sorptions at 1795, 1750, and 1730 cm^{-1} (NaCl, neat) for the β-lactam, ester, and ketone moieties, respectively. The mass spectrum (CH_4, CI) gave peaks at m/z 254 and 198 for ($M^+ + 1$) and ($M^+ - C_4H_9$), respectively. The ^1H NMR exhibited the characteristic one-proton singlet at δ 4.7 for the C-2 methine; a multiplet centered at δ 2.9 for the C-8 methine reflects a 0.6 ppm upfield shift of this resonance from the monocyclic precursors **9–12** and probably reflects both increased sp^3 character on nitrogen as well as shielding by the C-3 carbonyl.

The relatively surprising stability of **13** opens the possibility that numerous, stable "anti-Bredt" β-lactams can be synthesized and studied for novel chemical and possibly biological properties. Investigations along these lines are in progress in these laboratories and shall be reported on in due course.

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Supplementary Material Available: Physical data for all new compounds (2 pages). Ordering information is given on any current masthead page.

Oxazoline Route to Azomethine Ylides

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Recent progress[1,2] in generation of nonstabilized azomethine ylides allows synthesis of relatively simple five-membered nitrogen rings by 2 + 3 dipolar cycloaddition. Acyl-stabilized analogues **3** can be similarly used to prepare more complex cycloadducts,[3,4] but the most practical method to date for their generation via aziridine pyrolysis has limitations. Only the most reactive dipolarophiles can trap aziridine-derived dipoles stereospecifically,[3] and the behavior of alkyl-substituted aziridines (**2**, $R^1 = CH_3$, etc.) is surprisingly complex in certain systems.[5,6]

An alternative route to **3** from 4-oxazolines **4** has been contemplated[7] ever since the reverse reaction was demonstrated in a study of the valence bond tautomers **1–4**.[8] However, we can find only one example where pyrolysis of **4** with a dipolarophile is claimed to result in adduct formation.[7f] The other known 4-oxazolines **4**[7,8] are remarkably resistant to this process. They are also relatively inaccessible, and so far, all have been made directly or indirectly by acylaziridine pyrolysis, as in **2** → **3** → **4**.

We have developed an independent route to 4-oxazolines **4** by reduction of oxazolium salts **5** with $PhSiH_3/CsF$.[9] This reagent provides active hydride under aprotic, essentially neutral conditions, and overreduction of **4** is easily avoided. Most important, the silane/fluoride reagent selectively reduces oxazolium salts in the presence of dipolarophiles such as acrylate or acetylenedicarboxylate and permits in situ trapping of unstable oxazolines.

Isolation of the 4-oxazolines from oxazolium salt reductions has not been achieved due to their hydrolytic sensitivity but the 4,5-diphenyl derivative **4a** is stable in solution at room temperature (NMR, CD_3CN, CH_3CH, 5.02 ppm, quartet, J = 5.5 Hz). Addition of dimethyl acetylenedicarboxylate (DMAD) results in conversion into a 1:1 cycloadduct to which we assign the bicyclic structure **6** based on NMR evidence.[10] Similar adducts are obtained from other 4,5-disubstituted 4-oxazolines made in situ (Table I).

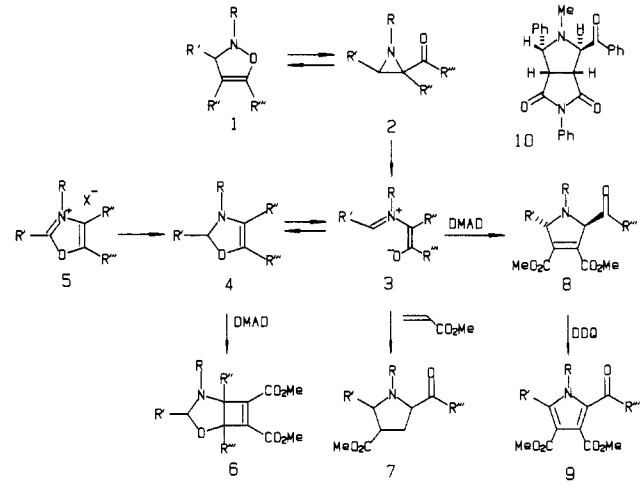
Table I. 2 + 2 Cycloadducts from 4-Substituted 4-Oxazolines (R = CH_3)

entry	R′	R″	R‴	product	yield
a	CH_3	Ph	Ph	**6a**	70%
b	CH_3	CH_3	CH_3	**6b**	82%
c	Ph	CH_3	Ph	**6c**	81%

Table II. 2 + 3 Cycloadducts from 4-Unsubstituted 4-Oxazolines (R = CH_3)

				yields	
				7	**9**[a]
d	Ph	H	Ph	55%[b]	95%
e	Ph	H	CH_3	87%	90%
f	Ph	H	OC_2H_5	63%[b]	93%
g	Ph	H	H	57%	
h	CH_3	H	OC_2H_5	61%	64%
i	CH_3	H	Ph	40%[b]	85%

[a] After DDQ oxidation of the crude product. [b] The other regioisomer (single stereoisomer) is formed in (d) 9%, (f) 10%, (i) 20%.



In contrast, several oxazolium salts having no substituent at C_4 are reduced by the in situ method ($PhSiH_3/CsF$/dipolarophile)

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(10) For example, **6b**: ^1H NMR ($CDCl_3$, ppm) 3.94 (1 H, q, J = 5.2 Hz), 3.78 (6 H, s), 1.43 (3 H, s), 1.33 (3 H, s), 1.31 (3 H, d, J = 5.2 Hz); ^{13}C NMR ($CDCl_3$, ppm) 167.2 (s), 162.6 (s), 142.9 (s), 140.8 (s), 89.0 (d), 85.7 (s), 74.5 (s), 52.0 (q), 51.9 (q), 31.6 (q), 17.9 (q), 16.1 (q), 15.9 (q).

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to give 4-oxazolines (**4**, R″ = H) which open spontaneously to the dipoles **3** at room temperature. Further reduction occurs in the absence of dipolarophiles, but in the presence of DMAD, **3d** affords a single cycloadduct **8d** in excellent yield.[11] Attempts to purify the 2,5-dihydropyrrole are complicated by double-bond migration and aromatization. For this reason, related DMAD cycloadducts have been assayed after aromatization to the pyrroles **9** with DDQ (Table II).[12] The trans stereochemistry for **8d** is assigned by NMR comparisons with related dihydropyrroles.[3c,d] The corresponding dipole geometry **3d** is also supported by formation of the *N*-phenylmaleiimide adduct **10**.[13] An experiment where **3d** is generated from **4d** in the presence of methyl acrylate again affords a 2 + 3 cycloadduct **7d** assumed to have similar stereochemistry. Several related acrylate adducts are likewise formed as single stereoisomers (Table II).

Our findings suggest that the relative stability of valence bond tautomers **1**–**4** is strongly influenced by the presence of a substituent R″ at C_4. When R″ = alkyl, aryl, etc., **4** resists opening to dipole **3** and there are several examples where **4** can be made by heating the aziridine **2**.[7,8] For R″ = H, however, ring opening of **4** to **3** is rapid at room temperature. Valence bond tautomerization of the corresponding aziridines **2** is much slower and requires ≥ca. 60 °C, so the relative stability of **4** vs. **2** (R″ = H) now favors the aziridine **2**. We have no comment on the reasons for the reversal of 4-oxazoline vs. aziridine stability, but the greater ease of oxazoline ring cleavage to **3** when R″ = H compared to R″ = aryl, alkyl, etc. can be attributed to eclipsing effects which destabilize the planar dipole when R″ is larger than hydrogen.

We expect that the 4-oxazoline route to azomethine ylides **3** demonstrated here[16] will prove superior to the aziridine approach in most cases, especially when alkyl substitution on the dipole is desired. Precursor oxazoles are easily made and modified, and a variety of applications of this technique are under investigation. We also note that controlled reduction of imidate salts to the aldehyde oxidation state is central to our procedure. The potential of the $PhSiH_3/CsF$ reagent for this purpose in other synthetic applications is clear.

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Registry No. 3 (R = Me; R′ = R‴ = Ph; R″ = H), 102537-03-1; **3** (R = R‴ = Me; R′ = Ph; R″ = H), 102537-04-2; **3** (R = Me; R′ = Ph; R″ = H; R‴ = OC_2H_5), 102537-05-3; **3** (R = Me; R′ = Ph; R″ = R‴ = H), 102537-06-4; **3** (R = R′ = Me; R″ = H; R‴ = OC_2H_5), 102537-07-5; **3** (R = R′ = Me; R″ = H; R‴ = Ph), 102537-08-6; **4** (R = R′ = Me; R″ = R‴ = Ph), 102536-93-6; **4** (R = R′ = R″ = R‴ = Me), 102536-94-7; **4** (R = R″ = Me; R′ = R‴ = Ph), 102536-95-8; **5** (R = H; R′ = Me; R″ = R‴ = Ph), 102536-90-3; **5** (R = H; R′ = R″ = R‴ = Me), 102536-91-4; **5** (R = H; R′ = R‴ = Ph; R″ = Me), 102536-92-5; **5** (R = R″ = H; R′ = R‴ = Ph), 59973-27-2; **5** (R = R″ = H; R′ = Ph; R‴ = Me), 102536-99-2; **5** (R = R″ = H; R′ = Ph; R‴ = OC_2H_5), 102537-00-8; **5** (R = R″ = R‴ = H; R′ = Ph), 64001-60-1; **5** (R = R″ = H; R′ = CH_3; R‴ = OC_2H_5), 102537-01-9; **5** (R = R″ = H; R′ = CH_3; R‴ = Ph), 102537-02-0; **5** (R = R′ = Me; R″ = R‴ = Ph), 102537-21-3; **5** (R = R′ = R″ = R‴ = Me), 102537-22-4; **5** (R = R″ = Me; R′ = R‴ = Ph), 102537-23-5; **5** (R = Me; R′ = R‴ = Ph; R″ = H), 54901-89-2; **5** (R = R‴ = Me; R′ = Ph; R″ = H), 102537-24-6; **5** (R = Me; R′ = Ph; R″ = H; R‴ = OC_2H_5), 102537-25-7; **5** (R = Me; R′ = Ph; R″ = R‴ = H), 102537-26-8; **5** (R = R′ = Me; R″ = H; R‴ = OC_2H_5), 102586-38-9; **5** (R = R′ = Me; R″ = H; R‴ = Ph), 64988-40-5; **6a**, 102536-96-9; **6b**, 102536-97-0; **6c**, 102536-98-1; **7** (R = Me; R′ = R‴ = Ph), 102537-15-5; **7** (R = R‴ = Me; R′ = Ph), 102537-16-6; **7** (R = Me; R′ = Ph; R‴ = OC_2H_5), 102537-17-7; **7** (R = Me; R′ = Ph; R‴ = H), 102537-18-8; **7** (R = R′ = Me; R‴ = OC_2H_5), 102537-19-9; **7** (R = R′ = Me; R‴ = Ph), 102537-20-2; **8d**, 102537-09-7; **9** (R = Me; R′ = R‴ = Ph), 102537-10-0; **9** (R = R‴ = Me; R′ = Ph), 102537-11-1; **9** (R = Me; R′ = Ph; R‴ = OC_2H_5), 102537-12-2; **9** (R = R′ = Me; R‴ = OC_2H_5), 102537-13-3; **9** (R = R′ = Me; R‴ = Ph), 102537-14-4; DMAD, 762-42-5; CH_2=$CHCO_2Me$, 96-33-3.

(11) **8d**: ^1H NMR (CD_3CN, ppm) 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).

(12) For example, **9d**: ^1H NMR ($CDCl_3$, ppm) 7.8–7.45 (10 H, m), 3.57 (3 H, s), 3.53 (3 H, s), 3.23 (3 H, s).

(13) **10**: ^1H NMR ($CDCl_3$, ppm) H_2 at 5.54 (s, $J_{2,3} \sim 0$ Hz); H_5 at 4.9 (d, $J_{4,5}$ = 9.1 Hz); see ref 3c,e for analogous structures.

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(15) Note that **3** is not necessarily formed from **2** since two isomeric dipoles can be formed by conrotatory aziridine opening, both of which would give **8**.

(16) Typical procedure: methyl triflate (0.249 mmol) was added to a solution of 5-methyl-2-phenyloxazole (0.226 mmol) in 3 mL of dry acetonitrile. After the mixture was stirred for 2 h at room temperature, phenyl silane (0.339 mmol) and methyl acrylate (0.747 mol) were added and this mixture was added by cannula to anhydrous cesium fluoride (0.452 mmol) in acetonitrile (4 mL). After 2 h, solvent removal and flash chromatography gave **7e** (0.197 mmol, 87%) as a white solid (mp 54–55 °C).

Stereochemistry of the 5-(*p*-Aminophenyl)-1,2,3,4-tetrahydroxypentane Portion of Methanopterin

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Methanopterin (Figure 1), a recently characterized cofactor[1,2] involved in the biological reduction of CO_2 to CH_4,[3,4] is currently postulated to function in its reduced state (tetrahydromethanopterin) as a C_1 carrier at the oxidation levels of formyl, methenyl, methylene, and methyl in a manner similar to that described for folic acid.[5] Recent work, aimed at defining the biosynthesis of this coenzyme, has shown that the pterin ring most likely arises from guanosine triphosphate[6,7] and that the 7-methyl group arises from methionine.[8] The aromatic portion of the 5-(*p*-aminophenyl)-1,2,3,4-tetrahydroxypentane has been shown to arise from *p*-aminobenzoic acid[6] and the side chain polyol from a pentose[6,8] with the C-1 through C-5 carbons of the side chain arising from the C-5 through C-1 carbons of the pentose. It is proposed that the reaction proceeds by the addition of the para carbon opposite the amino group of the *p*-aminobenzoic acid to the C-1 of the pentose with the subsequent loss of CO_2 in a reaction sequence analogous to that observed in the formation of indoleglycerol phosphate from phosphoribosyl anthranilate during the biosynthesis of tryptophan.[9] Since the configuration of carbon atoms 2–4 of the pentose is not expected to change during this type of reaction, the determination of the stereochemistry of the asymmetric carbons 2–4 of the 5-(*p*-aminophenyl)-1,2,3,4-tetrahydroxypentane will define which pentose is involved in the biosynthesis. This stereochemistry was determined to be ribo by the synthesis of each of the four possible stereoisomers. Only the ribose-derived isomer has the same chromatographic properties as the isomer present in methanogenic bacteria.

Each of the stereoisomers was prepared by the synthetic scheme outlined in Figure 2 starting with the known pentoses D-arabinose, D-ribose, D-xylose, and D-lyxose. The conversion of the pentoses into their diethyl dithioacetal derivatives (step a) and the subsequent conversion of these derivatives into their diisopropylidene derivatives (step b) have been previously described.[10-12] The

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