$J_{2'-3'}$ = 2.8 Hz, 1, $H_{2'}$), 8.60 (br, 1, 6-NH-pivalyl), 8.56 and 8.86 (s and s, 1 and 1, H_8 and H_2); mass spectrum (of the 3′-*O*-trimethylsilyl derivative of **4a**) calcd for $C_{23}H_{35}N_5O_5Si$ 489.2407, found 489.2425. Deblocking of **4a** with methanolic sodium methoxide gave (in 84% yield from **3a**) 6-amino-9-(2-deoxy-D-*erythro*-pent-1-enofuranosyl)purine (**4b**): mp 196–198°, resolidifies at ~202–210°, and melts with decomposition at 224–235°; $[\alpha]^{27}D$ 100.5° (*c* 0.96, DMF); uv (MeOH) max 250 nm (ϵ 16,500), sh 281, 290 nm (ϵ 7200, 4700), min 222 nm (ϵ 10,700); uv (0.1 *N* NaOH) max 251 nm (ϵ 16,400), sh 279, 290 nm (ϵ 6200, 3300), min 221 nm (ϵ 10,600); nmr (DMSO-d_6, TMS internal) δ 3.59 ("t," $J_{apparent}$ = 6 Hz, 2, $H_{5',5''}$), 4.43 ("sextet," $J_{4'-5',5''}$ = 5.0 Hz, $J_{4'-3'}$ = 3.0 Hz, 1, $H_{4'}$), 4.84 ("quintet," $J_{3'-4'}$ = 3.0 Hz, $J_{3'-3'-OH}$ = 6.0 Hz, 1, $H_{3'}$), 5.03 (t, $J_{5'-OH-5',5''}$ = 6.0 Hz, 1, 5′-OH); 5.35 (d, $J_{3'-OH-3'}$ = 6.0 Hz, 1, 3′-OH), 5.69 (d, $J_{2'-3'}$ = 2.8 Hz, 1, $H_{2'}$), 7.47 (s, 2, 6-NH_2), 8.30 and 8.34 (s and s, 1 and 1, H_2 and H_8); mass spectrum calcd for $C_{10}H_9N_5O_2$ ($M^+ - H_2O$) 231.0756, found 231.0752; mass spectrum [of the tris(trimethylsilyl) derivative of **4b**] calcd for $C_{19}H_{35}N_5O_3Si_3$ 465.2047, found 465.2062; spectrophotometrically determined $pK_a \sim 3.31$.

Anal. Calcd for $C_{10}H_{11}N_5O_3$: C, 48.19; H, 4.45; N, 28.10. Found: C, 48.28; H, 4.74; N, 27.92.

It is interesting to note that conjugation of the adenine ring with the 1′–2′ double bond shifts the uv spectrum hypsochromically as found with 9-(5-methyl-2-furyl)adenine.[3a] Heating **4b** gives 9-(5-methyl-2-furyl)adenine[3a] and attempted determination of the uv spectrum at pH 1 results in rapid cleavage to adenine. Blue fluorescence is observed when **4b** is visualized under 2537-Å light, which could be useful if this presumably base-sugar planar 2′-deoxyadenosine derivative can be incorporated into DNA and/or oligonucleotides.

Hydrogenation of **4b** at 3 psi over palladium/charcoal in alcohol–water containing sodium bicarbonate gave 2′-deoxyadenosine and 6-amino-9-(2-deoxy-α-D-*erythro*-pentofuranosyl)purine[13] in yields of 60 and 12%. It is interesting that the β:α stereoselectivity (5:1) is so high. A preliminary attempt at reduction of **4a** appeared to give no detectable α anomer, although accompanying hydrogenolysis of the glycosidic linkage to give 6-*N*-pivalyladenine made evaluation difficult.

The present study provides a possible route for the conversion of an intact ribo nucleoside to its 2′-deoxy-α anomer. As well, the new nucleoside 1-ene system is now available for biochemical, fluorescence, and synthetic studies.

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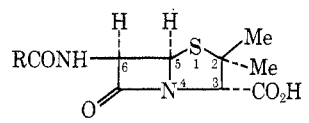
An Exocyclic Thio Analog of the Penicillin System[1]

Summary: A number of 3-arylidene-2-thioalkyl-1-pyrrolines were synthesized from 2-pyrrolidone *via* a three-step sequence and condensation of these thioimidates with phenoxyacetyl chloride in presence of triethylamine led to novel penicillin analogs in which substituents at C-5 have been interchanged to give an exocyclic alkylthio substituent and a carbocyclic five-membered ring; the stereochemistry of these fused β-lactams was established from a study of their nmr spectra.

Sir: An important structural feature of penicillins (**1**) in clinical use is a fused thiazolidine β-lactam system. In the course of research directed toward the synthesis of penicillin and cephalosporin analogs we became interested in the possibility of interchanging the substituents at C-5 to obtain derivatives of a novel fused β-lactam system (**2**) with an exocyclic alkylthio substituent. We describe here the preparation of some derivatives of this previously unknown class of compounds.



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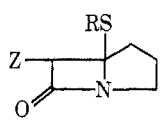

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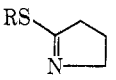
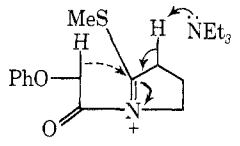


3

In recent years we[2] have synthesized diverse types of mono- and polycyclic β-lactams by the reaction of appropriate acid chlorides with imines in the presence of triethylamine. To take advantage of this approach we sought thioimidates of type **3** as intermediates for **1**. The reaction of phenoxyacetyl chloride and triethylamine with 2-methylthio-1-pyrroline (**3**, R = Me), however, led to the pyrroline derivative **5** instead of the desired β-lactam **6**. Evidently the initial reaction intermediate was **4** which underwent an elimination reaction in preference to cyclization.

To preclude the elimination pathway and thereby favor cyclization to a β-lactam, thioimidates of type **9** were examined next as imine components in the reaction with acid chlorides and triethylamine. Following the method of Zimmer[3] a series of pyrrolidone derivatives of type **7** were prepared by treating *N*-acetylpyrrolidone with aromatic aldehydes in the presence of sodium hydride. A suspen-



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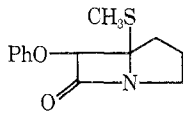

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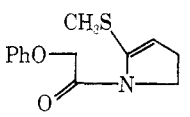
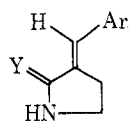


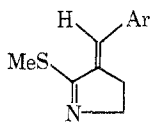
5

sion of 7 (Ar = Ph) and a 0.2 molar equiv of phosphorus pentasulfide was heated under reflux in pyridine for 1 hr and poured through filter paper into a large volume of warm (50°) water.[4] The thioamide 8 (Ar = Ph), mp 163–165°, obtained in quantitative yield, was heated with methyl iodide in tetrahydrofuran solution; the product was neutralized with triethylamine, extracted with dichloromethane, and purified by distillation to give the desired thioimidate (**9**, Ar = Ph), 68%, mp 94–95°. Several other members of this series were prepared in an analogous manner with yields of 33, 50, and 60% for **9b**, **9c**, and **9d**, respectively.

The reaction of **9a** with methoxyacetyl chloride and triethylamine in dichloromethane gave a single product, ir (Nujol) 1780 cm^{-1}, mp 73–74°, in 68% yield, which was shown to be the bicyclic β-lactam **10** on the basis of ir, mass spectral and pmr characteristics.

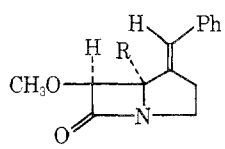


7, Y = O
8, Y = S



9a, phenyl
b, 3,4-dimethoxyphenyl
c, *p*-chlorophenyl
d, *m*-nitrophenyl

The stereochemistry of the β-lactam **10** was established by studying the pmr spectrum of the sulfoxide, **11**, mp 122–123°, and the sulfone **12**, mp 145–146°, obtained by successive oxidations of **10a** with *m*-chloroperoxybenzoic acid.[5] The sulfur was confirmed to be the site of oxidation by the progressive downfield shift of the methylthio group in the pmr spectrum, going from 2.20 ppm in **10a** to 2.45 ppm in 11 to 3.17 ppm in **12**. For this series of compounds



10, R = CH_3S
11, R = $CH_3S\rightarrow O$
12, R = CH_3SO_2

the methoxyl resonance position was virtually unchanged while the C-6 proton shifted from 4.41 ppm in **10** to 4.68 ppm in **11** and 4.60 ppm in **12**.

The 16-Hz anisotropic deshielding effect observed for the C-6 proton upon oxidation of the C-5 methythio substituent is clearly appropriate only for a situation in which the methythio group is oriented cis to the C-6 proton and thus trans to the C-6 methoxy group. In all of these compounds the olefinic proton showed a characteristic trans allylic coupling of 1–2 Hz. On the basis of the pmr data the stereostructure **10a** can be deduced. The trans disposition of the methoxy group in **10a** with respect to the thio function is in agreement with the directive influence and stereospecificity observed earlier by us in forming β-lactams from thioimidates.[6] In view of our earlier studies on the cycloaddition of various acid chlorides—in particular azidoacetyl chloride—to imines, it can be expected that the method described above could be extended to the synthesis of diverse bicyclic β-lactams of type **2**. Further work along these lines is in progress.

Acknowledgment. The authors are grateful to Stevens Institute of Technology for support of this work.

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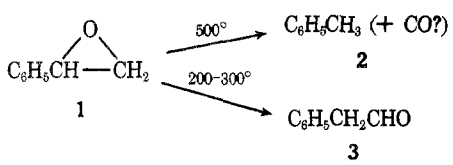
Thermal Rearrangement of 1,2-Epoxyethylbenzene

Summary: Thermolysis of 1,2-epoxyethylbenzene at 500° has been found to produce toluene while thermal rearrangement at 200–300° gives phenylethanal *via* a first-order process; $k = 6.02 \pm 0.12 \times 10^{-2}$ hr^{-1} at 200° in benzene.

Sir: We wish to communicate the results of our investigation of the thermal lability of 1,2-epoxyethylbenzene (**1**). While subjection of **1** to temperatures in the range of 500° leads to a clean thermolysis to toluene (**2**) (Figure 1) and, presumably, carbon monoxide with traces of phenyl acetylene (~1.6%) also being formed, the use of more moderate temperatures gives selective rearrangement of **1** to phenylethanal (**3**) *via* epoxide ring opening and a formal 1,2-hydrogen shift.



1 → (500°) **2** $C_6H_5CH_3$ (+ CO?)
1 → (200–300°) **3** $C_6H_5CH_2CHO$

Rate data, obtained under liquid phase conditions in benzene solution, show this rearrangement to obey first-order kinetics and to have rate constants as tabulated in Table I. Activation parameters derived from these data are $E_a = 29.2 \pm 0.6$ kcal/mol, $\Delta H^*_{200} = 28.3 \pm 0.6$ kcal/mol, and $\Delta S^*_{200} = +11.0 \pm 1.2$ cal/mol°K. In addition, the rate of rearrangement appears to be somewhat influenced by solvent, being ~35% more rapid in benzene (at 200°) than in toluene.

The dramatic influence of the phenyl substituent on the direction of ring opening of **1** is demonstrated by the absence of acetophenone (**6**) from the product mixture. This contrasts markedly with the complete lack of selectivity in C_1–O *vs.* C_2–O bond breakage reported by Gritter and Sabatino[1] for the photolysis of **1** at 2537 Å. A rather selec-