2-formylimidazole, 10111-08-7; 1-methyl-2-formylimidazole, 13750-81-7; 1-benzyl-2-formylimidazole, 10045-65-5; 2-furaldehyde, 98-01-1.

Supplementary Material Available: An example of the procedure for the synthesis of 1 is provided. Additional procedures needed to obtain **1e**, **1h**, **1i**, and **1k** are provided and outlined in Schemes I and II. Table II with % yield, mp, and recrystallization solvent for **1b–k** is included as well (6 pages). Ordering information is given on any current masthead page.

An Unusual Bisulfite Addition Compound from 3,5-Dipyrrolidinophenol

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Earlier investigations have shown that 3,5-dipyrrolidinophenol (1) exhibits a facile tautomerism in solution between phenolic and dienone forms depending on the nature of the solvent. In solvents capable of accepting a hydrogen bond, such as dimethyl sulfoxide, the molecule exists as the phenolic form,[1] while in solvents that donate a hydrogen bond, such as water or trichloroethanol, it exists in a dienone form.[2] This note describes the formation of a zwitterionic bisulfite addition derivative of the carbonyl form.

In the course of exploratory studies of a series of solvents, a solution of 1 in sulfur dioxide was examined. ^1H and ^{13}C NMR spectra of the solution showed only the phenolic form, but addition of water led to an unexpected product. Although no carbonyl peak appeared in the ^{13}C spectrum, in view of the facile tautomerism of 1, it seemed reasonable to view the material as a derivative of the ketonic form. The presence of a fully saturated carbon atom with a chemical shift of 83.2 ppm suggested that the sulfurous acid generated by addition of water produced a bisulfite addition product, with the balancing positive charge borne by the vinamidinium system, i.e., 4, (Scheme I).

The spectra of 4 and other NMR data in Table I support this structure. All of the spectra of 4 show the presence of an element of symmetry. The AB quartet of the methylene protons of the alicyclic ring is approximately four times the area of the olefinic singlet. Peaks in ^{13}C spectrum show heights approximately proportional to the number of atoms represented of protonated (C-2 plus C-6 vs. C-4) and nonprotonated carbon atoms (C-3 plus C-5 vs. C-1). A single peak appears in the ^{15}N spectrum, with a midfield resonance appropriate to an vinamidinium nitrogen.[3] The observed chemical shifts and multiplicities in off-resonance spectra are appropriate to the nature of the assigned carbon atoms. The difference in chemical shifts of the methylene protons evidently arises from the adjacent C-1 substituents. In the rigidly planar vinamidinium system, the two α (or β) carbon atoms of a pyrrolidine ring differ, being cis to the alicyclic methylene group or to the olefinic carbon. As a consequence, they show different chemical shifts.

Scheme I. Conversion of 1 to Dienone Tautomers 2 and 3 and to the Bisulfite Addition Compound 4

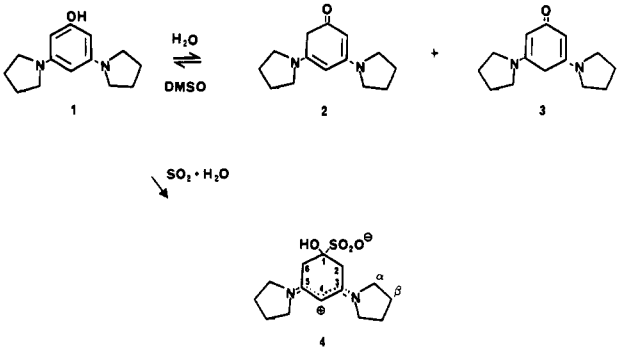

Table I. NMR Characteristics of Compounds 1–4

C	^{13}C NMR, ppm 1	2	3	4	^1H NMR, ppm (J, Hz) 4
1	158.6	179.6	185.0	83.2	
2	88.4	89.2[a]	92.0	33.8	3.01, 3.05 (−17.3)
3	149.4	161.6[b]	154.7	162.0	
4	87.8	82.8[a]	30.60	87.8	5.10
5	149.4	155.6[b]	154.7	162.0	3.01, 3.05 (−17.3)
6	88.4	36.2	92.0	33.8	
α	47.3	46.1, 46.7	[c]	48.8, 48.6	3.2–3.0
β	24.9	23.0	[c]	23.6, 23.1	2.0–2.15

^{15}N NMR, ppm 1	2	3	4
74.3	121.4, 115.6	109.3	143.8

[a,b] Assignments can be interchanged. [c] Obscured.

^{15}N spectra offered a further characterization of the series. The parent phenol in dimethyl sulfoxide showed a chemical shift somewhat downfield from that of *N,N*-dimethylaniline (71.9 vs. 44.6 ppm; cf., *N*-methylpyrrolidine, 43.6 ppm, vs. trimethylamine, 17.1 ppm).[4] The trichloroethanol solution showed the three peaks listed in Table I, although earlier studies had shown only the existence of the 2,4-dienone 2. However, ^{13}C spectra of the solution at the higher field and sensitivity now available showed the presence of a second dienone in approximately 10% of the concentration of the major material, with the peaks listed in Table I, attributable to the symmetrical 2,5-dienone 3. The ^{15}N frequencies observed are comparable to that of 3-(*N*-pyrrolidinyl)cyclohexenone, 105.8 ppm.[4]

The formation of sodium bisulfite addition compounds from ketones and aldehydes is known to proceed via the sulfite dianion.[5] In this case, the reaction is assisted by the increased stability of the resonating vinamidinium system of 4.

Evaporation of the sulfur dioxide from the solution of 4 left a white powder, which was insoluble in organic solvents and reverted to the phenol 1 in water. Preparation of 4 in a solution of sulfur dioxide and ca. 30% dioxane produced colorless prisms, which also reverted to the phenol on standing.

Experimental Section

Nuclear magnetic resonance spectra were obtained on a Varian XL-200 NMR spectrometer. Solutions for ^1H and ^{13}C spectra of 1 were approximately 0.5 M and included tetramethylsilane as an internal reference (=0 ppm). Solutions for ^{15}N spectra included nitromethane as an internal reference (=379 ppm, NH_3 = 0 ppm);[4]

(1) Effenberger, F.; Niess, R. *Chem. Ber.* **1966**, *101*, 3787.
(2) Highet, R. J.; Chou, F. E. *J. Am. Chem. Soc.* **1977**, *99*, 3538.
(3) Rabiller, C.; Ricolleau, G.; Martin, M. L.; Martin, G. J. *Nouv. J. Chim.* **1980**, *4*, 35.
(4) Levy, G. C.; Lichter, R. L. *Nitrogen-15 Nuclear Magnetic Resonance Resonance Spectroscopy*; Wiley: New York, 1979.
(5) Green, L. R.; Hine, J. *J. Org. Chem.* **1974**, *39*, 3896.

those in dimethyl sulfoxide and trichloroethanol included tris(acetylacetonato)chromium(III) (approximately 0.05 M) as a relaxation reagent. ^{15}N spectra in sulfur dioxide were obtained by the INEPT procedure.[6]

3,5-Dipyrrolidinophenol prepared as described previously was contaminated by a green oxidation product which could not be removed by crystallization or chromatography.[1,2] Pure material could be obtained by the careful exclusion of oxygen. Phloroglucinol (3.0 g) was charged into a bomb tube of approximately 100-mL capacity, which was swept with nitrogen while 5.0 mL of chilled pyrrolidine was added. The tube was sealed and heated to 150 °C for 90 min. After the tube was opened it was held under reduced pressure to remove excess pyrrolidine, flushed with nitrogen, charged with 50 mL of ethanol, flushed with nitrogen, and sealed. The mixture was heated to solution and allowed to cool. The tube was again opened and the supernatant removed by pipet, leaving 2.3 g of yellow crystals, mp 187.5–189 °C. On standing in air the crystals turned gray green. Spectrometric characteristics were identical with those previously reported.

3-*N*-Pyrrolidinyl-5-*N*-pyrrolidinio-1-hydroxy-3-cyclohexene Sulfonate (4). Solutions of 4 prepared for ^1H and ^{13}C NMR spectra were prepared by placing ca. 50 mg of 1 in a 5-mm NMR sample tube and chilling in a dry ice–acetone bath while 0.5 mL of sulfur dioxide was passed in. Water (0.004 mL) and a small amount of tetramethylsilane were then added before the tube was sealed. Conversion to 4 was prompt and complete. Samples for ^{15}N spectra were prepared similarly from 100 mg of 1 and 0.01 mL of water, with the substitution of 6 mg of nitromethane for the tetramethylsilane. Crystalline samples of 4 were prepared by allowing the sulfur dioxide to evaporate from the solution of 100 mg of 1 and 0.01 mL of water and crystallizing the residue from 1:1 dioxane–sulfur dioxide at −10 °C, mp 145–148 °C.

Registry No. 1, 16857-92-4; 2, 102869-96-5; 3, 102869-97-6; 4, 102869-98-7; SO_2, 7446-09-5; phloroglucinol, 108-73-6; pyrrolidine, 123-75-1.

(6) Morris, G. A.; Freeman, R. *J. Am. Chem. Soc.* **1979**, *101*, 760.

An Unusual Oxazolone from α-Bromopenicillin G

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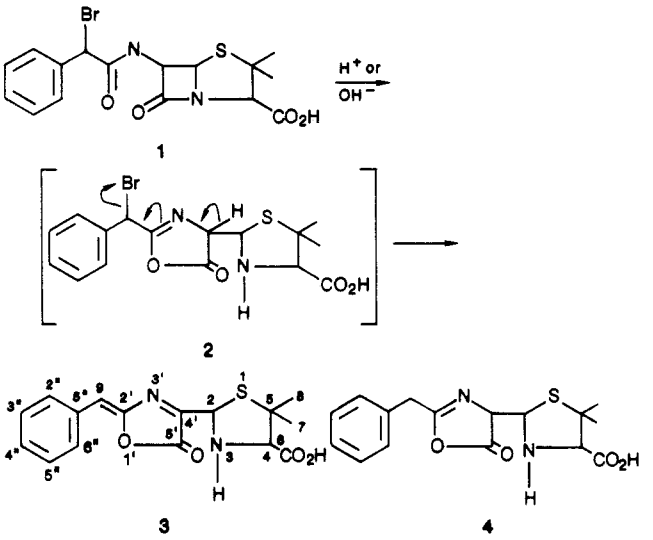
During an attempted preparation of a penicillin from 6-aminopenicillanic acid and α-bromophenylacetic acid, an unusual oxazolone–thiazolidine **3** was isolated. This oxazolone was very similar to the original azalactone formula proposed by early workers[1] and suggests that the acid degradation of a penicillin may proceed through a oxazolone–thiazolidine intermediate. Although the existence of the oxazolone–thiazolidine structure **4** has been proposed as early as 1942 by the Robinson group, numerous attempts to prepare this class of compounds proved to be elusive because of their inherent instability. Hitomi[2a] studied the decomposition of penicillin G under mild conditions and identified ten products. Johnson and Panetta[2b] studied the decomposition of methicillin in weakly acidic solutions and Dennen and Davis[2c] indicated

Scheme I



that penillic and penicilloic acids were the main products formed in a decomposition study of natural and semisynthetic penicillins. More recently Awang et al.[2d] investigated the degradation of penicillin in acidic media and proposed an oxazolone–thiazolidine intermediate as the mechanism for the degradation of a penicillin. None of the above investigators reported the isolation of any oxazolone with an intact thiazolidine ring. Therefore, we wish to describe the formation and characterization of **3**[3] which represents an example of this elusive oxazolone–thiazolidine.

When 6-aminopenicillanic acid was treated in aqueous sodium bicarbonate solution with α-bromophenylacetyl chloride, followed by an acid workup, a crystalline yellow amphoteric compound was isolated. The infrared spectrum showed a carbonyl absorption band at 1780 cm^{-1} consistent for a β-lactam carbonyl. However, the ^1H NMR spectrum was not consistent for the desired β-lactam because the β-lactam C_4' proton was missing and a new band appeared at 6.78 ppm. The mass spectrum showed no halogen. Combined evidence from the IR, ^{13}C NMR, ^1H NMR, MS, and microanalysis identified the compound as **3** shown in Scheme I.

Compound **3** shows ultraviolet maxima at 242, 359, and 377, reminiscent of a penicillenic acid, and its isolation offers credence to the rationalization that an oxazolone–thiozolidine intermediate is indeed the progenitor to the other reported degradation compounds. In the formation of **3** it is thought that the α-bromopenicillin **1** underwent dehydrohalogenation to the intermediate oxazolone **2** to form the stable isolatable compound **3**. Although in prior cases the oxazolone–thiazolidine system was readily degraded, the conjugation from C-9 to C-4′ in compound **3** stabilizes the two five-membered rings and permits isolation. The stereochemistry of carbon–carbon double bond at C2′ and C9 was not determined.

Experimental Section

General NMR spectra were recorded on a JEOL FY 90Q or a Bruker 360 spectrometer. Chemical shifts are reported in δ values relative to the tetramethylsilane as an internal standard. Infrared spectra were determined on a Nicolet 5DX FT-IR spectrophotometer. Mass spectra were recorded on a Dupont DP-102 Kratos MS-30 or Kratos MS-50 mass spectrometer. Melting point was taken on Fischer Johns melting point apparatus.

(1) Clarke, H. T.; Johnson, J. R.; Robinson, R. *The Chemistry of Penicillins*; Princeton University Press: Princeton, NJ, 1949; p 447, 730.

(2) (a) Hitomi, H. *Yakugaku Zasshi* **1959**, *79*, 1600; *Chem. Abstr.* **1959**, *54*, 10996g. (b) Johnson, D. A.; Panetta, C. A. *J. Org. Chem.* **1963**, *29*, 1826–1830. (c) Denner, D. W.; Davis, W. W. *Antimicrobial Agents Chemother.* **1961**, 531. (d) Awang, D. V. C.; Kindrac, D.; LeBelle, M. J.; Lauriault, G. 19th National Medicinal Symposium June 1984, Abstract #9, p 14.

(3) For convenience the numbering system used for the name does not coincide with the numbering system used for identification in the ^{13},c NMR and ^1H NMR.

0022-3263/86/1951-3232$01.50/0