= 7.3 Hz, H-3, H-4), 3.63 (2 H, m, H-5).

Anal. Calcd for $C_{26}H_{27}FO_4$: C, 73.91; H, 6.44; F, 4.49. Found: C, 73.77; H, 6.38; F, 5.00.

General Method for the Preparation of 2-Substituted 2-Deoxy-1,3,5-tri-*O*-benzyl-α-D-arabinofuranosides 10b–e. To a mixture of triflate **9** (552.5 mg, 1 mmol) and anhydrous HMPA (269 mg, 1.5 mmol) in dry Me_2SO (2 mL) was added 1.1 mmol of the salt (LiCl, LiBr, NaI, or LiN_3). After vigorous stirring (see Table I for reaction time) at room temperature, ice–water (30 mL) was added, and the product was extracted with petroleum ether (bp 30–60 °C) several times. The combined extracts were washed with water, dried over anhydrous Na_2SO_4, and evaporated to dryness in vacuo. The products were isolated by silica gel column chromatography with petroleum ether (bp 30–60 °C)–acetone (98:2) as the eluent and characterized (see Table I) by ^1H NMR and elemental analysis.

Acknowledgment. We thank Drs. B. A. Otter and K. A. Watanabe for their useful suggestions and Mr. M. Olsen for recording the NMR spectra.

Registry No. **1**, 54429-44-6; **2**, 80765-77-1; **3**, 80795-53-5; **4**, 80765-78-2; **5**, 80795-54-6; **6**, 54623-25-5; **9**, 80765-79-3; **10a**, 80765-80-6; **10b**, 80765-81-7; **10c**, 80765-82-8; **10d**, 80765-83-9; **10e**, 80765-84-0; 3,5-di-*O*-benzyl-1,2-*O*-isopropylidene-α-D-ribofuranose, 55735-86-9.

Biogenesis of Epidithiadioxopiperazines. Nucleophilic Additions to Benzene Oxide and *sym*-Oxepin Oxide

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The additions of amine nucleophiles to benzene oxide (**10**) and to *sym*-oxepin oxide (**14**) serve as models for the biogenesis of the epidithiadioxopiperazines of the gliotoxin and aranotin family. Also reported are the additions of a thiolate and an amide anion to *sym*-oxepin oxide (**14**).

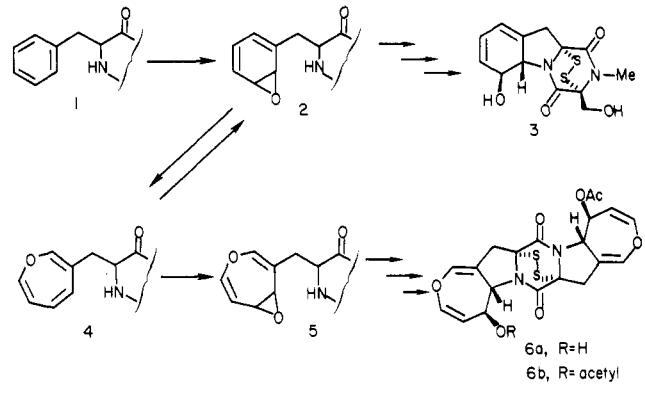
The biogenesis of the fungal metabolites gliotoxin[2] (**3**, Scheme I) and aranotin[2e-g,3] (**6a**) from phenylalanine (see **1**) occurs through oxidative elaboration of the amino acid. Neuss and co-workers[2e,f] have suggested that an enzyme-bound arene oxide, **2**, serves as a direct precursor to the dihydroarene ring of gliotoxin (**3**). Valence tautomerization of oxide **2** (**2** ⇄ **4**) and further enzymatic oxidation (**4** → **5**) would provide oxepin oxide **5**, the proposed[2e,f] precursor of the aranotins (see **6**).

Though plausible, Neuss' scheme has remained without chemical precedent. Arene oxides are prone to rearrangement, and consequently their "nucleophilic susceptibility"[4] is low. Thus, 3-(β-aminoethyl)benzene oxide (**7**), a model for enzyme-bound oxide **2**, fails to cyclize (**7** → **8**) under a variety of conditions.[5] Rather, conditions which might facilitate ring closure also accelerate the rearrangement of **7** to phenol **9**.

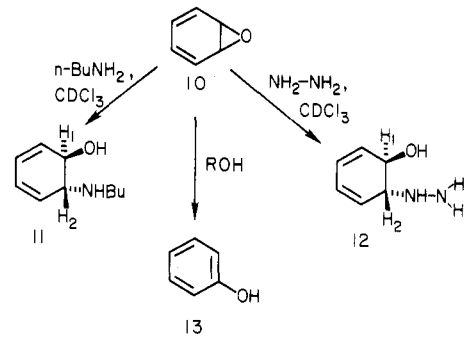
The reactivity of oxepin oxides toward nucleophiles has not been reported previously. Upon contact with untreated glassware or protic solvents, the parent, *sym*-oxepin oxide (**14**), undergoes rapid ring contraction (**14** → **20**).[6] A priori, the lability of the ring system might preclude successful nucleophilic reactions of **14** in a biogenetic fashion (see **5** → **6**). Certainly, *sym*-oxepin oxide (**14**) is incompatible with the protic conditions which facilitate nucleophilic additions to simple epoxides.[7]

Herein we present chemical precedent for both epoxide-opening steps of Neuss' scheme, **2** → **3** and **5** → **6**. Under appropriate conditions benzene oxide (**10**, Scheme

Scheme I



Scheme II



(1) Alfred P. Sloan Fellow, 1980–1982; current address: Genentech, Inc., South San Francisco, California, 94080.

(2) (a) Bell, M. R.; Johnson, J. R.; Wildi, B. S.; Woodward, R. B. *J. Am. Chem. Soc.* **1958**, *80*, 1001. (b) Bu'Lock, J. D.; Ryles, A. P. *Chem. Commun.* **1970**, 1404. (c) Johns, N.; Kirby, G. W. *Ibid.* **1971**, 163. (d) Kirby, G. W.; Patrick, G. L.; Robins, D. J. *J. Chem. Soc., Perkin Trans. 1* **1978**, 1336. (e) Neuss, N.; Nagarajan, R.; Molloy, B. B. *Tetrahedron Lett.* **1968**, 4467. (f) Neuss, N.; Boeck, L. D.; Brannon, D. R.; Cline, J. C.; DeLong, D. C.; Gorman, M.; Huckstep, L. L.; Lively, D. H.; Mabe, J.; Marsh, M. M.; Molloy, B. B.; Nagarajan, R.; Nelson, J. D.; Stark, W. M. *Antimicrob. Agents Chemother.* **1968**, 213. (g) Brannon, D. R.; Mabe, J.; Molloy, B. B.; Day, W. A. *Biochem. Biophys. Res. Commun.* **1971**, *43*, 588.

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(7) For examples, see the following: (a) Enikolopiyan, N. S. *Pure Appl. Chem.* **1976**, *48*, 317. (b) Parker, R. E.; Rockett, B. W. *J. Chem. Soc.* **1965**, 2569. (c) Burfield, D. R.; Gan, S.; Smithers, R. H. *J. Chem. Soc., Perkin Trans. 1* **1977**, 666.

0022-3263/82/1947-1509$01.25/0

Scheme III

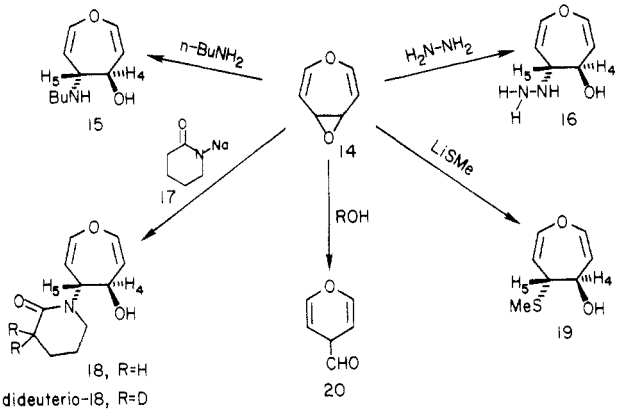


Table I. ^{1}H NMR Absorptions[a] for Nucleophilic Adducts and Model Compounds

compd	$\delta(H_1)$	$\delta(H_2)$	$J_{1,2}$	$\delta(H_4)$	$\delta(H_5)$	$J_{4,5}$
11	4.44	3.55	12.5			
12	4.58	3.64	12.1			
15				3.98	3.16	7.9
16				4.30	3.40	7.7
18				5.21	4.37	8.5
19				4.22	3.33	7.2
6b				5.68	5.09	8.7
21				4.21	5.06	7.7

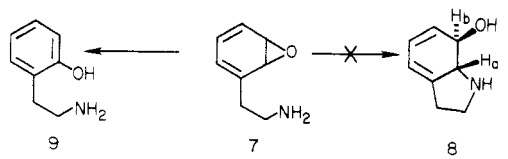
[a] Chemical shifts for H_1, H_2, H_4 and H_5 are reported downfield from tetramethylsilane on the δ scale. Coupling constants, $J_{1,2}$ and $J_{4,5}$ are reported in hertz.

II) and *sym*-oxepin oxide (**14**, Scheme III) add simple amines intermolecularly without significant competing rearrangement.

Results

Amine Nucleophiles. In aprotic media ($CDCl_3$) *n*-butylamine and hydrazine add slowly to benzene oxide (**10**). The addition of *n*-butylamine to **10** affords 11% of adduct **11** after 7 weeks and 56% of **11** after 8 months (Scheme II). The addition of amines to benzene oxide, though slow in $CDCl_3$, proceeds without significant aromatization (see **13**) of the arene oxide. The ^{1}H NMR spectra of adducts **11** and **12** clearly show the trans relationship of the vicinal protons H_1 and H_2 (see $J_{1,2}$, Table I and ref 8). Further, the NMR data (also see Experimental Section) show that the amine additions have occurred in 1,2- and/or 1,6-[8] rather than 1,4-fashion.

Gliotoxin model arene oxide **7**[5] was allowed to stand in $CDCl_3$ at ambient temperature. After 3 months ^{1}H NMR spectroscopy showed conversion of oxide **7** predominantly into phenol **9**. No absorptions attributable to cyclized product **8**[9] were discernible.



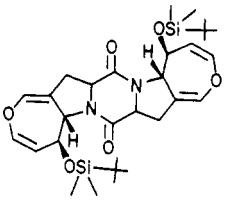
Addition of amine nucleophiles to *sym*-oxepin oxide (**14**) occurs readily in aprotic media ($CDCl_3$). The additions of *n*-butylamine and hydrazine are complete after 72 h at ambient temperature (see Scheme III).

Other Nucleophiles. The additions of nonamine nucleophiles to benzene oxide (**10**) have been carefully examined by Berchtold, Jerina, and co-workers.[8]

Valerolactam sodium salt (**17**) in dimethyl sulfoxide adds to *sym*-oxepin oxide (**14**), giving adduct **18** in modest yield (27%). The addition performed in dimethyl-d_6 sulfoxide affords dideuterated **18** (31%).

Lithium thiomethoxide adds rapidly to *sym*-oxepin oxide, giving thioether **19** in good yield (77%).

The assignment of structure to dihydrooxepin adducts **15**, **16**, **18**, and **19** follows from comparison of the adduct ^{1}H NMR spectra with the spectra for acetylaranotin (**6b**) and the bis-dethio derivative **21**.[10] The spectra (see Table I and the Experimental Section) indicate that the nucleophilic additions have occurred cleanly in the 1,2- rather than the 1,4-fashion. Further, the magnitude of the coupling constant $J_{4,5}$ (see Table I) for each adduct is consistent with the trans rather than the cis relationship of vicinal protons H_4 and H_5.



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Discussion

Structure influences the rate of nucleophilic addition to epoxides as well as the rate of epoxide rearrangement. The balance of the two rates determines the "nucleophilic susceptibility"[4] of an epoxide. High mutual reactivity between epoxide and nucleophile does not ensure that nucleophilic addition will take place. A more rapid rearrangement may actually predominate under a given set of reaction conditions. Structural parameters influencing the relative rates of epoxide rearrangement, hydration and addition of nucleophiles have been discussed by Bruice[4,11] and by Harvey.[12] Additions of amine nucleophiles to arene oxides previously have been observed only in cases[4] where rearrangement is impeded by the structure of the epoxide.

The reactivity of benzene oxide (**10**) toward nucleophiles is high,[4] yet the extremely facile rearrangement of **10** to phenol (**13**) has precluded observation of the nucleophilic addition of all but strong and/or polarizable nucleophiles.[8] Amine additions to **10** are possible (vide supra) but apparently only in aprotic media where the competing rearrangement, **10** → **13**, of the arene oxide is retarded.

The *intra*molecular epoxide opening, **7** → **8**, fails under conditions which promote the intermolecular addition of *n*-butylamine to benzene oxide (**10**). An examination of a Dreiding model of **7** suggests that the appropriate approach vector[5] is attainable for the initial approach of the amine to the epoxide. However, considerable strain may develop during the conversion **7** → **8** if the incoming amine and the leaving alkoxide are held in the trans-diaxial

(8) Jeffrey, A. M.; Yeh, H. J. C.; Jerina, D. M.; DeMarinis, R. M.; Foster, C. H.; Piccolo, D. E.; Berchtold, G. A. *J. Am. Chem. Soc.* **1974**, *96*, 6929.

(9) The absorptions expected for vicinal protons H(a) and H(b) (see 8) in the regions δ 3.5–4.2 and 4.0–5.6, respectively, were absent in the ^{1}H NMR (250 MHz) spectrum of the crude cyclization mixture. The expected chemical shifts are taken from model compounds including **11** and **12**, various synthetic gliotoxin precursors (Fukuyama, T. F. Ph. D. Thesis, Harvard University, 1977), and nucleophilic adducts of benzene oxide reported in ref 8.

(10) Prepared by the silylation [Corey, E. J.; Venkateswarlu, A. *J. Am. Chem. Soc.* **1972**, *94*, 6190] of bis(dethioaranotin) kindly supplied by Drs. N. Neuss and R. Nagarajan, Eli Lilly Co.

(11) Becker, A. R.; Janusz, J. M.; Rogers, D. Z.; Bruice, T. C. *J. Am. Chem. Soc.* **1978**, *100*, 3244.

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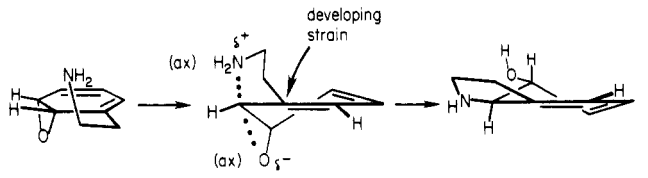
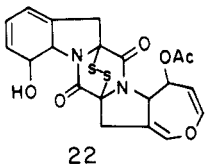


7 23 8

orientation (see **23**) required to maximize bonding in the transition state for epoxide nucleophilic opening. A model of product **8** is stain free only when the alcohol and amine groups are in pseudoequatorial positions. Geometrical constraints, thus, may impede the closure of **7**, while aromatization, **7** → **9**, is apparently facilitated by the electron-donating β-aminoethyl substituent (cf. **10**).

The failure to cyclize model arene oxide **7** cannot rule out the involvement of **2** (Scheme I) during the biogenesis of gliotoxin (**3**). In light of labeling studies,[2b-d] arene oxide **2** remains an attractive biosynthetic intermediate. Circumstantial evidence for the in vivo intermediacy of the valence tautomeric mixture **2** ⇄ **4** is provided in the structure of apoaranotin (**22**)[2e-g] which displays both the



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gliotoxin dihydroarene ring system and the aranotin dihydrooxepin ring system. Nonetheless, the present results (also see ref 5) strongly suggest that the cyclization **2** → **3** may occur only through enzyme intervention. The nature of the presumed enzyme catalysts remains, however, an intriguing and unanswered question.

The facile additions of amines to *sym*-oxepin oxide (**14**, cf. **10**) provide good precedent for the proposed[2e,f] biogenetic reaction **5** → **6**. A Dreiding molecular model of **5** shows that the entering amine and departing alkoxide can maintain the preferred antiperiplanar relationship during the closure reaction (**5** → **6**). Thus, unlike model oxide **7**, a model for oxepin oxide **5** would likely undergo biomimetic cyclization (cf. **5** → **6**).

Experimental Section

General Methods. Reagent grade dimethyl sulfoxide and dimethyl-d_6 sulfoxide (Kor Isotopes) were dried over 4-Å activated sieves (72 h) and distilled in vacuo onto fresh 4-Å activated sieves. All solvents were passed through basic alumina immediately prior to use.

n-Butylamine and anhydrous hydrazine were distilled under an atmosphere of nitrogen immediately prior to use. Lithium thiomethoxide was prepared by addition of *n*-butyllithium to a solution of methanethiol in tetrahydrofuran at −78 °C, followed by removal of the solvent in vacuo at ambient temperature. Valerolactam sodium salt was prepared from valerolactam and sodium hydride in tetrahydrofuran at −78 °C followed by removal of the solvent in vacuo at ambient temperature.

Infrared (IR) spectra were recorded on a Perkin-Elmer 567 spectrometer. ^{1}H (250 MHz) and ^{13}C (62.9 MHz) NMR spectra were obtained on a Brüker WM-250 spectrometer. Chemical shifts are reported downfield from tetramethylsilane on the δ scale. Residual $CHCl_3$ (δ 7.24, ^{1}H NMR) and $CDCl_3$ (δ 77.0, ^{13}C NMR) were used as internal standards for computation of chemical shifts relative to Me_4Si. Mass spectra were determined on a CEC-110B Mattauch-Herzog (Du Pont Instruments) high-resolution mass spectrometer.

All glassware was base treated (soaked in 1 N KOH and then NH_4OH) and oven dried.

Preparative work with benzene oxide and *sym*-oxepin oxide adducts is complicated by the lability of the starting materials and products. The propensity of the products to undergo acid-catalyzed or glass-surface-catalyzed rearrangements and the oxygen sensitivity of the dihydrooxepin products have often precluded their purification by standard techniques. We have characterized all products as fully as possible by analytical and/or spectroscopic techniques. The purity of each product as judged by ^{1}H NMR (250 MHz) is indicated.

Addition of *n*-Butylamine to Benzene Oxide. To a solution of benzene oxide[13] (**10**; 0.257 g, 2.73 mmol) in $CDCl_3$ (0.5 mL) was added *n*-butylamine (0.199 g, 2.73 mmol). After 8 months ^{1}H NMR spectroscopy indicated consumption of all starting oxide **10**. Exhaustive evaporation of the product solution afforded adduct **11** as a red oil (0.255 g, 56%) which was judged to be ≥95% pure: ^{1}H NMR ($CDCl_3$) 5.97–5.85 (4 H, m), 4.44 (1 H, d, J = 12.5 Hz), 4.01 (2 H, br s), 3.55 (1 H, d, J = 12.5 Hz), 2.87–2.61 (2 H, m), 1.63–1.22 (4 H, m), 0.90 (3 H, t); ^{13}C NMR ($CDCl_3$) 130.99, 128.63, 124.16, 123.54, 70.29, 60.84, 45.91, 31.90, 20.16, 13.68; IR (neat) 3100–3600 (br), 3030, 2940, 2860, 1640, 1600, 1455, 1060, 680 cm^{-1}; exact mass calcd for $C_{10}H_{17}NO$ (M^+) m/e 167.129 63, found 167.131 01.

Adduct **11** was derivatized as the *tert*-butyldiphenylsilyl ether:[14] ^{1}H NMR ($CDCl_3$) 7.69 (2 H, m), 7.38 (3 H, m), 5.85 (2 H, m), 5.70 (1 H, m), 5.64 (1 H, dd, J = 9.6, 3.3 Hz), 4.48 (1 H, ddd, J = 9.6, 3.3, 1.5 Hz), 3.52 (1 H, dd, J = 9.6, ~2 Hz), 2.50–2.30 (2 H, m), 1.50 (1 H, br s), 1.25 (4 H, m), 1.05 (9 H, s), 0.84 (3 H, t); IR (CCl_4) 3350 (br), 3050, 2960, 2920, 2850, 1425, 1100 cm^{-1}; exact mass calcd for $C_{26}H_{35}NOSi$ (M^+) m/e 405.248 79, found 405.249 90.

Addition of Hydrazine to Benzene Oxide. To a solution of benzene oxide[13] (**10**; 0.669 g, 7.11 mmol) in $CDCl_3$ (3.7 mL) was added anhydrous hydrazine (1.14 g, 35.6 mmol). After 7 weeks ^{1}H NMR spectroscopy showed partial conversion of benzene oxide (**10**) into adduct **12**. Exhaustive evaporation of the solvent and remaining, volatile starting materials yielded impure **12** as an oil: 0.509 g (66%); ^{1}H NMR ($CDCl_3$) 5.98–5.59 (4 H, m), 4.58 (1 H, d, J = 12.1 Hz), 3.64 (1 H, dt, J = 12.1, 2.6 Hz), 3.40 (br s); integration of the ^{1}H NMR spectrum indicates that 68% of the nonexchangeable proton absorptions are attributable to adduct **12**; IR ($CHCl_3$) 3400–3200, 3000, 1595, 1060 cm^{-1}. Upon being allowed to stand as an oil, adduct **12** undergoes rapid decomposition and aromatization (^{1}H NMR). The decomposition mixture displays the following: exact mass calcd for $C_6H_5NHNH_2$ (M^+) m/e 108.0687, found 108.0685.

Attempted Cyclization of 3-(β-Aminoethyl)benzene Oxide (7). A solution of **7**[5] (0.0233 g, 0.17 mmol) in $CDCl_3$ (0.5 mL) was allowed to stand at ambient temperature. After 3 months ^{1}H NMR spectroscopy showed no remaining starting material (**7**) and no absorptions attributable to cyclized product **8**.[9] Removal of solvent in vacuo, passage of a methanol solution of the residue through a Waters C-18 Sep Pak filter, and removal of methanol in vacuo afforded phenol **9**[5] (0.0118 g, 51%). Duplicate runs, performed as above, also failed to yield cyclized material **8**.

Addition of *n*-Butylamine to *sym*-Oxepin Oxide. To a solution of *sym*-oxepin oxide (**14**; generated from 0.035 g, 0.26 mmol, of the azo diepoxide precursor)[6] in $CDCl_3$ (0.5 mL) was added *n*-butylamine (0.019 g, 0.26 mmol). After 72 h ^{1}H NMR spectroscopy indicated consumption of **14**. The solvent and residual *n*-butylamine were removed by exhaustive evaporation, yielding adduct **15** as a light brown, air-sensitive oil (0.035 g, 75%) judged to be ≥95% pure by ^{1}H NMR ($CDCl_3$): 6.20 (1 H, dd, J = 7.7, 2.6 Hz), 6.16 (1 H, dd, J = 7.7, 2.2 Hz), 4.88 (1 H, dd, J = 7.7, 2.3 Hz), 4.69 (1 H, dd, J = 7.7, 2.8 Hz), 3.98 (1 H, ddd, J = 7.9, 2.3, 2.2 Hz), 3.16 (1 H, ddd, J = 7.9, 2.8, 2.6 Hz), 2.83–2.73 (1 H, m), 2.59–2.49 (1 H, m), 1.48–1.28 (4 H, m), 0.88 (3 H, t); ^{1}H decoupling and irradiation at δ 3.16 gives 6.20 (1 H, d, J = 7.7 Hz), 6.16 (1 H, dd, J = 7.7, 2.2 Hz), 4.88 (1 H, dd, J = 7.7, 2.3 Hz), 4.69 (1 H, d, J = 7.7 Hz), and 3.98 (1 H, dd, J = 2.3, 2.2 Hz); ^{13}C NMR ($CDCl_3$) 141.56, 139.82, 109.88, 107.94, 68.88, 61.19, 46.62, 32.31, 20.27, 13.80; IR (neat) 3200–3500, 1660, 1640 cm^{-1}; exact mass calcd for $C_{10}H_{15}NO$ $(M - H_2O)^+$ m/e 165.115 36, found 165.116 17, calcd for $C_6H_7O_2$ $(M - NHC_4H_9)^+$ m/e 111.044 60, found 111.044 17.

Addition of Hydrazine to *sym*-Oxepin Oxide. To a solution of *sym*-oxepin oxide (**14**; generated from 0.147 g, 1.07 mmol, of

(13) Vogel, E.; Gunther, G. *Angew. Chem.* **1967**, *79*, 429.

the azo diepoxide precursor)[6] in $CDCl_3$ (0.5 mL) was added anhydrous hydrazine (0.045 g, 1.39 mmol). After 72 h ^1H NMR spectroscopy indicated consumption of **14**. The solvent and excess hydrazine were removed in vacuo, affording adduct **16** as a pale yellow, air-sensitive oil (0.061 g, 41%) judged to be ≥95% pure by ^1H NMR ($CDCl_3$): 6.30 (1 H, dd, J = 7.7, 2.4 Hz), 6.18 (1 H, dd, J = 8.0, 2.1 Hz), 4.84 (1 H, dd, J = 8.0, 2.2 Hz), 4.63 (1 H, dd, J = 7.7, 2.8 Hz), 4.30 (1 H, ddd, J = 7.7, 2.2, 2.1 Hz), 3.46 (4 H, br s), 3.40 (1 H, ddd, J = 7.7, 2.8, 2.4 Hz); ^{13}C NMR ($CDCl_3$) 143.06, 140.05, 110.91, 106.35, 68.23, 64.75; IR (neat) 3200–3500, 3010, 1660, 1640 cm^{-1}; exact mass calcd for $C_6H_{10}N_2O_2$ (M^+) m/e 142.074 22, found 142.074 44.

Addition of Valerolactam Sodium Salt to *sym*-Oxepin Oxide. To a solution of *sym*-oxepin oxide (**14**; generated from 0.169 g, 1.23 mmol, of the azo diepoxide precursor)[6] in dimethyl sulfoxide (1.5 mL) was added valerolactam sodium salt (0.281 g, 2.33 mmol). The suspension was stirred at ambient temperature for 160 h. The product mixture was partitioned between equal volumes of Et_2O and H_2O (40 mL total volume), and the organic phase was discarded. The aqueous layer was extracted twice with CH_2Cl_2 (2 × 25 mL). The combined CH_2Cl_2 layers were washed with water (2 × 15 mL), dried (Na_2SO_4), and concentrated to yield adduct **18** as a yellow, air-sensitive oil (0.070 g, 27%) judged to be ≥90% pure by ^1H NMR ($CDCl_3$): 6.29 (1 H, dd, J = 8.1, 2.6 Hz), 6.18 (1 H, dd, J = 7.9, 2.4 Hz), 5.20 (1 H, ddd, J = 8.5, 2.9, 2.6 Hz), 4.95 (1 H, dd, J = 7.9, 2.4 Hz), 4.47 (1 H, dd, J = 8.1, 2.9 Hz), 4.37 (1 H, ddd, J = 8.5, 2.4, 2.4 Hz), 3.48, (1 H, br s, D_2O exchangeable), 3.35–3.26 (2 H, m), 2.43 (2 H, m), 1.86–1.74 (4 H, m); ^1H decoupling and irradiation at δ 5.21 gives 6.28 (1 H, d, J = 8.1 Hz), 6.18 (1 H, dd, J = 7.9, 2.2 Hz), 4.95 (1 H, dd, J = 7.9, 2.6 Hz), 4.46 (1 H, d, J = 8.1 Hz), and 4.37 (1 H, dd, J = 2.6, 2.2 Hz); ^{13}C NMR ($CDCl_3$) 171.44, 142.47, 139.23, 111.59, 104.11, 67.05, 56.39, 42.76, 32.19, 23.07, 20.80; exact mass calcd for $C_{11}H_{15}NO_3$ (M^+) m/e 209.1052, found 209.1059.

Addition of valerolactam sodium salt to *sym*-oxepin oxide as above with dimethyl-d_6 sulfoxide as solvent afforded dideuterated adduct **18** (31%). The ^1H NMR of dideuterated **18** lacks absorption at δ 2.43. The ^1H-decoupled ^{13}C NMR spectrum of dideuterated **18** displays a quintet for the CD_2 absorption at δ 31.55. The off-resonance ^1H-decoupled ^{13}C NMR spectrum displays the following: 171.46 (s), 142.50 (d), 139.29 (d), 111.59 (d), 104.11 (d), 67.05 (d), 56.36 (d), 42.73 (t), 31.55 (quintet), 23.01 (t), 20.57 (t); exact mass calcd for $C_{11}H_{13}D_2NO_3$ (M^+) m/e 211.117 74, found 211.116 84, calcd for $C_{11}H_{12}D_2NO_2$ $(M - OH)^+$ m/e 194.115 00, found 194.113 62, calcd for $C_{11}H_{11}D_2NO_2$ $(M - H_2O)^+$ m/e 193.107 18, found 193.108 47.

Addition of Lithium Thiomethoxide to *sym*-Oxepin Oxide. To a solution of *sym*-oxepin oxide (**14**; generated from 0.125 g, 0.91 mmol, of the azo diepoxide precursor)[6] in dimethyl sulfoxide (Me_2SO, 2.5 mL) was added lithium thiomethoxide (0.109 g, 2.00 mmol). The resulting mixture was stirred for 10.5 h and then diluted with H_2O (30 mL). The aqueous Me_2SO layer was extracted twice with Et_2O (2 × 25 mL), and the organic layers were combined and washed with H_2O (6 × 25 mL). Drying of the Et_2O layer ($MgSO_4$) and removal of solvent in vacuo yielded adduct **19** as a yellow, air-sensitive oil. Bulb-to-bulb distillation [90 °C (0.5 mmHg)] afforded pure **19**: 0.111 g (77%); ^1H NMR ($CDCl_3$) 6.22 (1 H, dd, J = 7.9, 1.9 Hz), 6.17 (1 H, dd, J = 7.5, 1.5 Hz), 5.07 (1 H, dd, J = 7.5, 3.5 Hz), 4.77 (1 H, dd, J = 7.9, 4.0 Hz), 4.22 (1 H, ddd, J = 7.2, 3.5, 1.5 Hz), 3.33 (1 H, ddd, J = 7.2, 4.0, 1.9 Hz), 2.89 (1 H, br s, D_2O exchangeable), 2.06 (3 H, s); ^{13}C NMR ($CDCl_3$) 142.98, 141.10, 110.83, 105.31, 67.52, 49.92, 11.15; IR (neat) 3400–3500, 2923, 1665, 1641 cm^{-1}; UV (EtOH) 225 nm (ε 1.79 × 10^3), 212 (1.88 × 10^3); exact mass calcd for $C_7H_{10}O_2S$ (M^+) m/e 158.040 15, found 158.038 37.

The adduct was derivatized as the *tert*-butyldiphenylsilyl ether:[14] ^1H NMR ($CDCl_3$) 6.35 (1 H, d, J = 7.5 Hz), 6.25 (1 H, d, J = 7.4 Hz), 5.01 (1 H, d, J = 7.4 Hz), 4.94 (1 H, d, J = 7.5 Hz), 4.38 (1 H, d, J = 5.3 Hz), 4.35 (1 H, d, J = 5.3 Hz), 3.27 (1 H, d, J = 5.3 Hz), 3.24 (1 H, d, J = 5.3 Hz), 1.82 (3 H, s), 1.11 (9 H, s); IR (neat) 3040–3080, 2820–2980, 1665, 1650 cm^{-1}; exact mass calcd for $C_{23}H_{28}O_2SiS$ (M^+) m/e 396.157 93, found 396.158 61. Anal. Calcd for $C_{23}H_{28}S$: C, 69.65; H, 7.12; S, 8.08. Found: C 69.38; H, 7.19; S, 8.25.

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Registry No. 6b, 20485-01-2; **7**, 72251-59-3; **9**, 2039-66-9; **10**, 1488-25-1; **11**, 80764-83-6; **11** ether, 80764-84-7; **12**, 80764-85-8; **14**, 52748-31-9; **15**, 80764-86-9; **16**, 80764-87-0; **17**, 34938-64-2; **18**, 80764-88-1; **18** (dideuterated), 80780-60-5; **19**, 80764-89-2; **19** ether, 80764-90-5; **21**, 80764-91-6; *n*-butylamine, 109-73-9; hydrazine, 302-01-2; lithium thiomethoxide, 35638-70-1.

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