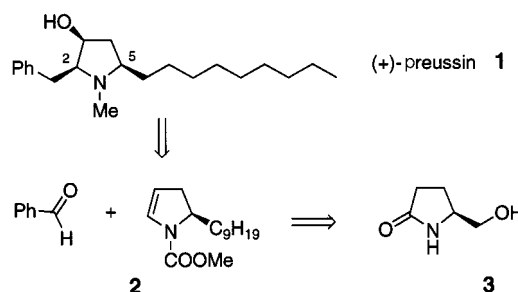


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- [13] The potential is converted into ΔG with the equation $\Delta G = -nFE$, where n is the number of electrons per mole, F is Faraday's constant, and E is the experimental reduction potential for the stated reaction.
- [14] In the case of compound **B** the value of $\Delta G_{\text{overall}}^B$ can be compared to the standard ΔG value for the conversion of O₂ into H₂O since the concentrations of all pertinent species are known.
- [15] The ΔG value for the O₂/H₂O₂ couple will be more negative if the activity of H₂O₂ is below 1.0M in our experimental conditions.
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Unprecedented Facial Diastereoselectivity in the Paternò–Büchi Reaction of a Chiral Dihydropyrrole—A Short Total Synthesis of (+)-Preussin**

Thorsten Bach* and Harm Brummerhop

The Paternò–Büchi reaction^[1] of aromatic aldehydes with enol and enamine derivatives gives 3-heteroatom-substituted 2-aryloxetanes in good yield.^[2] Subsequent Pd-catalyzed hydrogenolysis of these compounds leads to a bond cleavage between the oxygen atom and the C2 atom of the oxetane and yields the products of a formal carbohydroxylation.^[3] The carbohydroxylation of the N-acceptor-substituted 2,3-dihydropyrrole **2** appealed to us as an approach to the antifungal pyrrolidinol alkaloid (+)-preussin^[4] (**1**). A straightforward synthesis^[5] of this natural product appeared possible from the commercially available (*S*)-pyroglutaminol (**3**; Scheme 1).



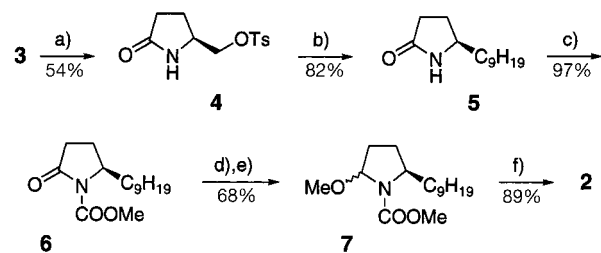
Scheme 1. Retrosynthesis of (+)-preussin (**1**).

We now report on the realization of this goal in which the pivotal Paternò–Büchi reaction of **2** proceeded with a substrate-induced facial diastereoselectivity previously unobserved in photocycloaddition reactions. Indeed, a bulky substituent within a five-membered ring is known to direct the attack of a reactant to the opposite face (*anti* attack). Examples of this are found in Paternò–Büchi reactions^[6] and in intermolecular [2+2] photocycloadditions.^[7] The thermal addition of ketenes to dihydropyrroles, which are analogues of **2**, also proceeded with *anti* attack to the existent substituent.^[8] The notion that made us hope for the *syn* attack shown in Scheme 1 was based on an observation by Beckwith and Chai^[9] in which they showed that in radical reactions of N-acceptor-substituted five-membered rings that bear a stereogenic center in the C2 position the radical center in the C5 position is attacked from the same face as the large substituent at C2 points to. Since Paternò–Büchi reactions are known to occur via radical intermediates^[1, 10] a selection at

[*] Prof. Dr. T. Bach, Dipl.-Chem. H. Brummerhop
Fachbereich Chemie der Philipps-Universität
Hans-Meerwein-Strasse, D-35032 Marburg (Germany)
Fax: (+49) 6421-288917
E-mail: bach@chemie.uni-marburg.de

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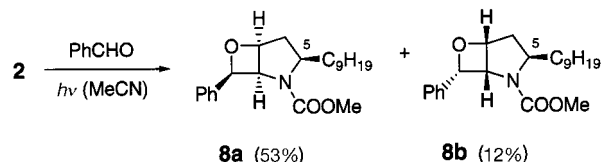
the triplet-1,4-biradical^[11] stage was deemed to be likely and we turned to the synthesis of dihydropyrrole **2** (Scheme 2). The primary alcohol of (*S*)-pyroglutaminol^[12] (**3**) was converted into the known tosylate **4**.^[13] The nonyl side chain was then established by a nucleophilic substitution reaction with



Scheme 2. Synthesis of dihydropyrrole **2**. a) TsCl, pyridine, 25 °C, 5 h; b) Li₂Cu(*n*C₈H₁₇)₂CN in THF/hexane (2/1), -78 → 25 °C, 16 h; c) BuLi in THF/hexane (4/1), -78 °C, 1 h, then ClCOOMe, -78 → 0 °C, 3 h; d) LiBEt₃H in THF, -78 → 0 °C, 3 h; e) Me₂C(OMe)₂, CSA in CH₂Cl₂, 0 °C, 0.5 h; f) TMSOTf, EtNiPr₂ in CH₂Cl₂, 0 °C, 0.5 h. CSA = camphor-sulfonic acid, TMS = trimethylsilyl, Tf = trifluoromethanesulfonyl, Ts = toluene-4-sulfonyl.

a higher order dioctyl cuprate.^[14] The endocyclic double bond was introduced in three steps after the pyrrolidinone **5** had been acylated with methyl chloroformate. The pyrrolidinone **6** was reduced with LiBEt₃H to the hemiaminal, which was transformed without isolation into the *N,O*-acetal **7** by treatment with dimethoxypropane. The subsequent elimination to the target compound **2** was conducted with NiPr₂Et/TMSOTf.^[15]

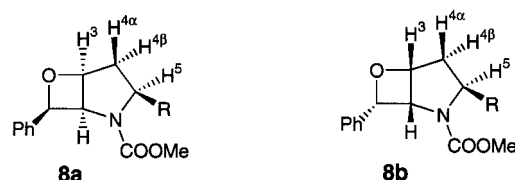
The Paternò–Büchi reaction of dihydropyrrole **2** with benzaldehyde proceeded smoothly and yielded three products (Scheme 3). One of the products was a 2-aminoxetane as determined by NMR spectroscopy, but because of its acid



Scheme 3. Paternò–Büchi Reaction of dihydropyrrole **2**.

lability it could not be isolated. The two other products were diastereoisomers of a 3-aminoxetane, and they were obtained in yields of 53 and 12%. NOESY NMR studies revealed that both products **8a** and **8b** exhibited an all-*cis* substitution pattern within the oxetane nucleus, which was to be expected from previous studies.^[16] Consequently, the products differed from each other only in the relative configuration of the annelated four-membered ring and the nonyl substituent at the C5 position.

The structural proof of the products is based on the different ¹H NMR coupling patterns of the two diastereoisomers (Figure 1). The comparison with calculated coupling constants^[17] facilitated an unambiguous correlation, which was confirmed by NOESY experiments. They clearly revealed that the attack of the photoexcited benzaldehyde on dihydropyrrole **2** had taken place on the face of the nonyl chain.

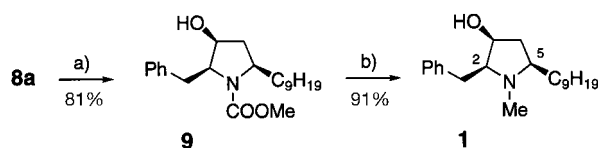


$J_{4\beta,5} = 9.1$ (8.3),	$J_{4\beta,3} = 5.2$ (5.9)	$J_{4\beta,5} = 6.2$ (7.3),	$J_{4\beta,3} = 2.2$ (2.6)
$J_{4\alpha,5} = 1.9$ (2.1),	$J_{4\alpha,3} < 1$ (1.7)	$J_{4\alpha,5} = 7.2$ (7.5),	$J_{4\alpha,3} = 7.2$ (6.8)

Figure 1. Measured (and calculated^[17]) vicinal coupling constants [Hz] of the protons in the pyrrolidine ring of **8a** and **8b**.

The question why this is the case is currently being studied. On one hand, it is possible that a selection occurs in the intermediate 1,4-biradical as a consequence of the pyramidalization of the nitrogen atom.^[18] On the other hand, hydrophobic interactions between the nonyl side chain and the phenyl nucleus may favor an approach from the *syn* face. Indeed force field calculations^[17] revealed a clear preference for a conformation of the major diastereoisomer **8a** in which the alkyl chain and the phenyl group are oriented fully parallel to each other.

The synthesis of (+)-preussin was completed by hydrogenation of the major photocycloaddition product **8a** to the pyrrolidinol **9** (Scheme 4). The LiAlH₄ reduction of the methoxycarbonyl group to the methyl group was facile and we isolated (+)-preussin (**1**) as a yellowish oil. The optical rotation ($[\alpha]_D^{25} = +22.1$, *c* = 1 in CHCl₃) and the other analytical data are in accord with the literature data.^[4]



Scheme 4. Completion of the synthesis of (+)-preussin (**1**). a) H₂, Pd(OH)₂/C in MeOH, 25 °C, 3.5 h; b) LiAlH₄ in THF, 66 °C, 2.5 h.

Overall the synthesis of **1** from (*S*)-pyroglutaminol (**3**) proceeded in a total yield of 10% over nine steps. In the chosen synthetic sequence the alkyl substituent in the C5 position can be varied at will by appropriate choice of the cuprate reagent. In previous studies^[2, 19] it has already been shown that various aromatic aldehydes can be employed for the Paternò–Büchi reaction of heteroatom-substituted alkenes. Consequently, the arylmethyl substituent in the C2 position can also be varied over a broad range.

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Ethenedithione (S=C=C=S): Does It Obey Hund's Rule?*

Ngai Ling Ma and Ming Wah Wong*

One of the fundamental rules governing the electronic structure of molecules is Hund's rule of maximum multiplicity. In order to minimize Coulombic repulsion, two electrons in a pair of degenerate orbitals prefer to be unpaired. Thus, for a molecule like O₂, the stability of the three lowest electronic states is in the order $^3\Sigma_g^- > ^1\Delta_g > ^1\Sigma_g^+$.

For the linear cumulated carbon oxides and carbon sulfides, XC_nX (X=O and S; n is even), such species have two electrons in the degenerate π HOMO, and hence are expected to have a triplet ground state. However, for the smallest member of the cumulated carbon sulfides, ethenedithione (S=C=C=S), the nature of its ground state remains controversial. C₂S₂ was first predicted by Schaefer et al. to be an experimentally accessible species in the gas phase that should have a triplet ground state.^[1] The existence of this transient molecule has been demonstrated by mass spectrometry^[2–4] and matrix isolation IR^[3, 5] and UV^[3, 5, 6] spectroscopy. Based on the unusual thermodynamic stability and extreme intermolecular activity, Wentrup et al. suggested that C₂S₂ is a triplet species.^[3] On the other hand, Maier et al. observed a very weak signal in the ESR spectrum of C₂S₂, which indicated that it could possess a singlet ground state. In addition, they performed complete active space (CAS) SCF and CISD calculations and found that the ground state of C₂S₂ is $^1\Delta_g$, with a singlet–triplet (S–T) gap estimated to be 3 and 9 kJ mol^{–1}, respectively. Hence, C₂S₂ was suggested by Maier et al. to be one of the first examples for the “violation of Hund's rule in an equilibrium structure”.^[5]

Given that the reported S–T gap is rather small using moderate levels of theory, whether C₂S₂ exists as a singlet or triplet remains uncertain. Herein we report ab initio calculations that are at a significantly higher level of theory than those reported previously in order to establish definitively the nature of the ground electronic state for ethenedithione.

First, we examined the energy difference of the three lowest states of C₂S₂, namely $^3\Sigma_g^-$, $^1\Delta_g$, and $^1\Sigma_g^+$, using various single-determinant methods (Table 1). The $^3\Sigma_g^-$ and $^1\Delta_g$ states were obtained by using an unrestricted Hartree–Fock (UHF) starting point. At the HF/6-31G* level, the $^1\Delta_g$ and $^1\Sigma_g^+$ states lie 31 and 98 kJ mol^{–1}, respectively, above the $^3\Sigma_g^-$ state. Inclusion of electron correlation at the MP2 level significantly lowers the energy gap by 15 and 61 kJ mol^{–1}, respectively. It is important to note that the $\langle S^2 \rangle$ values of the UHF wavefunctions of the $^3\Sigma_g^-$ (2.10) and $^1\Delta_g$ (1.07) states are significantly different from that of the corresponding pure spin states. In particular, the $^1\Delta_g$ state is severely spin contaminated

[*] Prof. Dr. M. W. Wong, Dr. N. L. Ma
Department of Chemistry,
National University of Singapore
Kent Ridge, Singapore 119260 (Singapore)
Fax: (+65) 7791691
E-mail: chmwmw@nus.edu.sg

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