) 1706 (C=O); 270-MHz NMR ($CDCl_3$) δ 7.50–7.40 (4 H, m), 7.36–7.25 (2 H, m), 4.30 (2 H, q, J = 7.1 Hz), 4.08 (2 H, q, J = 7.1 Hz), 3.68 (3 H, s), 1.36 (3 H, t, J = 7.1 Hz), 1.10 (3 H, t, J = 7.1 Hz).

Minor pyrrole (0.009 g, 0.029 mmol, 13%): oil; flash silica gel Kieselgel 60, 5:2 hexane/EtOAc, R_f 0.37; exact mass calcd for $C_{17}H_{19}O_4N$ 301.1309, found 301.1249, error 20 ppm; IR (CH_2Cl_2, cm^{-1}) 1715 (C=O), 1705 (C=O); 270-MHz NMR ($CDCl_3$) δ 7.45–7.32 (5 H, m), 6.49 (1 H, s), 4.35 (2 H, q, J = 7.1 Hz), 4.29 (2 H, q, J = 7.1 Hz), 3.71 (3 H, s), 1.35 (3 H, t, J = 7.1 Hz), 1.33 (3 H, t, J = 7.1 Hz).

3. Entry c. Major pyrrole (0.010 g, 0.036 mmol, 16%): oil; analytical TLC (silica gel F254), 5:2 hexane/EtOAc, R_f 0.38; exact mass calcd for $C_{16}H_{17}O_3N$ 271.1204, found 271.1208, 1.4 ppm; IR (CH_2Cl_2, cm^{-1}) 1709 (C=O), 1698 (C=O); 200-MHz NMR ($CDCl_3$) δ 7.48 (1 H, s), 7.46–7.25 (5 H, m), 4.09 (2 H, q, J = 7 Hz), 3.68 (3 H, s), 2.46 (3 H, s), 1.09 (3 H, t, J = 7 Hz).

Minor pyrrole (0.002 g, 0.007 mmol, 3%): oil; analytical TLC (silica gel F254), 5:1 hexane/EtOAc, R_f 0.20; exact mass calcd for $C_{16}H_{17}O_3N$ 271.1204, found 271.1195, error 3.4 ppm; IR (CH_2Cl_2, cm^{-1}) 1720 (C=O), 1705 (C=O); 270-MHz NMR ($CDCl_3$) δ 7.49–7.29 (5 H, m), 6.56 (1 H, s), 4.32 (2 H, q, J = 7.1 Hz), 3.65 (3 H, s), 2.63 (3 H, s), 1.35 (3 H, t, J = 7.1 Hz).

4. Entry d. Pyrrole (0.008 g, 0.032 mmol, 14%): oil; flash silica gel Kieselgel 60, 5:4 hexane/EtOAc, R_f 0.54; exact mass calcd for $C_{15}H_{15}O_3N$ 257.1048, found 257.1047, error 0.4 ppm; IR (CH_2Cl_2, cm^{-1}) 1710 (C=O), 1640 (C=O); 200-MHz NMR ($CDCl_3$) δ 7.76–7.65 (2 H, m), 7.60–7.31 (3 H, m), 7.08 (1 H, s), 3.92 (3 H, s), 3.80 (3 H, s), 2.62 (3 H, s).

5. Entry e. Major pyrrole (0.019 g, 0.079 mmol, 35%): oil; analytical TLC (silica gel F254), 5:4 hexane/EtOAc, R_f 0.62; exact mass calcd for $C_{12}H_{17}O_4N$ 239.1153, found 239.1151, error 0.8 ppm; IR (CH_2Cl_2, cm^{-1}) 1690 (C=O), 1712 (C=O); 270-MHz NMR ($CDCl_3$) δ 7.31 (1 H, s), 4.24 (4 H, q, J = 7.1 Hz), 3.82 (3 H, s), 2.52 (3 H, s), 1.31 (6 H, t, J = 7.1 Hz).

Minor pyrrole (0.012 g, 0.047 mmol, 9%): oil; analytical TLC (silica gel F254), 5:4 hexane/EtOAc, R_f 0.45; exact mass calcd for $C_{12}H_{17}O_4N$ 239.1153, found 239.1151, error 0.8 ppm; IR (CH_2Cl_2, cm^{-1}) 1726 (C=O), 1705 (C=O); 270-MHz NMR ($CDCl_3$) δ 6.21 (1 H, s), 4.35–4.09 (4 H, m), 3.78 (3 H, s), 2.20 (3 H, s), 1.40–1.08 (6 H, m).

6. Entry f. Minor pyrrole (0.004 g, 0.013 mmol, 6%): oil; flash silica gel Kieselgel 60, 5:4 hexane/EtOAc, R_f 0.67; exact mass calcd for $C_{15}H_{15}O_3N$ 257.1048, found 257.1055, error 2.7 ppm; IR ($CDCl_3$, cm^{-1}) 1712 (C=O), 1640 (C=O); 270-MHz NMR ($CDCl_3$) δ 7.83–7.76 (2 H, m), 7.58–7.38 (4 H, m), 7.12 (1 H, d, J = 1.6 Hz), 4.26 (2 H, q, J = 7.1 Hz), 4.03 (3 H, s), 1.30 (3 H, t, J = 7.1 Hz).

Major pyrrole (0.012 g, 0.047 mmol, 21%): oil; flash silica gel Kieselgel 60, 5:4 hexane/EtOAc, R_f 0.67; exact mass calcd for $C_{15}H_{15}O_3N$ 257.1048, found 257.1055, error 2.7 ppm; IR ($CDCl_3$, cm^{-1}) 1712 (C=O), 1640 (C=O); 270-MHz NMR ($CDCl_3$) δ 7.83–7.76 (2 H, m), 7.58–7.38 (3 H, m), 6.73 (1 H, d, J = 2.8 Hz), 6.62 (1 H, d, J = 2.8 Hz), 3.77 (2 H, q, J = 6.7 Hz), 3.71 (3 H, s), 0.78 (3 H, t, J = 6.7 Hz).

7. Entry g. Major pyrrole (0.010 g, 0.045 mmol, 20%): solid; mp 79–80 °C (crystallized from hexane); exact mass calcd for $C_{10}H_{13}O_4N$ 211.0841, found 211.0852, error 5.3 ppm; IR (CH_2Cl_2, cm^{-1}) 1700 (C=O); 270-MHz NMR (C_2D_6CO) δ 7.56 (1 H, d, J = 1.9 Hz), 7.18 (1 H, d, J = 1.9 Hz), 4.25 (2 H, q, J = 7.1 Hz), 3.95 (3 H, s), 3.73 (3 H, s), 1.31 (3 H, t, J = 7.1 Hz).

Minor pyrrole (0.004 g, 0.020 mmol, 9%): oil; flash silica gel Kieselgel 60, 5:2 hexane/EtOAc, R_f 0.35; exact mass calcd for $C_{10}H_{13}O_4N$ 211.0841, found 211.0841, error 0.1 ppm; IR (CH_2Cl_2, cm^{-1}) 1700 (C=O), 1710 (C=O); 200-MHz NMR (C_2D_6CO) δ 6.89 (1 H, d, J = 2.7 Hz), 6.39 (1 H, d, J = 2.7 Hz), 4.28 (2 H, q, J = 6.8 Hz), 3.81 (3 H, s), 3.73 (3 H, s), 1.30 (3 H, t, J = 6.8 Hz).

Alkylation and Reduction of Oxazoles in the Presence of Acrylate. Table III Results. Methyl triflate (0.028 mL, 0.249 mmol) was added to a solution of the oxazole (0.226 mmol) in 2 mL of acetonitrile. After the mixture was stirred for 2 h at room temperature, phenylsilane (distilled from CaH_2; 0.049 mL, 0.339 mmol) and methyl acrylate (0.061 mL, 0.678 mmol) were added, and the mixture transferred by cannula to anhydrous cesium fluoride (0.069 g, 0.452 mmol) in acetonitrile (4 mL). After the mixture was vigorously stirred for 2 h at ambient temperature, the solvent was removed (rotary evaporator), and the resultant residue was purified by silica gel chromatography. The details are given in each individual case as follows.

1. Entry a. Major pyrrolidine (0.040 g, 0.124 mmol, 55%): oil; separated on flash silica gel Kieselgel 60, 5:2 hexane/EtOAc, R_f 0.41; exact mass calcd for $C_{20}H_{21}O_3N$ 323.1516, found 323.1574, error 17.9 ppm; IR ($CDCl_3$, cm^{-1}) 1690 (C=O), 1740 (C=O); 200-MHz NMR ($CDCl_3$) δ 8.01–7.26 (10 H, m), 4.98 (1 H, dd, J = 8.8, 1.5 Hz), 4.64 (1 H, d, J = 10 Hz), 3.56 (1 H, q, J = 9.4 Hz), 3.04 (3 H, s), 2.88 (1 H, dt, J = 12.9, 9.1 Hz), 2.26 (3 H, s), 2–1.93 (1 H, m).

Minor pyrrolidine (0.007 g, 0.020 mmol, 9%): oil; flash silica gel Kieselgel 60, 5:2 hexane/EtOAc, R_f 0.43; exact mass calcd for $C_{20}H_{21}O_3N$ 323.1516, found 323.1572, error 17.3 ppm; IR (CH_2Cl_2, cm^{-1}) 1730 (C=O), 1685 (C=O); 200-MHz NMR ($CDCl_3$) δ 8.13–8.01 (2 H, m), 7.63–7.23 (8 H, m), 5.38 (1 H, d, J = 3.2 Hz), 4.33 (1 H, dd, J = 8.2, 7.9 Hz), 3.75 (3 H, s), 3.13 (1 H, ddd, J = 9.5, 5.3, 3.2 Hz), 2.63 (1 H, ddd, J = 13.1, 9.5, 7.9 Hz), 2.35–2.15 (1 H, m), 2.21 (3 H, s).

2. Entry b. Major pyrrolidine (0.041 g, 0.142 mmol, 63%): oil; separated on flash silica gel Kieselgel 60, 5:1 hexane/EtOAc, R_f 0.50; exact mass calcd for $C_{16}H_{21}O_4N$ 291.1465, found 291.1439, error 9 ppm; IR ($CDCl_3$, cm^{-1}) 1740 (C=O), 1720 (C=O); 270-MHz NMR ($CDCl_3$) δ 7.27–7.18 (5 H, m), 4.38 (1 H, d, J = 9.8 Hz), 4.18 (2 H, q, J = 7.1 Hz), 3.97 (1 H, dd, J = 8, 1.3 Hz), 3.61 (1 H, q, J = 9.8 Hz), 3.04 (3 H, s), 2.71 (1 H, ddd, J = 13, 8, 9.8 Hz), 2.24 (3 H, s), 2.03 (1 H, ddd, J = 13.0, 9.8, 1.3 Hz), 1.28 (3 H, t, J = 7.1 Hz).

Minor pyrrolidine (0.007 g, 0.0226 mmol, 10%): oil; flash silica gel Kieselgel 60, 5:2 hexane/EtOAc, R_f 0.33; exact mass calcd for $C_{16}H_{21}O_4N$ 291.1465, found 291.1483, error 6.1 ppm; IR (CH_2Cl_2, cm^{-1}) 1725 (C=O), 1730 (C=O); 270-MHz NMR ($CDCl_3$) δ 7.37–7.18 (5 H, m), 4.24 (1 H, d, J = 7.3 Hz), 4.14 (2 H, q, J = 7.1 Hz), 3.86 (1 H, dd, J = 8.3, 2.1 Hz), 3.59 (3 H, s), 2.89 (1 H, ddd, J = 10.8, 7.3, 5.1 Hz), 2.48 (1 H, ddd, J = 13.3, 10.8, 8.3 Hz), 2.31 (1 H, ddd, J = 13.3, 5.1, 2.1 Hz), 2.15 (3 H, s), 1.24 (3 H, t, J = 7.1 Hz).

3. Entry c. Pyrrolidine (0.0513 g, 0.197 mmol, 87%): oil; separated on flash silica gel Kieselgel 60, 5:2 hexane/EtOAc, R_f 0.27; exact mass calcd for $C_{15}H_{19}O_3N$ 261.136; found 261.1392, error 12.3 ppm; IR ($CDCl_3$, cm^{-1}) 1720 (C=O), 1740 (C=O); 270-MHz NMR ($CDCl_3$) δ 7.33–7.17 (5 H, m), 4.54 (1 H, d, J = 9.7 Hz), 4.02 (1 H, dd, J = 9.1, 2.5 Hz), 3.55 (1 H, q, J = 9.1 Hz), 3.15 (3 H, s), 2.82 (1 H, dt, J = 13, 9.7 Hz), 2.26 (3 H, s), 2.19 (3 H, s), 1.96 (1 H, ddd, J = 13, 8.7, 2.5 Hz).

4. Entry d. Major pyrrolidine (0.023 g, 0.099 mmol, 40%): oil; separated on flash silica gel Kieselgel 60, 5:4 hexane/EtOAc, R_f 0.33; exact mass, no match, parent M − 2 259.1188, calcd 259.1200, error 7.8 ppm, formula $C_{15}H_{19}O_3N$; IR ($CDCl_3$, cm^{-1}) 1684 (C=O), 1726 (C=O); 200-MHz NMR ($CDCl_3$) δ 8.16–7.91 (2 H, m), 7.62–7.37 (3 H, m), 4.46 (1 H, dd, J = 10, 4.7 Hz), 3.7–3.65 (1 H, m), 3.68 (3 H, s), 3.31 (1 H, q, J = 9.0 Hz), 2.78 (1 H, dt, J = 13.2, 10 Hz), 2.39 (3 H, s), 2 (1 H, ddd, J = 13.2, 9, 4.7 Hz), 0.96 (3 H, d, J = 6.5 Hz).

Minor pyrrolidine (0.011(7 g, 0.045 mmol, 20%): oil; separated on flash silica gel Kieselgel 60, 5:4 hexane/EtOAc, R_f 0.44; exact mass, no match, parent M − 2 259.1172, calcd 259.1208, error 14.2 ppm, formula $C_{15}H_{19}O_3N$; IR ($CDCl_3$, cm^{-1}) 1738 (C=O), 1738 (C=O); 270-MHz NMR ($CDCl_3$) δ 8.05–7.88 (2 H, m), 7.59–7.16 (3 H, m), 5.06 (1 H, d, J = 4.0 Hz), 3.69 (3 H, s), 3.37 (1 H, sextet, 6.7), 3.06 (1 H, ddd, J = 9.8, 5.9, 4 Hz), 2.39–2.3 (1 H, m), 2.36 (3 H, s), 1.85 (1 H, dt, J = 12.7, 6.3 Hz), 1.1 (3 H, d, J = 6.3 Hz).

5. Entry e. Pyrrolidine (0.035 g, 0.138 mmol, 63%): oil; separated on flash silica gel Kieselgel 60, 5:2 hexane/EtOAc, R_f 0.36; exact mass calcd for $C_{11}H_{19}O_4N$ 229.1309, found 229.1307, error 0.8 ppm; IR ($CDCl_3$, cm^{-1}) 1722 (C=O), 1745 (C=O); 270-MHz NMR ($CDCl_3$) δ 4.15 (2 H, q, J = 7.1 Hz), 3.67 (3 H, s), 3.59 (1 H, dd, J = 8.7, 2.8 Hz), 3.44 (1 H, dq, J = 6.3, 6.3 Hz), 3.3 (1 H, q, J = 8.3 Hz), 2.54 (1 H, dt, J = 13.4, 9.1 Hz) 2.36 (3 H, s), 2.0 (1 H, ddd, J = 13.4, 8.6, 2.8 Hz), 1.25 (3 H, t, J = 7.1 Hz), 0.91 (3 H, d, J = 6.3 Hz).

6. Entry f. Pyrrolidine (0.0374 g, 0.151 mmol, 67%): oil; separated on flash silica gel Kieselgel 60, 5:2 hexane/EtOAc, R_f 0.08; exact mass, no match, parent M - 2 245.1042, calcd 245.1052, error 4.1 ppm, formula $C_{14}H_{17}O_3N$; IR ($CDCl_3$, cm^{-1}) 1740 (C=O), 1685 (C=O); 270-MHz NMR ($CDCl_3$) δ 8.04-7.97 (2 H, m), 7.61-7.38 (3 H, m), 4.23 (1 H, d, J = 7.5 Hz), 3.58 (3 H, s), 3.25-3.13 (2 H, m), 2.59 (1 H, q, J = 7.9 Hz), 2.37 (3 H, s), 2.34-2.22 (1 H, m), 2.16-2.08 (1 H, m).

7. Entry g. Major pyrrolidine (0.019 g, 0.061 mmol, 27%): oil; analyzed by HPLC, M-9 silica gel, 2:3 hexane/EtOAc, 110 mL; exact mass calcd for $C_{10}H_{17}O_4N$ 215.1153, found 215.116, error 3.3 ppm; IR (CH_2Cl_2, cm^{-1}) 1730 (C=O), 1740 (C=O); 270-MHz NMR ($CDCl_3$) δ 4.27 (2 H, br q, J = 7.1 Hz), 3.69 (3 H, s), 3.29-3.17 (2 H, m), 3.16-3.04 (1 H, m), 2.54-2.41 (1 H, m), 2.41 (3 H, s), 2.28-2.10 (1 H, m), 2.09-1.97 (1 H, m), 1.25 (3 H, t, J = 7.1 Hz).

Minor pyrrolidine (0.014 g, 0.045 mmol, 20%): oil; analyzed by HPLC, M-9 silica gel, 2:3 hexane/EtOAc, 100 mL; exact mass calcd for $C_{10}H_{17}O_4N$ 215.1153, found 215.116, error 3.3 ppm; IR (CH_2Cl_2, cm^{-1}) 1740 (C=O), 1730 (C=O); 270-MHz NMR ($CDCl_3$) δ 4.24 (2 H, q, J = 7.0 Hz), 3.67 (3 H, s), 3.37-3.31 (1 H, m), 3.22-3.06 (2 H, m), 2.55-2.34 (2 H, m), 2.39 (3 H, s), 2.24-2.13 (1 H, m), 1.21 (3 H, t, J = 7.0 Hz).

8. Entry h. Pyrrolidine (0.032 g, 0.129 mmol, 73%): oil; separated on flash silica gel Kieselgel 60, 5:2 hexane/EtOAc, R_f 0.32; exact mass, no peak match, parent, formula $C_{14}H_{17}O_3N$; IR ($CDCl_3$, cm^{-1}) 2800 (CH=O), 1735 (C=O), 1720 (C=O); 270-MHz NMR ($CDCl_3$) δ 9.7 (1 H, d, J = 2.4 Hz), 7.33-7.11 (5 H, m), 4.47 (1 H, d, J = 9.1 Hz), 3.79 (1 H, dt, J = 9.5, 2.4 Hz); 3.5 (1 H, q, J = 9.1 Hz), 3.18 (3 H, s), 2.78 (1 H, dt, J = 13.8, 9.5 Hz), 2.34 (3 H, s), 2.12 (1 H, ddd, J = 13.8, 9.1, 2.4 Hz).

Alkylation, Reduction, and [2 + 3] DMAD Trapping of 2,4,5-Trisubstituted Oxazoles and Subsequent DBU Isomerization. Scheme II Results. The reactions were carried out as described for the 2,5-disubstituted oxazoles. The crude 3-pyrrolines obtained from the reactions were isolated by silica gel chromatography and isomerized to the 2-pyrrolines by treatment with DBU in THF overnight. The details for each case are described as follows.

1. Oxazole 25a. 3-Pyrroline **26a** (2:1 inseparable mixture of diastereomers; 0.042 g, 0.120 mmol, 53%): oil; analytical TLC (silica gel F254), 5:1 hexane/EtOAc, R_f 0.18; exact mass, no peak match, parent M + 1 348.1449, calcd 348.1372, error 21.6 ppm, formula $C_{18}H_{21}O_6N$; IR (CH_2Cl_2, cm^{-1}) 1720 (C=O), 1730 (C=O); 270-MHz NMR ($CDCl_3$) δ 7.31-7.16 (5 H, m), 6.19 (0.33 H, s), 4.83 (0.67 H, s), 3.72 (3 H, s), 3.70 (3 H, s), 3.49 (3 H, s), 2.09 (3 H, s), 1.57 (3 H, s).

DBU isomerization gave a 1:1 mixture of diastereomers **27a** and **27a'**. 2-Pyrroline **27a**: Oil; flash silica gel Kieselgel 60, 5:4 hexane/EtOAc, R_f 0.41; exact mass calcd for $C_{18}H_{21}O_6N$ 347.1363, found 347.1373, error 2.8 ppm; IR (CH_2Cl_2, cm^{-1}) 1735 (C=O), 1586 (C=C-N); 270-MHz NMR ($CDCl_3$) δ 7.48-7.27 (5 H, m), 4.13 (1 H, s), 3.80 (3 H, s), 3.75 (3 H, s), 3.41 (3 H, s), 2.58 (3 H, s), 1.54 (3 H, s).

2-Pyrroline **27a'**: oil; flash silica gel Kieselgel 60, 5:4 hexane/EtOAc, R_f 0.32; exact mass calcd for $C_{18}H_{21}O_6N$ 347.1363, found 347.1364, error 0.3 ppm; IR (CH_2Cl_2, cm^{-1}) 1745 (C=O), 1590 (C=C-N); 270-MHz NMR ($CDCl_3$) δ 7.45-7.23 (5 H, m), 3.98 (1 H, s), 3.72 (3 H, s), 3.68 (3 H, s), 3.40 (3 H, s), 2.55 (3 H, s), 1.67 (3 H, s); ^{13}C NMR $CDCl_3$ (DEPT) δ 173.1 (s), 171.3 (s), 165.2 (s), 163.5 (s), 131.3 (s), 129.0 (d), 128.0 (d), 127.9 (d), 95.0 (s), 71.2 (s), 54.8 (d), 54.7 (q), 52.8 (q), 51.9 (q), 30.2 (q), 17.3 (q).

2. Oxazole 25b. 3-Pyrroline **26b** (0.031 g, 0.074 mmol, 33%): oil; analytical TLC (silica gel F254), 5:1 hexane/EtOAc, R_f 0.17; exact mass, no peak match, parent M + 1 420.1658, calcd 420.1657, error 0.24 ppm, formula $C_{21}H_{25}O_8N$; IR (CH_2Cl_2, cm^{-1}) 1700 (C=O), 1750 (C=O), 1650 (C=C); 270-MHz NMR ($CDCl_3$) δ 7.44-7.15 (5 H, m), 4.91 (1 H, s), 4.32-4.17 (4 H, m), 3.74 (3 H, s), 3.51 (3 H, s), 2.41 (3 H, s), 1.32-1.21 (6 H, m).

26b Isomerization. 2-Pyrroline **27b**: oil; analytical TLC (silica gel F254), 5:2 hexane/EtOAc, R_f 0.15; exact mass calcd for $C_{21}H_{25}O_8N$ 419.1573, found 419.1582, error 2.1 ppm; IR (CH_2Cl_2, cm^{-1}) 1740 (C=O), 1750 (C=O), 1690 (C=O), 1600 (C=C-N); 200-MHz NMR ($CDCl_3$) δ 7.57-7.08 (5 H, m), 4.72 (1 H, s), 4.31-4.10 (4 H, m), 3.70 (3 H, s), 3.41 (3 H, s), 2.72 (3 H, s), 1.41-1.03 (6 H, m).

Alkylation, Reduction, and [2 + 2] DMAD Trapping of Oxazoles. Scheme III, Table IV Results. Methyl triflate (0.028 mL, 0.249 mmol) was added to a solution of the oxazole (0.226 mmol) in 2 mL of acetonitrile. After the mixture was stirred for 2 h at room temperature, phenylsilane (distilled from CaH_2; 0.049 mL, 0.339 mmol) and dimethyl acetylenedicarboxylate (DMAD; 0.083 mL, 0.678 mmol) were added, and the mixture was transferred by cannula to anhydrous cesium fluoride (0.069 g, 0.452 mmol) in acetonitrile (4 mL). After the mixture was vigorously stirred for 2 h at ambient temperature, the solvent was removed (rotary evaporator), and the resulting residue was purified by silica gel chromatography to leave the oxazolidine as an oil.

1. Entry a. Oxazolidine **30a**: oil; separated on flash silica gel Kieselgel 60, 5:2 hexane/EtOAc, R_f 0.24; exact mass calcd for $C_{23}H_{23}O_5N$ 393.1571, found 393.157, error 0.1 ppm; IR ($CDCl_3$, cm^{-1}) 1739 (C=O), 1723 (C=O); 270-MHz NMR (CD_3CN) δ 7.24-7 (10 H, m), 4.44 (1 H, q, J = 5.2 Hz), 3.85 (3 H, s), 3.77 (3 H, s), 2.35 (3 H, s), 1.61 (3 H, d, J = 5.2 Hz); ^{13}C NMR $CDCl_3$ (DEPT) δ 163.0 (s), 161.4 (s), 144.1 (s), 141.1 (s), 134.4 (s), 134.3 (s), 129.9 (d), 127.8 (d), 127.6 (d), 127.5 (d), 127.4 (d), 126.4 (d), 92.6 (s), 89.6 (d), 86.0 (s), 52.3 (q), 52.1 (q), 31.8 (q), 18.1 (q).

2. Entry b. Oxazolidine **30b** (0.058 g, 0.185 mmol, 82%): oil; separated on flash silica gel Kieselgel 60, 5:2 hexane/EtOAc, R_f 0.19; exact mass calcd for $C_{13}H_{19}O_5N$ 269.1258, found 269.122, error 14.1 ppm; IR ($CDCl_3$, cm^{-1}) 1738 (C=O), 1724 (C=O); 200-MHz NMR ($CDCl_3$) δ 3.94 (1 H, q, J = 5.2 Hz), 3.78 (6 H, s), 2.26 (3 H, s), 1.43 (3 H, s), 1.33 (3 H, s), 1.31 (3 H, d, J = 5.2 Hz); ^{13}C NMR $CDCl_3$ (DEPT) δ 162.6 (s), 161.7 (s), 142.8 (s), 140.8 (s), 88.9 (d), 85.7 (s), 74.5 (s), 52.0 (q), 51.8 (q), 31.5 (q), 17.9 (q), 16.1 (q), 15.9 (q).

3. Entry c. Oxazolidine **30c** (0.073 g, 0.185 mmol, 81%): oil; separated on flash silica gel Kieselgel 60, 5:2 hexane/EtOAc, R_f 0.43; exact mass calcd for $C_{23}H_{23}O_5N$ 393.1571; found 393.1558, error 3.2 ppm; IR ($CDCl_3$, cm^{-1}) 1735 (C=O), 1720 (C=O); 200-MHz NMR ($CDCl_3$) δ 7.67-7.3 (10 H, m), 4.88 (1 H, s), 3.87 (3 H, s), 3.74 (3 H, s), 2.19 (3 H, s), 1.09 (3 H, s); ^{13}C NMR $CDCl_3$ (DEPT) δ 162.5 (s), 161.3 (s), 145.4 (s), 138.7 (s), 136.9 (s), 135.6 (s), 129.6 (d), 128.4 (d), 128.3 (d), 128.2 (d), 126.4 (d), 126.3 (d), 94.7 (d), 92.0 (s), 76.3 (s), 52.1 (q), 52.0 (q), 31.0 (q), 16.7 (q).

Conversion of 2-Methyl-4,5-diphenyloxazoline (29a) into Pyrrole 33a. The 4-oxazoline was generated as described above in the absence of DMAD, and the reaction mixture was concentrated to 0.5 mL under N_2. Thermolysis of the oxazoline in refluxing MeOH or toulene lead to the pyrrole **33a**. Pyrrole **33a**: oil; separated on flash silica gel Kieselgel 60, 5:1 hexane/EtOAc, R_f 0.47; exact mass calcd for $C_{17}H_{15}N$ 233.1201, found 233.1208, error 3 ppm; 200-MHz NMR (CD_3CN) δ 7.72-7.32 (12 H, m), 3.26 (3 H, s).

Thermolysis of Oxazolidine 30 to 2-Pyrroline 31. Scheme III, Table IV Results. Oxazolidine **30** was dissolved in 1 mL of xylene and heated at 120 °C for 2 h. The solvent was removed (rotary evaporator), and the oily residue was purified on a silica gel column to yield 2-pyrroline **31**.

1. Entry a. 2-Pyrroline **31a**: oil; analytical TLC (silica gel F254), 5:2 hexane/EtOAc, R_f 0.4; exact mass calcd for $C_{23}H_{23}O_5N$ 393.1571, found 393.1561, error 2.4 ppm; IR (CH_2Cl_2, cm^{-1}) 1735 (C=O), 1721 (C=O), 1675 (C=O), 1589 (N-C=C); 270-MHz NMR ($CDCl_3$) δ 7.89-7.77 (2 H, m), 7.57-7.29 (8 H, m), 4.53 (1 H, q, J = 7.0 Hz), 3.69 (3 H, s), 3.24 (3 H, s), 2.68 (3 H, s), 1.31 (3 H, d, J = 7.0 Hz); ^{13}C NMR $CDCl_3$ (DEPT) δ 196.0 (s), 173.1 (s), 165.3 (s), 163.2 (s), 132.1 (s), 131.6 (s), 129.2 (d), 128.8 (d), 128.2 (d), 128.0 (d), 127.9 (d), 127.8 (d), 99.6 (s), 70.9 (s), 65.7 (d), 52.7 (q), 49.9 (q), 33.3 (q), 15.4 (q).

2. Entry b. 2-Pyrroline **31b** (0.067 g, 0.245 mmol, 43%): oil; flash silica gel Kieselgel 60, 5:4 hexane/EtOAc, R_f 0.13; exact mass calcd for $C_{13}H_{19}O_5N$ 269.1258, found 269.1264, error 2.3 ppm; IR (CH_2Cl_2, cm^{-1}) 1705 (C=O), 1710 (C=O), 1720 (C=O), 1580 (other); 270-MHz NMR ($CDCl_3$) δ 3.94 (1 H, q, J = 6.7 Hz), 3.69 (3 H, s), 3.59 (3 H, s), 2.73 (3 H, s), 2.23 (3 H, s), 2.14 (3 H, s), 1.22 (3 H, d, J = 6.7 Hz), ^{13}C NMR ($CDCl_3$ δ 204.5 (s), 172.3 (s), 166.4 (s), 162.8 (s), 98.0 (s), 70.6 (s), 65.7 (d), 52.4 (q), 50.1 (q), 31.5 (q), 29.0 (q), 14.5 (q), 12.7 (q).

2-Pyrroline **31b'** (0.031 g, 0.114 mmol, 20%): oil; flash silica gel Kieselgel 60, 5:4 hexane/EtOAc, R_f 0.17; exact mass calcd for $C_{13}H_{19}O_5N$ 269.1258, found 269.1265, error 2.6 ppm; IR (CH_2Cl_2, cm^{-1}) 1710 (C=O), 1705 (C=O), 1720 (C=O), 1585 (other); 270-MHz NMR ($CDCl_3$) δ 4.40 (1 H, q, J = 6.7 Hz), 3.70 (3 H, s), 3.62 (3 H, s), 2.81 (3 H, s), 2.33 (3 H, s), 2.19 (3 H, s), 1.07 (3 H, d, J = 6.7 Hz); ^{13}C NMR $CDCl_3$ δ 203.3 (s), 170.3 (s), 166.3 (s), 162.2 (s), 94.6 (s), 70.3 (s), 63.4 (d), 52.0 (q), 50.0 (q), 31.1 (q), 28.0 (q), 14.7 (q), 13.1 (q).

3. Entry c. 2-Pyrroline **31c**: oil; flash silica Kieselgel 60, 5:4 hexane/EtOAc, R_f 0.23; exact mass calcd for $C_{23}H_{23}O_5N$ 393.1571, found 393.157, error 0.1 ppm; IR ($CDCl_3$, cm^{-1}) 1730 (C=O), 1693 (C=O), 1675 (C=O), 1570 (other); 270-MHz NMR ($CDCl_3$) δ 7.35-7.28 (2 H, m), 7.27-6.93 (8 H, m), 5.53 (1 H, s), 3.65 (3 H, s), 3.47 (3 H, s), 2.73 (3 H, s), 2.42 (3 H, s); ^{13}C NMR $CDCl_3$ (DEPT) δ 194.9 (s), 173.5 (s),

166.5 (s), 162.6 (s), 137.8 (s), 134.8 (s), 131.3 (d), 128.5 (d), 128.1 (d), 128.0 (d), 127.9 (d), 127.2 (d), 96.6 (s), 73.6 (d), 71.8 (s), 52.6 (q), 49.9 (q), 32.1 (q), 12.9 (q).

Alkylation and Reduction of Oxazoles in the Presence of *N*-Phenylmaleimide. Scheme IV and Table V Results. The experiments were carried out as described for the acrylate trappings except *N*-phenylmaleimide (0.039 g, 0.226 mmol) was used as the acceptor. The details are given in each individual case as follows.

1. Entry a. Pyrrolidine **35a** (0.051 g, 0.124 mmol, 55%): solid; mp 196–198 °C (crystallized from EtOAc); exact mass calcd for $C_{26}H_{22}O_3N_2$ 410.1625, found 410.1636, error 2.7 ppm; IR ($CDCl_3$, cm^{-1}) 1710 (C=O); 270-MHz NMR ($CDCl_3$) δ 8.25–8.13 (2 H, m), 7.72–7.13 (13 H, m), 5.54 (1 H, s), 4.90 (1 H, d, J = 9.1 Hz), 3.78 (1 H, dd, J = 9.1, 8.3 Hz), 3.50 (1 H, d, J = 8.3 Hz), 2.33 (3 H, s).

Pyrrolidine **36a** (0.019 g, 0.045 mmol, 20%): oil; flash silica gel Kieselgel 60, 5:2 hexane/EtOAc, R_f 0.17; exact mass calcd for $C_{26}H_{22}O_3N_2$ 410.1625, found 410.163, error 1.2 ppm; IR ($CDCl_3$, cm^{-1}) 1710 (C=O); 270-MHz NMR ($CDCl_3$) δ 8.04–7.97 (2 H, m), 7.65–7.23 (13 H, m), 5.40 (1 H, d, J = 8.3 Hz), 4.56 (1 H, d, J = 5.6 Hz), 4.01 (1 H, dd, J = 9.9, 8.3 Hz), 3.54 (1 H, dd, J = 9.9, 5.6 Hz), 2.11 (3 H, s).

2. Entry b. Same as entry a, but the solvent employed was chloroform.

3. Entry d. Pyrrolidine **35d** (0.023 g, 0.061 mmol, 27%): oil; analytical TLC (silica gel F254, 5:1 hexane/EtOAc, R_f 0.14; exact mass calcd for $C_{22}H_{22}O_4N_2$ 378.1574, found 378.1571, error 0.7 ppm; IR (CH_2Cl_2, cm^{-1}) 1714 (C=O), 1723 (C=O); 200-MHz NMR ($CDCl_3$) δ 7.54–7.08 (10 H, m), 4.52 (1 H, d, J = 9.4 Hz), 4.42 (1 H, s), 4.25 (2 H, q, J = 7 Hz), 3.76 (1 H, dd, J = 9.4, 8.2 Hz), 3.49 (1 H, d, J = 8.2 Hz), 2.27 (3 H, s), 1.34 (3 H, t, J = 7 Hz).

Pyrrolidine **36d** (0.031 g, 0.081 mmol, 36%): oil; analytical TLC (silica gel F254), 5:4 hexane/EtOAc, R_f 0.1; exact mass calcd for $C_{22}H_{22}O_4N_2$ 378.1574, found 378.1529, error 11.9 ppm; IR (CH_2Cl_2, cm^{-1}) 1710 (C=O), 1725 (C=O); 200-MHz NMR ($CDCl_3$) δ 7.50–7.21 (10 H, m), 4.40 (1 H, d, J = 5.9 Hz), 4.28 (1 H, d, J = 9.1 Hz), 4.20 (2 H, q, J = 7.3 Hz), 3.87 (1 H, dd, J = 9.7, 9.1 Hz), 3.43 (1 H, dd, J = 9.7, 5.9 Hz), 2.16 (3 H, s), 1.26 (3 H, t, J = 7.3 Hz).

4. Entry e. Pyrrolidine **35e** (0.029 g, 0.095 mmol, 42%): oil; analytical TLC (silica gel F254), 5:4 hexane/EtOAc, R_f 0.39; exact mass calcd for $C_{16}H_{18}O_4N_2$ 302.1262, found 302.1239, error 7.6 ppm; IR ($CDCl_3$, cm^{-1}) 1710 (C=O), 1725 (C=O), 1740 (C=O); 200-MHz NMR ($CDCl_3$) δ 7.56–7.15 (5 H, m), 4.19 (1 H, s), 3.73 (3 H, s), 3.49–3.22 (3 H, m), 2.34 (3 H, s), 1.21 (3 H, d, J = 5.9 Hz).

Pyrrolidine **36e** (0.025 g, 0.081 mmol, 36%): oil; analytical TLC (silica gel F254), 5:4 hexane/EtOAc, R_f 0.15; exact mass calcd for $C_{16}H_{18}O_4N_2$ 302.1262, found 302.1272, error 3.3 ppm; IR ($CHCl_3$, cm^{-1}) 1710 (C=O), 1730 (C=O), 1750 (C=O); 200-MHz NMR ($CDCl_3$) δ 7.51–7.32 (3 H, m), 7.30–7.21 (2 H, m), 3.98 (1 H, d, J = 9.0 Hz), 3.70 (3 H, s), 3.64 (1 H, dd, J = 9.0, 9.0 Hz), 3.60 (1 H, dq, J = 4.4, 6.4 Hz), 3.06 (1 H, dd, J = 9.0, 4.4 Hz), 2.29 (3 H, s), 1.22 (3 H, d, J = 6.4 Hz).

5. Entry f. Pyrrolidine **35f** (0.017 g, 0.049 mmol, 22%): oil; analytical TLC (silica gel F254), 5:4 hexane/EtOAc, R_f 0.46; exact mass calcd for $C_{20}H_{18}O_3N_2$ 334.1313, found 334.1317, error 1.2 ppm; IR ($CHCl_3$, cm^{-1}) 1690 (C=O), 1710 (C=O), 1720 (C=O); 200-MHz NMR ($CDCl_3$) δ 8.17–8.07 (2 H, m), 7.66–7.27 (8 H, m), 5.04 (1 H, s), 3.56–3.44 (3 H, m), 3.36–3.27 (1 H, m), 2.39 (3 H, s).

Pyrrolidine **36f** (0.036 g, 0.113 mmol, 50%): oil; analytical TLC (silica gel F254), 5:4 hexane/EtOAc, R_f 0.1; exact mass calcd for $C_{20}H_{18}O_3N_2$ 334.1313, found 334.1325, error 3.6 ppm; IR ($CDCl_3$, cm^{-1}) 1690 (C=O), 1705 (C=O), 1720 (C=O); 200-MHz NMR ($CDCl_3$) δ 8.07–7.97 (2 H, m), 7.60–7.18 (8 H, m), 4.11 (1 H, d, J = 7.9 Hz), 3.79 (1 H, dd, J = 7.9, 7.9 Hz), 3.65 (1 H, d, J = 10 Hz), 3.41 (1 H, dd, J = 7.9, 7.9 Hz), 2.68 (1 H, dd, J = 10, 7.9 Hz), 2.34 (3 H, s).

6. Entry g. Pyrrolidine **35g** (0.027 g, 0.090 mmol, 40%): oil; analytical TLC (silica gel F254), 5:4 hexane/EtOAc, R_f 0.37; exact mass calcd for $C_{16}H_{18}O_4N_2$ 302.1262, found 302.127, error 2.7 ppm; IR (CH_2Cl_2, cm^{-1}) 1700 (C=O), 1730 (C=O), 1740 (C=O); 200-MHz NMR ($CDCl_3$) δ 7.58–7.26 (5 H, m), 4.26 (2 H, q, J = 7 Hz), 4.04 (1 H, s), 3.61–3.46 (2 H, m), 3.38–3.18 (2 H, m), 2.45 (3 H, s), 1.35 (3 H, t, J = 7 Hz).

Pyrrolidine **36g** (0.011 g, 0.036 mmol, 16%): oil; analytical TLC (silica gel F254), 5:4 hexane/EtOAc, R_f 0.17; exact mass calcd for $C_{16}H_{18}O_4N_2$ 302.1262, found 302.1267, error 2.6 ppm; IR (CH_2Cl_2, cm^{-1}) 1704 (C=O), 1718 (C=O), 1740 (C=O); 200-MHz NMR ($CDCl_3$) δ 7.56–7.24 (5 H, m), 4.38–4.20 (2 H, m), 3.68 (1 H, d, J = 7.9 Hz), 3.61 (1 H, dd, J = 9.9, 8.5 Hz), 3.41 (1 H, dd, J = 7.6, 7.6 Hz), 3.28 (1 H, d, J = 8.5 Hz), 2.63 (1 H, dd, J = 9.8, 7.9 Hz), 2.39 (3 H, s), 1.33 (3 H, t, J = 7.3 Hz).

7. Entry h. Pyrrolidine **35h** (0.036 g, 0.097 mmol, 43%): oil; analytical TLC (silica gel F254), 5:2 hexane/EtOAc, R_f 0.15; exact mass calcd for $C_{19}H_{22}O_6N_2$ 374.1472, found 374.1475, error 0.8 ppm; IR ($CHCl_3$, cm^{-1}): 1720 (C=O); 270-MHz NMR ($CDCl_3$) δ 7.48–7.21 (5 H, m), 4.27–4.15 (5 H, m), 4.10 (1 H, d, J = 8.3 Hz), 3.76 (1 H, t, J = 8.3 Hz), 3.49 (1 H, dd, J = 8.3, 1.2 Hz), 2.39 (3 H, s), 1.34–1.22 (6 H, m).

N-Isopropylation, Reduction, and Maleimide Trapping of 2,5-Diphenyloxazole: Pyrrolidines 35c, 36c. Table V, Entry c Result.[49] AgOTf (0.136 g, 0.532 mmol) was suspended in 5 mL of dichloromethane and cooled to 0 °C. Isopropyl bromide (0.050 mL, 0.266 mmol) was added, and the reaction mixture was stirred for 1 h at 0 °C. The AgBr formed was allowed to settle, and the supernatant liquid was transferred via cannula to a solution of 2,5-diphenyloxazole (0.059 g, 0.266 mmol) in 5 mL of dichloromethane. The reaction mixture was stirred for 1 h at 0 °C when it was warmed up to room temperature and stirred for an additional hour. The dichloromethane was blown off under N_2, and 3 mL of acetonitrile was added. Phenylsilane (0.058 mL, 0.399 mmol) and *N*-phenylmaleimide (0.046 g, 0.266 mmol) were added. This mixture was transferred by cannula to anhydrous cesium fluoride (0.080 g, 0.532 mmol) in 4 mL of acetonitrile, and the reaction mixture was stirred vigorously for 2 h. The solvent was evaporated, and the resulting residue was purified by silica gel chromatography to leave pyrrolidine **35c** (0.002 g, 0.0045 mmol, 8%) and **36c** (0.014 g, 0.032 mmol, 60%). (Yields are based on recovered oxazole (0.047 g, 0.212 mmol).)

Pyrrolidine **35c**: oil; analytical TLC (silica gel F254), 5:4 hexane/EtOAc, R_f 0.66; exact mass calcd for $C_{22}H_{22}O_3N_2$ 362.1625, found 362.1633, error 2.2 ppm; IR (CH_2Cl_2, cm^{-1}) 1710 (C=O); 270-MHz NMR ($CDCl_3$) δ 8.19–8.12 (2 H, m), 7.65–7.27 (8 H, m), 5.24 (1 H, s), 3.73–3.63 (1 H, m), 3.54 (1 H, d, J = 9.9 Hz), 3.45–3.44 (2 H, m), 3.19 (1 H, heptet, J = 6.3 Hz), 1.06 (3 H, d, J = 6.3 Hz), 0.94 (3 H, d, J = 6.3 Hz).

Pyrrolidine **36c**: oil; analytical TLC (silica gel F254), 5:4 hexane/EtOAc, R_f 0.47; exact mass calcd for $C_{22}H_{22}O_3N_2$ 362.1625, found 362.1626, error 0.3 ppm; IR (CH_2Cl_2, cm^{-1}) 1710 (C=O); 270-MHz NMR ($CDCl_3$) δ 8.07–8.01 (2 H, m), 7.68–7.18 (8 H, m), 4.67 (1 H, d, J = 8.3 Hz), 3.72 (1 H, dd, J = 8.3, 8.3 Hz), 3.60 (1 H, dd, J = 9.5, 1.9 Hz), 3.45 (1 H, dt, J = 1.9, 8.3 Hz), 3.06–2.90 (2 H, m), 1.09 (3 H, d, J = 6.7 Hz), 0.93 (3 H, d, J = 6.7 Hz).

Alkylation, Reduction, and Phenyl Vinyl Sulfone Trapping [2 + 3] of 2-Phenyl-5-ethoxyoxazole. Subsequent Sulfone Sodium Amalgam Reduction: Pyrrolidine 41.[50] Methyl triflate (0.036 mL, 0.313 mmol) was added to a solution of the oxazole (0.036 mL, 0.285 mmol) in 2 mL of acetonitrile. After the mixture was stirred for 2 h at room temperature, phenylsilane (distilled from CaH_2; 0.049 mL, 0.339 mmol) and phenyl vinyl sulfone (0.096 mL, 0.570 mmol) were added, and the mixture was transferred by cannula to anhydrous cesium fluoride (0.069 g, 0.452 mmol) in acetonitrile (4 mL). After the mixture was vigorously stirred for 2 h at ambient temperature, the solvent was removed (rotary evaporator), and the resultant residue was passed through a plug of silica gel (5:4 hexane/EtOAc). The resulting oil was dissolved in 1 mL of THF. This solution was added to a mixture of Na(Hg) (0.282 g) and Na_2HPO_4 (0.093 g, 0.653 mmol) in 2 mL of methanol, and the reaction was stirred overnight. The reaction was poured into 30 mL of hexane and washed with H_2O (2 × 20 mL). The organic layer was separated and dried over K_2CO_3, the solvent was removed (rotary evaporator), and the resulting residue was purified by silica gel chromatography to leave a clear oil (0.026 g, 0.116 mmol, 41%).

Pyrrolidine **41**: oil; analytical TLC (silica gel F254), 5:4 hexane/EtOAc, R_f 0.63; exact mass calcd for $C_{13}H_{17}O_2N$ 219.1255, found 219.126, error 2.3 ppm; IR (CH_2Cl_2, cm^{-1}) 1705 (C=O); 270-MHz NMR ($CDCl_3$) δ 7.33–7.16 (5 H, m), 3.99 (1 H, dd, J = 7.9, 6.7 Hz), 3.92 (1 H, dd, J = 8.3, 2.3 Hz), 3.71 (3 H, s), 2.49–2.17 (2 H, m), 2.21 (3 H, s), 1.98–1.85 (1 H, m), 1.83–1.67 (1 H, m).

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