lapping doublets centered at ca. 0.90 and 0.86 and 0.84 (9 H, J = ca. 6.8 Hz); ^{13}C NMR 153.09, 153.01, 143.29, 141.86, 141.14, 119.35, 117.14, 116.56, 90.38, 90.29, 79.42, 78.52, 53.83, 48.03, 46.98, 46.69, 35.27, 32.02, 29.20, 29.11, 28.09, 27.78, 26.72, 26.66, 26.35, 26.13, 25.22, 24.11, 23.87, 22.61, 22.34, 20.84, 18.85, 18.46, 16.62 ppm; mass spectrum, m/z (relative intensity) 265 (1), 264 (M^+, 7), 263 (3), 262 (3), 248 (10), 247 (8), 246 (35), 236 (10), 203 (16), 179 (58), 177 (26), 175 (9), 163 (11), 161 (38), 155 (38), 152 (19), 151 (100), 147 (22), 139 (22), 137 (30), 135 (23), 121 (38), 111 (15), 110 (38), 109 (42), 95 (43), 91 (29), 81 (67), 79 (27), 77 (28), 69 (48), 67 (26), 55 (57), 53 (21), 43 (36), 41 (78), 39 (25). Anal. Calcd for $C_{17}H_{28}O_2$: C, 77.22; H, 10.67. Found: C, 77.40; H, 10.53.

(*E*)- and (*Z*)-4-[5-Methyl-2-(1-methylethyl)cyclohexylidene]-2-cyclohexen-1-one (14b, Each as Four Diastereomeric Pairs). Similar treatment of 778 mg (5.04 mmol) of (-)-menthone (**14**), as described for **11b**, yielded 1.029 g (4.44 mmol, 88%) of **14b** as a colorless oil: bp 105-110 °C (0.1 Torr); IR (film) 3040, 2950, 2925, 2900, 2880, 2860, 1665, 1650, 1600, 1565, 1450, 1400, 1280, 1240, 1205, 1155, 1100, 1010, 960, 815 cm^{-1}; ^{1}H NMR δ 7.59 (1 H, dd, J = 10.2, 4.5 Hz), 5.85 (1 H, dd, J = 10.2, 3.1 Hz), 2.75 (2 H, m, apparent quintet, J = ca. 6.3 Hz), 2.47 (3 H, m, $W_{1/2}$ = 1.7 Hz), 2.30-2.23 (1 H, m), 2.04-1.85 (2 H, m), 1.82-1.08 (5 H, complex m), doublets centered at 0.99 and 0.92 (6 H, J = 6.8 Hz), three overlapping doublets centered at 0.77 and 0.74 and 0.72 (3 H, J = ca. 6.4 Hz); ^{13}C NMR 196.82, 147.17, 146.96, 144.98, 140.25, 140.10, 139.86, 123.59, 121.49, 121.41, 121.26, 41.85, 41.01, 34.11, 33.96, 32.16, 31.86, 31.81, 31.38, 29.32, 27.34, 26.03, 25.80, 25.67, 23.94, 23.79, 23.30, 22.45, 22.31, 22.02, 20.86, 19.37, 19.29, 17.74, 17.45, 17.31, 14.66 ppm; mass spectrum, m/z (relative intensity) 233 (8), 232 (M^+, 40), 189 (100), 188 (10), 161 (12), 147 (33), 145 (40), 133 (17), 131 (10), 121 (12), 119 (16), 117 (15), 115 (12), 109 (19), 107 (17), 105 (28), 95 (52), 93 (30), 91 (51), 81 (30), 79 (21), 77 (28), 69 (12), 67 (22), 65 (18), 55 (19), 53 (17), 51 (10), 43 (20), 41 (50), 39 (25). Anal. Calcd for $C_{16}H_{24}O$: C, 82.70; H, 10.41. Found: C, 82.48; H, 10.21.

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Bimanes. 23. The Synthesis and Properties of Vinyl-9,10-dioxabimanes

Edward M. Kosower,*,†,‡ David Zbaida,† Michel Baud'huin,† Daniele Marciano,† and Israel Goldberg†

Contribution from the Biophysical Organic Chemistry Unit, School of Chemistry, Sackler Faculty of Exact Sciences, Tel-Aviv University, Ramat-Aviv, Tel-Aviv 69978, Israel, and the Department of Chemistry, State University of New York, Stony Brook, New York 11794-3400.
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Abstract: Syntheses and useful reactions of *syn*-vinylbimanes are reported. The precursors are *syn*-(ethyl,methyl)bimane (4,6-diethyl-3,7-dimethyl-1,5-diazabicyclo[3.3.0]octa-3,6-diene-2,8-dione) (*syn*-(CH_3CH_2,CH_3)B) (**2**) and *syn*-(ethyl,chloro)bimane (4,6-diethyl-3,7-dichloro-1,5-diazabicyclo[3.3.0]octa-3,6-diene-2,8-dione) (*syn*-(CH_3CH_2,Cl)B) (**4**). Bromination of **2** yields the 1-bromoethyl derivative (*syn*-(CH_3CHBr,CH_3)(CH_3CH_2,CH_3)B) and both diastereomers of the bis-1-bromoethyl derivative (*syn*-(CH_3CHBr,CH_3)B) (Radkowsky; Kosower; Eisenberg; Goldberg *J. Am. Chem. Soc.* **1986**, *108*, 4532-4541). Elimination of HBr (Et_3N/CH_3CN) leads to monovinylbimane (*syn*-(CH_2=CH,CH_3)(CH_3CH_2,CH_3)B) and divinylbimane (*syn*-(CH_2=CH,CH_3)B), respectively. *syn*-(CH_3CH_2,CH_3)(CH_3,CH_3)B may be converted to *syn*-(CH_2=CH,CH_3)(CH_3,CH_3)B. Vinylbimanes can also be prepared via 2-hydroxyethylbimanes from paraformaldehyde and the anion of *syn*-(CH_3,CH_3)B. The novel reaction of pure bromine with *syn*-(ethyl,chloro)bimane (**4**) or *syn*-(methyl,chloro)bimane (**13**) yields monobromo or dibromo derivatives in high yields. The (1-bromoethyl,chloro)bimanes are converted into (vinyl,chloro)bimanes via phenyl thioethers, oxidation to sulfoxides, and thermal elimination. The synthesis of bimane precursors, chloropyrazolinones, is improved through removal of HCl with *t*-BuOH and dry $MgSO_4$. Vinylbimanes are stable, with UV absorption maxima similar to those of the corresponding ethylbimanes; the fluorescence maxima are at longer wavelengths, showing that excited state interaction of vinyl groups with the bimane ring is greater than in the ground state. Nucleophiles (water, chloride, amines, and bisulfite ion) add to give good yields of 2-adducts. The sulfonate (sulfite adduct) and Vilsmeier reagent ($(CH_3)_2N^+$=CHCl,Cl^-) react to form the sulfonyl chloride. The latter reacts with amines to yield fluorescent derivatives useful for identification. Tricyclic bimanes with an eight-membered ring, are readily obtained by bis addition of bifunctional nucleophiles (CH_3NH_2,S^{2-}). Dialkyl malonate anions yield both tricyclic monoadducts and bisadducts. The crystal structure of μ-(2-thiatrimethylene)-*syn*-(methylene,methyl)-9,10-dioxabimane is reported.

Introduction

9,10-Dioxabimanes ("bimanes") are stable, small heterocyclic systems, readily synthesized,[1-3] and converted via halogen derivatives into many other compounds.[4,5] The syn isomers are usually strongly fluorescent. Vinylbimanes are of interest as reactive intermediates, as potential biological thiol labeling agents,[6-25] and for analyzing the photophysics of conjugated 9,10-dioxabimanes.[26-31] We now report syntheses of monovinyl- and divinylbimanes, which are of interest in all these respects, along with some novel derivatives.

The effectiveness of bromobimanes as biological thiol labeling agents stimulated us to study bimanesulfonyl chlorides as protein labeling agents targeted at amino groups. Such agents might be useful in analysis of picomole quantities of amines, as is the case for thiols.[8,11,12,23]

* Address correspondence to this author at Tel-Aviv University.
† Tel-Aviv University.
‡ State University of New York, Stony Brook.

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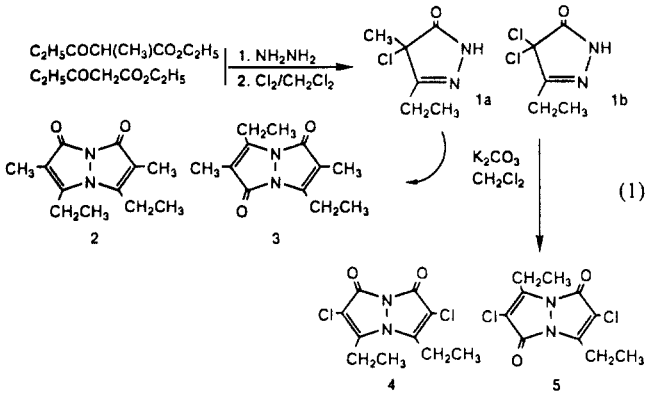
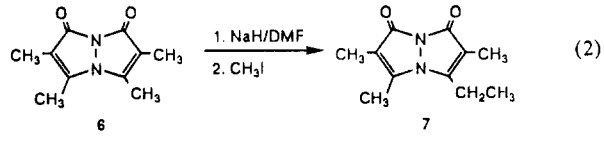
Results

Ethylbimanes. Vinylbimanes are most readily prepared from ethylbimanes which are derived by the "bimane synthesis".[1] The reaction of 3-ethyl-4-chloro-4-methyl-5-pyrazolinone (**1a**) and K_2CO_3 yields both *syn*-(CH_3CH_2,CH_3)B (**2**) and *anti*-(CH_3CH_2,CH_3)B (**3**) (eq 1). Similarly, 3-ethyl-4,4-dichloro-5-pyrazolinone (**1b**) is converted to *syn*-(CH_3CH_2,Cl)B (**4**) and *anti*-(CH_3CH_2,Cl)B (**5**) (eq 1). Reaction of *syn*-(CH_3,CH_3)B



(1)

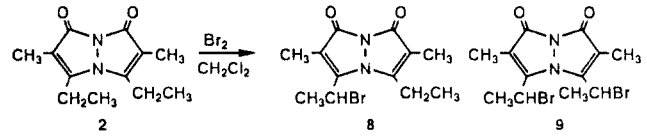
(**6**)[1] via the anion with methyl iodide in DMF leads to 30% of the unsymmetrical *syn*-(CH_3CH_2,CH_3)(CH_3,CH_3)B (**7**) eq 2).



(2)

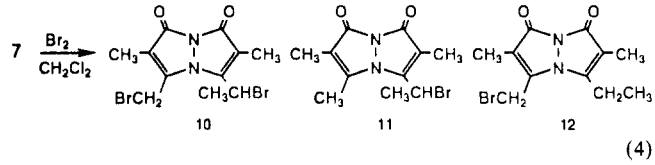
The latter is isolated from the mixture of three *syn*-bimanes and three *anti*-bimanes, produced by the "bimane synthesis" by using a mixture of 3-ethyl-4-chloro-4-methyl-5-pyrazolinone (**1a**) and 3,4-dimethyl-4-chloro-5-pyrazolinone (**1c**), by multiple chromatographies. A significant improvement in conversion of pyrazolinones to chloropyrazolinones is achieved by removal of HCl with *t*-BuOH and dry $MgSO_4$.

Bromoalkylbimanes. Treatment of **2** with 1 equiv of bromine in CH_2Cl_2 leads mainly to the monobromo derivative, *syn*-(CH_3CHBr,CH_3)(CH_3CH_2,CH_3)B (**8**), a typical yellow nonfluorescent bromobimane.[1,4] Reaction of 2 equiv of bromine with **2** leads to a mixture of diastereomeric dibromo derivatives, **9**[13] (eq 3). The unusual reaction of **9** with the tripeptide thiol,



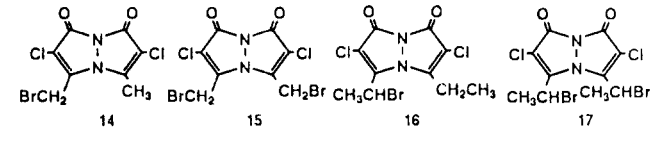
(3)

glutathione has been described in detail.[13] Bromination of the unsymmetrical bimane, **7**, leads to a 50:50 mixture of a dibromibimane (**10**) and the two possible monobromo compounds, **11** and **12**, as shown by ^1H NMR and kinetics[32] (eq 4).

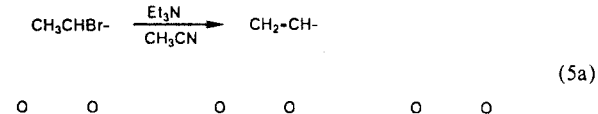


(4)

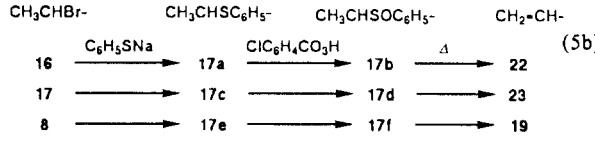
Bimanes with electron-withdrawing groups (e.g., Cl) at positions next to the carbonyl react slowly with bromine in CH_2Cl_2. The bromine concentration is raised by using pure bromine as solvent for reaction with *syn*-(methyl,chloro)bimane (**13**). After stirring a suspension of **13** in Br_2 for 1 h, evaporation of the bromine gives a mixture of starting material and monobromo derivative **14**. Repeating the procedure on the bromination product leads to a mixture of the dibromobimane **15** (60% yield), the monobromo derivative **14** (30% yield), and some starting material. Bromination of *syn*-(CH_3CH_2,Cl)B (**4**), yields monobromo (**16**) and dibromo (**14**) derivatives. Free radical bromination (*N*-bromosuccinimide and benzoyl peroxide) of *syn*-(CH_3,Cl)B (**13**) produces only modest yields of bromo derivatives.



Vinylbimanes. Elimination of HBr from 1-(bromoethyl)bimanes with triethylamine in CH_3CN gives good yields of the vinylbimanes, *syn*-(CH_2=CH,CH_3)(CH_3,CH_3)B (**18**), *syn*-(CH_2=CH,CH_3)(CH_3CH_2,CH_3)B (**19**), and *syn*-(CH_2=CH,CH_3)B (**20**) (eq 5a). The conversion of **6** to **18** by methylation, bromination, and elimination proceeds in only 4% overall yield.



(5a)



(5b)

A "one-pot" synthesis of monovinylbimane **18** and divinylbimane **20** begins with reaction of **6** and sodium hydride in DMF, addition

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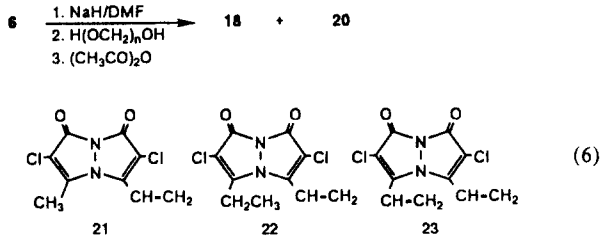
of paraformaldehyde in DMF to the anion, and removal of DMF and ends with conversion of two blue-fluorescent intermediates to vinylbimanes with hot acetic anhydride. The striking yellow-green fluorescence of the vinylbimanes is not detectable before the last step (eq 6). The overall yield of vinylbimane product



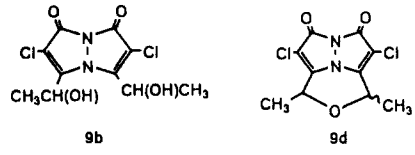
(6)

is as much as 75%, with conversions of 40%. The amount of NaH used to form the anion affects the **18**:**20** product ratio, with molar amounts favoring **18** (15:1) and 2.5 equiv favoring the divinyl derivative **20** (1:3).

Similarly, the anion of *syn*-(CH_3,Cl)B reacted with paraformaldehyde to give, after treatment with hot acetic anhydride, the monovinylbimane **21**. An unsuccessful attempt to eliminate HBr from the dibromo compound **17** with triethylamine gave only small amounts of *syn*-(ethyl,hydro)bimanes.

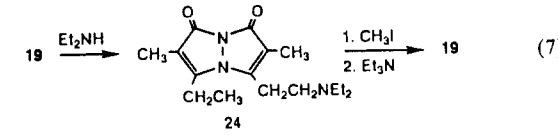
A different route is used to prepare *syn*-(vinyl,chloro)bimanes (eq 5b). The monobromo compound **16** is reacted with dry sodium thiophenolate in dry tetrahydrofuran to yield the phenyl thioether **17a** which is then oxidized with 3-chloroperbenzoic acid to the sulfoxide **17b**. The sulfoxide forms *syn*-(vinyl,chloro)(ethyl,-chloro)bimane (**22**) on heating in benzene solution at reflux for 1 h. A similar reaction sequence with bis-(bromoethyl,chloro)-bimane (**17**) yields the divinylbimane **23** via the diphenyl thioether **17c** and the bis-sulfoxide **17d**. The sulfoxide route yields the monovinylbimane **19** in good yield from **8** although the elimination step requires four times as long for **17f** as for **17b**. Attempts to prepare 2-nitrophenyl selenoethers from *syn*-(1-bromoalkyl,-chloro)bimanes led to quantitative formation of diselenides and reduction to the *syn*-(alkyl,chloro) and *syn*-(alkyl,hydro)bimanes, precluding synthesis of (vinyl,chloro)bimanes via selenoxides.

Attempts to eliminate HBr from *syn*-(1-bromoethyl,chloro)-bimane (**9**) with weak bases led to substitution products. *syn*-(1-Acetoxyethyl,chloro)bimane (**9a**) was formed with potassium acetate and *syn*-(1-hydroxyethyl,chloro)bimane (**9b**), and *syn*-(1-hydroxyethyl,chloro)(1-bromoethyl,chloro)bimane (**9c**) with sodium trifluoroacetate. In the last case, the tricyclic bimane, μ-(O)-*syn*-(methylmethylene,chloro)bimane (**9d**) was also obtained, a compound which could be prepared by reaction of *syn*-(1-bromoethyl,chloro)bimane (**9**) and $KHCO_3$ in warm water for two weeks.



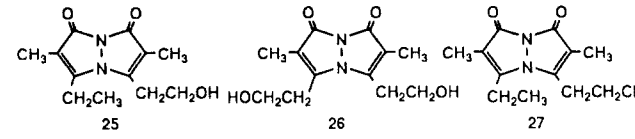
Four other syntheses using the anion of **6** (NaH/DMF) led to yields of no more than 2–4% of the monovinylbimane **18**. (a) Dihalomethanes (XCH_2Y; X = I, Y = Cl or X = Y = Br) gave neither haloethyl nor vinylbimane products, except for 3% of **18** from the reaction of ICH_2Cl in the presence of dibenzo-18-crown-6 ether. (b) Dimethyl(methylene)ammonium iodide [CH_2=N-(CH_3)$_2^+I^-$],[33] followed by methyl iodide and then triethylamine, afforded **18** in 3% yield. (c) (Iodomethyl)trimethylammonium iodide and then triethylamine also gave 3% of **18**. (d) The red anion derived from the diethyl phosphonate (from the phosphonium salt obtained from *syn*-(CH_2Br,CH_3)(CH_3,CH_3)B (**22**) and triethyl phosphite)[34] reacted with paraformaldehyde to yield 2% of **18**.

Addition of Nucleophiles to Vinylbimanes. Diethylamine reacts with *syn*-(CH_2=CH,CH_3)(CH_3CH_2,CH_3)B (**19**) to form *syn*-((CH_3CH_2)$_2$N—CH_2CH_2,CH_3)(CH_3CH_2,CH_3)B (**23**) eq 7). The adduct is reconverted into **19** by quaternization with methyl iodide and treatment with a catalytic amount of triethylamine.

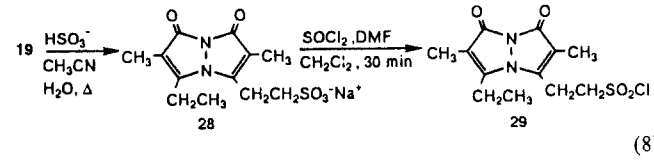


(7)

The vinylbimanes **18** and **20** yield the 2-hydroxy adducts **25** and **26** on heating with water and $NaHCO_3$; water is lost on heating with acetic anhydride. Adducts **25** and **26** have chromatographic mobilities identical with those of the two blue-fluorescent intermediates formed from the anion of **6** and paraformaldehyde. Hydrogen chloride in xylene reacts with *syn*-(CH_2=CH,CH_3)(CH_3CH_2,CH_3)B (**19**) to form a 2-(chloroethyl)bimane, *syn*-($ClCH_2CH_2$,CH_3)(CH_3CH_2,CH_3)B (**27**). The adduct reforms **19** by treatment with triethylamine.



Bimanesulfonyl Chlorides. Bimanesulfonates are formed by reaction of bisulfite with vinylbimanes; *syn*-(CH_2=CH,CH_3)-(CH_3CH_2,CH_3)B (**19**) gives 2-(oxysulfonyl)ethylbimane ("sulfonate") (**28**) (eq 8). The bimanesulfonate **28** yields the sulfonyl chloride **29** with Vilsmeier reagent, *N*,*N*-dimethylchloroformiminium chloride, [$(CH_3)_2N$=$CHCl^+Cl^-$][35] (eq 8).

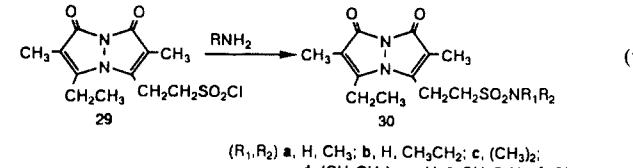


(8)

The bimanesulfonyl chloride (**29**) is fluorescent and can be observed on thin-layer chromatograms. The structure is confirmed by IR, mass spectrum, ^{1}H NMR, and elemental analysis. The sulfonyl chloride shows fairly strong infrared absorption bands at 1360 cm^{-1} (SO_2 symmetrical stretching) and at 1150 cm^{-1} (asymmetrical SO_2 stretch).[36] The mass spectrum does not show the parent peak (M^+ 318), but a strong peak for an SO_2 fragment appears.

The ^{1}H NMR spectrum of a very dilute solution (ca. 10^{-4} M) of **29** in $CDCl_3$ (300 MHz) exhibits the expected peaks. At higher concentrations, broad peaks in the 3.151–3.551 and 4.056–4.400 ppm regions are seen, and broadening of the expected quartet and triplet for the ethyl group is observed. The ^{1}H NMR spectrum of **29** in CF_3COOH at high concentrations is highly resolved.

Bimanesulfonyl ("bimsyl") chlorides are converted into sulfonamide derivatives (**30**) through reaction with an amine in acetonitrile, either at room temperature or at reflux (eq 9). The mass spectra of most of the sulfonamides include a molecular peak (M^+) along with a peak at *m/e* 218 due to the fragment ion ((vinyl,methyl)(ethyl,methyl)bimane$^+$). IR bands appear at 1150



(9)

(R_1,R_2) **a**, H, CH_3; **b**, H, CH_3CH_2; **c**, $(CH_3)_2$; **d**, $(CH_3CH_2)_2$; **e**, H, 3-$CH_3C_6H_4$; **f**, CH_3, C_6H_5

and 1330 cm^{-1}.[37] All sulfonamides melt with decomposition

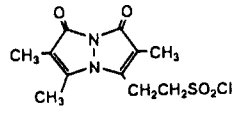
(33) Schreiber, J.; Maag, H.; Hashimoto, N.; Eschenmoser, A. *Angew. Chem. Int. Ed. Engl.* **1971**, *10*, 330–331.
(34) Horner, L.; Hoffmann, H.; Wippel, H. G. *Chem. Ber.* **1958**, *91*, 61–3.
(35) Bosshard, H. H.; Mory, R.; Schmid, M.; Zollinger, U. *Helv. Chim. Acta* **1959**, *42*, 1653.
(36) Sulfonyl chloride SO_2 bands (IR) are reported at 1410–1368 and 1195–1168 cm^{-1}. Robinson, A. *Can. J. Chem.* **1961**, *39*, 247.

(bubbling, SO_2?), forming the vinylbimane, *syn*-(CH_2=CH,-CH_3)(CH_3CH_2,CH_3)B (**19**). Thin-layer chromatography of the sulfonamides showed reasonably good separation between derivatives of closely related amines.

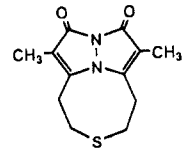
Sulfonamide formation and stability were examined for the reaction of sulfonyl chloride **29** and diethylamine in carbonate buffer, pH 9.2. After 20 h, sulfonamide (**30d**), vinylbimane (**19**), and sulfonate (**28**) TLC) were noted. After 48 h, the sulfonamide had disappeared. At pH 9.9, only traces of sulfonamide and sulfonate were found after 20 h. After incubation of sulfonamide **30d** at pH 9.2 for 20 h, ca. 50% was converted into vinylbimane and sulfonate. Sulfonyl chloride **29** was hydrolyzed in water to give only sulfonate **28** after 18 h.

Bimsyl chlorides **29** and **31**, labeled proteins weakly under the usual conditions.[6] The chloride **31** can be converted to the *N,N*-dimethyl sulfonamide (**32c**) which had a somewhat different chromatographic mobility than **30c**.

Other Addition Reactions. Reaction of Na_2S and divinylbimane **20** afforded the S-bridged compound, μ-(2-thiatrimethylene)-*syn*-(methylene,methyl)-9,10-dioxabimane[38] (**33**) in 40% yield. The structure was established on the basis of ^1H NMR, IR, and UV spectra and confirmed by X-ray crystallography. The two



31

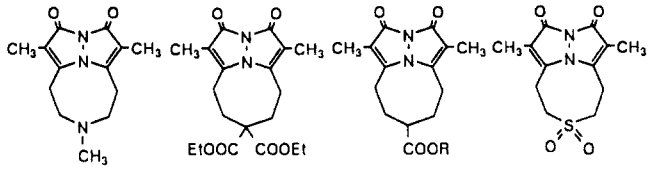


33

sets of methylene proton signals overlapped in the 2.7–3.2 ppm region, as expected from $C_6H_5CONHCH(COOH)CH_2CH_2SCH_3$ (2.66 ppm), $CH_3CH_2CH_2CH_2SCH_3$ (2.50 ppm), $CH_3CH_2SCH_3$ (2.53 ppm), and the α-methylene protons at the β-position of bimanes (2.7 ppm).

The divinylbimane, *syn*-(CH_2=CH,CH_3)B (**20**), reacts with methylamine (in CH_3CN or CH_3OH) to form μ-(2-azatrimethylene)-*syn*-(methylene,methyl)bimane (**34**) and with diethyl malonate anion to yield μ-($CH_2(EtO_2C)_2CCH_2$)-*syn*-(CH_2,CH_3)B (**35**) which can be converted to a monoester (**36a**) or monoacid (**36b**). Bis-adducts [*syn*-(3-carboalkoxyethyl,methyl)bimane] (**37**) are also formed in the latter reaction; **37m** is the major product from dimethyl malonate anion in methanol, possibly due to the greater acidity of dimethyl malonate.

The sulfone **38** is produced through oxidation of the thia-bridged bimane **33** with *m*-perchlorbenzoic acid.



34 35 36 38

R: a, CH_3CH_2; b, H

Crystallographic Results. The molecular structure of **33** is characterized by an approximate C_s symmetry (Figure 1). The dioxabimane framework is bent about the central N–N bond, the dihedral angle α between the mean planes of the two five-membered rings being 158.4°. The bond lengths and bond angles found for **33** are given in Figure 2 (Table II, supplementary material, contains more detail). The vibrational amplitudes of N in a

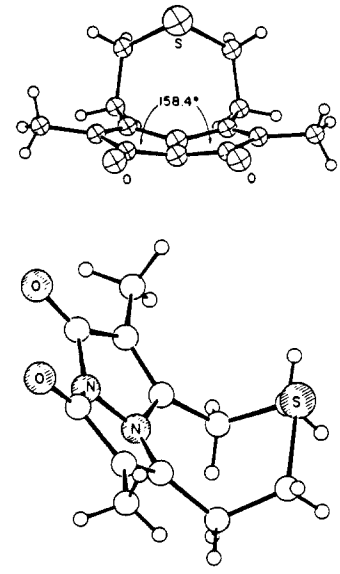


Figure 1. Two views of the structure of μ-(2-thiatrimethylene)-*syn*-(methylene,methyl)bimane (**33**). The dihedral angle is 158.4°. The lower view shows the approach of the sulfur to the bimane ring.

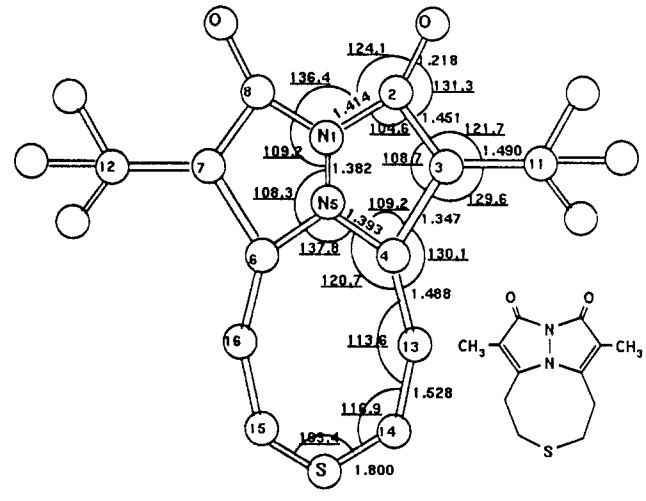


Figure 2. Atom numbering, bond distances (estimated standard deviation 0.002–0.003 Å), and angles (underlined) (estimated standard deviation 0.1–0.2°) for μ-(2-thiatrimethylene)-*syn*-(methylene,methyl)bimane (**33**).

direction perpendicular to the mean plane of the bimane framework are significantly larger than those in directions parallel to this plane. Within the structure of **33**, the respective components of the vibration tensors are 0.060 Å^2 (for N1) and 0.053 Å^2 (for N5) along the perpendicular axis as compared to 0.019 and 0.036 Å^2 (for N1) and 0.020 and 0.030 Å^2 for N5 along the other axes.

The eight-membered ring resembles a cradle with the sulfur converging on the concave side of the dioxabimane to form a van der Waals contact of 3.25 Å with N5. This is associated with average torsions of 38.5° about the CH_2–CH_2 bonds and 66° about the CH_2–S bonds. The crystal packing arrangement of **33** is stabilized by van der Waals forces and shows no unusual features.

Discussion

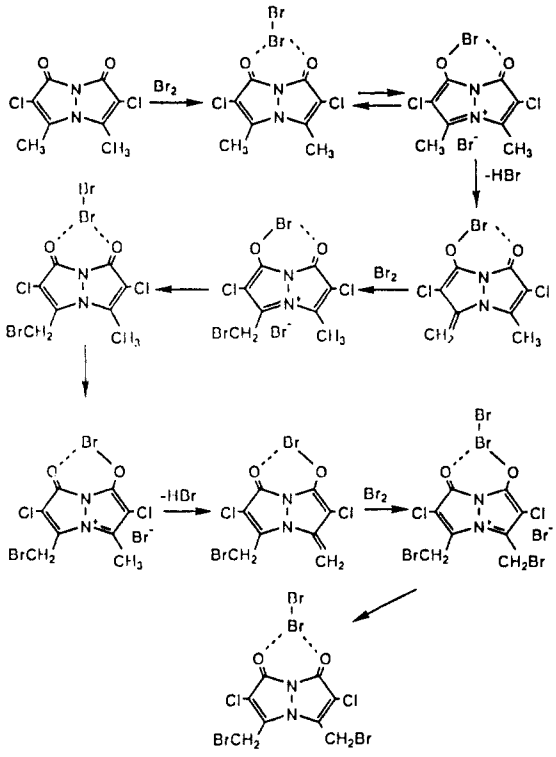
Vinylbimanes are of interest as reactive intermediates, as biological labeling agents, and for studies of the effect of conjugation on the photophysical properties of bimanes.

Synthesis. Practical syntheses of *syn*- and *anti*-(ethyl,-methyl)bimanes (**2** and **3**) and *syn*- and *anti*-(ethyl,chloro)bimanes (**4** and **5**) have been developed, via the "bimane synthesis" from ethyl propionate and ethyl 3-oxopentanoate, respectively. A key step, chlorination of pyrazolinones, is improved in rate and yield by removal of hydrogen chloride with *tert*-butyl alcohol and dry magnesium sulfate, a combination which might serve well in other chlorinations and brominations. The bimanes are converted to

(37) Sulfonamide SO_2 bands (IR) are found at 1159–1178 and 1370–1330 cm^{-1}. Baxter, J. N.; Cymerman-Craig, J.; Willis, J. B. *J. Chem. Soc.* **1955**, 669–679.

(38) The nomenclature (9,10-dioxa-*syn*-bimanes, 4,6-bridged-(or μ-)9,10-dioxa-*syn*-bimanes, and 9,10-dioxa-*anti*-bimanes), which we have developed for efficient discussion of 1,5-diazabicyclo[3.3.0]octadienediones, has been thoroughly discussed in ref 1. The use of μ- as an abbreviation for the bridged compounds (cf. description in ref 5) is done in analogy with the usage of μ- for bridged inorganic compounds.

Scheme I. Mechanism of Bromination of (Alkyl,chloro)bimanes in Pure Bromine[a]

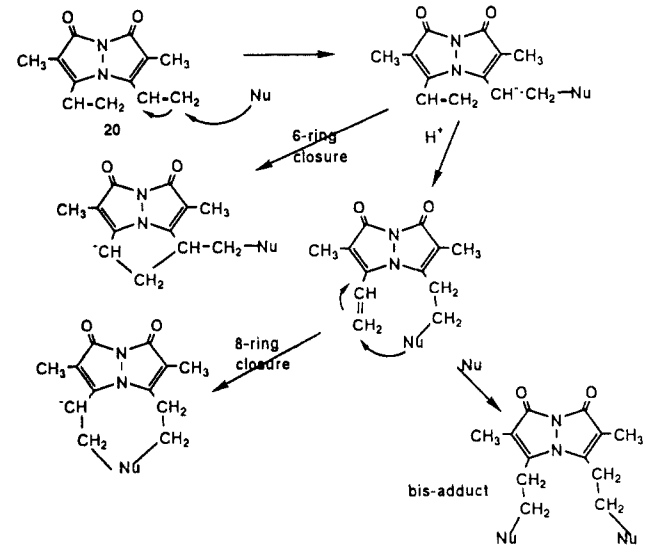


[a] A bimane–bromine complex is formed and is ionized to a bimane–bromonium bromide. The latter loses H^+, yielding an unsaturated compound which reacts with bromine to yield a bromo-substituted bimane–bromonium bromide. The latter forms a bromine complex which in turn reionizes and loses H^+ from the second alkyl group. Reaction with bromine yields a dibromobimane–bromine complex. Each successive bromine substituent makes formation of the bimane–bromonium ion more difficult, implying that formation of the dibromo derivative would be slower than formation of the monobromo derivative, as observed.

vinylbimanes in various ways. The most convenient synthesis of vinylbimanes involves bromination of an alkylbimane followed by elimination. A longer route involves displacement of bromide from a 1-bromoethyl derivative by thiophenolate, oxidation to sulfoxide, and thermal elimination of the vinylbimane. *syn*-(Vinyl,chloro)bimane (**23**) could be obtained only via the sulfoxide. *anti*-(Vinyl,methyl)bimane has been prepared from *anti*-(ethyl,methyl)bimane by the bromination–elimination route and will be reported elsewhere.

Bromination of bimanes substituted with electron-donating groups proceeds rapidly in good yields.[1] The low rate of reaction of bromine in low concentration with bimanes substituted with electron-withdrawing groups prompted us to maximize the concentration of bromine, i.e., to use pure bromine. Complex formation between bromine and *syn*-(methyl,chloro)bimane (**13**) or *syn*-(ethyl,chloro)bimane (**4**) is indicated by the evolution of heat on mixing of the bimane with bromine. Even with excess bromine, bromination is inhibited by the hydrogen bromide produced, probably by displacing bromine from its complex with carbonyl groups. We suppose that the structure of the acetone–bromine[39] and bimane–bromine complexes are similar, since bimanes are (a) weakly basic[1] and (b) have carbon–oxygen bond lengths closer to those of acetone than amides.[40] A plausible mechanism for the bromination reaction is given in Scheme I, which differs from the mechanism of bromination of bimanes like *syn*-(methyl,methyl)bimane in that the oxygens, rather than the 3 (or 7) positions are the sites for attachment of electrophilic bromine and

Scheme II. Reaction of Bifunctional Nucleophiles with *syn*-(Vinyl,methyl)bimane[a]

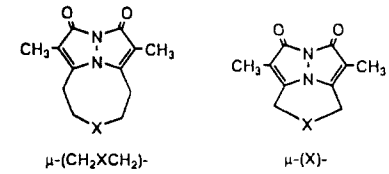


[a] The intermediate anion can react with H^+ to form a monovinyl monoadduct (intermediate A) or can undergo "6-ring closure". The 6-ring formation is obviously slower than protonation. Intermediate A can undergo 8-ring closure of reaction with an external nucleophile. The internal nucleophile has lower reactivity than the external nucleophile (less charge or more restrictive transition state geometry for 8-ring formation) but the high effective concentration of the internal nucleophile leads to the 8-ring derivative as a major product.

that allylic rearrangement of an intermediate bromide is unnecessary.

A more complex route to vinylbimanes involves reaction of the anion of a methylbimane with formaldehyde and elimination of water from the resulting hydroxyethyl or bis(hydroxyethyl)-bimanes. Monovinyl, chlorobimane is formed in low yield by "methylenation". Both the methylenation and the methylation reactions show that the anion of a β-alkylbimane is a convenient and useful synthetic intermediate.

Addition Reactions. Vinylbimanes are fairly reactive toward nucleophiles, yielding potentially useful derivatives. Elimination of the β-substituent can be facile and forms the vinylbimane, decreasing the usefulness of the bimsyl chlorides as amine labeling agents.[42] The instability of the sulfonamides (and sulfonyl chlorides) arises from the acidity of the hydrogen on the carbon next to the bimane ring and the presence of a leaving group on the β-position. One of the important discoveries of the present work is that addition of bifunctional nucleophiles to divinylbimanes readily gives tricyclic derivatives with an 8-membered ring (Formula: μ-(CH_2XCH_2)-). Tricyclic bimanes with a 6-membered ring (Formula: μ-(X)-) can be produced from the same bifunctional nucleophiles and the dibromobimane, *syn*-($BrCH_2$,CH_3)B.[5] The reason that 8-membered rings are so



μ-(CH_2XCH_2)- μ-(X)-

readily produced from bifunctional nucleophiles is due to the success of protonation in comparison with 6-ring closure after initial addition. The mono-adduct can either undergo 8-ring closure by intramolecular addition of the nucleophile or can react with a second nucleophile to form a bis-adduct (Scheme II). A completely different synthesis of tricyclic bimanes with carbon

(39) Hassel, O.; Strømme, K. O. *Nature* **1958**, *182*, 1155; *Acta Chem. Scand.* **1959**, *13*, 275.
(40) Goldberg, I.; Bernstein, J.; Kosower, E. M.; Goldstein, E.; Pazhenchevsky, B. *J. Heterocycl. Chem.* **1982**, *20*, 903–912.
(41) Goldberg, I.; Bernstein, J.; Kosower, E. M. *Acta Crystallogr.* **1982**, *B38*, 1990–2000.
(42) Takadate, A.; Yagashiro, I.; Irikura, M.; Fujino, H.; Goya, S. *Chem. Pharm. Bull.* **1989**, *37*, 373–376.

Table I. Absorption and Emission Maxima of Vinylbimanes in Dioxane

bimane	absorption: λ_{max}, nm (ϵ)	emission: λ_{max}, nm
syn-(CH_2=CH,CH_3)(CH_3,CH_3)B (**18**)	373 (5300)	464
syn-(CH_2=CH,CH_3)(CH_3CH_2,CH_3)B (**19**)	374 (5200)	464
syn-(CH_2=CH,CH_3)B (**20**)	379 (5100)	468
syn-(CH_2=CH,Cl)(CH_3,Cl)B (**21**)	379 (4800)	470
syn-(CH_2=CH,Cl)B (**23**)	379 (4800)	470

bridges is reported elsewhere.[43]

Crystal Structure of Thia-Bridged Bimane 33. The observed conformation of the bimane reflects less strain in the 2-thiatrimethylene-bridged compound than that found in compounds with smaller bridges such as μ-(S)- and μ-(SO_2)-*syn*-(methylene,-methyl)-9,10-dioxabimanes, which have dihedral angles around N–N of about 140°.[40,41] In this respect, the present structure (α = 158.4°) resembles that of the unbridged 4,6-bis(carboalkoxy)-9,10-dioxabimane,[2] in which folding of the molecular skeleton (α = 161.2°) is the apparent result of a peripheral dipolar interaction between the two ester groups. The hybridization in bonds involving partly pyramidal nitrogens and the details of molecular geometry, which reflect the limited extent of π-electron delocalization, are similar in the two compounds. The structure of **33** is also similar to that of μ-($(CH_2)_3$)-*syn*-(CH_2,CH_3)B, in which a methylene group is present in place of sulfur.[43] It is worth emphasizing that C=O bond distances in all bimanes thus far examined are 1.21–1.22 Å, as found for unconjugated carbonyl groups.

Photophysical Properties of Vinylbimanes. The vinylbimanes are bright yellow compounds with absorption maxima in solution at wavelengths (~374 nm), somewhat longer than that of *syn*-(CH_3,CH_3)B or *syn*-(CH_3CH_2,CH_3)B (360 nm, ΔE_A 2.98 kcal/mol). The fluorescence maxima are at considerably longer wavelengths (470 nm versus 423 nm, ΔE_F 6.76 kcal/mol), indicating that the vinyl group interaction with the bimane rings is stronger in the excited state than in the ground state. We infer that the vinyl group is not coplanar with the bimane ring in the ground state; the increased interaction in the excited state might be due to a decrease in the angle of the vinyl group with respect to one bimane ring. For *syn*- and *anti*-(phenyl,chloro)bimanes, crystal structures show that the phenyl groups are at an angle 65° to the plane of the bimane ring. Absorption and emission maxima for some vinylbimanes are listed in Table I.

Experimental Section

General. Instruments used are as follows: ^{1}H NMR spectra (chemical shifts are δ values referred to $(CH_3)_4Si$ as 0.00), Bruker WH-90 and AM-360 spectrometers; ultraviolet and visible spectra, Cary Model 17 spectrophotometer; fluorescence spectra, Hitachi Perkin-Elmer MPF-4 fluorescence spectrometer; mass spectra, DuPont 21-491B mass spectrometer; IR spectra, Perkin-Elmer Model 177 spectrophotometer; HPLC, Waters Associates Model 6.

Solvents and Materials. Dichloromethane (Anal.), acetonitrile, and 2-propanol (Merck) were used without further purification. Dimethylformamide (DMF) was dried by refluxing over calcium hydride. Tetrahydrofuran (THF) was distilled from the sodium ketyl of benzophenone. Absorption and emission spectra were measured in Spectrograde acetonitrile or dioxane.

Crystal Structure Analysis of the μ-(Thiatrimethylene)-*syn*-(methylene,methyl)-9,10-dioxabimane (33). Diffraction data were measured at room temperature on an Enraf-Nonius CAD-4 diffractometer equipped with a graphite monochromator, employing Mo Kα radiation (λ_{mean} = 0.71069 Å). Crystal data: $C_{12}H_{14}N_2O_2S$, M_r = 250.3; orthorhombic; a = 7.853 (2), b = 15.184 (3), c = 20.143 (3) Å; V = 2401.8 Å^3; Z = 8; d_c = 1.384 g cm^{-3}; $F(000)$ = 1056; space group *Pbca*.

The intensities of all reflections with $1 < \theta < 27°$ were recorded by using an $\omega - 2\theta$ scan technique with a varying scan angle of 0.9 + 0.3 tan θ. The scan rate varied according to the detected intensity between 1.0 and 4° min^{-1}. Possible deterioration of the crystal under examination was tested by frequent measurement of the intensities of standard reflections and found to be negligible. The data were not corrected for absorption and extinction effects. Final refinement of the structural model was based only on those observations that satisfied the condition $F_o^2 > 3\sigma(F_o^2)$.

The structure was solved by direct methods using the MULTAN system of computer programs. Refinement was carried out by full-matrix least-squares methods including positional parameters of all atoms, anisotropic thermal parameters for the non-hydrogen atoms, and isotropic thermal parameters for hydrogens. All hydrogen atom positions were initially obtained from difference maps. The weighted least-squares refinement of the structure converged smoothly at R = 0.041 for 1615 observations above threshold (excluding the extremely strong (020) reflection which appeared to suffer from secondary extinction). The final difference map did not show any unusual features. The positional and thermal atomic parameters are of interest because of the flexibility of the bimane nucleus. These are given in Table III (supplementary material).

9,10-Dioxa-*syn*-(ethyl,methyl)bimane (2). Ethyl propionate was treated with NaH/toluene/95–105 °C, the mixture neutralized with H_2SO_4/Et_2O, the solvent removed, and the residue distilled at 95–96 (20 mm) to yield the β-keto ester, ethyl propionylpropionate. The β-keto ester and hydrazine were reacted in hot ethanol to form in 50% yield, 3-ethyl-4-methyl-5-pyrazolinone, mp 230–240 °C, and the latter was treated with Cl_2/CH_2Cl_2 to produce a 60% yield of 3-ethyl-4-chloro-4-methyl-5-pyrazolinone, mp 92 °C (Et_2O/petroleum ether): ^{1}H NMR ($CDCl_3$) 1.30 (t, 3 H), 1.62 (s, 3 H), 2.65 (q, 2 H) ppm. The chloropyrazolinone (70 g, 0.44 mol) was mixed with $K_2CO_3 \cdot 1.5H_2O$ (210 g, 1.27 mol) in CH_2Cl_2, the mixture mechanically stirred for 16 h, the suspension filtered, and the solvent evaporated. After fast chromatography through silica H (230–400 mesh, Merck 9385) with CH_2Cl_2, chromatography on silica gel (70–230 mesh) yielded first, *anti*-(CH_3CH_2,CH_3)B (**3**), 4.0 g (8.3%), followed by the major product, *syn*-(CH_3CH_2,CH_3)B (**2**), 18.9 g (39.4%), which was crystallized from CH_3CN.

***anti*-(CH_3CH_2,CH_3)B (3).** White crystals (CH_3CN), mp 109 °C. IR (KBr): 3000, 2940, 1675, 1415, 1375, 1250, 1030, 890, 730 cm^{-1}. ^{1}H NMR ($CDCl_3$): 1.30 (t, 3 H, J = 7 Hz), 1.80 (s, 3 H), 2.75 (q, 2 H, J = 7 Hz) ppm. UV (CH_3CN): λ_{max} 322 nm (ϵ 14000). Mass spectrum: m/e 220 (M^+).

***syn*-(CH_3CH_2,CH_3)B (2).** Pale yellow crystals (CH_3CN), mp 165 °C. IR (KBr): 2940, 2880, 1730, 1670, 1595, 1220, 1060, 965, 740 cm^{-1}. ^{1}H NMR ($CDCl_3$): 1.30 (t, 3 H, J = 7 Hz), 1.85 (s, 3 H), 2.70 (q, 2 H, J = 7 Hz) ppm. UV (CH_3CN): λ_{max} 371 nm (ϵ 6300), 231 (17000). Fluorescence maxima (dioxane): λ_{max} 423 nm; (crystals) λ_{max} 460, 480 sh nm. Excitation fluorescence maxima (crystals): λ_{max} 360 sh, 400, 420 nm. Mass spectrum: m/e 220 (M^+).

9,10-Dioxa-*syn*-(ethyl,methyl)(methyl,methyl)bimane (7). Sodium hydride (oil-free, 0.184 g, 35 mmol) was added to *syn*-(methyl,methyl)bimane (**6**) (1.34 g, 7 mmol) and methyl iodide (4.97 g, 35 mmol) in DMF (100 mL) cooled to 0 °C. (Similar results were obtained with 0.302 g NaH, 1.8 equiv.) After 30 min, the solution became dark yellow. After 1 h at 0 °C, the stirred mixture was allowed to warm to room temperature overnight, acidified with 10% HCl (pH 6–7), the solvent removed under vacuum, and the residue chromatographed on silica gel to yield (eluant/chloroform) *syn*-(CH_3CH_2,CH_3)B (**2**), 0.46 g (2.1 mmol) (30%), (chloroform/EtOAc (1:1)) *syn*-(CH_3CH_2,CH_3)-(CH_3,CH_3)B (**7**), 0.43 g (2.1 mmol) (30%), and (EtOAc) *syn*-(CH_3,CH_3)B (**6**), 0.40 g (2.1 mmol) (30%).

***syn*-(CH_3CH_2,CH_3)(CH_3,CH_3)B (7).** Light yellow crystals (ethyl acetate), mp 156 °C. IR (KBr): 2895, 1745, 1660, 1610, 1390, 1020 cm^{-1}. ^{1}H NMR ($CDCl_3$) 1.30 (t, 3 H, J = 7 Hz), 1.80 (s, 6 H), 2.32 (s, 3 H), 3.70 (q, 2 H, J = 7 Hz) ppm. UV (dioxane): λ_{max} 360 nm (ϵ 6400), 258 sh (5200), 238 (14700). Mass spectrum: m/e 206 (M^+).

9,10-Dioxa-*anti*-(ethyl,chloro)bimane (5). Ethyl 3-oxopentanoate (Lonza) and a small excess of hydrazine were heated in methanol for 1 h to form 3-ethyl-2-pyrazolin-5-one (80% yield). A mixture of the 3-ethyl-2-pyrazolin-5-one (28 g, 0.25 mol), 1,2-dichloroethane (500 mL), 2-methyl-2-propanol (40 mL), and anhydrous magnesium sulfate (64 g) was stirred and chlorine introduced at a rate such that the mixture refluxed gently. After all the solid pyrazolinone had dissolved and the solution had a deep yellow color, excess chlorine was removed with an air stream, the solution filtered, the solvent removed, and the residue dissolved in hot 1,2-dichloroethane. On cooling, the 3-ethyl-4,4-dichloro-2-pyrazolin-5-one (**1b**) crystallized (88–95% yield). *N,N*-Diisopropylethylamine (5.4 mL, 4 g, 31 mmol) in CH_2Cl_2 (30 mL) was added dropwise over 1 h to 3-ethyl-4,4-dichloro-2-pyrazolin-5-one (5.43 g, 30 mmol) in CH_2Cl_2 (60 mL) cooled in ice. During addition, the initially colorless mixture became pale yellow, then deep yellow, and, finally, deep red. The ice was then removed and the mixture stirred until the chloropyrazolinone had disappeared (TLC, ca. 4 h). The solvent was evaporated and the residue purified by flash chromatography on silica gel

(43) Marciano, D.; Baud'huin, M.; Zinger, B.; Goldberg, I.; Kosower, E. M. Bimanes 25. *J. Am. Chem. Soc.*, third of three papers in this issue.

(elution with CH_2Cl_2) to yield *anti*-(CH_3CH_2,Cl)B (**5**), 1.36 g (35% yield), and *syn*-(CH_3CH_2,Cl)B (**4**), 0.666 g (17% yield).

3-Ethyl-2-pyrazolin-5-one. Slightly pink crystals. IR (KBr): 3000–2500, 1610 (C=O), 1325, 1245, 1195, 1160, 1065, 1025, 995, 945, 800, 760, 745 cm^{-1}. ^1H NMR (DMSO-d_6): 1.120 (t, 3 H, CH_3CH_2, J = 7.5 Hz), 2.455 (q, 2 H, CH_3CH_2, J = 7.5 Hz), 5.226 (s, 2 H) ppm.

3-Ethyl-4,4-dichloro-2-pyrazolin-5-one (1b). White crystals (1,2-dichloroethane), mp 92–94 °C. IR ($CHCl_3$): 3250, 1745, 1225, 940, 860, 785 cm^{-1}. ^1H NMR (CH_3CN-d_3): 1.233 (t, 3 H, CH_3CH_2, J = 7.35 Hz), 2.623 (q, 2 H, CH_3CH_2, J = 7.35 Hz) ppm.

***anti*-(CH_3CH_2,Cl)B (5).** Pale yellow crystals (CH_3CN), mp 107–108 °C. IR (KBr): 2940, 1695, 1590, 1400, 1355, 1255, 1175, 1060 cm^{-1}. ^1H NMR ($CDCl_3$): 1.36 (t, 3 H, CH_3CH_2, J = 7.5 Hz), 2.90 (q, 2 H, CH_3CH_2, J = 7.5 Hz) ppm. UV (dioxane): λ_{max} 325 nm (ϵ 14 900). Mass spectrum: m/e 264, 262, 260 (M^+) (mass distribution fits 2Cl with m/e 260 = 100%).

9,10-Dioxa-*syn*-(ethyl,chloro)bimane (4). 3-Ethyl-4,4-dichloro-2-pyrazolin-5-one (45.26 g, 0.25 mol) in CH_2Cl_2 (400 mL) was added over 1 h to a vigorously mechanically stirred mixture of $K_2CO_3 \cdot 1.5H_2O$ (51.6 g, 0.3125 mol, 1.25 equiv) and CH_2Cl_2 (100 mL) cooled in an ice bath. The suspension became deep yellow to orange-brown. After an additional hour of stirring, the ice bath was removed and both stirring and ultrasonic agitation used for another hour without cooling. Some starting chloropyrazolinone remained (TLC). More $K_2CO_3 \cdot 1.5H_2O$ (5.2 g, 31.5 mmol) was added and the stirring and agitation treatment repeated. Celite (25 g) was added and the solution was filtered through a thick Celite layer. The Celite was washed well with CH_2Cl_2 and then with acetonitrile. The orange-red residue (ca. 25 g) obtained after evaporation of solvent was dissolved in boiling acetonitrile (400 mL) and filtered hot. After cooling, yellowish crystals of *syn*-(CH_3CH_2,Cl)B, 6 g (mp 211–212 °C) (18.3%), were deposited. The filtrate was concentrated to ca. 200 mL, and another 4.45 g (mp 210–111 °C) (13.5%) crystallized. The combined filtrates were evaporated and the residue chromatographed on silica gel (275 g) (eluants: CH_2Cl_2, then CH_2Cl_2/EtOAc) (9:1)), yielding *anti*-(CH_3CH_2,Cl)B, 4.75 g (14.5% yield) followed by somewhat less pure *syn*-(CH_3CH_2,Cl)B 5.61 g, mp 187–190 °C (17.1%).

***syn*-(CH_3CH_2,Cl)B (4).** Yellow crystals (CH_3CN), mp 211–212 °C. IR (KBr): 2960, 2940, 2880, 1760, 1690, 1590, 1555, 1465, 1435, 1370, 1270, 1240, 1165, 1085, 1055, 885, 725 cm^{-1}. ^1H NMR ($CDCl_3$): 1.375 (t, 3 H, CH_3CH_2, J = 7 Hz), 2.81 (q, 2 H, CH_3CH_2, J = 7 Hz) ppm. UV (dioxane): λ_{max} 370 nm (ϵ 7200), 232 (13 700); (CH_3CN) 377 nm (6900), 231 (11 900). Fluorescence maxima (CH_3CN): λ_{max} 442 nm, 463 sh (ϕ_F 0.73). Mass spectrum: m/e 264, 262, 260 (M^+) (mass distribution fits 2Cl with m/e 260 = 59.4).

9,10-Dioxa-*syn*-(bromomethyl,chloro)(methyl,chloro)bimane (14) and 9,10-Dioxa-*syn*-(bromomethyl,chloro)bimane (15). Bromine (15 mL, 46.78 g, 293 mmol) was added all at once to *syn*-(CH_3Cl)B (**13**) (7 g, 30 mmol) at room temperature (exothermic reaction in a 500-mL flask protected from light. After 2 h, unreacted bromine was removed under vacuum (ca. 10 mmHg), CH_2Cl_2 (75 mL) was added and then evaporated, a treatment repeated twice to ensure complete removal of HBr and Br_2. Bromine (15 mL) was added to the yellow-orange residue all at once at room temperature (exothermic reaction) and the mixture stirred for 2 h. Removal of HBr and Br_2 with CH_2Cl_2 was repeated as before, yielding an orange residue containing *syn*-($BrCH_2$,Cl)(CH_3,Cl)B (55%) and *syn*-($BrCH_2$,Cl)B (40%) along with a small quantity of starting material *syn*-(CH_3Cl)B (5%). Separation by flash chromatography on a silica column protected from light (eluant, CH_2Cl_2) gave pure *syn*-($BrCH_2$,Cl)B (**15**), 5.83 g (50% yield), and pure *syn*-($BrCH_2Cl$)-(CH_3,Cl)B (**14**), 2.37 g (25% yield), and a mixture of **14** and **13**, 1.6 g.

***syn*-($BrCH_2$,Cl)(CH_3,Cl)B (14).** Yellow crystals from EtOAc, mp 190–191 °C. IR (KBr) 3040, 2980, 1755, 1680, 1595, 1565, 1415, 1290, 1225, 1170, 725 cm^{-1}. ^1H NMR ($CDCl_3$): 2.63 (s, 3 H), 4.43 (s, 2 H) ppm. UV (dioxane): λ_{max} 381 nm (ϵ 6850), 247 (11 800). Mass spectrum: m/e 316, 314, 312, 310 (M^+) (mass distribution fits $BrCl_2$ with m/e 312 = 100), 235, 233, 231 (M^+ – Br) (mass distribution fits 2Cl with m/e 231 = 46.9).

***syn*-($BrCH_2$,Cl)B (15).** Yellow crystals, mp 190–191 °C. IR (KBr) 3060, 2990, 1760, 1695, 1595, 1570, 1445, 1425, 1385, 1305, 1225, 1180, 1135, 1120, 915, 880, 740, 680, 645 cm^{-1}. ^1H NMR ($CDCl_3$) 4.61 (s) ppm. UV (dioxane): λ_{max} 392 nm (ϵ 7300), 259 (12 600). Mass spectrum: m/e 396, 394, 392, 390, 388 (M^+) (mass distribution fits Br_2Cl_2 with m/e 390 = 8.5), 315, 313, 311, 309 (M^+ – Br) (mass distribution fits $BrCl_2$ with m/e 311 = 14.7), 234, 232, 230 (M^+ – 2Br) (mass distribution fits 2Cl with m/e 230 = 100).

9,10-Dioxa-*syn*-(1-bromoethyl,chloro)(ethyl,chloro)bimane (16) and 9,10-Dioxa-*syn*-(1-bromoethyl,chloro)bimane (17). Bromine (10 mL) was reacted with *syn*-(CH_3CH_2,Cl)B (**4**) (5.22 g, 20 mmol) as described for **13**. The products were separated by flash chromatography on silica gel protected from light (eluant, CH_2Cl_2), giving pure *syn*-($BrCH(CH_3)$,Cl)B (**17**), 6.95 g (83%) (two diastereomers [meso/racemic(*dl*) can be observed by ^1H NMR and by TLC on silica (petroleum ether/EtOAc(3:1)), R_f = 0.38 and 0.47)], pure *syn*-($BrCH(CH_3)$,Cl)-(CH_3CH_2,Cl)B (**16**), 0.274 g (4% yield), and 0.367 g of a **17** and **16** mixture containing only traces of **4**. In another experiment, *syn*-(CH_3CH_2,Cl)B (**4**) (5.22 g, 20 mmol) was reacted with bromine (10 mL) only once for 2 h at room temperature. After workup and purification as noted above, **17**, 3.871 g (46%), **16**, 2.324 g (34%), and **4**, 0.902 g (17%) were obtained.

***syn*-($BrCH(CH_3)$,Cl)(CH_3CH_2,Cl)B (16).** Yellow crystals, mp 178–180 °C. IR (KBr): 3060, 2990, 1770, 1685, 1590, 1420, 1370, 1285, 1250, 1240, 1190, 1175, 1140, 1100, 1075, 1025, 985, 920, 735, 670, 650, 625 cm^{-1}. ^1H NMR ($CDCl_3$): 1.43 (t, 3 H, CH_3CH_2, J = 7.6 Hz), 2.24 (d, 3 H, CH_3CH, J = 7.2 Hz), 2.97 (q, 2 H, CH_3CH_2, J = 7.6 Hz), 5.06 (q, 1 H, CH_3CH, J = 7.2 Hz) ppm. UV (dioxane): λ_{max} 380 nm (ϵ 6700), 248 (11 800). Mass spectrum: m/e 344, 342, 340, 338 (M^+) (mass distribution fits $BrCl_2$ with m/e 340 = 39.5), 263, 261, 259 (M^+ – Br) (mass distribution fits 2Cl with m/e 259 = 25.9).

***syn*-($BrCH(CH_3)$,Cl)B (17).** Yellow crystals, mp 218–219 °C. IR (KBr): 2990, 1760, 1695, 1580, 1560, 1450, 1425, 1385, 1370, 1290, 1250, 1185, 1080, 1070, 1050, 1010, 980, 945, 930, 800, 740, 710, 685, 660 cm^{-1}. ^1H NMR ($CDCl_3$) (2 diastereoisomers) 2.21 (d, 3 H, J = 7 Hz), 5.31 (q, 1 H, J = 7 Hz), and 2.29 (d, 3 H, J = 7 Hz), 5.56 (q, 1 H, J = 7 Hz) ppm. UV (dioxane): λ_{max} 385 nm (ϵ 6900), 257 (12 150). Mass spectrum: m/e 424 (M^+), 422, 420, 418, 416 (mass distribution fits Br_2Cl_2), 343 (M^+ – Br), 341, 339, 337 (mass distribution fits $BrCl_2$), 262 (M^+ – 2Br), 260, 258 (mass distribution fits 2Cl).

9,10-Dioxa-*syn*-(1-acetoxyethyl,chloro)bimane (9a). A mixture of *syn*-(1-bromoethyl,chloro)bimane (**9**) (8.9 mg, 0.02 mmol) and potassium acetate (8 mg, 0.089 mmol) in acetonitrile (3 mL) is refluxed for 15 h. After cooling, the solvent is evaporated and the residue separated by flash chromatography on silica gel 60 (eluant, ethyl acetate), affording 2 diastereomers (1:8) of *syn*-($CH_3COOCH(CH_3)$,Cl)B (**9a**), 1 mg (0.003 mmol) (13% yield). No divinylbimane was observed among the products.

9,10-Dioxa-*syn*-(1-acetoxyethyl,chloro)bimane (9a) (Two Diastereomers). Yellow solid. ^1H NMR ($CDCl_3$): (main isomer) 1.784 (d, 3 H, 7 Hz), 2.169 (s, 3 H), 6.112 (q, 1 H, J = 7 Hz) ppm; (second isomer) 1.812 (d, 3 H, 7 Hz), 2.141 (s, 3 H), 5.905 (q, 1 H, J = 7 Hz) ppm. UV (dioxane): λ_{max} 373 nm (ϵ 2600), 260 sh (2700), 234 (5300). Fluorescence maxima (dioxane): λ_{max} 440 nm, 466 nm (ϕ_F 0.9).

A mixture of *syn*-(1-bromoethyl,chloro)bimane (**9**) (100 mg, 0.26 mmol) and sodium trifluoroacetate (155 mg, 1.14 mmol) in 5 mL of acetonitrile is refluxed for 15 h. After cooling, the solvent is evaporated and the residue chromatographed by flash chromatography on silica gel 60 (eluants, CH_2Cl_2/ethyl acetate, 9:1 to 1:1), affording *syn*-($HOCH(CH_3)$,Cl)B (**9b**), 17 mg (0.06 mmol) 22% yield), together with *syn*-($HOCH(CH_3)$,Cl)($BrCH(CH_3)$,Cl)B (**9c**), 4 mg, 0.01 mmol (4% yield), and *μ*-(*O*)-*syn*-($CH(CH_3)$,Cl)B (**9d**), 2 mg, 0.008 mmol (3% yield).

9,10-Dioxa-*syn*-(1-hydroxyethyl,chloro)bimane (9b) (One Isomer). Yellow solid, mp 178 °C. IR (KBr): 3340 br, 2880, 1740, 1720 sh, 1645, 1550, 1430, 1400, 1260, 1160, 1080, 700 cm^{-1}. ^1H NMR ($CDCl_3$): 1.676 (d, 3 H, 7 Hz), 1.721 (d, 3 H, 7 Hz), 5.448 (m, 1 H), 3.493 (m, 1 H) ppm. UV (CH_3CN): λ_{max} 390 nm (ϵ 3000), 255 sh (3200), 239 (4400). Fluorescence maxima (CH_3CN): λ_{max} 442 nm, 460 nm (ϕ_F 0.9). Mass spectrum: m/e 296 (8), 294 (64), 292 (100) (M^+), 277 (15), 276 (18), 274 (24).

9,10-Dioxa-*syn*-(1-hydroxyethyl,chloro)(1-bromoethyl,chloro)bimane (9c) (One Isomer). Yellow solid. ^1H NMR ($CDCl_3$): 1.620 (d, 3 H, 7 Hz), 1.691 (d, 3 H, 7 Hz), 4.704 (q, 1 H, J = 7 Hz), 5.051 (q, 1 H, J = 7 Hz) ppm. Mass spectrum: m/e 359 (18), 357 (17) (M^+), 277 (77), 275 (100), 261 (9), 194 (11).

μ-(Oxo)-*syn*-(methylmethylene,chloro)-9,10-dioxabimane (9d) (Two Diastereomers). Yellow solid. IR (KBr): 2860, 1740, 1720 sh, 1340, 1230, 1150, 1000, 800 cm^{-1}. ^1H NMR ($CDCl_3$): 1.620 (d, 3 H, J = 4 Hz), 1.650 (d, 3 H, J = 4 Hz), 5.052 (q, 1 H, J = 4 Hz), 5.146 (q, 1 H, J = 4 Hz) ppm. UV (CH_3CN): λ_{max} 350 nm (ϵ 3000), 236 (8000). Fluorescence maxima (CH_3CN): λ_{max} 440 nm, 460 sh (ϕ_F 0.4). Mass spectrum: m/e 278 (5), 276 (65), 274 (94) (M^+), 257 (17), 193 (21), 178 (8), 170 (11), 141 (12), 139 (11).

9,10-Dioxa-*syn*-(1-(phenylthio)ethyl,chloro)(ethyl,chloro)bimane (17a) and 9,10-Dioxa-*syn*-(1-(phenylthio)ethyl,chloro)bimane (17c). A round-bottomed flask equipped with an oil bubbler was flame dried while being flushed with nitrogen (an atmosphere maintained throughout the reaction). A solution of *syn*-($BrCH(CH_3)$,Cl)(CH_3CH_2,Cl)B (**16**) (204 mg, 0.6 mmol) in dry THF (30 mL) was placed in the flask. Freshly prepared sodium thiophenolate (C_6H_5SNa) (99 mg, 0.75 mmol) was added all at once at room temperature. After 30 min of stirring (the reaction mixture became slightly orange), the solvent was evaporated and the residue flash chromatographed on silica gel (eluant, petroleum ether/EtOAc (7:3)) to yield *syn*-($PhSCH(CH_3)$,Cl)(CH_3CH_2,Cl)B (**17a**),

155 mg (70%). By use of the same procedure, *syn*-(BrCH(CH_3),Cl)B (**17**) (838 mg, 2 mmol) in THF (100 mL) was reacted with PhSNa (740 mg, 5.6 mmol) (instantaneous red-orange color and then quickly brown) to yield, after flash chromatography on silica gel (eluant, petroleum ether/EtOAc (3:1)), *syn*-(PhSCH(CH_3),Cl)B (**17c**), 717 mg (75% yield).

***syn*-(PhSCH(CH_3),Cl)(CH_3CH_2,Cl)B (17a).** ^{1}H NMR ($CDCl_3$): 1.362 (t, 3 H, CH_3CH_2, J = 7.6 Hz), 1.962 (d, 3 H, CH_3CH, J = 7.3 Hz), 3.052 (q, 2 H, CH_3CH_2, J = 7.6 Hz), 4.433 (q, 1 H, CH_3CH, J = 7.3 Hz), 7.484–7.857 (m, 5 H_{arom}) ppm.

***syn*-(PhSCH(CH_3),Cl)B (17c).** Yellow crystals from CH_3CN, mp 135–136 °C. IR (KBr): 3060, 2980, 2940, 1765, 1700, 1580, 1475, 1440, 1410, 1380, 1310, 1275, 1190, 1175, 1160, 1130, 1090, 1070, 1025, 1010, 930, 770, 755, 735, 710, 695, 660 cm^{-1}. ^{1}H NMR ($CDCl_3$): (2 diastereomers) 1.71 (d, 3 H, CH_3CH, J = 7 Hz), 4.37 (q, 1 H, CH_3CH, J = 7 Hz), 7.4 (m, 5 H) and 1.74 (d, 3 H, CH_3CH, J = 7 Hz), 4.69 (q, 1 H, CH_3CH, J = 7 Hz), 7.4 (m, 5 H) ppm. UV (dioxane): λ_{max} 382 nm (ϵ 6600), 248 (17 400). Fluorescence maxima (dioxane): λ_{max} 455 nm, 466 (ϕ_F 0.11). Mass spectrum: m/e 480 (M^+), 478, 476 (mass distribution fits 2Cl).

9,10-Dioxa-*syn*-(1-(phenylsulfoxy)ethyl,chloro)(ethyl,chloro)bimane (17b) and 9,10-Dioxa-*syn*-(1-(phenylsulfoxy)ethyl,chloro)bimane (17d). 3-Chloroperbenzoic acid (192 mg, 1 mmol) in CH_2Cl_2 (10 mL) was added dropwise over 30 min to a solution of *syn*-(PhSCH(CH_3),Cl)-(CH_3CH_2,Cl)B (**17a**) (369.3 mg, 1 mmol) in CH_2Cl_2 (10 mL) cooled in ice. After 15 min of additional stirring at 0 °C, the solvent was evaporated and the residue flash chromatographed on silica gel (eluant, EtOAc/CH_2Cl_2 (1:9)) to give an almost quantitative yield of *syn*-(PhSOCH(CH_3),Cl) (CH_3CH_2,Cl)B (**17b**).

A solution of 3-chloroperbenzoic acid (575 mg, 3 mmol) in CH_2Cl_2 (10 mL) was added dropwise over 15 min to a solution of *syn*-(PhSCH-(CH_3),Cl)B (**17c**) (716 mg, 1.5 mmol) in CCl_4 (15 mL) cooled in dry ice/CCl_4. The mixture was stirred at −20 °C for 30 min, then allowed to warm to room temperature over ca. 45 min and the solvent evaporated to yield crude 9,10-dioxo-*syn*-(1-(phenylsulfoxy)ethyl,chloro)bimane (**17d**) which was used without purification in the next reaction.

***syn*-(PhSOCH(CH_3),Cl)(CH_3CH_2,Cl)B (17b).** Yellow solid. ^{1}H NMR ($CDCl_3$): (2 diastereoisomers) 1.095 and 1.401 (t, 3 H, CH_3CH_2, J = 7.6 Hz), 1.628 and 2.021 (d, 3 H, CH_3CH, J = 7.34 Hz), 2.471–2.691 and 2.862–3.115 (m, 2 H, CH_3CH_2), 3.956 and 4.080 (q, 1 H, CH_3CH, J = 7.34 Hz), 7.470–7.796 (m, 5 H, H_{arom}) ppm.

9,10-Dioxa-*syn*-(1-(phenylthio)ethyl,methyl)(ethyl,methyl)bimane (17e). *syn*-(BrCH(CH_3),CH_3)(CH_3CH_2,CH_3)B (**8**) (598 mg, 2 mmol) in THF (100 mL) was reacted with PhSNa (330.4 mg, 2.5 mmol) in the manner described for **17a** and **17c**. After 20 min at room temperature, the starting material had disappeared (TLC), the mixture was filtered through $MgSO_4$, the solvent evaporated, and the residue flash chromatographed on silica gel (eluant, EtOAc/CH_2Cl_2 (1:9)) to yield *syn*-(PhSCH(CH_3),CH_3)(CH_3CH_2,CH_3)B (**17f**), 593.4 mg (90.3% yield) along with *syn*-(CH_3CH_2,CH_3)B (**2**), 38.6 mg (8.8% yield).

***syn*-(PhSCH(CH_3),CH_3)(CH_3CH_2,CH_3)B (17e).** Yellow solid, mp 114–116 °C. IR (KBr): 1740, 1665, 1585, 1410, 1230, 1155, 970, 690 cm^{-1}. ^{1}H NMR ($CDCl_3$): 1.193 (t, 3 H, CH_3CH_2, J = 7.6 Hz), 1.724 (d, 3 H, CH_3CH, J = 7.27 Hz), 1.795 (s, 3 H, CH_3), 1.850 (s, 3 H, CH_3), 2.589 (q, 2 H, CH_3CH_2, J = 7.6 Hz), 4.253 (q, 1 H, CH_3CH, J = 7.27 Hz), 7.320–7.374 (m, 3 H, H_{arom}), 7.407–7.433 (m, 2 H, H_{arom}) ppm. ^{13}C NMR ($CDCl_3$): 6.69, 8.00 (CH_3), 12.81 (CH_3CH_2), 19.19 (CH_3CH), 19.51 (CH_3CH_2), 39.88 (CH_3CH), 112.85, 114.32 (CO—*C*=), 129.49, 134.75, 134.97 (C_{arom}), 150.45, 152.22 (=C—N), 160.70, 160.86 (C=O) ppm. UV (dioxane) λ_{max} 366 nm (ϵ 5700); (CH_3CN) 373 (5200), 234 (14 100). Fluorescence maxima (dioxane): λ_{max} 428 nm, 460, 494 sh (ϕ_F 0.14); (CH_3CN) 439 nm, 464 (ϕ_F 0.16). Mass spectrum: m/e 328 (M^+).

9,10-Dioxa-*syn*-(1-(phenylsulfoxy)ethyl,methyl)(ethyl,methyl)bimane (17f). 3-Chloroperbenzoic acid (230 mg, 1.2 mmol) in CH_2Cl_2 (12 mL) was added dropwise over 30 min to a solution of *syn*-(PhSCH(CH_3),-CH_3)(CH_3CH_2,CH_3)B (**17e**) (394 mg, 1.2 mmol) in CH_2Cl_2 (12 mL) cooled in ice. After 15 min of stirring at 0 °C, the solvent was evaporated and the residue flash chromatographed on silica gel (eluant, EtOAc/CH_2Cl_2 (1:1)) to yield quantitatively *syn*-(PhSOCH(CH_3),CH_3)-(CH_3CH_2,CH_3)B (**17f**).

***syn*-(PhSOCH(CH_3),CH_3)(CH_3CH_2,CH_3)B (17f).** Yellow solid. ^{1}H NMR ($CDCl_3$): (2 diastereoisomers) 0.998 and 1.311 (t, 3 H, CH_3CH_2, J = 7.6 Hz), 1.615 and 1.896 (d, 3 H, CH_3CH, J = 7.34 Hz), 1.714, 1.802, 1.855 and 1.987 (s, 6 H, CH_3), 2.283–2.475 and 2.644–2.854 (m, 2 H, CH_3CH_2), 3.970 and 4.163 (q, 1 H, CH_3CH, J = 7.34 Hz), 7.383–7.688 (m, 5 H) ppm.

9,10-Dioxa-*syn*-(vinyl,methyl)(methyl,methyl)bimane (18) (Hydroxymethylation, Elimination). The dark yellow anion of *syn*-(CH_3,CH_3)B (**6**) (3.84 g, 20 mmol) was produced with sodium hydride (0.53 g, 22 mmol) at 0 °C after 30 min in DMF (180 mL). Paraformaldehyde (0.68 g, 22 mmol) (dissolved by warming to 80–100 °C) in DMF (50 mL) was added over a period of 10 min, and the mixture was stirred mechanically for 1 h at 0 °C and then 3 h at 20 °C). Acetic anhydride (50 mL) was added, the solution refluxed for 1 h, the solvent distilled off, and the residue chromatographed on silica gel to yield [eluant, CH_2Cl_2] *syn*-(CH_2=CH,CH_3)B (**20**), 0.2 g (5% yield), *syn*-(CH_2=CH,CH_3)-(CH_3,CH_3)B (**18**), 1.02 g (25% yield), and (ethyl acetate) *syn*-(CH_3,CH_3)B (**6**), 2.3 g (60% yield). The use of 2.5 equiv of NaH per mole of **6** gave *syn*-(CH_2=CH,CH_3)B (**20**) (19% yield), *syn*-(CH_2=CH,CH_3)(CH_3,CH_3)B (**18**) (5%), and *syn*-(CH_3,CH_3)B (**6**) (70%). Reaction of *syn*-(CH_3,Cl)B with paraformaldehyde and 2 equiv of NaH gave *syn*-(CH_2=CH,Cl)(CH_3,Cl)B (**21**) in 15% yield.

***syn*-(CH_2=CH,Cl)(CH_3,Cl)B (21).** Yellow needles, mp 161 °C (CCl_4). IR (KBr): 1740, 1660, 1440, 1210, 1200, 1050, 950, 750 cm^{-1}. ^{1}H NMR ($CDCl_3$): 2.49 (s, 3 H), 5.69–5.89 (m, 2 H), 6.33–6.65 (m, 1 H) ppm. UV (CH_3CN): λ_{max} 379 nm (ϵ 5100), 261 (14 500). Fluorescence maxima (dioxane): 410 sh, 440, λ_{max} 460 nm, 482 sh (ϕ_F 0.78). Mass spectrum: m/e 244, 246, 248 (M^+).

9,10-Dioxa-*syn*-(vinyl,methyl)(methyl,methyl)bimane (18) (Bromination, Elimination). Bromine (1.6 g, 10 mmol) in CH_2Cl_2 was added to *syn*-(ethyl,methyl)(methyl,methyl)bimane (**7**) (2.06 g, 10 mmol) in CH_2Cl_2 (80 mL), forming both monobromo and dibromo derivatives (TLC). After removal of solvent, triethylamine (10 g, 100 mmol) in acetonitrile (40 mL) was added to the residue, and the whole was refluxed overnight. The solvent was removed, the residue dissolved in CH_2Cl_2, the solution washed twice with water to remove salts, the organic phase dried ($MgSO_4$), and the solvent evaporated. The residue was chromatographed on silica gel (eluant, CH_2Cl_2) to afford *syn*-(CH_2=CH,CH_3)(CH_3,CH_3)B (**18**) 86 mg (4%).

9,10-Dioxa-*syn*-(vinyl,methyl)(methyl,methyl)bimane (18) (Thermal Elimination of Phenylsulfinic Acid). A solution of the sulfoxide (**17f**) in benzene (420 mg, 1.22 mol) (stored at −20 °C) was refluxed for 4 h, the solvent removed, and the residue flash chromatographed on silica gel (eluants, CH_2Cl_2/EtOAc (3:1) and (6:4)) to yield pure *syn*-(CH_2=CH,CH_3)B (**18**), 223.6 mg (84% yield).

***syn*-(CH_2=CH,CH_3)B (20) from *syn*-(CH_3CH_2,CH_3)B (2).** Bromine (3.2 g, 20 mmol) in CH_2Cl_2 (80 mL) was added slowly (1 h) to *syn*-(CH_3CH_2,CH_3)B (2.2 g, 10 mmol) in CH_2Cl_2 (80 mL). Immediately after addition, the solvent was removed and the residue reacted overnight with triethylamine (10 mL) in acetonitrile (50 mL) at reflux. After removal of the solvent, chromatography on silica gel (eluant, CH_2Cl_2) gave *syn*-(CH_2=CH,CH_3)B (**20**), 1.4 g (65% yield).

***syn*-(CH_2=CH,CH_3)(CH_3,CH_3)B (18).** Yellow needles (CCl_4), mp 155–156 °C. IR (KBr) 1740, 1650, 1620, 1440, 1410, 1220, 1030, 970, 750, 740 cm^{-1}. ^{1}H NMR ($CDCl_3$): 1.836 (s, 3 H), 1.950 (s, 3 H), 2.259 (s, 3 H), 5.738–5.996 (m, 2 H), 6.368–6.687 (m, 1 H). UV (CH_3CN): λ_{max} 379 nm (ϵ 5300), 262 nm (15 000). Fluorescence maxima (dioxane): λ_{max} 464 nm (ϕ_F 0.30). Mass spectrum m/e 204 (M^+).

***syn*-(CH_2=CH,CH_3)B (20).** Yellow needles (CCl_4), mp 137 °C. IR (KBr): 1730, 1650, 1430, 1210, 1030, 750 cm^{-1}. ^{1}H NMR ($CDCl_3$): 2.263 (s, 3 H), 5.600–5.901 (m, 2 H), 5.940–6.345 (m, 1 H). UV (CH_3CN): λ_{max} 379 nm (ϵ 5100), 260 nm (14 200). Fluorescence maxima (CH_3CN): λ_{max} 468 nm, 480 sh, 495 sh (ϕ_F 0.6); (dioxane) λ_{max} 468 nm; (crystals) λ_{max} 510 nm, 550 sh. Fluorescence excitation maxima (crystals): λ_{max} 398 nm, 450 nm, 463 nm. Mass spectrum: m/e 216 (M^+).

***syn*-(Vinyl,chloro)bimane (23) (Thermal Elimination of Phenylsulfinic Acid).** A solution of the sulfoxide **17d** (stored at −20 °C) (239 mg, 0.479 mmol) in benzene was refluxed for 1 h, the solvent removed and pure *syn*-(CH_2=CH,Cl)B (**23**), 51 mg (42% yield), obtained by flash chromatography on silica gel (eluant, CH_2Cl_2/EtOAc (98:2)).

***syn*-(CH_2=CH,Cl)B (20b).** Yellow solid, mp 154–155 °C. IR (KBr): 1760, 1690, 1620, 1580, 1430, 1340, 1280, 1260, 1150, 970, 750 cm^{-1}. ^{1}H NMR ($CDCl_3$): 6.167, 6.200, 6.364, 6.414, 6.505, 6.538, 6.554, 6.567 ppm (typical ABX pattern). ^{13}C NMR ($CDCl_3$): 109.67 (CCl), 120.92 (CH_2), 131.00 (CH), 146.75 (C-N), 155.59 (C=O) ppm. UV (dioxane): λ_{max} 370 nm (ϵ 4800). Fluorescence maxima (dioxane): λ_{max} 470 nm (ϕ_F). Mass spectrum: m/e 260 (M^+), 258, 256 (mass distribution fits 2Cl).

***syn*-(Vinyl,chloro)(ethyl,chloro)bimane (22) (Thermal Elimination of Phenylsulfinic Acid).** A solution of the sulfoxide **17b** in benzene was refluxed for 1 h to form the monovinyl derivative **22** as judged by TLC (yellow-green fluorescence) but the material was not further characterized.

9,10-Dioxa-*syn*-(2-(*N*,*N*-diethylamino)ethyl,methyl)(ethyl,methyl)-bimane (24). *syn*-(CH_2=CH,CH_3)(CH_3CH_2,CH_3)B (**19**) (218 mg, 1 mmol) and diethylamine (73 mg, 1 mmol) in $CHCl_3$ (35 mL) were reacted overnight at room temperature, solvent was removed, and the residue was chromatographed (neutral alumina; eluant, EtOAc/$CHCl_3$

(4:1)) to yield a yellow solid which gave, after trituration (petroleum ether) and recrystallization from $CHCl_3$/petroleum ether (40–60) (4:1), *syn*-((CH$_3$CH$_2$)$_2$NCH$_2$CH$_2$,CH$_3$)(CH$_3$CH$_2$,CH$_3$)B (**24**), 261 mg (90% yield).

***syn*-((CH$_3$CH$_2$)$_2$NCH$_2$CH$_2$,CH$_3$)(CH$_3$CH$_2$,CH$_3$)B (24).** Mp 59–60 °C. IR (KBr): 2920, 1740, 1660, 1590, 1430, 1380, 1220, 1050, 730 cm^{-1}. ^{1}H NMR ($CDCl_3$): 0.90–1.50 (m, 9 H), 1.87 (s, 6 H), 2.50 (q, 6 H, J = 7 Hz), 2.80 (s, 4 H) ppm. UV (CH_3CN): λ_{max} 370 nm (ϵ 4300), 234 (9800). Mass spectrum: m/e 291 (M^+). Anal. Calcd for $C_{16}H_{25}N_3O_2$: C, 65.97; H, 8.59; N, 14.43 Found: C, 65.83; H, 8.52; N, 14.13.

A small amount of the amine was treated with excess methyl iodide in CH_3CN, the solvent evaporated, and the residue refluxed with Et_3N in CH_3CN. After evaporation of the solvent, the residue was found to contain ca. 50% *syn*-(CH$_2$=CH,CH$_3$)(CH$_3$CH$_2$,CH$_3$)B (**19**) and ca. 50% unreacted amine **24** (TLC).

9,10-Dioxa-*syn*-(2-chloroethyl,methyl)(ethyl,methyl)bimane (27). A suspension of *syn*-(vinyl,methyl)(ethyl,methyl)B (**19**) (218 mg, 1 mmol) in xylene (50 mL) saturated with HCl was refluxed for 2 h. After cooling, 9,10-dioxa-*syn*-(2-chloroethyl,methyl)(ethyl,methyl)bimane (**27**), 229 mg (90% yield), a pale yellow solid, was filtered off and recrystallized from $CHCl_3$/petroleum ether.

***syn*-(ClCH$_2$CH$_2$,CH$_3$)(C$_2$H$_5$,CH$_3$)B (27).** Mp 166 °C dec 190–200 °C to vinylbimane. IR (KBr): 2910, 1730, 1660, 1590, 1430, 1230, 1210, 1100, 1060, 1030, 730, 690, 660 cm^{-1}. ^{1}H NMR ($CDCl_3$): 1.35 (t, 3 H, J = 7 Hz), 1.85 (s, 3 H), 1.93 (s, 3 H), 2.75 (q, 2 H, J = 7 Hz), 3.18 (t, 2 H, J = 7 Hz), 3.82 (t, 2 H, J = 7 Hz) ppm. UV (CH_3CN): λ_{max} 372 nm (ϵ 4780), 250 sh (6300), 242 (11 400). Mass spectrum m/e 254 (9.7) (M^+), 255 (20.2), 253 (64.5), (vinylbimane$^+$) 218 (21.4). Anal. Calcd for $C_{12}H_{15}ClN_2O_2$: C, 56.47; H, 5.94; N, 11.02. Found: C, 56.06; H, 5.82; N, 10.94.

Sodium 9,10-Dioxa-*syn*-(2-(oxysulfonyl)ethyl,methyl)(ethyl,methyl)bimane (28). *syn*-(Vinyl,methyl)(ethyl,methyl)B (**19**) (218 mg, 1 mmol) in CH_3CN (40 mL) and aqueous sodium bisulfite (156 mg, 1.5 mmol) were refluxed for 2 h, the solvent evaporated and the residue extracted with CH_3CN for 48 h (Soxhlet). The CH_3CN was evaporated, the solid dissolved in hot ethanol and the hot solution quickly filtered. After several hours, yellow hygroscopic *syn*-(Na$^+$$^-O_3SCH_2CH_2$,CH$_3$)-(CH$_3CH_2$,CH$_3$)B, 305 mg (95% yield) separated.

***syn*-(Na$^+$$^-O_3SCH_2CH_2$,CH$_3$)(CH$_3CH_2$,CH$_3$)B (28).** IR (KBr): 3480 (H_2O), 1735, 1570, 1400, 1200, 1040, 730 cm^{-1}. UV (H_2O): λ_{max} 380 nm (ϵ 1000), 260 nm (7500) (ϵ low since **27** absorbs water during weighing). ^{1}H NMR (CF_3COOH) ($CHCl_3$ 7.25 ppm): 1.42 (t, 3 H, J = 7 Hz), 1.92 (s, 3 H), 1.99 (s, 3 H), 2.90 (q, 2 H, J = 7 Hz), 3.50 (br s, 4 H) ppm.

9,10-Dioxa-*syn*-(2-(chlorosulfonyl)ethyl,methyl)(ethyl,methyl)bimane (29). Dimethylformamide (36.5 mg, 0.5 mmol) in CH_2Cl_2 (5 mL) and thionyl chloride (59.5 mg, 0.5 mmol) in CH_2Cl_2 (5 mL) were added to a stirred suspension of the sulfonate (**28**) (161 mg, 0.5 mmol) in CH_2Cl_2 (30 mL). After 0.5 h at room temperature, the solvent was evaporated and the oily residue was poured onto crushed ice to give yellow, fluorescent 9,10-dioxa-*syn*-(2-(chlorosulfonyl)ethyl,methyl)(ethyl,methyl)-bimane (**29**) which was filtered off, dried, and crystallized twice from chloroform/petroleum ether, 150 mg (94% yield). Catalytic amounts (0.1 equiv) of DMF gave a similar result.

***syn*-(ClSO$_2$CH$_2$CH$_2$,CH$_3$)(CH$_3$CH$_2$,CH$_3$)B (29).** Mp 152–153 °C dec 190–200 °C to vinylbimane (**19**) and other products. IR (KBr): 2980, 2900, 1740, 1660, 1650, 1620, 1590, 1420, 1360, 1150, 1100, 1020, 1000, 790, 645 cm^{-1}. ^{1}H NMR ($CDCl_3$) (300 MHz): 1.33 (t, 3 H, J = 7.43 Hz), 1.814 (s, 3 H), 1.877 (s, 3 H), 2.688 (t, 2 H, J = 7.43 Hz), 3.151–3.551 (m, 2 H), 4.056–4.400 (m, 2 H) ppm. UV (CH_3CN): λ_{max} 370 nm (ϵ 4800), 250 sh (6150), 239 (6540). Mass spectrum: m/e 254 (2.9) ($M^+ - SO_2$), (vinylbimane$^+$) 218 (84.3), SO_2+ 64 (100). Anal. Calcd for $C_{12}H_{15}ClN_2O_4S$: C, 45.21; H, 4.71; N, 8.79; S, 10.04; Cl, 11.14. Found: C, 45.41; H, 4.84; N, 9.01; S. 10.07; Cl, 11.37.

Sulfonamides. Sulfonyl chloride and 2 equiv of amine were reacted in CH_3CN for 12 h at room temperature or 0.5 h at reflux. The solvent was removed, water added, the whole extracted twice with chloroform, the solution dried ($MgSO_4$), the solvent removed, the residue chromatographed (silica gel; eluant EtOAc/$CHCl_3$ (4:1)), and the product crystallized and characterized by mp, IR, ^{1}H NMR, UV, and mass spectrum. Data for one derivative are given in full along with melting points for an additional five. The thin-layer chromatographic properties are quite sensitive to structure, suggesting that the derivatives may be useful for identification of amines.

9,10-Dioxa-*syn*-(2-((*N*,*N*-dimethylamino)sulfonyl)ethyl,methyl)-(ethyl,methyl)bimane (*syn*-((CH$_3$)$_2$NSO$_2$CH$_2$CH$_2$,CH$_3$)(CH$_3$CH$_2$,CH$_3$)B (30c)). Pale yellow solid (80% yield), mp 162–164 °C ($CHCl_3$/petroleum ether). IR (KBr): 1740, 1655, 1590, 1330, 1230, 1150, 950, 720, 715 cm^{-1}. ^{1}H NMR ($CDCl_3$) 1.30 (t, 3 H, J = 7Hz), 2.60 (q, 2 H, J = 7 Hz), 1.85 (s, 6 H), 3.00 (s, 6 H), 3.22 (br s, 4 H) ppm. UV (CH_3CN): λ_{max} 370 nm (ϵ 4200), 252 sh (5600), 230 (11 900). Mass spectrum: m/e 327 (M^+), ($M^+ - SO_2$) 263, (vinylbimane$^+$) 218, (SO_2^+) 64, (CH$_2$=N(CH$_3$)$_2^+$) 58.

9,10-Dioxa-*syn*-(2-((*N*,*N*-diethylamino)sulfonyl)ethyl,methyl)-(ethyl,methyl)bimane (*syn*-((CH$_3$CH$_2$)$_2$NSO$_2$CH$_2$CH$_2$,CH$_3$)-(CH$_3$CH$_2$,CH$_3$)B (30d)). Pale yellow solid (84% yield), mp 181–182 °C dec to vinylbimane ($CHCl_3$/petroleum ether). Mass spectrum: m/e 355 (M^+). Anal. Calcd for $C_{16}H_{25}N_3O_4S$: C, 54.08; H, 7.04; N, 11.83. Found: C, 54.28; H, 7.14; N, 11.96. **9,10-Dioxa-*syn*-(2-((*N*-methyl-*N*-phenylamino)sulfonyl)ethyl,methyl)(ethyl,methyl)bimane (*syn*-(C$_6$H$_5$-(CH$_3$)NSO$_2$CH$_2$CH$_2$,CH$_3$)(CH$_3$CH$_2$,CH$_3$)B (30f).** Pale yellow solid (84% yield), mp 139–140 °C dec. **9,10-Dioxa-*syn*-(2-((*N*-(3-methylphenyl)amino)sulfonyl)ethyl,methyl)(ethyl,methyl)bimane (*syn*-((3-CH$_3$C$_6$H$_4$)NHSO$_2$CH$_2$CH$_2$,CH$_3$)(CH$_3$CH$_2$,CH$_3$)B (30e)).** Pale yellow solid (75% yield), mp 176–7 °C dec. **9,10-Dioxa-*syn*-(2-((*N*-methylamino)sulfonyl)ethyl,methyl)(ethyl,methyl)bimane (*syn*-(CH$_3$NHSO$_2$CH$_2$CH$_2$,CH$_3$)(CH$_3$CH$_2$,CH$_3$)B (30a)).** Pale yellow solid (64% yield), mp 127–130 °C dec. **9,10-Dioxa-*syn*-(2-((*N*-ethylamino)sulfonyl)ethyl,methyl)(ethyl,methyl)bimane (*syn*-(CH$_3$CH$_2$NHSO$_2$CH$_2$CH$_2$,CH$_3$)(CH$_3$CH$_2$,CH$_3$)B (30b)).** Pale yellow solid (67% yield), mp 145–146 °C dec.

R_f values for sulfonamides on thin-layer silica. (R_f, ethyl acetate; R_f, ethyl acetate/ethanol (9:1)): BSO$_2$NR$_1$R$_2$, **30** (R$_1$, R$_2$) **a** (H, CH$_3$), 0.10, 0.40; **b** (H, CH$_3$CH$_2$), 0.18, 0.50; **c** ((CH$_3$)$_2$), 0.16, 0.45; **d** ((CH$_3$CH$_2$)$_2$), 0.19, 0.56; **e** (H, *m*-CH$_3$C$_6$H$_4$), 0.37, 0.57; **f** (CH$_3$, C$_6$H$_5$), 0.44, 0.60.

9,10-Dioxa-*syn*-(2-(chlorosulfonyl)ethyl,methyl)(methyl,methyl)-bimane (31). *syn*-(CH$_2$=CH,CH$_3$)(CH$_3$,CH$_3$)B (**18**) (102 mg, 0.5 mmol) in CH_3CN (15 mL) and aqueous sodium bisulfite (60 mg, 0.57 mmol) were refluxed for 1 h, the solvent evaporated, the solid (154 mg) suspended in CH_2Cl_2 (20 mL), and dimethylformamide (36.5 mg, 0.5 mmol) in CH_2Cl_2 (5 mL) and thionyl chloride (59.5 mg, 0.5 mmol) in CH_2Cl_2 (5 mL) were added with stirring. After 0.5 h, the solvent was evaporated, the oily residue poured onto crushed ice, the yellow fluorescent 9,10-dioxa-*syn*-(2-(chlorosulfonyl)ethyl,methyl)(methyl,methyl)-bimane (**31**) filtered off, dried, and crystallized twice from chloroform/petroleum ether (40–60), 136 mg (90% yield).

***syn*-(ClSO$_2$CH$_2$CH$_2$,CH$_3$)(CH$_3$,CH$_3$)B.** Yellow solid, mp 139–140 °C ($CHCl_3$/petroleum ether (40–60)), dec 190–200 °C to vinylbimane **17**. IR (KBr): 1740, 1450, 1370, 1220, 1160, 735, 725 cm^{-1}; ^{1}H NMR ($CDCl_3$) 1.70 (s, 3 H), 1.75 (s, 3 H), 2.35 (s, 3 H), 2.90–3.45 (m, 2 H), 3.90–4.30 (m, 2 H) ppm. UV (CH_3CN) λ_{max} 370 nm (ϵ 5600), 245 nm (6800), 220 nm (15 400). Mass spectrum: m/e 304 (M^+). Anal. Calcd for $C_{11}H_{13}ClN_2O_4S$: C, 43.34; H, 4.26; N, 9.19; S, 10.50; Cl, 11.65. Found: C, 43.44; H, 4.38; N, 9.29; S, 10.84; Cl, 11.72.

9,10-Dioxa-*syn*-(2-((*N*,*N*-dimethylamino)sulfonyl)ethyl,methyl)-(methyl,methyl)bimane (*syn*-((CH$_3$)$_2$NSO$_2$CH$_2$CH$_2$,CH$_3$)(CH$_3$,CH$_3$)B (32c)). Pale yellow solid from $CHCl_3$/petroleum ether (78% yield), mp 175 °C (dec. to vinylbimane). R_f values for **32c**, TLC on silica (EtOAc or EtOAc/EtOH, 9:17), are 0.17 or 0.47, slightly different from those of **30c**.

μ-(2-*N*-Methylazatrimethylene)-*syn*-(methylene,methyl)bimane (34). *syn*-(CH$_2$=CH,CH$_3$)B (**20**) (216 mg, 1 mmol) in CH_2Cl_2 (15 mL) and methylamine (31 mg, 1 mmol) in ethanol (15 mL) were reacted overnight. The solvent was evaporated, and the residue chromatographed on neutral alumina (eluant, EtOAc/CH_2Cl_2 (1:1)) to yield as the major fluorescent product μ-(2-*N*-methylazatrimethylene)-*syn*-(methylene,-methyl)bimane (**34**), yellow solid, 197 mg (80% yield), mp 221 °C from $CHCl_3$ or $CHCl_3$/petroleum ether. IR (KBr): 2950, 1730, 1660, 1630, 1600, 1450, 1330, 1285, 1245, 1200, 1155, 1100, 1070, 1000, 970, 940, 870, 730 cm^{-1}. ^{1}H NMR ($CDCl_3$) 1.73 (s, 6 H), 2.20 (s, 3 H, NCH$_3$), 2.63–2.88 (m, 8 H) ppm. UV (CH_3CN): λ_{max} 363 nm (ϵ 6200), 253 sh (7800), 240 (17 400). Fluorescence (dioxane): λ_{max} 434 nm, 463 sh (ϕ_F 0.40). Mass spectrum: m/e 247 (100) (M^+).

μ-(2-Thiatrimethylene)-*syn*-(methylene,methyl)bimane (33). *syn*-(CH$_2$=CH,CH$_3$)B (**20**) (108 mg, 0.5 mmol) in CH_2Cl_2 (20 mL) and sodium sulfide (Na$_2$S·7–9H$_2$O) (40 mg, 0.5 mmol) in water (30 mL) containing hexadecyltrimethylammonium bromide (10 mg) were stirred together at room temperature for 2 h. The phases were separated, the aqueous layer was extracted three times with CH_2Cl_2, and the latter was washed with water, dried, and evaporated. The residue was chromatographed on silica gel (eluant, EtOAc/CH_2Cl_2 (1:1) then EtOAc) to give μ-(2-thiatrimethylene)-*syn*-(methylene,methyl)bimane (**33**), 22 mg (20% yield) and *syn*-(CH$_2$=CH,CH$_3$)B (**20**), 70 mg (40% yield).

μ-(2-Thiatrimethylene)-*syn*-(methylene,methyl)bimane (33). Yellow crystals from $CHCl_3$, mp 235–6 °C. IR (KBr): 2920, 1740, 1660, 1450, 1380, 1250, 1050, 960, 940, 840 cm^{-1}. ^{1}H NMR ($CDCl_3$): 1.79 (s, 3 H), 2.70–3.20 (m, 4 H) ppm. UV (CH_3CN): λ_{max} 355 nm (ϵ 4600), 260 sh (6100), 232 (15 400). Fluorescence (dioxane): λ_{max} 438 nm, 460 sh (ϕ_F 0.58). Mass spectrum: m/e 250 (M^+).

μ-(2,2-Dicarbethoxytrimethylene)-*syn*-(methylene,methyl)bimane (35). Sodium ethoxide (Na (45 mg, 1.96 mmol) in ethanol (20 mL)) and diethyl malonate (320 mg, 2.00 mmol) were refluxed for 1 h, then mixed with *syn*-(CH_2=CH,CH_3)B (**20**) (423 mg, 1.96 mmol) in EtOH (20 mL) at room temperature. After 12 h, the solvent was removed, the residue extracted with $CHCl_3$, the solution dried, the solvent evaporated, and the residue chromatographed on silica gel to give (eluant, CH_2Cl_2/EtOAc (1:1)) *syn*-(($C_2H_5OOC)_2CHCH_2CH_2$,CH_3)B (**37e**) as a pale yellow solid, 105 mg (10% yield), and (EtOAc/EtOH (8:2)) μ-($CH_2(C_2H_5O_2C)_2CCH_2$)-*syn*-(CH_2,CH_3)B (**35**), 293 mg (40% yield). Similar results were obtained from a reaction carried out in DMF with NaH as the base.

***syn*-(3,3-Dicarbomethoxypropyl,methyl)bimane (37m).** A mixture of sodium methoxide (sodium (45 mg, 1.96 mmol) in methanol (15 mL)) and dimethyl malonate (262 mg, 1.99 mmol) was refluxed for 1 h, then mixed with *syn*-(CH_2=CH,CH_3)B (**20**) (43 mg, 0.196 mmol) in methanol (10 mL) at room temperature. After 12 h, the solvent was removed, the residue extracted with chloroform, and the extract dried and evaporated. Chromatography of the residue on silica gel (eluant, CH_2Cl_2/EtOAc (1:1)) gave *syn*-(($CH_3O_2C)_2CHCH_2CH_2$,CH_3)B (**37m**), 84 mg (90% yield).

***syn*-(($CH_3O_2C)_2CHCH_2CH_2$,CH_3)B (37m).** Pale yellow solid, mp 99–101 °C (from $CHCl_3$/petroleum ether (40:60)). IR (KBr): 2980, 1730, 1580, 1450, 1350, 1260, 1210, 1150, 1050, 1040, 990, 950, 860, 770 cm^{-1}. ^1H NMR ($CDCl_3$): 1.90 (s, 3 H), 2.05–2.50 (m, 2 H), 2.60–3.05 (m, 2 H), 3.65 (t, 2 H), 3.81 (s, 6 H, OCH_3) ppm. UV (dioxane): λ_{max} 354 nm (ε 5700), 250 sh (6100), 230 (14 800); (CH_3CN) 373 nm (4500), 255 sh (5050), 232 (14 200). Fluorescence (dioxane): λ_{max} 425 nm, 455 sh, 465 sh, 480 sh (ϕ_F 0.26). Mass spectrum: *m/e* 480 (M^+).

***syn*-(($C_2H_5OOC)_2CHCH_2CH_2$,CH_3)B (37e).** Pale yellow solid, mp 72 °C (from $CHCl_3$/petroleum ether (40:60)). IR (KBr): 2950, 1730, 1590, 1460, 1360, 1260, 1200, 1150, 1050, 1040, 990, 950, 860, 760 cm^{-1}. ^1H NMR ($CDCl_3$) 1.29 (t, 6 H, *J* = 7 Hz), 1.85 (s, 3 H), 2.00–2.40 (m, 2 H), 2.60–2.90 (m, 2 H), 3.58 (t, 1 H, *J* = 7 Hz), 4.23 (q, 4 H, *J* = 7 Hz) ppm. UV (dioxane): λ_{max} 364 nm (ε 5800), 250 sh (6100), 230 (11 800); (CH_3CN) 373 nm (4600), 255 sh (5130), 232 (12 800). Fluorescence (dioxane): λ_{max} 425 nm, 465 sh, 480 sh (ϕ_F 0.80). Mass spectrum: *m/e* 536 (M^+).

μ-($CH_2(C_2H_5O_2C)_2CCH_2$)-*syn*-(CH_2,CH_3)B (35). Pale yellow solid, mp 291 °C (from ethanol). IR (KBr): 2960, 1730, 1620, 1420, 1360, 1300, 1260, 1210, 1080, 1010, 850, 740 cm^{-1}. ^1H NMR ($CDCl_3$): 1.20 (t, 3 H, *J* = 7 Hz), 1.70 (s, 3 H), 2.05–2.70 (m, 4 H), 4.15 (q, 2 H, *J* = 7 Hz) ppm. UV (CH_3CN): λ_{max} 368 nm (ε 5100), 253 sh (6300), 230 (14 800). Fluorescence (dioxane): λ_{max} 435 nm, 463 sh (ϕ_F 0.96). Mass spectrum: *m/e* 376 (M^+).

μ-($CH_2(C_2H_5O_2C)CHCH_2$)-*syn*-(CH_2,CH_3)B (36e). A mixture of lithium bromide (350 mg, 4 mmol) and μ-($CH_2(C_2H_5O_2C)_2CCH_2$)-*syn*-(CH_2,CH_3)B (**35e**) (376 mg, 1 mmol) in dry DMF (25 mL) was refluxed overnight. The solvent was removed, and the residue chromatographed on silica gel. Elution with CH_2Cl_2/EtOAc (1:1) gave μ-($CH_2(C_2H_5O_2C)CHCH_2$)-*syn*-(CH_2,CH_3)B (**36e**) as a white solid, 218 mg (72% yield).

μ-($CH_2(HO_2C)CHCH_2$)-*syn*-(CH_2,CH_3)B (36h). A suspension of μ-($CH_2(C_2H_5O_2C)_2CCH_2$)-*syn*-(CH_2,CH_3)B] (**35e**) (376 mg, 1 mmol) in 15% HCl (15 mL) was warmed at 90 °C until all the solid dissolved (45 min). The white solid which separated on cooling was filtered off and recrystallized from isopropyl alcohol to give μ-($CH_2(HO_2C)$-$CHCH_2$)-*syn*-(CH_2,CH_3)B (**36h**), 96 mg (35%).

μ-($CH_2(C_2H_5O_2C)CHCH_2$)-*syn*-(CH_2,CH_3)B (36e). White solid, mp 147 °C (from $CHCl_3$/petroleum ether). IR (KBr): 1730, 1620, 1450, 1360, 1250, 1210, 1100, 1020, 1010, 1000, 980, 950, 860, 750 cm^{-1}. ^1H NMR ($CDCl_3$): 1.92 (t, 3 H, *J* = 7 Hz), 2.00 (s, 3 H), 2.05 (s, 3 H), 2.10–2.50 (m, 8 H), 3.39 (m, 1 H), 4.05 (q, 2 H, *J* = 7 Hz) ppm. UV (CH_3CN): λ_{max} 368 nm (ε 5000), 254 sh (6500), 230 (14 500). Fluorescence (dioxane): λ_{max} 435, 463 sh (ϕ_F 0.88). Mass spectrum: *m/e* 304 (M^+).

μ-($CH_2(HO_2C)CHCH_2$)-*syn*-(CH_2,CH_3)B (36h). White solid, mp 203 °C. IR (KBr): 3590, 1735, 1610, 1450, 1360, 1240, 1205, 1100, 1050, 1000, 950, 850, 740 cm^{-1}. ^1H NMR ($CDCl_3$): 1.99 (s, 3 H), 2.05 (s, 3 H), 2.10–2.50 (m, 8 H), 3.71 (m, 1 H) ppm. UV (CH_3CN): λ_{max} 368 nm (ε 4800), 253 sh (6000), 230 (14 000). Fluorescence (dioxane): λ_{max} 435 nm, 463 sh (ϕ_F 0.82). Mass spectrum: *m/e* 276 (M^+).

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Supplementary Material Available: Tables of bond lengths and angles and final positional and thermal parameters for **33** (2 pages). Ordering information is given on any current masthead page.