II41, 86409-78-1; II42, 86409-79-2; II43, 60468-24-8; III31, 78-75-1; III32, 533-98-2; III33, 3234-49-9; III34, 10288-13-8; III38, 86409-76-9; III39, 84394-61-6; III40, 86409-77-0.

Supplementary Material Available: Spectral and analytical data for all new compounds (6 pages). Ordering information is given on any current masthead page.

Studies on the Oxidation of Imino Ethers

Alan J. Biloski[1] and Bruce Ganem*

Department of Chemistry, Baker Laboratory, Cornell University, Ithaca, New York 14853

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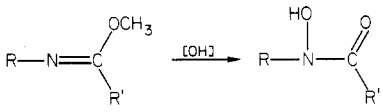
We have investigated the reactivity of imino ethers **1** toward several oxidizing agents with the hope of developing an efficient synthesis of hydroxamic acids **2** (eq 1), a family



(1)

1

3, R = *tert*-butyl; R′ = H
4, R = R′ = *tert*-butyl
5, R = *n*-C_7H_{15}; R′ = CH_3

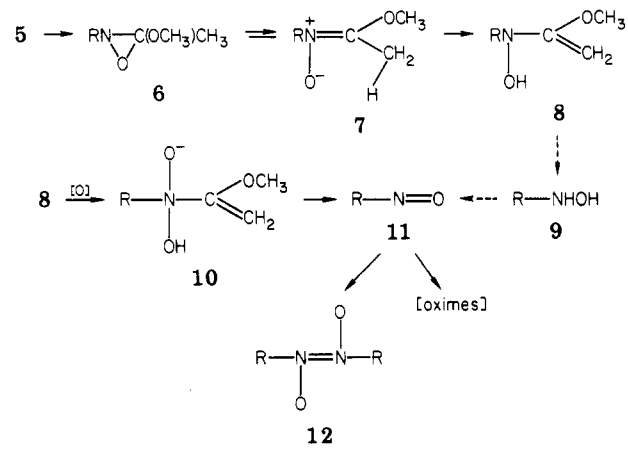
2

of naturally occurring substances with powerful iron-chelating properties.[2] Our unexpected findings constitute the subject of this paper.

The well-precedented epoxidation of imines[3] and imino ethers[4] to oxaziranes suggested that appropriately designed 3-alkoxyoxaziranes might produce hydroxamates upon acid hydrolysis. Indeed, it was first reported in 1971 that treatment of *O*-methylcaprolactim with peracid spontaneously furnished *N*-hydroxycaprolactam in ca. 3% yield.[5,6] Aue and Thomas[4] later showed that acyclic imino ethers such as **3** and **4** formed relatively stable alkoxyoxaziranes with peracetic acid and that in aqueous HCl, **3** decomposed to methyl formate and *N*-*tert*-butylhydroxylamine. Since the condensation of hydroxylamines with active esters furnishes hydroxamic acids, we were encouraged to explore further the chemistry of oxidized imino ethers.

When **5** was reacted with 1 equiv of buffered peracetic acid at −78 °C, only the nitroso dimer **12** could be isolated in 49% yield. No trace of alkoxyoxazirane was detected, even when the oxidation was terminated prematurely. However, NMR spectroscopy after brief reaction times clearly indicated the presence of *n*-heptanal (syn and anti) oximes. When 2 equiv of peracid was used, the yield of **12** rose to 70%. These unexpected results, which are wholly inconsistent with the behavior of **3** and **4**,[4] are best

Scheme I[a]



[a] R = *n*-C_7H_{15}.

explained by the mechanism presented in Scheme I. An initially formed alkoxyoxazirane, **6**, in equilibrium with alkoxynitrone **7**, may unergo a rapid 1,4 hydrogen shift to yield **8**, a migration which cannot occur in the oxidation of **3** and **4**. Intermediate **8** might then decompose directly to *N*-*n*-heptylhydroxylamine **9** in the presence of acetic acid or more probably might be oxidized again to **10**. Several pathways can be envisioned for the decomposition of **10** to nitroso-*n*-heptane **11**, the ultimate progenitor of **12**.[7]

Conversion of **6** to its *N*-oxide followed by direct extrusion of **11** could also in principle give rise to **12**, but the known rate of such oxidations[4] is inconsistent with the present reaction.

Two other epoxidizing agents were also examined. Reaction of **5** with either 2-(hydroperoxy)hexafluoro-2-propanol[8] or with *tert*-butyl hydroperoxide/vanadyl acetylacetonate[9] was extremely sluggish. In each instance only recovered **5** and its hydrolysis product, *N*-*n*-heptylacetamide, were detected.

As an alternative to epoxidation, the direct N-acetoxylation of imino ethers by lead tetraacetate (LTA) was investigated so as to preclude deleterious hydrogen shifts in the first-formed product. Unbuffered LTA promoted the rapid hydrolysis of **5** to *N*-*n*-heptylacetamide. The use of solid buffers such as NaOAc, Na_2HPO_4, or $CaCO_3$ under heterogeneous conditions (CH_2Cl_2 or hexane) afforded complex mixtures of products. With pyridine as the solvent,[10] LTA smoothly transformed **5** into acetoxy imino ether **13**. However, the use of pyridine complicated product isolation; therefore, in subsequent experiments it was replaced with a cross-linked 4-vinylpyridine polymer in hexane as the solvent. Under these conditions, **13** could be isolated in 75% yield (eq 2). The oxidation appears to be general, as lactim ether **14** similarly afforded **15** (79%; eq 3).

This LTA acetoxylation of imino ethers provides a convenient one-step alternative to the conventional NBS oxidation/$Et_4N^+OAc^-$ displacement sequence for preparing 3-acetoxy lactim ethers.[11] Such species are useful reagents

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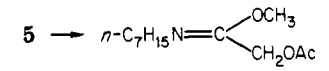
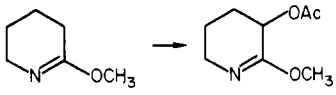


(2)

13



(3)

14 15

in the stereospecific synthesis of antitumor pyrrolizidine alkaloids.[12]

Experimental Section

Oxidation of 5 with Peracetic Acid. To a solution of 5 (0.27 g, 1.58 mmol) in CH_2Cl_2 (8 mL) in a 25-mL, oven-dried, round-bottomed flask was added anhydrous Na_2HPO_4 (0.45 g, 3.2 mmol). The resulting suspension was cooled to −78 °C under N_2, and then a standardized solution of peracetic acid (1.58 mmol) was added via a gas-tight syringe and Teflon needle. A white precipitate appeared upon completion of the addition; TLC of the reaction mixture at that time indicated a substantial quantity of 12 had already formed. The flask was allowed to warm to room temperature, and its contents were transferred to a separatory funnel. After being washed twice with 5% Na_2CO_3, the organic phase was dried ($MgSO_4$) and concentrated in vacuo to a pale yellow semisolid. Preparative thin-layer chromatography (Analtech silica gel plate, $CHCl_3$ eluant, two developments) gave 12 as a white solid: 49% yield; mp 53–55 °C (lit.[13] mp 57–58 °C).

Use of 2 equiv of peracid in the same experiment furnished 12 in 70% yield.

Oxidation of 5 with Lead Tetraacetate. To a suspension of poly(4-vinylpyridine) (Reilly Chemical Co., 5.3 g, 45 molar equiv) in dry hexane (20 mL) was added LTA (MC&B Corp., 98.6% pure; 1.33g, 3.0 mmol) followed 30 min later by the imino ether 5 (0.51 g, 3 mmol). The reaction mixture was stirred at room temperature for 30 min and then warmed to reflux for 75 min, whereupon a negative starch–iodide test was observed. The reaction mixture was cooled and filtered, and the precipitated solids were washed thoroughly with hexane. Concentration of the combined organic layers gave a quantitative yield of a clear, colorless oil (0.62 g) containing ca. 75% of 13 which could not be separated by distillation or chromatography from unreacted 5 (25%, the only other component of the mixture). For 13: ^1H NMR ($CDCl_3$) δ 4.60 (s, 2 H, CH_2OAc), 3.62 (s, 3 H, OCH_3), 3.27 (t, 2 H, J = 6 Hz, CH_2N), 2.1 (s, 3 H, CH_3CO); IR λ_{max} (film) 3.45 5.75, 6.0, 8.25, 9.6 μm; CIMS (isobutane) m/e (relative intensity) 230 (M + 1, base), 198 (M + 1 − CH_3OH, 54), 158 (M + 1 − H_2 − C_5H_{10}, 28); TLC R_f (EtOAc) 0.64.

Oxidation of 14 with Lead Tetraacetate. A mixture of poly(4-vinylpyridine) (75.5 g) and LTA (1.62 g) in dry THF (25 mL) was treated with imino ether 14 (0.39 g) at room temperature for 2 h and then at 50 °C for 1 h. The workup as described for 13 above afforded a pale yellow oil (0.46 g, 79%) of virtually pure 15: NMR ($CDCl_3$) δ 5.10 (t, 1 H, J = 6 Hz), 3.55 (s, 3 H), 2.11 (s, 3 H); IR λ_{max} (film) 5.85, 5.9 μM; CIMS, m/e (relative intensity) 172 (M + 1, 100), 112 (M + 1 − AcOH, 6); TLC R_f (EtOAc) 0.1.

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Registry No. 5, 86411-26-9; 12, 3378-34-5; 13, 86411-27-0; 14, 5693-62-9; 15, 86411-28-1; peracetic acid, 79-21-0; lead tetraacetate, 546-67-8.

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Synthesis of 2-Amino-7-(2′-deoxy-β-D-*erythro*-pentofuranosyl)-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one, a New Isostere of 2′-Deoxyguanosine

Heinz-Dieter Winkeler and Frank Seela*

Department of Chemistry, University of Paderborn, D-4790 Paderborn, Federal Republic of Germany

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The pyrrolo[2,3-*d*]pyrimidine nucleosides are rare constituents of nucleic acids and have been isolated in the monomeric form as nucleoside antibiotics.[1] Several transfer nucleic acids contain the rare nucleoside queuosine (**1b**,[2] Chart I) and related derivatives in the wobble position of the anticodon. Moreover, the nucleoside antibiotic cadeguomycin (**1c**)[3] has been recently obtained as a fermentation product of *Streptomyces hydroscopicus*. The parent nucleoside of queuosine and cadeguomycin is 7-deazaguanosine (**1a**).[4] The latter has been prepared in our laboratory by the technique of phase-transfer glycosylation of 4-methoxy-2-methylthio-7*H*-pyrrolo[2,3-*d*]pyrimidine with 1-bromo-2,3,5-tri-O-benzyl-D-ribofuranose followed by a multistep conversion of the condensation product.[5] By the same method *ara*-7-deazaguanosine[6] has also been obtained.

All attempts to use acetyl- or benzoyl-protected halogenoses in the synthesis of D-*ara*- or D-ribofuranosyl-nucleosides failed due to ortho amide formation.[7] Under the strongly alkaline conditions of phase-transfer glycosylation, nucleophilic displacement at the carbon of the acyloxonium intermediate is preferred, rather than a reaction at the carbon of the anomeric center. Acylated 2-deoxy sugars, however, cannot form an acyloxonium ion involving carbons 1 and 2 and should therefore be applicable to phase-transfer glycosylation reactions.

The total synthesis of sugar-modified 7-deazaguanosines has only been reported for the D-ribo- and D-arabino-furanosyl series. The 2′-deoxy series, e.g., compound **2**, is still unknown. Whereas 2′-deoxy-7-deazaadenosine can be prepared from the naturally occuring antibiotic tubercidin by nucleoside transformation[8] or by reduction of its triphosphate with ribonucleotide reductase,[9] these routes are not applicable to 2′-deoxy-7-deazaguanosine since 7-deazaguanosine has not been isolated from natural sources. We now report the total synthesis of 2′-deoxy-7-deazaguanosine (**2**), which is an isostere of the DNA constituent 2′-deoxyguanosine (**3**). Furthermore, we describe its O^4-methyl derivative **6**, which is structurally closely related to O^6-methyl-2′-deoxyguanosine[10] that causes mutations by mispairing in DNA.[11] The nucleosides **2** and

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