Heating of Ester 4b with Water. After prolonged heating of the tetracyano ester **4b** in acetonitrile at 80 °C for several days, the unsaturated tricyano ester **6** was formed, but not a trace of the unsaturated ester **7** could be detected (VPC).

Acknowledgment. We thank Professor Th. J. de Boer for stimulating discussions and Mr. C. Kruk for the ^{13}C NMR spectra and skillful assistance in their interpretation.

Registry No. 1a, 41330-13-6; **1b**, 30451-99-1; **1c**, 76430-11-0; **1e**, 76430-12-1; **2a**, 57260-86-3; **2b**, 76430-13-2; **2c**, 76430-14-3; **2d**, 57260-85-2; **2e**, 76430-15-4; **3c**, 76430-16-5; **3e**, 76430-17-6; **4b**, 76430-18-7; **4c**, 76430-19-8; **5c**, 76430-20-1; **6**, 76430-21-2; **7**, 924-50-5; 1-(methylthio)cyclopropyl bromide, 54376-40-8; 1-ethoxy-1-(methylthio)cyclopropane, 76430-22-3; dimethylketene dimethyl acetal, 5634-54-8; methylketene dimethyl acetal, 5634-52-6; methylketene diethyl acetal, 21504-43-8; tetracyanoethylene, 670-54-2; cyclopentanone dimethyl acetal, 931-94-2; 2-methylcyclopentanone dimethyl acetal, 76430-23-4; 3-methylcyclopentanone dimethyl acetal, 76430-24-5; **1d**, 18523-34-7.

Bimanes. 6. Reactive Halogen Derivatives of *syn*- and *anti*-1,5-Diazabicyclo[3.3.0]octadienediones (9,10-Dioxabimanes)

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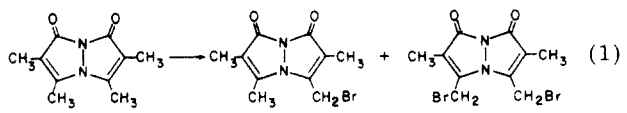
The preparation of reactive halogen derivatives of *syn*- and *anti*-1,5-diazabicyclo[3.3.0]octadienediones (9,10-dioxabimanes) is accomplished through the intermediate monobromo- and dibromobimanes previously described. Mono- and dihydroxy compounds are produced from the bromides by reaction with wet sodium trifluoroacetate in CH_3CN and are used to prepare the (a) monochlorides and dichlorides ($SOCl_2$) and (b) the monofluorides and difluorides (Et_2NSF_3). Monofunctional halides react with nucleophiles (amines, thiols, carboxylates) to yield direct substitution products, with some reduction accompanying the thiol reaction. Difunctional halides react with excess nucleophile to give direct disubstitution products. *syn*-Dihalides react with difunctional nucleophiles (actual or potential, e.g., RNH_2, S^{2-}, $(CN)_2C<$) to yield a new series of heterocyclic compounds, the "bridged" 9,10-dioxabimanes. The absorption spectra of both *syn*- and *anti*-$(XCH_2,CH_3)B$ are markedly affected by the nature of X. Most *syn*-bromobimanes are nonfluorescent and are moderately photosensitive, due to thermally reversible isomerizations and additional irreversible reactions. *syn*-Chlorobimanes are nonfluorescent to weakly fluorescent. *syn*-Monofluoro- and difluorobimanes are strongly fluorescent. At 77 K, the halogenated compounds are all phosphorescent to some extent and many of the syn derivatives are strongly fluorescent.

Introduction

In the course of investigating the reactions of *syn*-(methyl,methyl)bimane[2,3] (**1**), it was found that bromination led to either a monobromobimane (**2**) or a dibromobimane (**3**), the proportions depending on the number of equivalents of bromine used for the reaction (eq 1). The



(1)

1 2 3

usefulness of the bromobimanes in producing many other 9,10-dioxabimane derivatives as well as their successful application to the labeling of proteins and cells[4,5] suggested that it would be appropriate to describe their characteristics in detail, as we now do in the present article. We report also the preparation of chloro- and fluorobimanes.

Results

The properties and reactions of monobromo- and dibromobimanes are the primary subject of the present article. It was, however, of importance to make a comparison of their photophysical properties with other reactive halobimanes, and for this purpose, the transformation of the bromides into the corresponding alcohols and then to the desired halides has been carried out.

The conversion of *syn*-bromides to the alcohols in aqueous buffer, pH 7.4, at 50 °C proceeds slowly, and the alcohols produced are accompanied by more polar materials, which we suppose to be ring-opened products like those obtained in the reaction of hydroxide ion with dioxa-*syn*-bimanes.[2] More effective is the classical procedure of displacing halide with a carboxylate, using wet sodium trifluoroacetate in acetonitrile, which leads directly to the

(1) (a) Tel-Aviv University. (b) State University of New York.

(2) The formation and some of the uses of the bromobimanes were briefly mentioned in a communication: Kosower, E. M.; Pazhenchevsky, B.; Hershkowitz, E. *J. Am. Chem. Soc.* **1978**, *100*, 6516. A description of the bromination of some 9,10-dioxabimanes is given in Bimanes 5: Kosower, E. M.; Pazhenchevsky, B. *Ibid.* **1980**, *102*, 4983-4993.

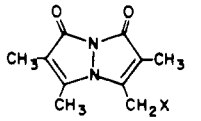
(3) The nomenclature of the *syn*- and *anti*-1,5-diazabicyclo[3.3.0]octadienediones (9,10-dioxabimanes) is thoroughly discussed in Bimanes 5. Briefly, a group in the position α to the carbonyl is labeled R_1, a group β is denoted R_2, the relationship of the carbonyl groups is indicated by syn or anti prefixes, and the 9,10-dioxabimane structure is referred to as 9,10-dioxabimane, bimane, or B.

(4) Kosower, N. S.; Kosower, E. M.; Newton, G. L.; Ranney, H. M. *Proc. Natl. Acad. Sci. U.S.A.* **1979**, *76*, 3382.

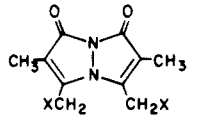
(5) Kosower, N. S.; Newton, G. L.; Kosower, E. M.; Ranney, H. M. *Biochim. Biophys. Acta* **1980**, *622*, 201. (a) Goldberg, I., unpublished results. Crystal structures for related bimanes have been reported: Bernstein, J.; Goldstein, E.; Goldberg, I. *Cryst. Struct. Commun.* **1980**, *9*, 285; *Ibid.* **1980**, *9*, 301; Goldberg, I. *Ibid.* **1980**, *9*, 329; Kosower, E. M.; Bernstein, J.; Goldberg, I.; Pazhenchevsky, B.; Goldstein, E. *J. Am. Chem. Soc.* **1979**, *101*, 1620.

0022-3263/81/1946-1666$01.25/0

desired alcohols in reasonable yield. Four of the possible alcohols derived from *syn*- and *anti*-$(CH_3,CH_3)B$ (1 and 4) have been prepared in the yields noted: *syn*-$(HOCH_2,CH_3)(CH_3,CH_3)B$ (**5**, 47%), *syn*-$(HOCH_2,CH_3)B$ (**6**, 51%), *anti*-$(HOCH_2,CH_3)(CH_3,CH_3)B$ (**7**, 50%), *anti*-$(HOCH_2,CH_3)B$ (**8**, 61%). The structure of the *anti*-diol **8** has been confirmed by X-ray crystallography.[5a]

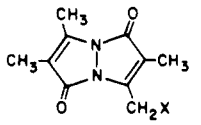


syn-$(XCH_2,CH_3)(CH_3,CH_3)B$

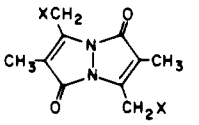


syn-$(XCH_2,CH_3)B$

X = OH, F, Cl, Br



anti-$(XCH_2,CH_3)(CH_3,CH_3)B$



anti-$(XCH_2,CH_3)B$

X = OH, Cl, Br

The alcohols (**5**–**7**) are converted to the chlorides **9**–**11** with thionyl chloride. Although the chlorides may also be prepared from the bromides by using lithium chloride in dimethyl sulfoxide, it is difficult to ensure that no bromide is present in the product. Purity is essential for an accurate determination of photophysical properties.

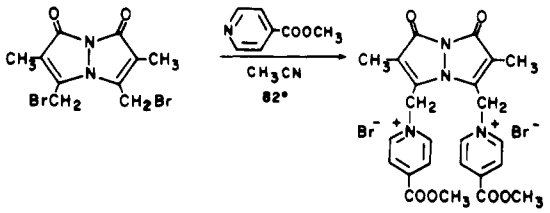
The fluorides (**12**, **13**) are prepared by the reaction of (diethylamino)sulfur trifluoride in CH_2Cl_2 at low temperature with the alcohols. The *syn*-difluoro derivative (**13**) does not exhibit long-range F–F coupling in an ^{19}F NMR spectrum.

Bromides may also be prepared from the alcohols by reaction with phosphorus tribromide, a pathway that might prove useful for cases in which R_1 = H (Br replaces R_1 in bromination).

Monofunctional Nucleophile Reactions. A limited number of oxygen, nitrogen, and sulfur nucleophiles were reacted with monobromo and dibromo derivatives of *syn*- and *anti*-$(CH_3,CH_3)B$, most of the examples involving the *syn*-dibromo compound **3**. A two-phase reaction of *syn*-$(BrCH_2,CH_3)B$ (**3**) with KOAc and a phase-transfer agent yielded 90% of the diacetate, *syn*-$(CH_3COOCH_2,CH_3)B$ (**16**). Potassium terephthalate reacted with the *syn*-dibromide (**3**) in CH_3CN at reflux in the presence of dibenzo-18-crown-6 to yield what appeared to be a fluorescent polymeric product (**17**), insoluble in all the usual solvents and decomposing, rather than melting, above 250 °C. Slow addition of methoxide ion to the dibromide (**3**) in methanol gave an 84% yield of *syn*-$(CH_3OCH_2,CH_3)B$ (**18**), whereas rapid mixing of the reagents gave a dark mixture which contained none of the dimethoxy product.

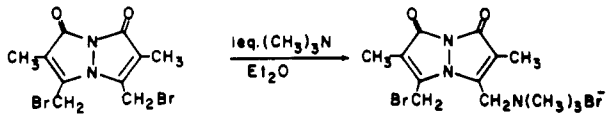
Slow addition of methanethiolate ion in ethanol to the dibromide (**3**) produced 58% of the *syn*-$(CH_3SCH_2,CH_3)B$ (**19**) along with 1.7% of the partially reduced compound, *syn*-$(CH_3SCH_2,CH_3)(CH_3,CH_3)B$ (**20**). Propanethiolate ion reacted with the dibromide **3** in a two-phase reaction to give 72% of the bis product, *syn*-$(CH_3CH_2CH_2S-CH_2,CH_3)B$ (**21**), along with 10% of the partially reduced compound, *syn*-$(CH_3CH_2CH_2SCH_2,CH_3)(CH_3,CH_3)B$ (**22**). The *anti*-dibromide (**15**) gave a good yield of the bis product (**23**) in a similar reaction with propanethiolate ion. The *syn*-monobromo derivative (**2**) led to 65% of the monosubstitution product, *syn*-$(CH_3CH_2CH_2SCH_2,-CH_3)(CH_3,CH_3)B$ (**22**), along with 2% of the reduction product, *syn*-$(CH_3,CH_3)B$ (**1**).

The product of the reaction of methyl isonicotinate with the *syn*-dibromide (**3**) in CH_3CN at reflux is a bis(pyridinium salt) (**24**,[6] eq 2). Reaction of 1 equiv of tri-



(2)

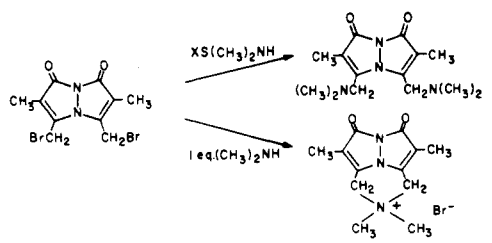
methylamine with the *syn*-dibromide (**3**) leads to the monobromomono(trimethylammonio)dioxa-*syn*-bimane (**25**), useful as a biological thiol-labeling agent which does not penetrate intact cell membranes[4,5] (eq 3). Excess



(3)

trimethylamine reacts with the dibromide **3** to form the bis(trimethylammonio salt) (**26**); reaction of trimethylamine with the *syn*-monobromide (**2**) yields the mono-(trimethylammonio salt) (**27**).

Difunctional Nucleophile Reactions. Two types of product result from the reaction of difunctional nucleophiles with *syn*-dibromide **3**. The first type is the bis product expected for displacement of two bromide ions by two nucleophiles. The second type of product is a compound containing an additional ring, formed by intramolecular reaction of the second functionality with the second bromide. The two types are illustrated for the reaction of dimethylamine in eq 4 (**3** → **28** or **29**).



(4)

The new cyclic compounds are referred to as "bridged" 9,10-dioxa-*syn*-bimanes and have been prepared with nitrogen (as in eq 4), carbon, or sulfur as bridging atoms. Their properties will be discussed in another article.[9]

In the case of ammonia, no disubstitution product could be obtained and the reaction of primary amines produces very small yields of disubstitution products. However, the reaction of ammonia with the monobromide, *syn*-$(BrCH_2,CH_3)(CH_3,CH_3)B$ (**2**), leads to the monoamino compound, *syn*-$(NH_2CH_2,CH_3)(CH_3,CH_3)B$ (**30**) and a small amount of an interesting side product, *syn*-$(CN,-CH_3)(CH_3,CH_3)B$ (**31**). The use of acetamide as both reactant (diminished nucleophilicity of nitrogen) and solvent (aprotic dipolar solvent) at elevated temperatures (the melting point of acetamide is 82 °C) leads to rea-

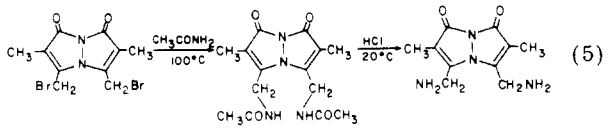
(6) Reduction of the bis(pyridinium salt) by Na(Hg) in CH_3CN leads to a solution with a visible absorption like the charge-transfer absorption of pyridinyl radical π-mers.[7] Reduction with magnesium metal gives rise to a solution with a strong visible absorption, which is probably related to that found for other intramolecular pyridinyl diradical magnesium halide complexes.[8] Teuerstein, A., unpublished results.

(7) Itoh, M.; Kosower, E. M. *J. Am. Chem. Soc.* **1968**, *90*, 1843. Hermolin, J.; Kosower, E. M., submitted for publication.

(8) Kosower, E. M.; Hajdu, J.; Nagy, J. H. *J. Am. Chem. Soc.* **1978**, *100*, 1186.

(9) Kosower, E. M.; Pazhenchevsky, B.; Dodiuk, H.; Ben-Shoshan, M.; Kanety, H. *J. Org. Chem.*, following paper in this issue.

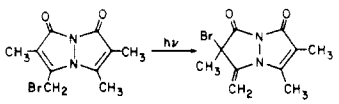
sonable yields of the diacetamido derivative (**32**) (accompanied by the bridged *N*-acetylimino derivative **33**) which then may be hydrolyzed to the diamino compound (**34**, eq 5).



(5)

In the case of secondary amines, the intramolecular ring closure which follows the introduction of the first amine group is slow enough so that a substantial excess of the nucleophile leads to formation of the disubstituted product. Diamino products have been characterized for dimethylamine (**28**), piperidine (**35**), and *N*-methylanilines with the following substituents: 3-Br (**36**), H (**37**), 4-Cl (**38**), 4-CH_3 (**39**), 4-$COOCH_3$ (**40**). A bis product (**41**) was also obtained from the reaction of the primary amine 1-naphthylamine. The monopiperidino (**42**) and monomethylamino (**43**) derivatives have been characterized, after preparation from the monobromobimane (**2**). The dipiperidino derivative (**44**) was prepared from the *anti*-dibromide (**15**).

The *syn*-bromo and dibromobimanes are photosensitive. Appreciable conversion of *syn*-($BrCH_2$,CH_3)(CH_3,CH_3)B to another compound occurs in CH_3CN on irradiation at 430 nm, as judged from the decrease in the absorption maximum at 245 nm and the broadening of the long-wavelength absorption band at 383 nm. Attempted isolation by evaporation of the solvent leads to the recovery of the starting monobromo compound. Irreversible photoreactions ensue on longer irradiations or after irradiation at shorter wavelengths (380 nm), yielding at least some fluorescent products which have not been characterized. The photoproduct reacts with glutathione in aqueous buffer about twice as fast as the starting bromide[10] and is also photosensitive. The initial photoproducts are tentatively identified as isomers of the starting bromides. The isomerization is shown in eq 6.



(6)

The photophysical properties of the halogen derivatives vary markedly with the nature of the halogen. While mono- and difluoro syn derivatives are strongly fluorescent in solution, like *syn*-(CH_3,CH_3)B, the mono- and dichloro derivatives are weakly fluorescent, and the bromo compounds are completely nonfluorescent. In matrices at 77 K, considerable enhancement of fluorescence is found, the chloro compounds being moderately fluorescent and the bromo derivatives weakly fluorescent under these conditions. The fluorescence quantum yield found for *syn*-($BrCH_2$,CH_3)B in a diethyl ether–pentane–ethanol (5:5:2) matrix at 77 K is 0.03, by comparison with the value of 0.6 for *syn*-(CH_3,Cl)B under the same conditions.[11] The fluorescence maxima and either quantum yield of fluorescence (25 °C, dioxane) or relative fluorescence intensities (77 K) for the halogenated bimanes are listed in Table I.

All of the *syn*-halobimanes are weakly phosphorescent, the phosphorescence to fluorescence ratio (Φ_P/Φ_F) being less than 0.01 as in the case of most *syn*-bimanes. The emission maxima are at longer wavelengths than the phosphorescence maximum for *syn*-(CH_3,CH_3)B. The phosphorescence lifetimes are 0.5 s or less. The phosphorescence maxima and relative intensities of phosphorescence are included in Table I.

Table I. Emission Data for Halogenated 9,10-Dioxa-*syn*- and -*anti*-(methyl,methyl)bimanes

derivative[a]	fluorescence, λ_{max} (ϕ_F) [relative intensity][b] dioxane, 25 °C	fluorescence, λ_{max} (ϕ_F) [relative intensity][b] EP,[d] 77 K	phosphorescence, λ_{max} [relative intensity],[c] EP,[d] 77 K
		syn-(XCH_2,CH_3)B	
H,H	420 (0.72)	426, 445 (s)[e]	528, 565 (s)[e]
H,Br	*f*	426 [2]	543 [4.3]
Br,Br	*f*	440 [1]	592 [1]
H,Cl	424 (0.016)	440 [6]	568 [1.2]
Cl,Cl	428 (0.001)	436 [17]	588 [2.8]
H,F	436 (0.62)	424 [20]	570 [7.2]
F,F	436 (0.84)	428 [30]	592 [2]
		anti-(XCH_2,CH_3)B	
H,H	463 (0.001)		480, 498 (s)[e]
Cl,Cl	496 (0.001)		470-490 [530]
H,Br			480-497 [73]
Br,Br			470-490 [5.3]

[a] Derivatives of *syn*- or *anti*-(XCH_2,CH_3)B, in which one or both X = H have been replaced by a halogen, as designated. [b] Relative to the fluorescence of *syn*-($BrCH_2$,CH_3)B as 1, using relative peak heights. [c] Relative to the phosphorescence of *syn*-($BrCH_2$,CH_3)B as 1, using relative peak heights. [d] Diethyl ether–isopentane (1:1). [e] Ether–pentane–ethanol (5:5:2) matrix. [f] Undetectable.

The *anti*-halobimanes exhibit only phosphorescence in matrices at 77 K, the intensities being greater than those of the corresponding syn compounds. The phosphorescence maxima are at wavelengths much shorter than those of the corresponding syn derivatives and at positions not very different from those of the weak fluorescences found in solution[11] (Table I). The lifetimes are consistent with the interpretation of these emissions as phosphorescence (0.5 s or less) but the emissions have not been investigated in detail.

Discussion

The conversions and syntheses described in the present article indicate how readily the bromobimanes are converted into a variety of useful derivatives. Since many of the derivatives are fluorescent in the case of 9,10-dioxa-*syn*-bimanes, the conversions described provide a route to a large number of compounds bearing a small, stable, fluorescent moiety, including those with the potential for acting as labeling and derivatizing agents.

The absorption maxima of the substituted *syn*- and *anti*-(methyl,methyl)bimanes (Table II) show that the S_0–S_1 electronic transition is moderately sensitive to the nature of the substituent. The shift of the maximum for the change from H to Cl to Br is particularly noteworthy. Possible influences on the position of the absorption maximum may include the polarizability of the substituent, the repulsion of the charge on the substituent and the charge in the ring in the S_1 state, the planarity of the bimane system, and the interaction of the σ bond of the substituent with the π system, especially in the excited π^* state. One of the novel possibilities is that the planarity of the bicyclic system is affected by the substituents, the planarity increasing with the number of substituents irrespective of their nature, provided these substituents are not too large. The planarity of bimane molecules is discussed in connection with the photophysical and photochemical properties of the bimanes.[11] It is worth men-

(10) Kosower, E. M.; Radkowski, A., unpublished results.
(11) Kosower, E. M.; Kanety, H.; Dodiuk, H., submitted for publication (Bimanes 8).

Table II. Longest Wavelength Absorption Maxima for Mono- and Disubstituted 9,10-Dioxa-*syn*- and -*anti*-(methyl,methyl)bimanes in Dioxane

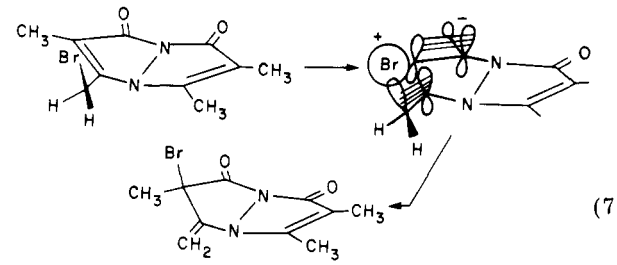
substituent	λ_{max} (ϵ_{max}) mono	bis
	syn-(XCH_2,CH_3)B	
H	359 (6500)	
Py^+ [a]		373 (7000) [b]
$Br,N(CH_3)_3^+$		380 (5200) [b]
$N(CH_3)_3^+$	376 (4700) [b]	393 (6700) [b]
$N(CH_3)C_6H_4X$		
X = H		370 (5400)
X = 3-Br		370 (6400)
X = 4-Cl		372 (6700)
X = 4-CH_3		373 (6400)
NH-1-$C_{10}H_7$		380 (7400)
OH	372 (6250)	378 (4700)
$OOCCH_3$		379 (6600)
OCH_3		380 (4700)
SCH_3	372 (5100)	380 (7000)
NH_2	370 (6600)	384 (6600)
$NHCOCH_3$		381 (6000) [c]
$NHCH_3$	370 (5200)	
$N(CH_3)_2$		382 (7800)
NC_5H_{10} [d]	373 (7000)	382 (7400)
NC_5H_{10} [d]	389 (5100) [b]	398 (5300) [b]
NC_5H_{10},$HNC_5H_{10}^+$ [d,e]		379 (5300) [b]
$HNC_5H_{10}^+$ [e]	379 (5400) [b]	386 (6100) [b]
F	373 (6200)	382 (6900)
Cl	374 (6400)	383 (6800)
Br	377 (7000)	390 (6600)
	anti-(XCH_2,CH_3)B	
H	322 (15100)	
OH	325 (14400)	328 (14100)
NC_5H_{10} [d]		330 (13600)
S-1-C_3H_7		330 (10800)
Cl		342 (12600)
Br	336 (11300)	349 (11500)

[a] 4-(Carbomethoxy)-1-pyridino. [b] Water. [c] Acetonitrile. [d] Piperidino. [e] Piperidinium.

tioning here the series of diacetylene derivatives reported some time ago by Armitage and Whiting[12] for which there was considerable dependence of the absorption maximum on the nature of the substituent. For the change from Cl to Br to I in $XCH_2C{\equiv}CC{\equiv}CCH_2X$, the maximum shifts from 253 to 260 to 281 nm, a change which the authors ascribed to the polarizability of the substituent. Halogen substitution on the β-methyl groups also affects the short-wavelength absorption bands. The 235-nm maximum and 255-nm shoulder found for *syn*-(CH_3,CH_3)B (**1**) in dioxane is changed in *syn*-($ClCH_2$,CH_3)B (**10**) to one band at 245 nm, in *syn*-($BrCH_2$,CH_3)(CH_3,CH_3)B (**2**) to one band at 248 nm, and in *syn*-($BrCH_2$,CH_3)B (**3**) to one band at 266 nm. The shift is not observed in the monochloro, monofluoro, or difluoro *syn*-bimanes of the same substitution type, leading to the possibility that the halogen–π^* interaction also affects the energies of excited states higher than S_1.

Placing a positively charged substituent on the methyl group at the β position of the bimane shifts the absorption maximum to much shorter wavelengths. However, a second positive charge (as in the case of bis(trimethylammonio)-9,10-dioxa-*syn*-bimane) shifts the maximum back toward longer wavelengths, reaching a value similar to that of the monobromobimane in water (393 nm for the bis salt, 394 nm for the monobromo derivative). We suppose that flattening of the ring counteracts the effect of the second positive charge; additional examples will be needed to probe this interesting finding further. The dipiperidinium derivative absorbs at appreciably shorter wavelengths than the bis(trimethylammonio) compound (386 nm vs. 393 nm), indicating how sensitive the maximum is to changes in the substitution of the bimane. In any case, the positions of the longest wavelength maximum for both syn and anti derivatives constitute a useful guide to structure which must be applied with some caution.

syn-Monobromo-, dibromo-, and dichlorobimanes are not fluorescent in solution. The quenching reaction is probably related to the photoisomerization process, typified by the transformation shown in eq 6. The simplest interpretation of these results is that the S_0–S_1 transition involves orbitals in which overlap between the C–X bond are the π system affects the transition energy. Such hyperconjugation is well-known in the case of metal–carbon bonds, as exemplified in the work of Traylor and coworkers,[13] and should be more important in the excited state than in the ground state. In other words, a σ–π^* interaction would be stronger than a σ–π interaction. The excited-state interaction would have the effect of labilizing the bromine. Since the negative charge which moved in the excitation is, in part, localized on the α-carbon of the bimane ring, very close to the bromine–carbon bond, the bromine can readily move from the carbon attached to the β-methyl to the ring α-carbon. A simple molecular picture for the σ–π^* state suggests that it would be quite easy for the bromine to move to the α-carbon in an intramolecular rearrangement. It would also be quite easy for the bromine to return to its original location by either thermal or photochemical means. The hyperconjugation and the rearrangement which follows are illustrated in eq 7. Pho-



(7)

toisomerization is known for allylic halides and has been explained with an ionic mechanism by Sammes.[14] An explanation for the heavy-atom effects on the phosphorescence of norbornenes by Chandra et al.[15] is related to that which we have given for the quenching. A number of points support this picture in addition to those already mentioned. The strength of the C–X bond affects not only the position of the absorption maximum but also the photochemical consequences of the excitation, since the chloro derivatives are markedly less photosensitive than the bromo compounds. Nevertheless, the very weak fluorescence of the monochloro compound indicates that an energy-dissipation pathway exists. Hyperconjugation in the S_1 state followed by internal conversion is the logical choice for the pathway. As noted below, freezing the halogenated bimanes into a matrix at 77 K diminishes the extent of both the photochemical reactions and the quenching process, even the bromobimanes being weakly fluorescent under these conditions.

Our studies of nucleophilic displacement reactions for many different nucleophiles indicate that the bromomethyl

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(14) Sammes, P. G. *In* "The Chemistry of the Carbon-Halogen Bond"; Patai, S., Ed.; J. Wiley and Sons: New York, 1973; Part 2, Chapter 11.

(15) Chandra, A. K.; Turro, N. J.; Lyons, A. L., Jr.; Stone, P. *J. Am. Chem. Soc.* **1978**, *100*, 4964.

and bis(bromomethyl)-*syn*- and -*anti*-9,10-dioxabimanes are readily substituted in such reactions. Competition between external and internal nucleophiles determines whether or not bis or "bridged" substitution products will be formed in the case of the *syn*-dibromobimanes. The course of the competition is dependent upon (a) the concentration of the external nucleophile, (b) the reactivity of the nucleophile (it is likely that the nucleophilicity of the intramolecular nucleophile is diminished with respect to that of the external nucleophile because of the electron-attracting character of the bimane nucleus), (c) steric effects around the reaction center, and (d) solvent effects. A number of these points are now being explored and will be reported at a later time.[10]

Experimental Section

The instrumentation used in this research has been described in a previous article.[2] The Experimental Section is divided into several sections, including (a) synthesis of alcohols, (b) preparation of various halogen derivatives, and (c) reaction of the bromide with various nucleophiles.

Alcohols. Dark reaction mixtures from which little or no product could be isolated resulted from the reaction of bromobimanes with aqueous base. A modification of the classical two-step procedure for the conversion of alkyl halides to alcohols (carboxylate ion, ester hydrolysis) was then used with success to prepare the bimane alcohols. It is more efficient to effect the conversion to the alcohols by using the crude bromobimanes obtained from the reaction of bromine with *syn*- or *anti*-(methyl,methyl)bimanes, since the chromatographic procedures for the separation of the alcohols are (a) more effective and (b) do not require the exclusion of light to avoid side products resulting from the photosensitivity of the bromobimanes.

9,10-Dioxa-*syn*-(hydroxymethyl,methyl)(methyl,methyl)bimane (5). The product mixture from the reaction of bromine (1.25 g, 7.8 mmol) and *syn*-(CH_3,CH_3)B (1; 1.5 g, 7.8 mmol; monobromobimane derivative predominant according to TLC) was mixed with wet sodium trifluoroacetate (1.3 g, 9.6 mmol) in CH_3CN (50 mL) and the whole refluxed for 15 h with exclusion of light. The precipitated NaBr was filtered off, the solvent was evaporated, the residue was washed with water (ca. 10 mL), the yellow solid was transferred to a silica gel column, and the products were eluted with CH_2Cl_2 and increasing amounts of CH_3CN. (An alumina column may also be used.) The major product obtained was *syn*-($HOCH_2$,CH_3)(CH_3,CH_3)B (5: 680 mg (42%); yellow crystals (CH_3CN–*i*-PrOH); mp 205 °C; IR (KBr) 3460, 2920, 1745, 1660, 1620, 1590, 1440 (sh), 1410, 1380, 1245, 1220 (sh), 1030, 1000, 740 cm^{-1}; ^1H NMR (Me_2SO-d_6) 1.73 (s), 1.85 (s, 6 H), 2.41 (s, 3 H), 4.46 (br s, 2 H), 5.70 (br s, 1 H) ppm; UV (dioxane) 372 nm (ϵ 6250), 255 (5000), 232 (14800); fluorescence (dioxane) 430 nm, 455 (sh) (ϕ_F 0.79); mass spectrum, *m/e* 208 (M^+).

9,10-Dioxa-*syn*-(hydroxymethyl,methyl)bimane (6). *syn*-($BrCH_2$,CH_3)B (3; 350 mg, 1 mmol; unpurified dibromobimane from the reaction of 2 equiv of bromine and *syn*-(CH_3,CH_3)B (1) may also be used) and wet sodium trifluoroacetate (1.0 g, 7.4 mmol) were dissolved in CH_3CN (25 mL) and the solution was refluxed for 15 h. The solvent was removed, and the residue was extracted with water and crystallized to yield *syn*-($HOCH_2$,CH_3)B (6), 150 mg (51%) (chromatographic separation is required if crude dibromobimane is used as starting material): yellow needles (CH_3CN–DMF); mp 234–235 °C; IR (KBr) 3340, 1755, 1660, 1605, 1425, 1245, 1045, 750 cm^{-1}; ^1H NMR (Me_2SO-d_6) 1.78 (s, 3 H), 4.62 (d, 2 H), 5.80 (t, 1 H) (added D_2O gave 1.75 (s, 3 H), 4.65 (s, 2 H)) ppm; UV (dioxane) 378 nm (ϵ 4700), 260 (3600, sh), 230 (12000); fluorescence (dioxane) 431 nm, 450 (sh) (ϕ_F 0.60); mass spectrum, *m/e* 224 (M^+).

9,10-Dioxa-*anti*-(hydroxymethyl,methyl)(methyl,methyl)bimane (7). The product mixture from the reaction of bromine (420 mg, 2.6 mmol) and *anti*-(CH_3,CH_3)B (4; 500 mg, 2.6 mmol; mostly monobromo compound) was mixed with sodium trifluoroacetate (650 mg, 4.8 mmol) in acetonitrile (50 mL) and the solution refluxed for 15 h with exclusion of light. The solvent was evaporated after filtering off NaBr, and the residue was washed with water (5 mL) and extracted with CH_2Cl_2 (50 mL). After removal of the CH_2Cl_2, the residue was chromatographed on alumina to yield *anti*-($HOCH_2$,CH_3)(CH_3,CH_3)B (7), *anti*-($HOCH_2$,CH_3)B (8), and *anti*-($BrCH_2$,CH_3)B (15). The first fraction was crystallized to give *anti*-($HOCH_2$,CH_3)(CH_3,CH_3)B (7): 270 mg (50%); white needles (EtOAc); mp 154 °C; IR ($CHCl_3$) 3380 (weak), 2970 (weak), 1715, 1660, 1620, 1415, 1380, 1360, 1265, 1190, 970, 900 cm^{-1}; ^1H NMR ($CDCl_3$) 1.80 (s), 1.78 (s) (6 H), 2.40 (s, 3 H), 4.60 (br s, 3 H) (added D_2O gave 4.60 (s, 2 H)) ppm; UV (dioxane) 325 nm (ϵ 14400); mass spectrum, *m/e* 208 (M^+), 209 ($M + 1^+$; CI).

9,10-Dioxa-*anti*-(hydroxymethyl,methyl)bimane (8). The product mixture from the reaction of bromine (850 mg, 5.3 mmol) and *anti*-(CH_3,CH_3)B (4; 500 mg, 2.6 mmol) was mixed with wet sodium trifluoroacetate (1.0 g, 7.35 mmol) in CH_3CN, the solution was refluxed for 15 h, the solvent was removed, and the residue was washed with water (5 mL) and chromatographed on alumina (eluant CH_2Cl_2), yielding as the major product *anti*-($HOCH_2$,CH_3)B (8): 350 mg (61%); white needles (EtOAc–CH_3CN); mp 143 °C; IR ($CHCl_3$) 3420 (weak), 2970 (weak), 1660, 1410, 1385, 1345, 1265, 1200, 1140, 960, 900, 875 cm^{-1}; ^1H NMR ($CDCl_3$) 1.84 (s, 3 H), 4.52 (s, 2 H), 4.25 (br s, 1 H) ppm; UV (dioxane) 328 nm (ϵ 14100); mass spectrum, *m/e* 224 (M^+).

Bromides. Two procedures are used to prepare the bromobimanes: either reaction of the parent bimane (with appropriate substitution, in the present instance, at least one β-methyl group) with bromine or reaction of the alcohols with phosphorus tribromide. The bromination reaction is by far the most convenient and has already been described for *syn*- and *anti*-(methyl,methyl)bimanes.[2]

9,10-Dioxa-*syn*-(bromomethyl,methyl)(methyl,methyl)bimane (2). *syn*-($HOCH_2$,CH_3)(CH_3,CH_3)B (5; 60 mg, 0.28 mmol) and PBr_3 (150 mg, 0.55 mol) were reacted in CH_2Cl_2 (3 mL). After the solid had dissolved, CH_2Cl_2 (15 mL) and water (5 mL) were added, the CH_2Cl_2 was separated and dried (Na_2SO_4), the solvent was removed, and the residue was recrystallized from ethyl acetate to yield 30 mg (39%) of *syn*-($BrCH_2$,CH_3)(CH_3,CH_3)B (2).

Chlorides. 9,10-Dioxa-*syn*-(chloromethyl,methyl)(methyl,methyl)bimane (9), 9,10-Dioxa-*syn*-(chloromethyl,methyl)bimane (10), and 9,10-Dioxa-*anti*-(chloromethyl,methyl)bimane (11). Two procedures were used to prepare the chlorobimanes: either reaction of the alcohols with thionyl chloride or reaction of bromobimanes with lithium chloride in dimethyl sulfoxide. The alcohol was dissolved in thionyl chloride at room temperature without warming during stirring, the solvent was removed, and the residue was recrystallized. In the second procedure, anhydrous LiCl and the bromobimane were warmed in Me_2SO until a clear solution resulted. After 1 h, the reaction mixture was cooled and diluted with water, and the precipitated product was recrystallized. Small amounts of bromine can be detected in the product prepared by displacement through mass spectrometric analysis. For photophysical measurements, the thionyl chloride route is preferred.

***syn*-($ClCH_2$,CH_3)(CH_3,CH_3)B (9)**: $SOCl_2$ method; 64% yield; yellow crystals (EtOAc–Et_2O); mp 132 °C; IR (KBr) 1725, 1660, 1630, 1600, 1410, 1220, 1155, 1090, 1020, 880, 740 cm^{-1}; ^1H NMR ($CDCl_3$) 1.81 (s), 1.90 (s) (6 H), 2.39 (s, 3 H), 4.38 (s, 2 H) ppm; UV (dioxane) 374 nm (ϵ 6400), 265 (4300, sh), 237 (13500); fluorescence (dioxane) 424 nm (ϕ_F 0.016); mass spectrum, *m/e* 226, 228 (M^+).

***syn*-($ClCH_2$,CH_3)B (10)**: LiCl method; 96% yield; yellow crystals (EtOAc); mp 166 °C; IR (KBr) 1745, 1675, 1600, 1430, 1390, 1240, 1165, 1110 cm^{-1}; ^1H NMR ($CDCl_3$) 1.98 (s, 3 H), 4.75 (s, 2 H) ppm; UV (dioxane) 383 nm (ϵ 6800), 245 (10500); mass spectrum, *m/e* 260, 262 (M^+).

anti-($ClCH_2$,CH_3)B (11): LiCl method; 40% yield; white crystals (benzene–petroleum ether (60–80 °C); mp 156 °C; IR (KBr) 1680, 1625 (sh), 1430, 1405, 1385, 1285, 1250, 1185, 1160, 1055, 920, 905, 740, 715 cm^{-1}; ^1H NMR ($CDCl_3$) 1.90 (s, 3 H), 4.60 (s, 2 H) ppm; UV (dioxane) 342 nm (ϵ 12600), 212 (13000); mass spectrum, *m/e* 260, 262 (M^+).

Fluorides. 9,10-Dioxa-*syn*-(fluoromethyl,methyl)bimane (13) and 9,10-Dioxa-*syn*-(fluoromethyl,methyl)(methyl,methyl)bimane (12). The reaction of the syn alcohols with (diethylamino)sulfur trifluoride at low temperatures was used to prepare two fluorobimanes. *syn*-($HOCH_2$,CH_3)B (6) (70 mg, 0.31 mmol) was added to (diethylamino)sulfur trifluoride[13] (200 mg,

1.24 mmol) in CH_2Cl_2 (10 mL) at −40 °C, and the mixture was stirred for 3 h as the temperature was allowed to rise slowly to 20 °C. The solid starting material dissolved completely during the reaction. Water (5 mL) was added, the CH_2Cl_2 separated, dried ($MgSO_4$), and evaporated, and the oily residue crystallized to give 28 mg (40%) of *syn*-(FCH_2,CH_3)B (**13**). A similar procedure applied to *syn*-($HOCH_2$,CH_3)(CH_3,CH_3)B (**5**; 40 mg) yielded 25 mg (61%) of *syn*-(FCH_2,CH_3)(CH_3,CH_3)B (**12**) after passing a solution of the crude product through a short alumina column.

***syn*-(FCH_2,CH_3)B (13)**: yellow crystals (*i*-PrOH); mp 116 °C; IR (KBr) 2920, 1750, 1665, 1600, 1415, 1380, 1245, 1220, 1165, 990, 885 cm^{-1}; ^1H NMR ($CDCl_3$) 1.91 (s), 1.94 (s) (6 H), 4.93 (s), 5.72 (s, 2 H, J_{FCH_2} = 48 Hz) ppm; ^{19}F NMR ($CDCl_3$) 217.37 (t, J_{CH_2F} = 49 Hz) ppm; UV (dioxane) 382 nm (ε 6900), 265 (sh), 232 (11 300); fluorescence (dioxane) 436 nm (ϕ_F 0.84); mass spectrum, *m/e* 228 (M^+).

***syn*-(FCH_2,CH_3)(CH_3,CH_3)B (12)**: yellow crystals (Et_2O–ca. 5% CH_2Cl_2); mp 129 °C; IR (KBr) 1745, 1660, 1595, 1410, 1380, 1230, 1015, 980 cm^{-1}; ^1H NMR ($CDCl_3$) 1.81 (s), 1.90 (d) (6 H), 2.33 (s, 3 H), 4.90 (s), 5.69 (s, 2 H, J_{FCH_2} = 48 Hz) ppm; ^{19}F NMR ($CDCl_3$) 215.42 (t, J_{CH_2F} = 49 Hz) ppm; UV (dioxane) 373 nm (ε 6200), 260 (sh), 232 (12 300); fluorescence (dioxane) 436 nm (ϕ_F 0.62); mass spectrum, *m/e* 210 (M^+).

Irradiation of Bromobimanes. The response of the bromobimanes, especially the monobromo derivative, *syn*-($BrCH_2$,CH_3)(CH_3,CH_3)B (**2**), to light was examined under several conditions. After irradiation with a known flux from the 150-W xenon source lamp of an MPF-4 spectrofluorimeter at 430 nm in CH_3CN, broadening of the long-wavelength absorption band at 383 nm and decrease in the absorption maximum at 245 nm were noted. Upon reaching 10% loss in the latter maximum in an irradiation, the solution was evaporated, the residue redissolved, and the UV spectrum shown to be very similar to that of the starting monobromo compound. TLC showed no trace of any other compound. Irradiation of the monobromo compound at 380 nm led to more rapid change (higher absorption coefficient) and the formation of fluorescent photoproducts.

The reactions of nucleophiles with bromobimanes are grouped according to the nature of the nucleophilic atom, as follows: (1) oxygen nucleophiles, (2) sulfur nucleophiles, and (3) nitrogen nucleophiles.

9,10-Dioxa-*syn*-(methoxymethyl,methyl)bimane (18). Sodium methoxide (0.1 N, 14 mL, 1.4 mmol) was added dropwise to a suspension of *syn*-($BrCH_2$,CH_3)B (**3**; 250 mg, 0.71 mmol) in methanol (10 mL) over 1 h, and after 3 h, the solvent was evaporated, the residue extracted with CH_2Cl_2, the solution passed through a short, neutral alumina column, and the *syn*-(CH_3OCH_2,CH_3)B (**18**) obtained as a yellow oil, 150 mg (84%), through elution with EtOAc–petroleum ether (60–80 °C): IR (neat) 2940, 1760, 1685, 1615, 1510, 1440, 1230, 1100 cm^{-1}; ^1H NMR ($CDCl_3$) 1.93 (s, 3 H), 3.42 (s, 3 H), 4.52 (s, 2 H) ppm; UV (dioxane) 380 nm (ε 4700), 260 (sh, 4000), 231 (11 200); fluorescence (dioxane) 428 nm, 450 (sh) (ϕ_F 0.84); mass spectrum, *m/e* 252 (M^+).

9,10-Dioxa-*syn*-(acetoxymethyl,methyl)bimane (16). *syn*-($BrCH_2$,CH_3)B (**3**; 0.50 g, 1.43 mmol) in CH_2Cl_2 (10 mL) was stirred vigorously with aqueous KOAc (2 M, 10 mL) containing hexadecyltrimethylammonium bromide (100 mg) for 12 h, the CH_2Cl_2 separated, washed with water, and dried (Na_2SO_4), the solvent evaporated, and the residue crystallized to yield 0.39 g (90%) of *syn*-($AcOCH_2$,CH_3)B (**16**): yellow needles (EtOAc–Et_2O); mp 134 °C; IR (KBr) 1740 (sh), 1720, 1660, 1610, 1430, 1375, 1210, 1030, 910 cm^{-1}; ^1H NMR ($CDCl_3$) 1.98 (s, 3 H), 2.16 (s, 3 H), 5.21 (s, 2 H) ppm; UV (dioxane) 379 nm (ε 6600), 255 (sh, 4400), 232 (11 800); fluorescence (dioxane) 431 nm, 460 (sh) (ϕ_F 0.90); mass spectrum, *m/e* 308 (M^+).

Bimane "Terephthalate" (17). Reaction of *syn*-($BrCH_2$,CH_3)B (**3**; 35 mg, 0.1 mmol) and potassium terephthalate (24 mg, 0.1 mmol) in CH_3CN containing dibenzo-18-crown-6 (72 mg, 0.1 mmol) at reflux for 48 h gave a yellow precipitate of **17**, 26 mg, which turned dark at 280 °C and did not melt up to 330 °C: IR (KBr) 1760, 1725, 1680, 1610, 1430, 1270, 1210, 1100, 1010, 725 cm^{-1}; UV (CH_3CN–Me_2SO, 9:1) 378 nm, 265 (sh); fluorescence (CH_3CN–Me_2SO, 9:1) 441 nm, 460 (sh) (ϕ_F 0.71).

9,10-Dioxa-*syn*-(methylthiomethyl,methyl)bimane (19) and 9,10-Dioxa-*syn*-(methylthiomethyl,methyl)(methyl,methyl)bimane (20). Sodium methanethiolate (0.3 M, EtOH, 10 mL, 3 mmol) was added dropwise to a suspension of *syn*-($BrCH_2$,CH_3)B (**3**; 350 mg, 1.0 mmol) in EtOH (20 mL) over 2 h. After 3 h, the solvent was removed, the residue extracted with CH_2Cl_2, the extract filtered, the solvent evaporated, and the oily residue purified by crystallization and chromatography to yield *syn*-(CH_3SCH_2,CH_3)B (**19**), 165 mg (58%), and *syn*-(CH_3SCH_2,CH_3)(CH_3,CH_3)B (**20**), 4 mg (1.7%).

***syn*-(CH_3SCH_2,CH_3)B (19)**: yellow crystals (*i*-PrOH); mp 94 °C; IR (KBr) 2920, 1745, 1660, 1625, 1590, 1430, 1235, 1170, 1110 cm^{-1}; ^1H NMR ($CDCl_3$) 1.93 (s, 3 H), 2.22 (s, 3 H), 3.98 (s, 2 H) ppm; UV (dioxane) 380 nm (ε 7000), 241 (15 600); fluorescence (dioxane) 428 nm, 455 (sh) (ϕ_F 0.63); mass spectrum, *m/e* 284 (M^+).

***syn*-(CH_3SCH_2,CH_3)(CH_3,CH_3)B (20)**: yellow crystals (THF–Et_2O); mp 109–110 °C; IR (KBr) 2920, 1740, 1660, 1620, 1595, 1430, 1415, 1240, 1215, 1155 cm^{-1}; ^1H NMR ($CDCl_3$) 1.86 (s), 1.92 (s) (6 H), 2.19 (s, 3 H), 2.44 (s, 3 H), 3.69 (s, 2 H) ppm; UV (dioxane) 372 nm (ε 5100), 260 (6500, sh), 234 (11 500); fluorescence (dioxane) 430 nm, 460 (sh) (ϕ_F 0.68); mass spectrum, *m/e* 238 (M^+).

9,10-Dioxa-*syn*-(1-propylthiomethyl,methyl)bimane (21), 9,10-Dioxa-*syn*-(1-propylthiomethyl,methyl)(methyl,methyl)bimane (22), and 9,10-Dioxa-*anti*-(1-propylthiomethyl,methyl)bimane (23). Reaction of 1-propanethiol with *syn*-($BrCH_2$,CH_3)B (**3**) in a two-phase mixture containing NaOH, benzene, and hexadecyltrimethylammonium bromide yielded, after purification, the bis(propylthiomethyl) derivative (**21**) in 72% yield as an oil and the mono(propylthiomethyl) compound (**22**) as a solid, mp 82 °C, in 10% yield. Reaction of 1-propanethiol with *syn*-($BrCH_2$,CH_3)(CH_3,CH_3)B (**2**) yielded 65% of the mono(propylthiomethyl) derivative [*syn*-($CH_3CH_2CH_2$-SCH_2,CH_3)(CH_3,CH_3)B (**22**)] and ca. 2% *syn*-(CH_3,CH_3)B (**1**). Reaction of 1-propanethiol with *anti*-($BrCH_2$,CH_3)B (**15**) yielded only the bis(propylthiomethyl) derivative (**23**) in 67% yield as a solid after trituration with hexane.

***syn*-($CH_3CH_2CH_2SCH_2$,CH_3)B**: yellow oil; IR (neat) 2930, 1755 (sh), 1745, 1675, 1620, 1600, 1410, 1225, 1160, 1110, 745 cm^{-1}; ^1H NMR ($CDCl_3$) 1.51 (t, 3 H), 1.69 (m, 2 H), 1.92 (s, 3 H), 2.61 (t, 2 H), 4.97 (s, 2 H) ppm; UV (dioxane) 380 nm (ε 6150), 255 (6000, sh); fluorescence (dioxane) 428 nm, 460 (sh) (ϕ_F 0.61); mass spectrum, *m/e* 340 (M^+).

***syn*-($CH_3CH_2CH_2SCH_2$,CH_3)(CH_3,CH_3)B (22)**: yellow solid (EtOAc–Et_2O); mp 82 °C; IR (KBr) 2960, 2920, 1740, 1660, 1625, 1600, 1420, 1235, 1080, 730 cm^{-1}; ^1H NMR ($CDCl_3$) 1.51 (t, 3 H), 1.65 (m, 2 H), 1.87 (s), 1.92 (s, 6 H), 2.44 (s, 3 H), 2.62 (t, 2 H), 3.70 (s, 2 H) ppm; UV (dioxane) 371 nm (ε 6500), 256 (sh); fluorescence (dioxane) 425 nm, 460 (sh) (ϕ_F 0.55); mass spectrum, *m/e* 268 (M^+).

***anti*-($CH_3CH_2CH_2SCH_2$,CH_3)B (23)**: white solid; mp 58 °C; IR (KBr) 2990, 2940, 1680, 1415, 1390, 1370, 1270, 1190, 1040, 900, 880 cm^{-1}; ^1H NMR ($CDCl_3$) 1.50 (t, 6 H), 1.70 (m, 4 H), 1.95 (s, 6 H), 2.65 (t, 4 H), 3.90 (s, 4 H) ppm; UV (dioxane) 330 nm (ε 10 800); mass spectrum, *m/e* 330 (M^+).

Various nitrogen nucleophiles were reacted with *syn*-($BrCH_2$,CH_3)B and *syn*-($BrCH_2$,CH_3)(CH_3,CH_3)B. The conditions which favor the production of at least some bis product involve the use of a large excess of nitrogen nucleophile; experiments which lead to tricyclic ("bridged") derivatives will be described in another article.[9]

9,10-Dioxa-*syn*-(*N*-aryl-*N*-methylaminomethyl,methyl)bimanes (36–40). *syn*-($BrCH_2$,CH_3)B (**3**; 2 mmol), *N*,*N*-diisopropylethylamine (0.5–1.0 mL), and an *N*-methylaniline (1 mL, 5–10 mmol) in CH_3CN are stirred for 1–7 days at room temperature, the precipitate (cyclic quaternary salt, see ref 9] filtered off, the filtrate evaporated, and the residue chromatographed on alumina or purified by recrystallization from *i*-PrOH. The properties and yields of the individual compounds are given below.

9,10-Dioxa-*syn*-(*N*-phenyl-*N*-methylaminomethyl,methyl)bimane (37) [*syn*-($C_6H_5N(CH_3)CH_2$,CH_3)B]: 3.5% yield; crystallized from *i*-PrOH; mp 69–70 °C; IR (KBr) 2920, 2850, 1745, 1660, 1600, 1500, 1450, 1420, 1380, 1340, 1310, 1260, 1220, 1190, 1150, 1120, 1110, 1030, 1000, 940, 870, 790, 750, 690 cm^{-1}; ^1H NMR ($CDCl_3$) 1.80 (s, 6 H), 2.75 (s, 6 H), 4.20 (s, 4 H), 6.65–7.10 (m, 8 H) ppm; UV (dioxane) 405 nm (sh), 370 (ε 5400), 294 (4400), 249 (27 200); fluorescence (dioxane) 428 nm (ϕ_F 0.054).

9,10-Dioxa-*syn*-(*N*-(4-methylphenyl)-*N*-methylaminomethyl,methyl)bimane (39) [syn-(4-$CH_3C_6H_4N(CH_3)$-CH_2,CH_3)B]: 8.5% yield; mp 181 °C (*i*-PrOH–*n*-hexane); IR (KBr) 3005, 2895, 1740, 1665, 1615, 1590, 1520, 1480, 1445, 1430, 1410, 1395, 1370, 1330, 1320, 1290, 1260, 1230, 1215, 1190, 1120, 1030, 1000, 950, 870, 800, 740 cm^{-1}; ^1H NMR ($CDCl_3$) 1.80 (s, 6 H), 2.20 (s, 6 H), 2.75 (s, 6 H), 4.20 (s, 4 H), 6.50–7.00 (q, 8 H) ppm; UV (dioxane) 405 nm (sh), 373 (ε 6400), 302 (4000), 250 (34 800); fluorescence (dioxane) 430 nm (ϕ_F 0.01); mass spectrum, *m/e* 430 (M^+).

9,10-Dioxa-*syn*-(*N*-(4-chlorophenyl)-*N*-methylaminomethyl,methyl)bimane (38) [*syn*-(4-$ClC_6H_4N(CH_2,CH_3)$B]: 22% yield; crystallized from *i*-PrOH–*n*-hexane; mp 179–180 °C; IR (KBr) 1745, 1665, 1600, 1500, 1440, 1390, 1360, 1320, 1260, 1240, 1220, 1190, 1160, 1140, 1100, 1000, 930, 815, 740, 690 cm^{-1}; ^1H NMR ($CDCl_3$) 1.80 (s, 6 H), 2.75 (s, 6 H), 4.18 (s, 4 H), 6.65–7.10 (m, 8 H) ppm; UV (dioxane) 405 nm (sh), 372 (ε 6700), 307 (4700), 255 (40 100); fluorescence (dioxane) 428 nm (ϕ_F 0.04); mass spectrum, *m/e* 471 (M^+).

9,10-Dioxa-*syn*-(*N*-(3-bromophenyl)-*N*-methylaminomethyl,methyl)bimane (36) [*syn*-(3-$BrC_6H_4N(CH_3)$-CH_2,CH_3)B]: 8% yield; crystallized from *i*-PrOH; mp 126–127 °C; IR (KBr) 2920, 2850, 1745, 1660, 1600, 1500, 1450, 1420, 1380, 1340, 1260, 1220, 1150, 1120, 1030, 1000, 940, 870, 790, 750, 690 cm^{-1}; ^1H NMR ($CDCl_3$) 1.80 (s, 6 H), 2.75 (s, 6 H), 4.25 (s, 4 H), 6.65–7.10 (m, 8 H) ppm; UV (dioxane) 400 nm (sh), 370 nm (ε 6400), 300 (5400), 251 (31 000); fluorescence (dioxane) 428 nm (ϕ_F 0.043).

9,10-Dioxa-*syn*-(*N*-(1-naphthyl)aminomethyl,methyl)bimane (41) [*syn*-(1-$C_{10}H_7NHCH_2,CH_3$)B]: 18% yield; mp 250–251 °C; IR (KBr) 3350, 3040, 2920, 1740, 1650, 1625, 1590, 1530, 1490, 1450, 1430, 1410, 1350, 1280, 1250, 1230, 1120, 1080, 1000, 940, 780, 760, 740 cm^{-1}; ^1H NMR (Me_2SO-d_6) 1.80 (s, 6 H), 4.50 (br s, 4 H), 6.5–8.2 (m, 14 H) ppm; UV (dioxane) 405 nm (sh), 380 (ε 7400), 330 (18 000), 245 (58 000); fluorescence (dioxane) 428 nm (ϕ_F 0.017).

9,10-Dioxa-*syn*-(piperidinomethyl,methyl)(methyl,methyl)bimane (42), 9,10-Dioxa-*syn*-(piperidinomethyl,methyl)bimane (35), 9,10-Dioxa-*anti*-(piperidinomethyl,methyl)bimane (44), 9,10-Dioxa-*syn*-(dimethylaminomethyl,methyl)bimane (28), and 9,10-Dioxa-*syn*-(methylaminomethyl,methyl)(methyl,methyl)bimane (43). *anti*-($BrCH_2,CH_3$)B (**3**; (100 mg, 0.29 mmol) and piperidine (500 mg, 5.9 mmol) in CH_3CN (5 mL) were stirred for 1 h, the solution was filtered from precipitated solid, the solvent was evaporated, and the residue was crystallized from $CHCl_3$–EtOAc to yield 44 as a solid, 30 mg (29%). The *syn*-monobromo (**2**) and dibromo (**3**) compounds were reacted with piperidine, methylamine, and dimethylamine in the same way.

***syn*-($C_5H_{10}NCH_2,CH_3$)(CH_3,CH_3)B (42)**: 44% yield; yellow crystals (EtOAc–Et_2O); mp 184 °C; IR (KBr) 2980, 2920, 2800, 1735, 1665, 1630, 1600, 1470, 1420, 1390, 1300, 1290, 1230, 1210, 1180, 1150, 1120, 1100, 1070, 1040, 1020, 1000, 960, 920, 870, 800, 750, 680 cm^{-1}; ^1H NMR ($CDCl_3$) 1.50 (m, 6 H), 1.85 (s, 6 H), 2.90 (s, t, 7 H), 3.30 (s, 2 H) ppm; UV (dioxane) 373 nm (ε 7000), 255 (5900, sh), 232 (15 500); fluorescence (dioxane) 426 nm (ϕ_F 0.82); mass spectrum, *m/e* 275 (M^+).

***syn*-($C_5H_{10}NCH_2,CH_3$)B (35)**: low yield; yellow crystals (*i*-PrOH–*n*-hexane); mp 177 °C; IR (KBr) 2920, 2850, 2790, 1755, 1665, 1630, 1610, 1450, 1440, 1380, 1340, 1300, 1280, 1255, 1240, 1210, 1160, 1120, 1100, 1060, 990, 910, 860, 810, 800, 780, 735, 680 cm^{-1}; ^1H NMR ($CDCl_3$) 1.50 (m, 6 H), 1.85 (s, 3 H), 2.40 (m, 4 H), 3.75 (s, 2 H) ppm; UV (dioxane) 405 nm (sh), 382 (ε 7400), 252 (6200, sh), 232 (16 800); fluorescence (dioxane) 427 nm (ϕ_F 0.29); mass spectrum, *m/e* 358 (M^+).

***anti*-($C_5H_{10}NCH_2,CH_3$)B**: white solid; mp 125 °C; IR (KBr) 2940, 1680, 1440, 1410, 1380, 1340, 1290, 1240, 1200, 1150, 1040, 990, 920, 860, 780, 730, 720, 640 cm^{-1}; ^1H NMR ($CDCl_3$) 1.5 (m, 12 H), 1.90 (s, 6 H), 2.6 (m, 8 H), 3.8 (s, 4 H) ppm; UV (dioxane) 330 nm (ε 13 600); mass spectrum, *m/e* 358 (M^+).

***syn*-($(CH_3)_2NCH_2,CH_3$)B (28)**: 10% yield; crystallized from *n*-hexane; mp 89–90 °C; IR (KBr) 2940, 2920, 2850, 2810, 2770, 1745, 1660, 1630, 1600, 1460, 1430, 1350, 1260, 1220, 1150, 1115, 1100, 1020, 790, 740 cm^{-1}; ^1H NMR ($CDCl_3$) 1.90 (s, 6 H), 2.30 (s, 12 H), 3.60 (s, 4 H) ppm; UV (dioxane) 405 nm (sh), 382 (ε 7800), 252 (5400, sh), 232 (15 500); fluorescence (dioxane) 427 nm (ϕ_F 0.35); mass spectrum, *m/e* 278 (M^+).

***syn*-(CH_3NHCH_2,CH_3)(CH_3,CH_3)B (43)**: 52% yield; mp 80 °C (*i*-PrOH–hexane); IR (KBr) 3300, 2920, 1735, 1650, 1620, 1600, 1420, 1230, 1140, 1120, 1090, 1010, 940, 830, 790, 740, 670 cm^{-1}; ^1H NMR ($CDCl_3$) 1.82 (s), 1.90 (s, 6 H), 2.28 (s, 1 H), 2.42 (s), 2.47 (s, 6 H), 3.70 (s, 2 H) ppm; UV (dioxane) 370 nm (ε 5200), 255 (4800, sh), 232 (9800); fluorescence (dioxane) 425 nm 0.35); 0.71); mass spectrum, *m/e* 221 (M^+).

9,10-Dioxa-*syn*-(trimethylammoniomethyl,methyl)(bromomethyl,methyl)bimane Bromide (25). Trimethylammonio quaternary salts were prepared by a straightforward procedure using a titrated solution of trimethylamine prepared by bubbling trimethylamine into dry CH_3CN. Trimethylamine in CH_3CN (0.025 M, 20 mL, 0.5 mmol) was added dropwise over 15 min to *syn*-($BrCH_2,CH_3$)B (**3**; 175 mg, 0.5 mmol) in CH_3CN (15 mL). After the mixture was stirred for 6 h at room temperature the yellow precipitate was filtered off and crystallized from EtOH–*i*-PrOH (15:2) to give *syn*-(($(CH_3)_3N^+CH_2,CH_3,Br^-$)($BrCH_2,CH_3$)B (**25**) as a solid: 164 mg (79%); yellow crystalline powder; dec 210–220 °C; IR (KBr) 3000, 2970, 1755 (br), 1675, 1660, 1470, 1400, 1330, 1215, 1105, 1050, 970, 900 cm^{-1}; ^1H NMR (D_2O) 1.937 (s, 3 H), 2.084 (s, 3 H), 3.401 (s, 9 H), 4.708 (s, 2 H), 4.809 (s, ca. 2 H) ppm; UV (H_2O) 380 nm (ε 5200), 243 (13 100).

9,10-Dioxa-*syn*-(trimethylammoniomethyl,methyl)bimane Dibromide (26). Reaction of trimethylamine in CH_3CN (4 equiv, 30 mL) with *syn*-($BrCH_2,CH_3$)B (**3**; 175 mg, 0.5 mmol) in CH_3CN (15 mL) over 16 h at room temperature gave *syn*-(($(CH_3)_3N^+$-CH_2,CH_3,Br^-)B (**26**) as a somewhat hygroscopic yellow solid, which was crystallized from ethanol: 193 mg (82%); yellow crystalline powder; dec 220–225 °C; IR (KBr) 3000, 2950, 1755, 1655, 1600, 1470, 1410, 1330, 1250, 1000, 955 cm^{-1}; ^1H NMR (D_2O) 2.119 (s, 3 H), 3.349 (s, 9 H), 4.888 (s, 2 H) ppm; UV (H_2O) 393 nm (ε 6700), 263 (sh), 237 (13 000); fluorescence (H_2O) 465 nm (ϕ_F 0.66).

9,10-Dioxa-*syn*-(trimethylammoniomethyl,methyl)(methyl,methyl)bimane Bromide (27). Trimethylamine in CH_3CN (0.55 mmol, 3 mL) and *syn*-($BrCH_2,CH_3$)(CH_3,CH_3)B (**2**; 135 mg, 0.5 mmol) in CH_3CN (15 mL) were stirred together for 16 h at room temperature, and the yellow solid was filtered off quickly, dried under vacuum, and crystallized from ethanol to give *syn*-(($(CH_3)_3N^+CH_2,CH_3,Br^-$)($CH_3,CH_3$)B (**27**) as a solid: 137 mg (86%); yellow crystalline powder; dec 210–215 °C; IR (KBr) 3000, 2950, 1740 (br), 1630, 1575, 1410, 1260, 1005, 955 cm^{-1}; ^1H NMR (D_2O) 1.826 (s, 3 H), 2.038 (s, 3 H), 2.517 (s, 3 H), 3.362 (s, 9 H), 4.773 (s, ca. 2 H) ppm; UV (H_2O) 376 nm (ε 4700), 267 (sh), 232 (15 700); fluorescence (H_2O) 477 nm (ϕ_F 0.062).

9,10-Dioxa-*syn*-(aminomethyl,methyl)(methyl,methyl)bimane (30). *syn*-($BrCH_2,CH_3$)(CH_3,CH_3)$_B$ (**2**; 500 mg, 1.85 mmol) in CH_3CN (10 mL) was reacted with aqueous ammonia (30%, 2 mL, 30 mmol). After 3 h, the solvent was removed and the residue chromatographed on silica gel (eluant CH_2Cl_2) to yield first *syn*-(CN,CH_3)(CH_3,CH_3)$_B$ (**31**), 15 mg (4%), and then *syn*-(NH_2CH_2,CH_3)(CH_3,CH_3)B (**30**), 173 mg (45%). Similar results were obtained from the reaction of NH_3 gas with a solution of *syn*-($BrCH_2,CH_3$)(CH_3,CH_3)B in CH_3CN.

***syn*-(NH_2CH_2,CH_3)(CH_3,CH_3)B (30)**: yellow crystals (*i*-PrOH); mp 183 °C; IR ($CHCl_3$) 3460, 3410 (weak), 2930 (weak), 1740, 1660, 1595, 1425, 1390, 1245, 1200, 1170, 1020, 970, 940, 910 cm^{-1}; ^1H NMR ($CDCl_3$) 1.50 (s, 2 H, +D_2O, lost), 1.79 (s), 1.84 (s) (6 H), 2.41 (s, 3 H), 3.81 (s, 2 H) ppm; UV (dioxane) 370 nm (ε 6600), 255 (7600, sh), 232 (13 200); fluorescence (dioxane) 425 nm (ϕ_F 0.76); mass spectrum (CI), *m/e* 208 (M + 1)$^+$.

9,10-Dioxa-*syn*-(cyano,methyl)(methyl,methyl)bimane (31) [*syn*-(CN,CH_3)(CH_3,CH_3)B]: yellow crystals; mp 225 °C; IR ($CHCl_3$) 2250, 1755, 1680, 1630, 1460, 1405, 1390, 1255, 1195, 910 cm^{-1}; ^1H NMR ($CDCl_3$) 1.80 (s, 1 H), 2.30 (s), 2.40 (s) (2 H) ppm; UV (dioxane) 365 nm (ε 4200), 265 (3100, sh), 227 (8800); fluorescence (dioxane) 424 nm (ϕ_F 0.83); mass spectrum, *m/e* 203 (M^+).

9,10-Dioxa-*syn*-(*N*-acetylaminomethyl,methyl)bimane (32) and 9,10-Dioxa-*syn*-(aminomethyl,methyl)bimane (34). Application of the synthesis for the monoamino derivative **30** to *syn*-($BrCH_2,CH_3$)B (**3**) under these conditions or with liquid NH_3 at either −78 °C or −33 °C (reflux) led only to the μ-NH-*syn*-(CH_2,CH_3)B (the "bridged" imino derivative).[9] The diamino compound was synthesized by a two-step procedure. *syn*-($BrCH_2,CH_3$)B (**3**; 150 mg, 0.43 mmol) was thoroughly mixed with

acetamide (7.5 g, 130 mmol, mp 82 °C) and the mixture heated at ca. 100 °C for 24 h. After cooling, the mixture is thoroughly triturated with CH_2Cl_2, in which CH_3CONH_2 is not very soluble, and chromatographed on silica gel, using EtOAc as eluant. The first compound eluted proved to be the diacetamido derivative **32**, produced in 25% yield (35 mg) after crystallization. The second product was the bridged *N*-acetylimino compound (**33**),[9] identical with a sample produced from the bridged imino compound and readily hydrolyzed to that compound. The bridged *N*-acetylimino compound was formed in this reaction in approximately 10–15% yield, but was the major product if the ratio of acetamide to dibromo compound were much smaller, e.g., 15:1. Hydrolysis of the diacetamido compound (20 mg) to the diamino derivative (**34**) was effected by 15% HCl at room temperature for 2 h. After neutralization of the acid with $NaHCO_3$, the product was extracted with CH_2Cl_2, and **34** was obtained as a yellowish solid, 10 mg (70%).

***syn*-($CH_3CONHCH_2,CH_3$)B (32)**: yellow needles (*i*-PrOH); mp 135 °C; IR (KBr) 3000 (weak), 2920 (weak), 1740, 1725 cm^{-1}; ^1H NMR ($CDCl_3$) 1.85 (1 H), 1.98 (3 H), 2.20 (3 H), 5.20 (2 H) ppm; UV (CH_3CN) 381 nm (ϵ 6000), 254 (4600), 232 (14400); mass spectrum, *m/e* 306 (M^+).

***syn*-(NH_2CH_2,CH_3)B (34)**: yellow crystals; mp 222 °C; IR (KBr) 3350 (strong), 2920 (weak), 1740 cm^{-1}; ^1H NMR (D_2O) 1.93 (s, 3 H), 3.39 (s, 2 H); UV (dioxane) 384 nm (ϵ 6600), 255 (7400, sh), 235 (15500); fluorescence (H_2O) 470 nm (ϕ_F 0.05); mass spectrum, *m/e* 222 (M^+).

9,10-Dioxa-*syn*-(4-(carbomethoxy)-1-pyridinomethyl,-methyl)bimane Dibromide (24). Methyl isonicotinate, a less active nucelophile, was refluxed with the dibromobimane without added *N,N*-diisopropylethylamine to give *syn*-(4-$CH_3OOCC_5H_4N^+CH_2,CH_3,Br^-$)B: yellow crystals (MeOH); mp 192 °C dec; IR (KBr) 3000, 1740, 1660, 1640, 1605, 1435, 1305, 1290, 1230, 1120 cm^{-1}; ^1H NMR (D_2O) 1.85 (s, 6 H), 4.30 (s, 6 H), 6.50 (s, 4 H), 8.85 (d, 4 H), 9.50 (d, 4 H) ppm; UV (methanol) 465 nm (ϵ 500), 363 (7000), 270 (7100, sh), 229 (27000).

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Bimanes. 7. Synthesis and Properties of 4,6-Bridged *syn*-1,5-Diazabicyclo[3.3.0]octa-3,6-diene-2,8-diones (μ-Bridged 9,10-Dioxabimanes)

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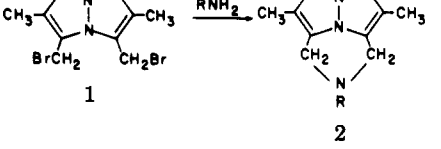
The reaction of *syn*-4,6-bis(bromomethyl)-1,5-diazabicyclo[3.3.0]octa-3,6-diene-2,8-diones with appropriate difunctional nucleophiles leads to 4,6-bridged *syn*-1,5-diazabicyclo[3.3.0]octa-3,6-diene-2,8-diones (μ-bridged 9,10-dioxabimanes), in which the bridging atoms are carbon, nitrogen, and sulfur. Substituents on the bridging atoms include the following: (a) (on carbon) H, $COOCH_3$, H, COOH, $(COOCH_3)_2$, $(COOC_2H_5)_2$, $(CN)_2$; (b) (on nitrogen) H, OH, $COCH_3$, CH_3, C_2H_5, $(CH_3)_3C$, CH_2CH_2OH, $C(CH_2OH)_3$, $C(CH_2OH)_n(CH_2OCOR)_{3-n}$ (n = 0, 1, 2; R = CH_3, $C_{15}H_{31}$, $C_{11}H_{23}$), $C(CH_2OH)(CH_2OC(CH_3)_2OCH_2$, $(CH_3)_2^+$, C_6H_4X (X = H, CH_3O, CH_3, CN, Br, Cl, $COOC_2H_5$), $(CH_3)(C_6H_4X)^+$ (X = CH_3, Cl); (c) (on sulfur) none, CH_3^+, O_2.

Introduction

In the course of studying the reaction of the *syn*-dibromodioxabimane **1** [*syn*-4,6-bis(bromomethyl)-3,7-dimethyl-1,5-diazabicyclo[3.3.0]octa-3,6-diene-2,8-dione or *syn*-($BrCH_2,CH_3$)B][2] with simple amines, RNH_2, products were isolated that were found to have properties consistent with a "bridged" structure, in which an atom linked the carbons substituted on the 4- and 6-positions of the 1,5-diazabicyclooctane structure (**2**, eq 1).[3]



1 2 (1)

The ring-forming reaction seemed so promising for the preparation of new heterocyclic compounds with interesting photophysical properties and strained rings that a substantial number of derivatives were prepared and ex-

(1) (A) Tel-Aviv University. (b) State University of New York, Stony Brook.

(2) The nomenclature of bimane derivatives is thoroughly discussed in Bimanes 5: Kosower, E. M.; Pazhenchevsky, B. *J. Am. Chem. Soc.* **1980**, *102*, 4983-4993.

(3) Kosower, E. M.; Pazhenchevsky, B.; Dodiuk, H.; Kanety, H.; Faust, D. *J. Org. Chem.*, preceding paper in this issue.

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