Electronically Mediated Selectivity in Ring Opening of 1-Azirines. The 3-X Mode: Convenient Route to 3-Oxazolines

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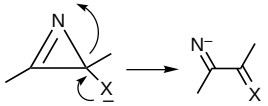
The mild base-promoted reaction of methyl 2-phenyl-1-azirine-3-acetate (**1**) with aldehydes and acetone provides a new and simple route to the 3-oxazolines **5**, which are formed in good yields by the electrophilic trapping of an imino anion produced by C−N bond cleavage in the 1-azirine enolate intermediate **6**. Chloranil oxidation of **5** containing an aromatic substituent at C-2 affords oxazoles **7**, while reaction of **5** containing an aliphatic group at C-2 produces 5-methylene-3-oxazolines **8** and 5-spiro-2-oxazolines **9** in addition to **7**.

While the chemistry of simple alkyl- and aryl-substituted 1-azirines has been extensively studied,[1] no methodology has been developed utilizing higher order functionality as an electronic probe for selective ring opening of the 1-azirine nucleus. In the present study, we focus attention on what shall be referred to as the "3-X mode" (eq 1), wherein an electron-rich substituent at the 3-position exerts a "pushing" effect on the three-membered ring. To the extent that this process results in C−N bond cleavage, the resulting imino anion might be induced to undergo reaction with electrophiles. As a simple precursor to a 3-X-substituted 1-azirine, we chose the 3-acetate derivative **1**. We herein report the mild base-catalyzed reaction of **1** with aldehydes and ketones, with special emphasis on synthetic and mechanistic implications.

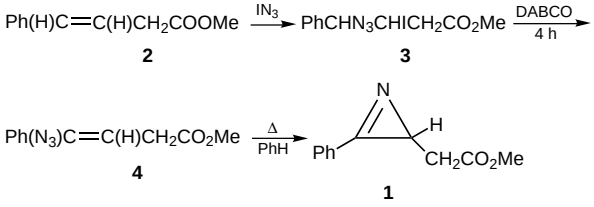


(1)

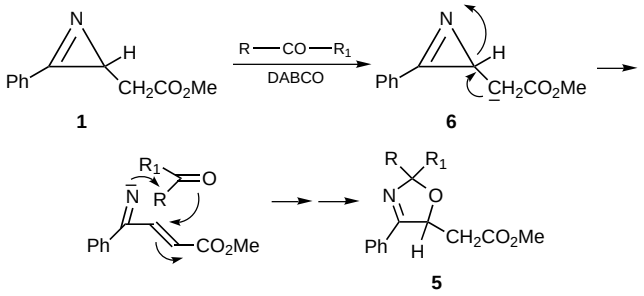
Results and Discussion

Methyl 2-phenyl-1-azirine-3-acetate **(1)** was conveniently prepared from methyl 4-phenyl-3-butenoate (**2**) via iodine azide addition (Scheme 1).[1b] While no reaction occurred between **1** and a series of aldehydes and ketones used as solvents in the absence of base, the presence of DABCO (1.5 equiv, 40 h, 25 °C) in the reaction medium resulted in a smooth conversion to 3-oxazolines **5**, as a 1:1 mixture of diastereomers where these exist (Scheme 2). The presence of the 3-oxazoline nucleus in **5** was suggested by the appearance, in the ^{1}H NMR spectra, of two strongly deshielded methine protons (δ 5.5−6.8, H-2 and H-5) in addition to diastereotopic methylene protons (δ 2.4−2.8). Each of these latter nuclei appeared as a doublet of doublets containing a J value identical with that found in the multiplet of the H-5 partner. In the cases of formation of diastereomers, the *cis* isomers could be conveniently obtained as colorless solids upon trituration of the purified product (see Experimental Section). A distinction between *cis* and *trans* isomers could be conveniently made on the basis of characteristic $J_{H\text{-}2-H\text{-}5}$ values. Thus, values observed in this study of 3.0−3.5 Hz (*cis*) and 4.5−5.5 (*trans*) are in total agreement with those previously reported[2] for 3-oxazoline isomers. In addition, an NOE difference experiment performed on **5d** (Figure 1) further confirms this designation.

Scheme 1



Scheme 2



compd	R	R_1	yield (%)
5a	CH_3	H	75
5b	$(CH_3)_3C$	H	70
5c	C_6H_5	H	50
5b	*p*-$CH_3OC_6H_4$	H	55
5e	$C_6H_5CH{=}CH$	H	50
5f	C_4H_3O	H	70
5g	CH_3	CH_3	55

Formation of **5** is consistent with participation of the intermediate 3-X-substituted 1-azirine **6**, generated in low concentration through proton abstraction from **1** by DABCO (Scheme 2). An alternative concerted process involving proton abstraction with ring opening in **1** must also be considered and, in fact, does not alter our original proposal. A nucleophilic role for DABCO in this reaction, which would invoke the participation of aziridine intermediates, was discarded inasmuch as potassium carbonate also produces **5**, albeit at a slower rate.

[⊗] Abstract published in *Advance ACS Abstracts,* May 1, 1996.

(1) (a) Padwa, A.; Woolhouse, A. D. In *Comprehensive Heterocyclic Chemistry*; Katritzky, A. R., Ed.; Pergamon Press: Oxford, U.K., 1984; Vol. 7, p 47. (b) Anderson, D. J.; Hassner, A. *Synthesis* **1975**, 483.

(2) Huisgen, R.; Raab, R.; Bunge, K.; Stangl, H. *Chem. Ber.* **1972**, *105*, 1279.

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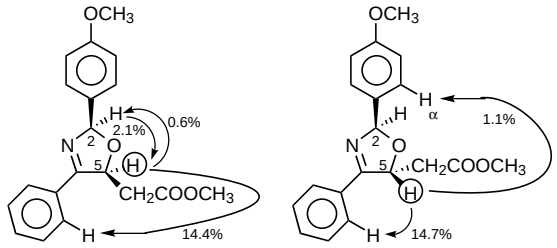
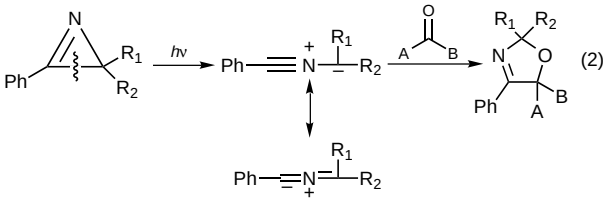


Figure 1.

In contrast to the well-known 2-oxazoline isomers,[3] 3-oxazolines are a rare class of compounds and only a few methods have been elaborated for their preparation. Of these methods,[2,4] one approach[4a] is extremely pertinent to the present discussion. Aldehydes and ketones react with nitrile ylides produced from 1-azirines by photochemically promoted C−C bond cleavage (eq 2). In

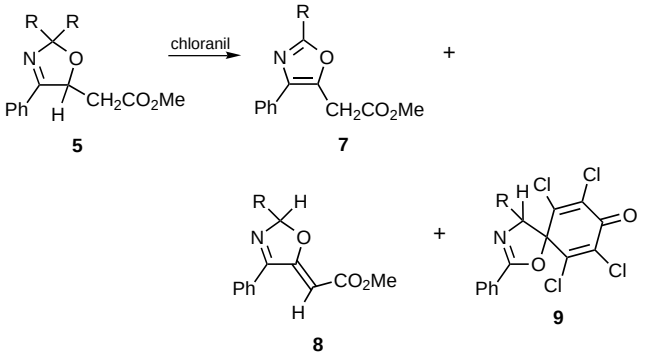


this case, the carbonyl moiety becomes the 1,5-fragment in the resulting 3-oxazoline. In the present study, the 1,2-fragment in **5** originates from the carbonyl component. The two methodologies are therefore complementary, although it should be noted that acceptable yields of 3-oxazolines in the photochemical process require the presence of electron-withdrawing substituents on the carbonyl moiety. The mild reaction conditions employed in the present study permit, for the first time, construction of a 3-oxazoline nucleus containing versatile functional groups at the 2-position (i.e. styryl (**5e**) and furyl (**5f**)).

2,4-Diaryl- and 2,4,5-triaryl-3-oxazolines may be readily converted to oxazoles utilizing chloranil (tetrachloro-1,4-benzoquinone) as the dehydrogenation agent.[2] The behavior of 3-oxazolines **5** (as 50:50 mixtures of diastereomers) under these oxidation conditions (1.5 equiv of chloranil, toluene, 40 h under reflux) proved to be a function of the electronic nature of the substituent at the 2-position.

Thus, derivatives containing an aromatic group (**5c**−**f**, including the styryl analogue **5e**) afforded oxazoles **7c**−**f** in 50−60% yields (Scheme 3). However, derivatives containing an aliphatic group (**5a**,**b**) furnished, in addition to oxazoles **7a**,**b** (20−30%),[5] 5-methylene-3-oxazolines **8a**,**b** (10−20%)[6] and 5-spiro-2-oxazolines **9a**,**b** (25−30%). That the latter are, in fact, 2-oxazolines was

Scheme 3



	product (yield, %)		
5a, R = CH_3	**7a** (20)	**8a** (20)	**9a** (25)
5b, R = $(CH_3)_3C$	**7b** (30)[a]	**8b** (10)[a]	**9b** (30)[a]
5c, R = C_6H_5	**7c** (50)		
5d, R = *p*-$CH_3OC_6H_4$	**7d** (60)		
5e, R = $C_6H_5CH{=}CH$	**7e** (50)		
5f, R= C_4H_3O	**7f** (55)		

[a] Yield based upon consumed **5b** (see Experimental Section).

readily deduced from the ^1H NMR spectra, wherein H-4 appeared 1 ppm upfield relative to H-2 of **5a**,**b**.[7] The reaction of **5b** revealed a severe steric effect of the *tert*-butyl group with recovery of 91% of the *trans*-**5b** isomer. When submitted separately to the reaction conditions, **7a** and **8a** were recovered unchanged, thus ruling out a route to **9** involving cycloaddition of **7** or **8** with chloranil. While one might be tempted to invoke the participation of nitrile ylides analogous to those of eq 2, generated from an oxidized form of **5**, in the formation of **9** by way of participation of chloranil as a dipolarophile, an experiment using benzaldehyde (a known probe for nitrile ylide intermediates[4a]) as an external carbonyl source in the oxidation of **5a** failed to produce any product of incorporation of the aldehyde. Also, the use of 5 equiv of chloranil in the reaction of **5a** did not significantly alter the product composition. The results of the above control experiments strongly suggest the participation of a reduced form of chloranil (perhaps an oxy anion species) in the formation of **9**. Interestingly, production of **9** may be totally suppressed by use of a quinone of higher oxidation potential (DDQ, 2,5-dichloro-3,6-dicyano-1,4-benzoquinone). With this reagent reaction of **5a** afforded **7a** and **8a** exclusively, as a 1:1 mixture, on the basis of ^1H NMR analysis of the crude product. We have been unable to determine the fate of the propionate fragment in **5** in the reactions producing **9**. The complex nature of the redox system involved in these transformations precludes further mechanistic interpretation.

Investigations of the reactions of the imino anion derived from **6** with various dicarbonyl compounds and other C-electrophiles are in progress in our laboratory.

Experimental Section

General Considerations. All chemicals were of reagent grade and were used as received. Melting points are uncorrected. ^1H NMR (300 MHz) and ^{13}C NMR (75 MHz) spectra were recorded in $CDCl_3$ solution, using TMS as internal standard. Elemental analyses were performed by UNICAMP,

(3) For reviews see: (a) Maryanoff, B. E. In *Oxazoles and Oxazolines in Organic Synthesis*; Turchi, I. J., Ed.; Interscience: New York, 1986; p 963. (b) Gant, T. G.; Meyers, A. I. *Tetrahedron* **1994**, *50*, 2297.

(4) (a) For a review see: Nair, V. Azirines. In *The Chemistry of Heterocyclic Compounds*; Hassner, A., Ed.; Interscience: New York, 1983; Vol. 42 (Small Ring Heterocycles, Pt. 1), p 215. (b) Pfoertner, K.-H.; Bernauer, K.; Kaufmann, F.; Lorch, E. *Helv. Chim. Acta* **1985**, *68*, 584. (c) Hassner, A.; Amarasekara, A. S.; Andisik, D. *J. Org. Chem.* **1988**, *53*, 27. (d) Singh, G. S. *Indian J. Chem.* **1987**, *26B*, 270.

(5) Oxazole **7a** has been cited in a patent: Meguro, K.; Fujita, T. (Takeda Chem. Ind. Ltd.) Eur. Pat. Appl. Ep 92,239, Oct 26, 1983.

(6) The isomer shown is suggested on the basis of a NOE difference experiment performed on **8a**, wherein irradiation of the phenyl hydrogens produced an enrichment (0.3%) of the vinyl hydrogen signal.

(7) In addition, a COLOC experiment (8 Hz) performed on **9a** showed a correlation ($^3J_{H-C}$) between the methyl protons and C_5 in support of the $CH_3-C_4-C_5$ connectivity.

Instituto de Química, Campinas, São Paulo, Brazil. Column chromatography utilized Florisil (Merck; 100−200 mesh particle size).

Methyl 2-Phenyl-1-azirine-3-acetate (1). A stirred suspension of NaN_3 (5.07 g, 78 mmol) in acetonitrile (38 mL) was treated with ICl (2.2 mL, 44 mmol) at −10 °C. After 15 min, methyl (*E*)-4-phenyl-3-butenoate (**2**;[8] 6.30 g, 36 mmol) was added; the resulting mixture was stirred for 12 h at room temperature, poured into water, and extracted with CH_2Cl_2 (2 × 50 mL). The organic layer containing crude iodo azide **3** was washed with 5% $Na_2S_2O_3$ solution, dried ($MgSO_4$), and reduced to half-volume in vacuo. DABCO (5.86 g, 51.9 mmol) was added and, after 4 h at room temperature, the DABCO. HI salt was separated and washed with CH_2Cl_2, and the combined organic fractions were washed with water and dried. Evaporation of the solvent under reduced pressure afforded the crude vinyl azide **4** as a yellow oil (7.32 g), which was immediately dissolved in benzene (900 mL). The resulting solution was heated at 80 °C for 20 h, after which time the solvent was removed under reduced pressure and the resulting oil was purified by column chromatography with benzene−hexane (1:1) as eluant to give 6.19 g (91%) of **1** as a pale yellow oil: IR (film) 1740 cm^{-1}; ^1H NMR δ 7.90 (m, 2H), 7.50 (m, 3H), 3.66 (s, 3H), 2.94 (dd, J = 16.5, 4.0 Hz, 1H), 2.34 (dd, J = 6.5, 4.0 Hz, 1H), 2.09 (dd, J = 16.5, 6.5 Hz, 1H); ^{13}C NMR δ 171.0, 169.7, 132.4, 129.6, 128.8, 125.4, 51.0, 38.7, 27.2. Anal. Calcd for $C_{11}H_{11}NO_2$: C, 69.83; H, 5.86; N, 7.40. Found: C, 70.02; H, 5.91; N, 7.29.

General Procedure for Obtaining 3-Oxazolines 5. A solution containing azirine **1** (189 mg, 1.0 mmol), aldehyde or acetone (1.5 mL), and DABCO (168 mg, 1.5 mmol) was stirred at 25 °C for 40 h. Excess aldehyde was removed either by evaporation in vacuo (aliphatic aldehydes and acetone) or by treatment with saturated $NaHSO_3$ solution (aromatic aldehydes). A CH_2Cl_2 extract was washed with water, dried, and concentrated "in vacuo". The residue was purified by column chromatography.

Methyl 2-methyl-4-phenyl-3-oxazoline-5-acetate (5a) was obtained from the reaction of azirine **1** (189 mg, 1.0 mmol) and acetaldehyde (1.5 mL, 27 mmol). Elution with PhH−Et_2O (32:1) afforded 3-oxazoline **5a** (175 mg, 75%) as a colorless oil which was a 50:50 mixture of diastereomers (based on ^1H NMR). When this oil was allowed to stand with petroleum ether (30−60 °C, 5 mL) in the refrigerator, 50 mg of pure and crystalline *cis*-**5a** could be isolated: mp 60−62 °C; IR (KBr) 1735, 1630 cm^{-1}; ^1H NMR δ 7.80 (m, 2H), 7.40 (m, 3H), 5.83 (m, 1H), 5.51 (ddd, J = 9.0, 3.0, 3.0 Hz, 1H), 3.63 (s, 3H), 2.81 (dd, J = 15.0, 3.0 Hz, 1H), 2.40 (dd, J = 15.0, 9.0 Hz, 1H), 1.45 (d, J = 6.0 Hz, 3H); ^{13}C NMR δ 169.5, 167.3, 131.7, 131.6, 129.2, 129.0, 102.6, 80.8, 51.2, 40.4, 23.0.

trans-**5a**: IR (film) 1740, 1635 cm^{-1}; ^1H NMR δ 7.80 (m, 2H), 7.40 (m, 3H), 5.82 (m, 1H), 5.63 (ddd, J = 9.0, 5.5, 3.0 Hz, 1H), 3.63 (s, 3H), 2.62 (dd, J = 15.0, 3.0 Hz, 1H), 2.41 (dd, J = 15.0, 9.0 Hz, 1H), 1.44 (d, J = 6.0 Hz, 3H); ^{13}C NMR δ 169.6, 167.4, 131.3, 129.1, 128.0, 101.8, 80.4, 51.3, 37.9, 21.9.

IR and NMR data were taken from the spectra of the *trans*-**5a**-enriched petroleum ether soluble fraction.

Elemental analysis was obtained for the 50:50 diastereomeric mixture. Anal. Calcd for $C_{13}H_{15}NO_3$: C, 66.94; H, 6.48; N, 6.00. Found: C, 67.08; H, 6.30; N, 6.12.

Methyl 2-*tert*-butyl-4-phenyl-3-oxazoline-5-acetate (5b) was obtained from the reaction of azirine **1** (107 mg, 0.6 mmol) and trimethylacetaldehyde (0.75 mL, 6.9 mmol). Elution with benzene afforded 3-oxazoline **5b** (110 mg, 70%) as a colorless oil which was a 50:50 mixture of diastereomers (based on ^1H NMR). When this oil was allowed to stand with petroleum ether (4 mL), crystalline *cis*-**5b** (35 mg) separated: mp 108−111 °C; IR (KBr) 1740, 1635 cm^{-1}; ^1H NMR δ 7.75 (m, 2H), 7.40 (m, 3H), 5.55 (ddd, J = 9.0, 4.5, 3.0 Hz, 1H), 5.34 (d, J = 4.5 Hz, 1H), 3.67 (s, 3H), 2.80 (dd, J = 16.0, 3.0 Hz, 1H), 2.41 (dd, J = 16.0, 8.5 Hz, 1H), 0.98 (s, 9H); ^{13}C NMR δ 169.7, 168.1, 131.4, 130.8, 128.6, 128.2, 112.6, 80.8, 51.3, 39.5, 36.2, 25.3.

trans-**5b:** IR (film) 1740, 1635 cm^{-1}; ^1H NMR δ 7.75 (m, 2H), 7.40 (m, 3H), 5.57 (m, 1H), 5.39 (d, J = 5.5 Hz, 1H), 3.64 (s, 3H), 2.65 (dd, J = 16.0, 3.0 Hz, 1H), 2.43 (dd, J = 16.0, 8.5 Hz, 1H), 0.95 (s, 9H); ^{13}C NMR δ 169.7, 167.9, 131.0, 130.7, 128.5, 127.9, 112.2, 80.8, 51.2, 38.1, 35.3, 25.0. IR and NMR data were taken from the spectra of the *trans*-**5b**-enriched petroleum ether soluble fraction.

Elemental analysis was obtained for the 50:50 diastereomeric mixture. Anal. Calcd for $C_{16}H_{21}NO_3$: C, 69.79; H, 7.69; N, 5.09. Found: C, 69.99; H, 7.82; N, 5.28.

Methyl 2,4-Diphenyl-3-oxazoline-5-acetate (5c). The reaction of azirine **1** (200 mg, 1.1 mmol) and benzaldehyde (1.5 mL, 15 mmol) using PhH−Et_2O (20:1) as eluant gave 3-oxazoline **5c** (155 mg, 50%) as a colorless oil which was a 50:50 mixture of diastereomers (based on ^1H NMR). When this oil was allowed to stand with petroleum ether (6 mL), solid *cis*-**5c** (60 mg) could be isolated: mp 67−68.5 °C; IR (KBr) 1730, 1630 cm^{-1}; ^1H NMR δ 7.70 (m, 2H), 7.20−7.30 (m, 8H), 6.71 (d, J = 3.5 Hz, 1H), 5.70 (ddd, J = 8.5, 3.5, 3.5 Hz, 1H), 3.58 (s, 3H), 2.77 (dd, J = 16.0, 3.5 Hz, 1H), 2.42 (dd, J = 16.0, 8.5 Hz, 1H); ^{13}C NMR δ 169.6, 168.0, 126.0−139.8, 105.4, 81.1, 51.3, 38.0.

trans-**5c**: IR (film) 1740, 1630 cm^{-1}; ^1H NMR δ 7.70 (m, 2H), 7.20−7.30 (m, 8H), 6.68 (d, J = 5.5 Hz, 1H), 5.80 (ddd, 8.5, 5.5, 3.5 Hz, 1H), 3.64 (s, 3H), 2.75 (dd, 16.0, 3.5 Hz, 1H), 2.55 (dd, 16.0, 8.5 Hz, 1H); ^{13}C NMR δ 169.6, 168.2, 126.0−140.4, 105.5, 81.4, 51.4, 39.6. IR and NMR data were taken from the spectra of the *trans*-**5c**-enriched petroleum ether soluble fraction.

Elemental analysis was obtained for the 50:50 diastereomeric mixture. Anal. Calcd for $C_{18}H_{17}NO_3$: C, 73.20; H, 5.80; N, 4.74. Found: C, 73.44; H, 5.67; N, 4.69.

Methyl 2-(*p*-methoxyphenyl)-4-phenyl-3-oxazoline-5-acetate (5d) was obtained from the reaction of azirine **1** (190 mg, 1.0 mmol) and anisaldehyde (1.5 mL, 12 mmol). Elution with PhH−Et_2O (32:1) afforded 3-oxazoline **5d** (178 mg, 55%) as a colorless oil which was a 50:50 mixture of diastereomers (based on ^1H NMR). When this oil was allowed to stand with petroleum ether (6 mL), crystalline *cis*-**5d** (65 mg) separated: mp 109−109.5 °C; IR (KBr) 1730, 1630 cm^{-1}; ^1H NMR δ 7.80 (m, 2H), 7.40 (m, 3H), 7.32 (d, J = 8.5 Hz, 2H), 6.80 (d, J = 8.5 Hz, 2H), 6.69 (d, J = 3.0 Hz, 1H), 5.69 (ddd, J = 8.5, 3.0, 3.0 Hz, 1H), 3.80 (s, 3H), 3.63 (s, 3H), 2.77 (dd, J = 16.0, 3.0 Hz, 1H), 2.41 (dd, J = 16.0, 8.5 Hz, 1H); ^{13}C NMR δ 169.1, 167.2, 159.0, 132.0, 130.5, 128.3, 127.9, 127.1, 113.2, 105.3, 81.0, 54.4, 51.1, 39.6.

trans-**5d**: IR (film) 1740, 1630 cm^{-1}; ^1H NMR δ 7.80 (m, 2H), 7.40 (m, 3H), 7.28 (d, J = 8.5 Hz, 2H), 6.77 (d, J = 8.5 Hz, 1H), 6.64 (d, J = 5.0 Hz, 1H), 5.76 (ddd, J = 8.5, 5.0, 3.0 Hz, 1H), 3.77 (s, 3H), 3.69 (s, 3H), 2.76 (dd, J = 16.0, 3.0 Hz, 1H), 2.56 (dd, J = 16.0, 8.5 Hz, 1H); ^{13}C NMR δ 169.4, 167.6, 159.5, 132.0, 131.0, 130.9, 128.5, 128.3, 127.6, 113.3, 105.2, 80.8, 54.5, 51.3, 38.1. IR and NMR data were taken from the spectra of the *trans*-**5d**-enriched petroleum ether soluble fraction.

Elemental analysis was obtained for the 50:50 diastereomeric mixture. Anal. Calcd for $C_{19}H_{19}NO_4$: C, 70.14; H, 5.89; N, 4.31. Found: C, 70.03; H, 5.79; N, 4.47.

Methyl 4-Phenyl-2-styryl-3-oxazoline-5-acetate (5e). The reaction of azirine **1** (328 mg, 1.7 mmol) and cinnamaldehyde (2.6 mL, 21 mmol) using benzene as eluant gave 3-oxazoline **5e** (275 mg, 50%) as a colorless oil which was a 50:50 mixture of diastereomers (based on ^1H NMR). When this oil was allowed to stand with petroleum ether (10 mL), solid *cis*-**5e** (110 mg) could be isolated: mp 133−135 °C; IR (KBr) 1735, 1625 cm^{-1}; ^1H NMR δ 7.75 (m, 2H), 7.40 (m, 3H), 7.10−7.30 (m, 5H), 6.74 (d, J = 16.0 Hz, 1H), 6.30 (dd, J = 5.0, 3.0 Hz, 1H), 6.21 (dd, J = 16.0, 5.0 Hz, 1H), 5.62 (ddd, J = 8.5, 3.0, 3.0 Hz, 1H), 3.64 (s, 3H), 2.78 (dd, J = 16.0, 3.0 Hz, 1H), 2.49 (dd, J = 16.0, 8.5 Hz, 1H); ^{13}C NMR δ 170.6, 169.1, 136.2, 132.7, 131.5, 130.6, 128.9, 128.2, 128.1, 127.4, 126.9, 105.8, 81.2, 52.0, 40.0.

trans-**5e**: IR (film) 1740, 1630 cm^{-1}; ^1H NMR δ 7.75 (m, 2H), 7.40 (m, 3H), 7.10−7.30 (m, 5H), 6.73 (d, J = 16.0 Hz, 1H), 6.27 (dd, J = 5.0, 5.0 Hz, 1H), 6.17 (dd, J = 16.0, 5.0 Hz, 1H), 5.71 (ddd, J = 8.5, 5.0, 3.0 Hz, 1H), 3.65 (s, 3H), 2.74 (dd, J = 16.0, 3.0 Hz, 1H), 2.51 (dd, J = 16.0, 8.5 Hz, 1H); ^{13}C NMR δ 169.6, 168.1, 127−136.5, 104.8, 80.6, 51.3, 38.0. IR and NMR

(8) Linstead, R. P.; Williams, L. T. D. *J. Chem. Soc.* **1926**, 2735.

data were taken from the spectra of the *trans*-**5e**-enriched petroleum ether soluble fraction.

Elemental analysis was obtained for the 50:50 diastereomeric mixture. Anal. Calcd for $C_{20}H_{19}NO_3$: C, 74.75; H, 5.96; N, 4.36. Found: C, 74.94; H, 6.07; N, 4.19.

Methyl 2-Furyl-4-phenyl-3-oxazoline-5-acetate (5f) was obtained from the reaction of azirine **1** (150 mg, 0.8 mmol) and 2-furaldehyde (1.2 mL, 15 mmol). Elution with benzene afforded 3-oxazoline **5f** (160 mg, 70%) as a colorless oil which was a 50:50 mixture of diastereomers (based on ^{1}H NMR). When this oil was allowed to stand with petroleum ether (5 mL), crystalline *cis*-**5f** (60 mg) separated: mp 104.5−105.5 °C; IR (KBr) 1730, 1630 cm^{-1}; ^{1}H NMR δ 7.75 (m, 2H), 7.40 (m, 4H), 6.68 (d, J = 3.0 Hz, 1H), 6.40 (d, J = 3.0 Hz, 1H), 6.35 (dd, J = 3.0, 2.0, 1H), 5.75 (ddd, J = 8.5, 3.0, 3.0 Hz, 1H), 3.62 (s, 3H), 2.80 (dd, J = 16.0, 3.0 Hz, 1H), 2.53 (dd, J = 16.0, 8.5 Hz, 1H); ^{13}C NMR δ 170.2, 169.8, 151.6, 142.6, 131.3, 130.4, 128.7, 128.3, 110.1, 108.0, 99.8, 81.1, 51.5, 39.5.

trans-**5f**: IR (film) 1740, 1630 cm^{-1}; ^{1}H NMR δ 7.75 (m, 2H), 7.40 (m, 3H), 7.35 (m, 1H), 6.65 (d, J = 4.5 Hz, 1H), 6.25−6.35 (m, 2H), 5.78 (ddd, J = 8.5, 4.5, 3.0 Hz, 1H), 3.60 (s, 3H), 2.77 (dd, J = 16.0, 3.0 Hz, 1H), 2.62 (dd, J = 16.0, 8.5 Hz, 1H); ^{13}C NMR δ 169.7, 169.6, 152.0, 142.3, 131.1, 130.5, 128.8, 128.6, 110.0, 107.7, 99.4, 80.9, 51.4, 38.0. IR and NMR data were taken from the spectra of the *trans*-**5f**-enriched petroleum ether soluble fraction.

Elemental analysis was obtained for the 50:50 diastereomeric mixture. Anal. Calcd for $C_{16}H_{15}NO_4$: C, 67.36; H, 5.30; N, 4.91. Found: C, 67.54; H, 5.14; N, 5.02.

Methyl 2.2-Dimethyl-4-phenyl-3-oxazoline-5-acetate (5g). The reaction of azirine **1** (125 mg, 0.7 mmol) and acetone (1.0 mL, 14 mmol) using PhH−Et_2O (20:1) as eluant gave 3-oxazoline **5g** (90 mg, 55%) as a colorless oil: IR (KBr) 1740, 1635 cm^{-1}; ^{1}H NMR δ 7.75 (m, 2H), 7.40 (m, 3H), 5.59 (dd, J = 9.0, 3.0 Hz, 1H), 3.66 (s, 3H), 2.75 (dd, J = 15.5, 3.0 Hz, 1H), 2.38 (dd, J = 15.5, 9.0 Hz, 1H), 1.49 (s, 3H), 1.45 (s, 3H); ^{13}C-NMR δ 169.5, 165.5, 131.2, 130.5, 128.4, 128.1, 109.0, 80.5, 51.2, 40.2, 28.8, 28.2. Anal. Calcd for $C_{14}H_{17}NO_3$: C, 68.00; H, 6.93; N, 5.66. Found: C, 67.88; H, 6.84; N, 5.81.

General Procedure for Chloranil Oxidation of 3-Oxazolines (5). A solution of 3-oxazoline **5** (0.4 mmol, 50:50 mixture of diastereomers) and chloranil (148 mg, 0.6 mmol) in toluene (8.0 mL) was heated at 110 °C for 40 h. After it was cooled to room temperature, the solution was washed with 2 N NaOH (4.0 mL), dried, and concentrated "in vacuo". The residue was purified by column chromatography using 20 g of Florisil with benzene as eluant.

Methyl 2-methyl-4-phenyloxazole-5-acetate (7a) was obtained from the reaction of 3-oxazoline **5a** (94 mg). The first component was 5-spiro-2-oxazoline **9a** (36 mg, 25%), a colorless solid: mp 130−133 °C; IR (KBr) 1680, 1665 cm^{-1}; ^{1}H NMR δ 7.95 (m, 2H), 7.50 (m, 3H), 4.80 (q, J = 7.0 Hz, 1H), 1.47 (d, J = 7.0 Hz, 3H); ^{13}C NMR δ 168.2, 160.7, 149.6, 148.0, 131.9, 131.6, 131.0, 128.7, 128.4, 126.0, 88.0, 75.1, 15.2. Anal. Calcd for $C_{15}H_9NO_2Cl_4$: C, 47.78; H, 2.41; N, 3.71. Found: C, 47.99; H, 2.57; N, 3.52.

The second component was oxazole **7a** (18 mg, 20%), a pale yellow oil: IR (film) 1745 cm^{-1}; ^{1}H NMR δ 7.55 (m, 2H), 7.30 (m, 3H), 3.75 (s, 2H), 3.73 (s, 3H), 2.47 (s, 3H); ^{13}C NMR δ 167.9, 159.2, 138.9, 137.3, 131.8, 128.3, 127.4, 126.9, 51.8, 31.7, 13.6. Anal. Calcd for $C_{13}H_{13}NO_3$: C, 67.52; H, 5,67; N, 6.06. Found: C, 67.71; H, 5.53; N, 6.21.

The third component was 5-methylene-3-oxazoline **8a** (18 mg, 20%), a pale yellow oil: IR (film) 1720, 1650 cm^{-1}; ^{1}H NMR δ 7.65 (m, 2H), 7.45 (m, 3H), 6.30 (q, J = 6.0 Hz, 1H), 5.30 (s, 1H), 3.65 (s, 3H), 1.65 (d, J = 6.0 Hz, 3H); ^{13}C NMR δ 164.3, 164.1, 160.4, 130.5, 130.4, 128.3, 128.2, 105.6, 91.5, 50.3, 20.5. Anal. Calcd for $C_{13}H_{13}NO_3$: C, 67.52; H, 5.67; N, 6.06. Found: C, 67.66; H, 5.79; N, 6.18.

Methyl 2-*tert*-butyl-4-phenyloxazole-5-acetate (7b) was obtained from the reaction of 3-oxazoline **5b** (110 mg). The first component was unreacted *trans*-**5b** (50 mg, 91%). The second component was 5-spiro-2-oxazoline **9b** (27 mg, 30%, based upon consumed **5b**), a colorless solid: mp 160−162 °C; IR (KBr) 1680, 1665 cm^{-1}; ^{1}H NMR δ 7.95 (m, 2H), 7.50 (m, 3H), 4.58 (s, 1H), 1.06 (s, 9H); ^{13}C NMR δ 168.7, 162.3, 149.8, 148.3, 132.2, 131.6, 131.1, 128.7, 128.5, 125.8, 89.4, 82.1, 29.0, 18.1. Anal. Calcd for $C_{18}H_{15}NO_2Cl_4$: C, 51.57; H, 3.61; N, 3.34. Found: C, 51.81; H, 3.79; N, 3.17.

The third component was oxazole **7b** (18 mg, 30%, based upon consumed **5b**), a pale yellow oil: IR (film) 1745 cm^{-1}; ^{1}H NMR δ 7.40−7.70 (m, 5H), 3.78 (s, 2H), 3.73 (s, 3H), 1.41 (s, 9H); ^{13}C NMR δ 168.3, 167.8, 138.8, 137.4, 131.7, 128.3, 127.5, 126.8, 51.8, 31.8, 23.2, 18.3. Anal. Calcd for $C_{16}H_{19}NO_3$: C, 70.31; H, 7.01; N, 5.12. Found: C, 70.12; H, 7.18; N, 5.26.

The fourth component was 5-methylene-3-oxazoline **8b** (6 mg, 10%, based upon consumed **5b**), a pale yellow oil. IR (film) 1720, 1650 cm^{-1}; ^{1}H NMR δ 7.65 (m, 2H), 7.40 (m, 3H), 5.89 (s, 1H), 5.28 (s, 1H), 3.66 (s, 3H), 1.07 (s, 9H); ^{13}C NMR δ 164.4, 164.1, 160.5, 130.7, 130.3, 128.4, 128.1, 116.2, 91.4, 50.3, 34.1, 23.1. Anal. Calcd for $C_{16}H_{19}NO_3$: C, 70.31; H, 7.01; N, 5.12. Found: C, 70.20; H, 7.15; N, 5.01.

Methyl 2,4-diphenyloxazole-5-acetate (7c) was obtained from the reaction of 3-oxazoline **5c** (116 mg): yield 55 mg (50%, a colorless solid); mp 67.0−67.5 °C; IR (KBr) 1735 cm^{-1}; ^{1}H NMR δ 8.10 (m, 2H), 7.70 (m, 2H), 7.20−7.40 (m, 6H), 3,89 (s, 2H), 3.76 (s, 3H); ^{13}C NMR δ 167.5, 159.7, 139.1, 138.5, 131.5, 129.6, 128.1, 128.0, 127.5, 127.4, 126.9, 126.1, 51.8, 31.9. Anal. Calcd for $C_{18}H_{15}NO_3$: C, 73.70; H, 5.16; N, 4.78. Found: C, 73.91; H, 5.33; N, 4.62.

Methyl 2-(*p*-methoxyphenyl)-4-phenyloxazole-5-acetate (7d) was obtained from the reaction of 3-oxazoline **5d** (129 mg): yield 78 mg (60%, a colorless solid); mp 94−95 °C; IR (KBr) 1735 cm^{-1}; ^{1}H NMR δ 8.00 (d, J = 8.5 Hz, 2H), 7.25−7.65 (m, 5H), 6.88 (d, J = 8.5 Hz, 2H), 3.85 (s, 2H), 3.81 (s, 3H), 3.74 (s, 3H); ^{13}C NMR δ 167.9, 160.9, 159.9, 138.5, 138.3, 131.6, 128.2, 127.8, 127.3, 126.9, 120.2, 113.6, 54.7, 51.9, 31.9. Anal. Calcd for $C_{19}H_{17}NO_4$: C, 70.58; H, 5.30; N, 4.33. Found: C, 70.40; H, 5.46; N, 4.23.

Methyl 4-phenyl-2-styryloxazole-5-acetate (7e) was obtained from the reaction of 3-oxazoline **5e** (126 mg): yield 62 mg (50%, a pale yellow oil); IR (film) 1745, 1640 cm^{-1}; ^{1}H NMR δ 7.25−7.65 (m, 11H), 6.88 (d, J = 16.0 Hz, 1H), 3.84 (s, 2H), 3.75 (s, 3H); ^{13}C NMR δ 167.5, 159.5, 138.8, 138.6, 135.5, 135.4, 131.4, 128.5, 128.4, 128.1, 127.4, 126.9, 126.8, 113.9, 51.8, 31.9. Anal. Calcd for $C_{20}H_{17}NO_3$: C, 75.22; H, 5.37; N, 4.39. Found: C, 75.03; H, 5.55; N, 4.34.

Methyl 2-furyl-4-phenyloxazole-5-acetate (7f) was obtained from the reaction of 3-oxazoline **5f** (120 mg): yield 64 mg (55%, a colorless solid); mp 68.5−69.0 °C; IR (KBr) 1735 cm^{-1}; ^{1}H NMR δ 7.70 (m, 2H), 7.49 (m, 1H), 7.40 (m, 3H), 6.98 (d, J = 3.5 Hz, 1H), 6.45 (dd, J = 3.5, 2.0 Hz, 1H), 3.84 (s, 2H), 3.69 (s, 3H); ^{13}C NMR^{13}C NMR δ 168.9, 153.3, 144.4, 142.7, 139.4, 138.5, 131.0, 128.7, 128.2, 127.1, 111.9, 111.7, 52.6, 32.0. Anal. Calcd for $C_{16}H_{13}NO_4$: C, 67.84; H, 4.63; N, 4.94. Found: C, 67.92; H, 4.70; N, 4.87.

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