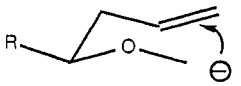
play an important role since, in Et_2O, these cyclizations fail to occur.



6

Employing our standard conditions, we have been unable to effect the cyclization of α-alkoxy lithiums derived from stannanes (exemplified by **5a,b**) in which the double bond bears a second alkyl substituent. These results are in keeping with the observations of Bailey[3c] and presumably reflect the fact that cyclization, in such cases, would lead to the generation of a relatively unstable secondary carbanion. The failure of these anions to cyclize is significant since it argues against the possible involvement of radical intermediates in the successful cyclizations. If these reactions were mediated by transient radical species derived from the α-alkoxy lithiums, the presence of alkyl substituents at the double bond terminus would be expected to facilitate rather than impede cyclization.[13]

In striking contrast to the behavior of **5a,b**, the methoxy-substituted stannanes **7a,b**, **9**, and **11** undergo cyclization, giving vinyl tetrahydrofurans in excellent yield (Scheme II). The facility of these reactions may be due to the fact that, in the transition state, anionic character can be partially displaced onto oxygen. From a synthetic standpoint these cyclization–eliminations are far more valuable than the simple cyclizations outlined in Scheme I. They not only proceed in better yield but give rise to versatile olefinic substituents suitable for further manipulation. An attractive feature of this method is its employment of the stable and easily generated methoxy unit as a leaving group.[14] In these cyclizations only a slight excess of *n*-BuLi need be employed since the formation of products analogous to **3a,b** is precluded by the rapid elimination of methoxide.

Although there appear to be certain limitations to its scope, the anionic cyclization of α-alkoxy lithiums provides an expedient and stereoselective route to a variety of tetrahydrofurans not easily accessible by other means. At the present time we are continuing to explore the generality of this new method and also attempting to adapt it for the preparation of pyrrolidines[15] from stannylmethyl amines.[16] The results of these investigations will be communicated in due course.

Acknowledgment. We thank the Research Board of the University of Illinois, Research Corporation, and the donors of the Petroleum Research Fund, administered by the American Chemical Society, for their support of this work.

(13) Beckwith, A. L. J.; Blair, I. A.; Phillipou, G. *Tetrahedron Lett.* **1974**, 2251.

(14) Compare: (a) Stork, G.; Schoofs, A. R. *J. Am. Chem. Soc.* **1979**, *101*, 5081. (b) Abeywickrema, A. N.; Beckwith, A. L. J.; Gerba, S. *J. Org. Chem.* **1987**, *52*, 4072. (c) Ishii, T.; Kawamura, N.; Matsubara, S.; Utimoto, K.; Kozima, S.; Hitomi, T. *J. Org. Chem.* **1987**, 52, 4416.

(15) Padwa has recently investigated a conceptually related approach to pyrrolidines involving an azahexenyl radical cyclization. (a) Padwa, A.; Nimmesgern, H.; Wong, G. S. K. *Tetrahedron Lett.* **1985**, 957. (b) Padwa, A.; Nimmesgern, H.; Wong, G. S. K. *J. Org. Chem.* **1985**, *50*, 5620.

(16) Peterson, D. J. *J. Am. Chem. Soc.* **1971**, *93*, 4027.

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Allene Epoxidation. Efficient Synthesis and Synthetic Conversions of 1,4-Dioxaspiro[2.2]pentanes[1]

Summary: The oxidation of simple allenes with dimethyldioxirane provides the corresponding 1,4-dioxaspiro[2.2]pentanes in good to excellent isolated yields; subsequent addition of various nucleophiles proceeds regioselectively to generate highly functionalized products of type **2**.

Sir: Earlier studies of the peracid oxidation of allenes has established the involvement of 1,4-dioxaspiro[2.2]pentanes (**1**) as one of several novel reactive intermediates that lead to an array of isolated products.[2-4] The overall conversion of allenes to ketones of structure **2** by the addition of nucleophiles to these spirodioxides **1** constitutes an attractive synthetic scheme that generates functionality at each of the three allenic carbons (Scheme I). However, spirodioxides have been isolated and characterized in only three instances to date, each of which involves a sterically hindered allene.[3,5] Furthermore, products of type **2** are not generally formed in acceptable yields, owing to the various reaction pathways in competition under the conditions of the peracid oxidations. In this paper we report on a method for the efficient generation of spirodioxides **1** and examine their reactions with various nucleophiles.

The recent discovery by Murray[6] that dimethyldioxirane (**3**) can be obtained as a dilute solution in acetone provided the key to our search for a suitable oxidant.[7] Use of this extraordinary reagent[8] in the presence of solid K_2CO_3 as a buffering agent provides the neutral, nonnucleophilic conditions that permit the isolation of spirodioxides. Thus, treatment of 2,5,5-trimethyl-2,3-hexadiene (**4a**) with 5 equiv of **3** for 10 min at room temperature, followed by removal of solvent in vacuo, gave the known[3] spirodioxide **5a** as a single diastereomer in good yield (84%) and purity.[9] In a similar manner, the less hindered allene **4b** was transformed to **5b** in 95% yield by 3.5 equiv of **3**. In this case a 9:1 ratio of stereoisomers was observed.[10] These

(1) This work was first presented at the 194th National Meeting of the American Chemical Society, New Orleans, LA, August 30–September 4, 1987. Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, and a Public Health Service Biomedical Research Support Grant administered by Indiana University for partial support of this work. Departmental equipment grants aided in the purchase of the Varian 300 NMR (PHS-SID-RR-1882-01) and the Kratos MS 80 (CHE-81-11957) instruments used in this work.

(2) Crandall, J. K.; Machleder, W. H.; Sojka, S. A. *J. Org. Chem.* **1973**, *38*, 1149–1154.

(3) Crandall, J. K.; Conover, W. W.; Komin, J. B.; Machleder, W. H. *J. Org. Chem.* **1974**, *39*, 1723–1729.

(4) For reviews of allene oxide chemistry, see: Stang, P. J. *The Chemistry of Functional Groups. Supplement E: The Chemistry of Ethers, Crown Ethers, Hydroxyl Groups and Their Analogs*; Patai, S., Ed.; Wiley: New York, 1983; pp 859–879. L'Abbe, G. *Angew. Chem., Int. Ed. Engl.* **1980**, *19*, 276–289. Chan. T. H.; Ong, B. S. *Tetrahedron* **1980**, *36*, 2269–2289. Smadja, W. *Chem. Rev.* **1983**, *83*, 263–320.

(5) Wolff, S.; Agosta, W. C. *Can. J. Chem.* **1984**, *62*, 2429–2434.

(6) Murray, R. W.; Jeyaraman, R. *J. Org. Chem.* **1985**, *50*, 2847–2853. Cassidei, L.; Fiorentino, M.; Mello, R.; Sciacovelli, O.; Curci, R. *J. Org. Chem.* **1987**, *52*, 699–700.

(7) Dimethyldioxirane solutions in acetone have been shown to epoxidize olefins in a syn-stereospecific manner.[6] An in situ method behaves similarly: Curci, R.; Fiorentino, M.; Troisi, L. *J. Org. Chem.* **1980**, *45*, 4758–4760.

(8) For other interesting reactions of **3**, see: Murray, R. W.; Jeyaraman, R.; Molan, L. *J. Am. Chem. Soc.* **1986**, *108*, 2470–2472. Murray, R. W.; Jeyaraman, R.; Molan, L. *Tetrahedron Lett.* **1986**, *27*, 2335–2336. Jeyaraman, R.; Murray, R. W. *J. Am. Chem. Soc.* **1984**, *106*, 2462–2463.

(9) Compound **5a** showed the following:[3] IR 1635 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.52 (s, 1), 1.53 (s, 3), 1.50 (s, 3), 0.97 (s, 9); ^{13}C NMR ($CDCl_3$) δ 88.3 (s), 69.4 (dm, J = 171, 5 Hz), 63.4 (m, J = 5 Hz), 31.1 (m, J = 4 Hz), 25.6 (qm, J = 125, 4 Hz), 22.4 (qd, J = 128, 4 Hz), 20.2 (qd, J = 128, 4 Hz).

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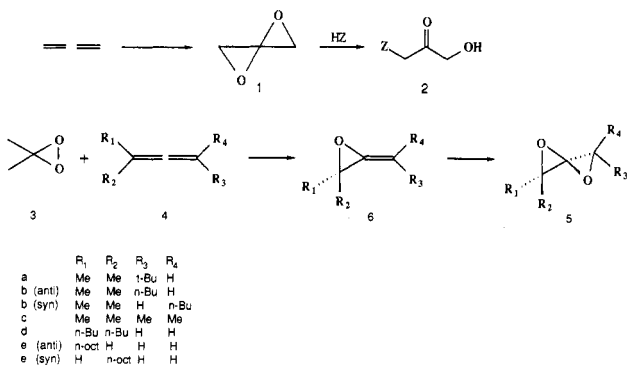
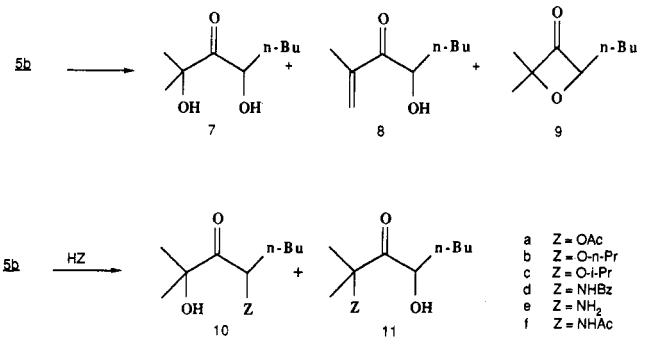
Scheme I



Scheme II



are assigned as the anti and syn isomers,[11] respectively, on the basis of the anticipated initial oxidation at the more substituted double bond[12] of **4b** from the π face away from the single substituent at the other allene terminus. This gives intermediate *E*-allene oxide **6b**,[3] which sets the stereochemistry of **5b** formed by a second oxidation. Most interestingly, no products derived from alternate reactions of allene oxides **6** were observed in this or other allene epoxidations using **3**. The anticipated high reactivity of allene oxides toward further oxidation helps to account for this.[3]

The formation of isolable spirodioxides appears to be reasonably general. This is evidenced by the conversion of tetramethylallene (**4c**) to highly volatile, crystalline **5c** in 44% yield[13] (4 equiv of **3** for 0.5 h at −50 °C) and the transformation of disubstituted allene **4d** to spirodioxide **5d** in 80% yield (10 equiv of **3** for 1.5 h at −40 °C).[14] Finally, monosubstituted allene **4e** is partially converted to a 5:1 mixture of anti and syn spirodioxide **5e** in 50% yield with 10 equiv of oxidant at −40 °C for 2.5 h.[15] Thus, spirodioxides **5** are available for exploitation as synthetic intermediates.

The chemistry of spirodioxides has been explored with the trisubstituted example **5b** (Scheme II). Attempted preparative TLC of **5b** on silica gel plates led to the formation of dihydroxy ketone **7** (34% yield), enone **8** (34%), and oxetanone **9** (30%).[16] These reactions are consistent with expectations for acid-catalyzed reactions of spirodioxides.[2,3] (Indeed, omission of K_2CO_3 in the epoxidation of **4b** resulted in the formation of these materials as well.) Nonetheless, various nucleophiles have been shown to add smoothly to **5b**. Thus, dissolving **5b** in aqueous THF resulted in clean conversion to dihydroxy ketone **7** in 80% yield. Reaction of **5b** with 2 equiv of tetrabutylammonium acetate and 1.3 equiv of acetic acid in THF led regioselectively to secondary acetate **10a** in nearly quantitative yield without detectable amounts of the tertiary isomer **11a**. On the other hand, dissolving **5b** in glacial acetic acid gave a mixture of regioisomers **10a** and **11a** along with a comparable amount of **8** and **9** (3:1 ratio). Following a reaction in acetic acid-d_4 by ^{1}H NMR indicated an initial ratio of **10a**/**11a** of 1:5.6 after 5 min, which gradually equilibrated to 34:1 over 4 days. These results suggest that nucleophilic opening of spirodioxide **5b** occurs by an S_N2-like process in the presence of acetate, whereas a carbocationic mechanism predominates under acidic conditions. These and further details of the unraveling of the spirodioxide in the presence of nucleophiles need to be substantiated by more detailed mechanistic investigation, but the implications of regioselective (and possibly stereoselective) nucleophilic additions to spirodioxides are of obvious synthetic utility.

Selective attack at the secondary site of **5b** under nonacidic conditions has also been documented with other nucleophilic systems. For example, reaction of **5b** with a large excess of 1-propanol in the presence of K_2CO_3 generated the isomeric ethers **10b** and **11b** in an 83:17 ratio in 95% yield. Importantly, substantially higher regioselectivity (97:3) was observed with 0.15 equiv of NaH in 1-propanol. The more hindered 2-propanol gave a 94:6 ratio of **10c**/**11c** in the presence of K_2CO_3. Similarly, benzylamine in $CDCl_3$ yielded **10d** (61%) as the only adduct. Ammonia behaves in a like fashion, leading to **10e**, which was isolated in moderate yield as **10f**, after subsequent reaction with acetic anhydride and pyridine.[17,18]

Other synthetic conversions of spirodioxide **5b** are also feasible. Thus, pyrolysis of **5b** at ca. 400 °C in a vacuum flow system efficiently generated oxetanone **9** as an 11:1 mixture with enone **8** in 89% yield. On the other hand, enone **8** is the major product from treatment of **5b** with lithium diethylamide in ether at 0 °C.

More limited experimentation with the other spirodioxides indicates a similar pattern of reactivity. We are continuing to explore the chemistry of spirodioxides, particularly nucleophilic additions in both inter- and intramolecular versions.[19] These reactions appear to hold

(10) The anti isomer **5b** showed the following: IR 1643 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.73 (dd, 1, J = 6, 5 Hz), 1.9–1.7 (m, 2), 1.55 (s, 3), 1.49 (s, 3), 1.4–1.3 (m, 4), 0.91 (t, 3, J = 7 Hz); ^{13}C NMR ($CDCl_3$) δ 89.4 (s), 63.3 (septet, J = 4 Hz), 61.7 (d, J = 174 Hz), 29.6 (t, J = 126 Hz), 27.3 (t, J = 129 Hz), 22.4 (q, J = 127 Hz), 21.5 (t, J = 128 Hz), 20.5 (q, J = 127 Hz), 13.8 (q, J = 125 Hz). The presence of the syn isomer **5b** was evidenced by ^{1}H NMR signals at δ 3.55 (dd, J = 6, 5 Hz), 1.53 (s), 1.47 (s).

(11) The designations anti and syn refer to the relative geometry of the highest priority alkyl group at one of the ring carbons relative to the oxygen of the second ring.

(12) For relative rates of epoxidation of variously substituted olefins by **3**, see: Baumstark, A. L.; McCloskey, C. J. *Tetrahedron Lett.* **1987**, *28*, 3311–3314.

(13) Compound **5c** showed the following: mp (sealed cap.) 52–53.5 °C; IR 1629 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.54 (s, 6), 1.47 (s, 6); ^{13}C NMR ($CDCl_3$) δ 93.6 (s), 64.5 (m, J = 5 Hz), 21.3 (qm, J = 128, 3 Hz), 20.1 (qm, J = 128, 3 Hz).

(14) Compound **5d** showed the following: IR 1619 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.37 (AB q, 2, J_{AB} = 3 Hz, $\Delta\nu$ = 27 Hz), 2.0–1.7 (m, 4), 1.5–1.2 (m, 8), 0.91 (t, 6, J = 7 Hz); ^{13}C NMR ($CDCl_3$) δ 85.6 (s), 68.8 (s), 48.8 (t, J = 175 Hz), 32.3 (t, J = 127 Hz), 31.9 (t, J = 127 Hz), 26.5 (tm, J = 120 Hz), 26.2 (tm, J = 120 Hz), 22.7 (t, J = 124 Hz), 13.9 (q, J = 124 Hz).

(15) The ^{1}H NMR spectrum of the mixture showed the presence of *anti*-**5e** [δ 3.76 (t, 1, J = 5 Hz), 3.40 (AB q, 2, J_{AB} = 3 Hz, $\Delta\nu$ = 26 Hz)] and *syn*-**5e** [δ 3.62 (t, 1, J = 5 Hz), 3.45 (AB q, 2, J_{AB} = 3 Hz, $\Delta\nu$ = 26 Hz)].

(16) All new compounds were fully characterized by spectral data including high-resolution mass spectra (with the exception of **5d** and **5e**). Complete details will be provided in our full publication.

(17) No spectroscopic evidence for the isomeric acetamide **11f** was detected.

(18) The reaction of ammonia with **5b** in THF or CH_2Cl_2 gave a product that decomposed rapidly upon concentration. However, ^{1}H NMR and IR analysis of a reaction in $CDCl_3$ confirmed **10e** as the initial major product.

(19) A study of oxidative cyclizations of allenic alcohols has been conducted: Crandall, J. K.; Batal, D. J., manuscript in preparation.

substantial potential for the synthesis of highly functionalized target molecules.

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Petrosamine, a Novel Pigment from the Marine Sponge *Petrosia* sp.

Summary: Petrosamine (1) is an alkaloid isolated from the marine sponge *Petrosia* sp. collected at Belize. The colors of petrosamine solutions vary significantly with solvent.

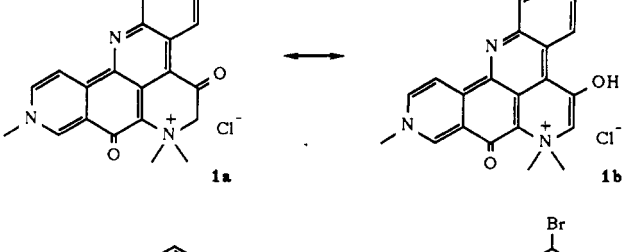
Sir: While attempting to purify an antimicrobial constituent from the marine sponge *Petrosia* sp., we isolated a new alkaloid, petrosamine (1), that has the same carbon skeleton as amphimedine (2), which is a cytotoxic constituent of the sponge *Amphimedon* sp.[1] Petrosamine (1) is remarkable because the colors exhibited by dilute organic or aqueous solutions of the compound are noticeably different. In this paper we report the isolation, spectral properties, and X-ray structure determination of petrosamine (1).

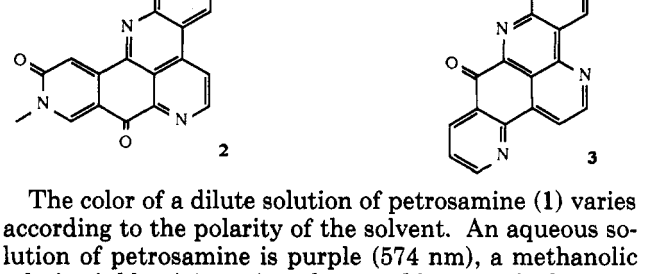
The marine sponge *Petrosia* sp. was collected in shallow water at Carrie Bow Cay, Belize. The deep blue colored methanol extracts of *Petrosia* sp. showed antimicrobial activity against *Staphylococcus aureus* and *Bacillus subtilis*. The methanol soluble material was partitioned to obtain ethyl acetate, *n*-butanol, and aqueous extracts. Both the blue color and the antimicrobial activity were concentrated in the *n*-butanol extract. Chromatography of the butanol-soluble material on Sephadex LH-20 (MeOH) resulted in separation of a blue band from a pale yellow band that contained the antimicrobial activity. Subsequent chromatography of the antimicrobial fraction on silica gel, Sephadex, or a variety of ion-exchange resins invariably led to partial loss of the antimicrobial activity and the isolation of tyramine.

The blue material was rechromatographed on Sephadex LH-20 to obtain petrosamine (1, 0.1% dry weight) as dark green crystals, mp. >330 °C, from dichloromethane–methanol. The high-resolution mass spectrum of petrosamine (1) required a molecular formula of $C_{21}H_{17}BrN_3O_2$. The ^1H and ^{13}C NMR spectra[2] were both highly solvent-dependent and gave few clues for structural elucidation. Both the ^1H and ^{13}C NMR spectra indicated the presence of three *N*-methyl signals, two of which were always equivalent. The remaining signals were all in the aromatic region of the spectra, except for a ^{13}C NMR signal at δ 187.4 (s) that could be assigned to a single quinone-type carbonyl.

Petrosamine (1) crystallized in the triclinic crystal class with diffractometer-measured lattice constants of a = 10.894 (3) Å, b = 12.394 (4) Å, c = 9.210 (2) Å, α = 107.852 (19)°, β = 112.755 (18)°, and γ = 93.447 (22)°. All unique diffraction maxima with $2\theta < 110°$ were collected using variable speed, 1° ω-scans and graphite monochromated Cu K$\bar{\alpha}$ radiation (1.54178 Å). Of the 2179 reflections surveyed, 1628 (75%) were judged observed after correction for Lorentz, polarization, and background effects.[3] Intensity statistics suggested the centrosymmetric space group $P\bar{1}$, and successful solution and refinement validated this choice. The structure was solved by a combination of heavy atom and tangent formula recycling techniques. Hydrogen atoms were located in a ΔF synthesis. Block-diagonal least-squares refinements have converged to the current residual of 0.082 for the observed data. Additional crystallographic details are available and are described in the paragraph entitled Supplementary Material Available at the end of this paper.

Figure 1 is a computer-generated perspective drawing of the final X-ray model of petrosamine (1). Hydrogens are omitted for clarity, as are the chloride counterion and the three waters of crystallization. In the crystalline form, petrosamine (1) clearly exists as a diketone [i.e., **1a**] with a C5 carbonyl (C=O, 1.20 Å) and a C6 methylene group (C5–C6, 1.50 Å). In solution, however, the C5 carbonyl exists in the enol form [**1b**, ^{13}C NMR δ ca. 161 (s)] and the C6 protons exchange so rapidly in deuteriated solvents that they could not be observed in the ^1H NMR spectra of D_2O or MeOH-d_4 solutions.





The color of a dilute solution of petrosamine (1) varies according to the polarity of the solvent. An aqueous solution of petrosamine is purple (574 nm), a methanolic solution is blue (595 nm), and a very dilute tetrahydrofuran

(1) Schmitz, F. J.; Agarwal, S. K.; Guunasekera, S. P.; Schmidt, P. G.; Shoolery, J. N. *J. Am. Chem. Soc.* **1983**, *105*, 4835.

(2) Petrosamine (1) mp >330 °C; IR (KBr) 3400 (br), 1670 (br), 1640, 1585, 1530 cm^{-1}; UV (MeOH) 289 nm (ϵ 42 600), 346 (12 400), 414 (sh, 6900), 595 (5300), (H_2O) 284 nm (ϵ 32 000), 345 (10 900), 574 (4700), (THF) 611 nm; ^1H NMR (MeOH-d_4) δ 3.93 (s, 6 H), 4.66 (s, 3 H), 7.90 (dd, 1 H, J = 8, 2 Hz), 8.46 (d, 1 H, J = 2 Hz), 9.05 (br d, 1 H, J = 6 Hz), 9.27 (d, 1 H, J = 8 Hz), 9.52 (d, 1 H, J = 6 Hz), 9.80 (br s, 1 H), (DMSO-d_6) δ 3.86 (s, 6 H), 4.62 (s, 3 H), 7.70 (s, 1 H), 7.94 (dd, 1 H, J = 8,2 Hz), 8.34 (d, 1 H, J = 2 Hz), 9.14 (d, 1 H, J = 8 Hz), 9.22 (br d, 1 H, J = 6 Hz), 9.27 (d, 1 H, J = 6 Hz), 9.89 (br s, 1 H), (D_2O) δ 3.70 (s, 6 H), 4.54 (s, 6 H), 7.02 (dd, 1 H, J = 8,2 Hz), 7.12 (d, 1 H, J = 2 Hz), 8.11 (d, 1 H, J = 8 Hz), 8.71 (d, J = 6 Hz), 8.82 (d, 1 H, J = 6 Hz), 9.49 (s, 1 H); ^{13}C NMR (DMSO-d_6) δ 187.4 (s), 161.4 (s), 145.6 (d), 142.6 (d), 142.3 (s), 141.7 (s), 140.1 (s), 135.3 (s), 132.1 (d), 131.7 (s), 128.9 (s), 126.4 (d), 123.0 (s), 122.1 (d), 120.4 (s), 114.6 (s), 114.5 (s), 53.4 (2 q), 48.6 (q), (D_2O) δ 187.3 (s), 160.3 (s), 144.6 (d), 142.0 (d), 141.6 (s), 140.9 (s), 138.5 (s), 134.5 (d), 131.1 (d), 127.1 (s), 125.0 (d), 122.4 (d), 120.9 (s), 114.9 (s), 54.4 (2 q), 48.6 (q); HRMS obsd m/z 422.0500, $C_{21}H_{17}{}^{79}BrN_3O_2$ requires m/z 422.0504.

(3) All crystallographic calculations were done on a PRIME 9950 computer operated by the Cornell Chemistry Computing Facility. Principal programs employed were: FOBS a data reduction program by G. D. Van Duyne, Cornell University, 1987; MULTAN 80 and RANTAN 80, systems of computer programs for the automatic solution of crystal structures from X-ray diffraction data (locally modified to perform all Fourier calculations including Patterson syntheses) written by P. Main, S. E. Hull, L. Lessinger, G. Germain, J. P. Declercq, and M. M. Woolfson, University of York, England, 1980; BDLS, an anisotropic block-diagonal least-squares refinement written by K. Hirotsu, E. Arnold, and G. D. Van Duyne, Cornell University, 1987; PLUTO78, a locally modified crystallographic illustration program by W. D. S. Motherwell, Cambridge Crystallographic Data Centre, 1978; BOND, a program to calculate molecular parameters and prepare tables written by K. Hirotsu and G. Van Duyne, Cornell University, 1985.

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