servations are consistent with the work of Negishi et al.,[2] who found recently internal addition favored in the $(\eta^5\text{-}C_5H_5)_2ZrCl_2$ promoted alkylation of alkynes. Finally, it was observed that the trimethylsilyl ether of 3-butyn-1-ol could be ethylated at −25 °C in high yield to give products I and II; at 0 °C, the overall yield was much lower; however, the product was nearly all *trans*-3-hexen-1-ol. Thus, it appears that the use of trimethylsilyl ether derivatives of alkynols may under certain conditions be used to modify carbometalation selectivity. Alexakis, Normant, and Villieras[23] have investigated the addition of alkylcopper–magnesium bromide reagents to the trimethylsilyl derivatives of 2-propynol and 3-butyn-1-ol. Compared with other analogous 2-propynyl and 3-butynyl systems, they found that "steric crowding on the heteroatom... enhances the ratio of branched to linear product". This substantial difference relative to our system (which favors the linear product) is not surprising at this point since the chemistry of organotitanium–aluminum systems is often quite different from that of organocopper reagents, e.g., olefin polymerization reactions.

In conclusion, we have found that the carbometalation of selected alkynols can be accomplished under mild conditions with transition metal–organoalane systems. It seems reasonable to expect that further studies with a variety of transition-metal species will lead to systems capable of giving stereo- and regioselective carbometalations of unsaturated substrates.

Acknowledgment. The authors thank the donors of the Petroleum Research Fund, administered by the American Chemical Society, for partial support of this work. We also thank the duPont Company for funds to purchase instrumentation used in these studies, the Ethyl Corporation for gifts of organoaluminum reagents, and Hercules Inc. for the gift of $(\eta^5\text{-}C_5H_4CH_3)_2TiCl_2$. Professors M. D. Schiavelli and R. A. Coleman are acknowledged for helpful discussions.

Registry No. I, 928-97-2; II, 1708-98-1; III, 24469-79-2; IV, 59518-08-0; V, 64275-74-7; VI, 71097-17-1; VII, 71097-18-2; VIII, 71097-19-3; IX, 63714-11-4; X, 71097-20-6; XI, 71097-21-7; XIII, 764-37-4; XIV, 763-32-6; 4-ethyl-4-penten-6-ol, 63714-12-5; *trans*-4-hepten-2-ol, 58927-81-4; 3-butyn-1-ol, 927-74-2; 4-pentyn-1-ol, 5390-04-5; 5-hexyn-1-ol, 928-90-5; 4-pentyn-2-ol, 2117-11-5; 5-hexyn-3-ol, 19780-84-8; 3-pentyn-1-ol, 10229-10-4; 3-hexyn-1-ol, 1002-28-4; bis(η^5-cyclopentadienyl)titanium dichloride, 1271-19-8; diethylaluminum chloride, 96-10-6; bis(η^5-methylcyclopentadienyl)titanium dichloride, 1282-40-2; triethylaluminum dimer, 15203-25-5; trimethylaluminum dimer, 15632-54-9; 3-butyn-1-ol trimethylsilyl ether, 17869-75-9; diethylaluminum chloride dimer, 51466-48-9; bis(η^5-cyclopentadienyl)zirconium dichloride, 1291-32-3.

(23) (a) A. Alexakis, J. F. Normant, and J. Villieras, *J. Mol. Catal.*, 1, 43 (1975/76); (b) *J. Organomet. Chem.*, **96**, 471 (1975).

Mercuric Trifluoroacetate Mediated Brominative Cyclizations of Dienes. Total Synthesis of *dl*-3β-Bromo-8-epicaparrapi Oxide

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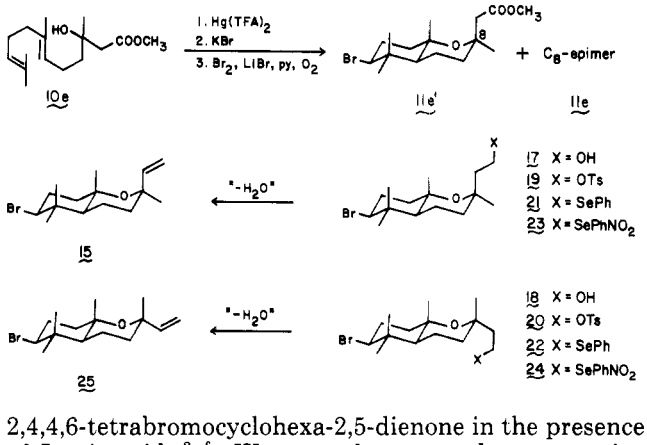
Received March 20, 1979

Mercuric trifluoroacetate induces the electrophilic cyclization of homogeranic acid and diene alcohols **10** with concomitant carbon–carbon bond formation to generate the bicyclic organomercury compounds **2** and **12**. The mercury substituent can be stereospecifically replaced by bromine with either retention or inversion of configuration to give the bromides **1** or **4** and **11** or **14**, respectively. Application of this net brominative cyclization to a synthesis of *dl*-3β-bromo-8-epicaparrapi oxide (**15**) in seven steps and 12% yield from geranylacetone is described.

The widespread occurrence of bromine-containing natural products from marine organisms[1] has prompted a number of investigations designed to establish methods for incorporation of a bromine atom into cyclic substrates via, formally, bromonium ion initiated polyolefin cyclizations.[2] Reagent systems that have been used successfully in this endeavor include *N*-bromosuccinimide,[3a–c] bromine in the presence of Lewis acids such as $AlBr_3$ and $SnBr_4$,[3d] bromine in the presence of silver(I) ion,[3d] and 2,4,4,6-tetrabromocyclohexa-2,5-dienone in the presence of Lewis acids.[3e,f] We recently reported an extensive investigation of the brominative cyclization of homogeranic acid to generate the trans-fused bromo lactone **1**.[4] The most efficient conditions for this cyclization appeared to

Scheme I



(1) For reviews and monographs with leading references see: Faulkner, D. J. *Tetrahedron* **1977**, *33*, 1421. Minale, L. *Pure Appl. Chem.* **1976**, *48*, 7. Baker, J. T. *Ibid.* **1976**, *48*, 35. Premuzic, E. *Fortschr. Chem. Org. Naturst.* **1971**, *29*, 417. Sinda, J. F.; DeBernardis, J. F. *Lloydia* **1973**, *36*, 107. Scheuer, P. J. "Chemistry of Marine Natural Products"; Academic Press: New York, N.Y., 1973. Baker, J. T.; Murphy, V. "Compounds from Marine Organisms"; CRC Press: Cleveland, Ohio, 1976; Vol. 1. Faulkner, D. J.; Fenical, W. "Marine Natural Products Chemistry"; Plenum Press: New York, 1977.

(2) Faulkner, D. J. *Pure Appl. Chem.* **1976**, *48*, 25.

(3) (a) van Tamelen, E. E.; Hessler, E. J. *Chem. Commun.* **1966**, 411; (b) Greenwood, J. M; Solomon, M. D.; Sutherland, J. K; Torre, A. *J. Chem. Soc. C* **1968**, 3004; (c) González, A. G.; Martin, J. D.; Pérez, C.; Ramírez, M. A. *Tetrahedron Lett.* **1976**, 137; (d) Wolinsky, L. E.; Faulkner, D. J. *J. Org. Chem.* **1976**, *41*, 597; (e) Kato, T.; Ichinose, I.; Kumazawa, S.; Kitahara, Y. *Bioorg. Chem.* **1975**, *4*, 188; (f) Kato, T.; Ichinose, I.; Kamoshida, A.; Kitahara, Y. *J. Chem. Soc., Chem. Commun.* **1976**, 518.

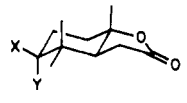
(4) Hoye, T. R.; Kurth, M. J. *J. Org. Chem.* **1978**, *43*, 3693.

0022-3263/79/1944-3461$01.00/0

be reaction of the diene acid with an excess (3 equiv) of bromine in the presence of an equimolar excess of silver fluoroborate in nitromethane, but the best yield for the desired conversion was only 15%. The excess brominating agent was necessary to eliminate competitive proton-initiated cyclizations to the nonbrominated lactones **6** and **9**.

It is known that mercuric ions can initiate cationic polyene cyclizations[5] and that carbon–mercury bonds can be converted to carbon–bromine linkages by reaction with molecular bromine.[6] Coupling of these two transformations would lead to a net brominative cyclization, and this paper reports the reduction of this concept to practice.

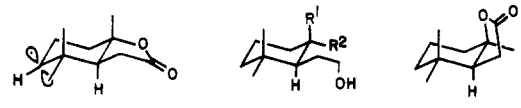
Homogeranic acid was the first substrate investigated since the desired ultimate product, bromo lactone **1**, was previously characterized.[4] Reaction of homogeranic acid with mercuric trifluoroacetate [$Hg(TFA)_2$] in nitromethane solution led after solvent removal to a crude, oily organomercuric trifluoroacetate, **2**. Rather than isolate the trifluoroacetate derivative, we routinely subjected the crude nitromethane reaction mixtures to saturated KBr solution to effect conversion to the more readily handled, powdery organomercuric bromide **3**. The stereochemistry at the mercury-bearing carbon was confirmed by the appearance of H_{ax} as a broad doublet of doublets (J = 12 and 5 Hz) at δ 2.86 and 2.67 in the ^1H NMR spectra[5b] of **2** and **3**, respectively.



1 X = Br Y = H_{ax}
2 X = HgTFA Y = H_{ax}
3 X = HgBr Y = H_{ax}
4 X = H_{eq} Y = Br
6 X = H Y = H

The question of stereoselectivity in the conversion of bromomercuri lactone **3** to bromo lactone **1** was investigated next. When **3** was treated with molecular bromine in pyridine solution at room temperature, it was rapidly (<1 h) transformed into a mixture (~2:1) of the epimeric bromides **1** [H_{ax}: δ 3.90 (dd, J = 12 and 5 Hz)] and **4** [H_{eq}: δ 4.24 (dd, J = 3 and 3 Hz)]. However, by simply adding a slight excess of lithium bromide to the Br_2/pyridine solution and saturating both that and the substrate/pyridine solution with oxygen before mixing the two, we were able to effect the stereospecific conversion of **3** into bromide **1**. Alternatively, if the bromine and substrate were rapidly mixed in pyridine and immediately exposed to 300-nm light through Pyrex, the solution became colorless within minutes and epimer **4**, the result of inversion of configuration at the mercury-bearing carbon, could be isolated to the exclusion of epimer **1**.

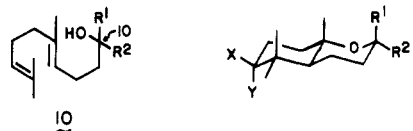
The stereospecificity displayed by these two reactions deserves comment. Predominant or sole retention of configuration has been observed previously for alkylmercurial to alkyl halide transformations.[7a] Bromine/pyridine complex and iodine in the presence of added iodide ion are particularly useful in maximizing this stereochemical control. The sometimes dramatic inhibitory effect of oxygen on radical pathways for halogenation has been noted.[7] Homolytic cleavage of the mercurials by halogen often leads to loss of stereochemistry. The present results are consistent with the following rationales. Competing radical and ionic processes lead to a mixture of **1** and **4** when bromine in pyridine alone is used for the halogenation. The addition of oxygen and lithium bromide then inhibits the homolytic pathway, promotes the frontside electrophilic halogenation reaction, possibly through the intervention of tribromide ion, and generates equatorial bromide **1** specifically. Alternatively, immediate irradiation at 300 nm initiates a rapid radical-chain reaction that leads to exclusive inversion of configuration, that stereochemistry resulting from preferential axial attack[8] of molecular bromine on the rigid neopentyl-like cyclohexyl radical **5**.



5 **7** R^1=CH_3 R^2=OH **9**
8 R^1=OH R^2=CH_3

The net brominative cyclization of homogeranic acid to bromo lactones **1** or **4** via the organomercury intermediates **2** and **3** proceeds on preparative scales in yields of 20–38%. The trans-fused nature of these bicyclic lactones was confirmed by sodium/liquid ammonia reduction of both **1** and **4** to the crystalline diol **7**. This compound was identical with the diol derived from lithium aluminum hydride reduction of the trans lactone **6** and not with the diol **8** from reduction of the cis lactone **9**. The stereochemistries of **6** and **9** are well established.[4]

The cyclization of diene alcohols of type **10** to bromo ethers of general structure **11** was also of interest.



10

11 X = Br Y = H_{ax}
12 X = HgTFA Y = H_{ax}
13 X = HgBr Y = H_{ax}
14 X = H_{eq} Y = Br

However, we were unable to observe the desired reaction mode by subjecting several **10** substrates to the previously used brominating conditions (vide supra).[3] Fortunately, these alcohols did undergo cationic cyclization with $Hg(TFA)_2$ to organomercuric trifluoroacetates of type **12**. These could then be transformed at will by the same methodology outlined above (i.e., via ligand exchange to the bromomercuri ethers **13** and subsequent stereospecific bromination) into the equatorial bromo ethers **11** or the axial bromo ethers **14**. It is noteworthy that proton H_{ax} in the ^1H NMR spectra at 80 and 100 MHz for the bicyclo[4.4.0] ethers **11** appeared as a characteristic six-line pattern, recognized as the X portion of an ABX system, rather than the simple doublet of doublets seen for the

(5) For examples of other mercuric ion initiated carbocycle formation see: (a) Julia, M.; Colomer, E.; Julia, S. *Bull Soc. Chim. Fr.* **1966**, 2397; (b) Julia, M.; Fourneron, J. D. *Tetrahedron* **1976**, *32*, 1113, and earlier papers in that series; (c) Julia, M.; Gasquez, E. C. *Bull Soc. Chim. Fr.* **1973**, 1796; (d) Kurbanov, M.; Semenovsky, A. V; Smit, W. A.; Shmelev, L. V.; Kucherov, V. F. *Tetrahedron Lett.* **1972**, 2175; (e) Dyadchenko, A. I.; Semenovskii, A. V.; Smit, V. A. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1976**, 2276, 2281, and references cited therein; (f) Misumi, S.; Ohfune, Y.; Furusaki, A.; Shirahama, H.; Matsumoto, T. *Tetrahedron Lett.* **1976**, 2865; (g) Misumi, S.; Ohtsuka, T.; Ohfune, Y.; Sugita, K.; Shirahama, H.; Matsumoto, T. *Tetrahedron Lett.* **1979**, 31; (h) Misumi, S.; Ohtsuka, T.; Hashimoto, H.; Ohfune, Y.; Shirahama, H.; Matsumoto, T. *Tetrahedron Lett.* **1979**, 35; (i) Matsuki, Y.; Kodama, M.; Ito, S. "Abstracts of Papers", 177th National Meeting of the American Chemical Society, Honolulu, Hawaii, April 1979; American Chemical Society: Washington, D.C., 1979; ORGN 328; (j) Bates, D. K.; Jones, M. C. *J. Org. Chem.* **1978**, *43*, 3775.

(6) (a) Jensen, F. R.; Rickborn, B. "Electrophilic Substitution of Organomercurials"; McGraw-Hill: New York, 1968; (b) Larock, R. C. *Angew. Chem., Int. Ed. Engl.* **1978**, *17*, 27.

(7) (a) See ref 6a, pp 75–99, and references cited therein; (b) Keller, J. Ph.D. Dissertation, University of California, Los Angeles, 1948, as noted by Winstein, S.; Traylor, T. G. *J. Am. Chem. Soc.* **1956**, *78*, 2597.

(8) Kaplan, L. In "Free Radicals"; Kochi, J., Ed.; Wiley: New York, 1973; Vol. II, pp 393–405 gives a discussion of the stereochemical aspects of conformationally anchored cyclohexyl radicals as well as a cautionary note (p 393) regarding extrapolation of the results from reactions of simple cyclohexyl radicals to structurally more complex systems.

Table I. Conversion of Diene Alcohols 10 to Equatorial Bromides 11 and to Axial Bromides 14

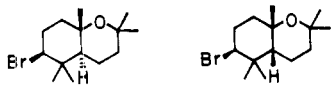
substrate alcohol (10)			equatorial bromide (11)				axial bromide (14)			
compd	R^1	R^2	compd	R^1	R^2	% yield[a]	compd	R^1	R^2	% yield[a]
10a[b]	H	H	11a	H	H	25[c]				
10b	Me	H	11b	Me	H	16	14b	Me	H	12
			11b′	H	Me	12	14b′	H	Me	10
10c	Me	Me	11c	Me	Me	26	14c	Me	Me	21
10d	Me	CN	11d	Me	CN	11				
			11d′	CN	Me	14				
10e	Me	CH_2CO_2Me	11e	Me	CH_2CO_2Me	>22[d]				
			11e′	CH_2CO_2Me	Me	>22				
10f	Me	$CH=CH_2$	no bicyclic ether formation with $Hg(TFA)_2$							

[a] Yields are for isolated and purified bromide and are based upon starting alcohol 10. [b] Sample 10a was actually a 3:1 mixture of *E* and *Z* isomers. [c] Product 11a consisted of a 3:1 mixture of trans- and cis-fused bicyclic ethers *trans*-11a (19% from 10a) and *cis*-11a (6% from 10a). [d] Esters 11e and 11e′ were reduced (DIBAL) before separation. Epimeric alcohols 17 and 18 were isolated each in 22% yield from 10e.

analogous proton in the bicyclo[4.3.0] lactone 1.

Table I summarizes the results of the $Hg(TFA)_2$ mediated brominative cyclizations of a variety of alcohols, **10a–10f**. The yields of bromo ethers 11 or 14 (19–44%) from 10 appear to be more or less independent of the primary (**10a**), secondary (**10b**), or tertiary (**10c–10e**) nature of the alcohol. Purification was generally not performed until after bromination of the crude organomercury intermediates. In an attempt to identify the portion of the overall process which accounts for the low to at best modest yields, **10c** was converted in the usual manner to **13c** ($R^1 = R^2 = CH_3$), and that organomercuric bromide was isolated by chromatography on silica gel as a white powder in 41% yield. On another occasion the pure bromomercuri lactone **3**, obtained by trituration with ethyl acetate, was converted into bromide **4** in 96% yield. These findings seem to implicate the cyclization rather than the bromination as the step responsible for the overall inefficiency.

The stereospecificity of the cyclization reactions and the stereochemical assignments outlined in Table I also deserve comment. Pure *E* olefins **10** gave trans-fused bicyclic bromo ethers **11** and **14** stereospecifically. The stereochemical nature of the ring fusion was proved rigorously for the products derived from **10a** and **10e**. In the former instance the sample of diene alcohol **10a** was actually a 3:1 mixture of *E* and *Z* olefins which led to a 3:1 ratio of products *trans*-**11a** and *cis*-**11a**, respectively. In the



IIa *trans* IIa *cis*

proton NMR spectra of these isomers the bridgehead methyl absorption had a larger width at half-height for *trans*-**11a** than for *cis*-**11a**.[9] In addition, the absorption for proton H_{ax} in *trans*-**11a** appeared at nearly the same chemical shift and had the same multiplicity as was observed for compounds **11b–11e**, **11b′**, **11d′**, and **11e′**, whereas the analogous proton in *cis*-**11a** differed in both these respects. In the case of **11e** and **11e′** the trans ring fusion was confirmed by ultimate conversion to a naturally occurring material of defined stereochemistry (vide infra). The remaining compounds in Table I are assigned a trans ring fusion by analogy to the mercuric ion initiated cyclizations just discussed and previously reported[5e] and on the assumption that the cyclizations proceed in a manner consistent with the Stork–Eschenmoser hypothesis.[10]

Enantiomeric substrates (**10b**, **10d**, and **10e**) gave nearly equal amounts of the two possible diastereomeric bromo ethers (cf., **11b/11b′**, **14b/14b′**, **11d/11d′**, and **11e/11e′** ratios), implying that the approach of mercuric ion to the terminal olefin is not influenced by the nature of the stereocenter at the remote end (C-10) of the dienes **10**. The relative stereochemical assignments for these epimeric pairs are based on proton NMR analyses. For instance, the crystalline nitriles **11d** ($R_1 = Me_{ax}$, $R_2 = CN_{eq}$) and **11d′** ($R_1 = CN_{ax}$, $R_2 = Me_{eq}$) could be distinguished by the fact that the bridgehead methyl group in the latter was deshielded[11] (δ 1.57) by the 1,3-diaxial cyano group relative to that methyl absorption in the former (δ 1.23). The assignments for **11b** ($R_1 = Me_{ax}$, $R_2 = H_{eq}$) and **11b′** ($R_1 = H_{ax}$, $R_2 = Me_{eq}$) as well as for **14b** ($R_1 = Me_{ax}$, $R_2 = H_{eq}$) and **14b′** ($R_1 = H_{ax}$, $R_2 = Me_{eq}$) are based upon the appearance of the ethereal methine proton at ~0.3 ppm lower field and with a smaller $W_{1/2}$ when it is equatorial (as in **11b** and **14b**) than when it is axial (as in **11b′** and **14b′**). The 1:1 mixture of epimeric esters **11e** and **11e′** was not readily separable by chromatography.

Finally, we would like to describe the application of this brominative cyclization to the total synthesis of *dl*-3β-bromo-8-epicaparrapi oxide (**15**), a natural product isolated from *Laurencia obtusa* collected from the English Channel,[12] and its C-8 epimer, **25**. The hindered nitriles **11d** and **11d′** were unreactive toward diisobutylaluminum hydride. In addition, the vinyl alcohol **10f**, which might have led to **15** and **25** directly, did not undergo the desired cyclization with $Hg(TFA)_2$, presumably due to interfering ionization of the labile allyl alcohol. Consequently, the ultimately successful strategy involved incorporation of a two-carbon precursor to the vinyl group into the alcohol **10** before the cyclization reaction. Thus the sequence (see Scheme I) began with the β-hydroxy ester **10e** derived from the Reformatsky reaction of geranylacetone and methyl bromoacetate. Cyclization of **10e** with $Hg(TFA)_2$, exposure to saturated KBr, and bromination gave the inseparable esters **11e** and **11e′**. These were reduced (DIBAL) and separated to provide the epimeric alcohols **17** and **18**, each in 22% isolated yield from hydroxy ester **10e**. Unam-

(9) Williamson, K. L.; Howell, T.; Spencer, T. A. *J. Am. Chem. Soc.* **1966**, *88*, 325.

(10) Stork, G.; Burgstahler, A. W. *J. Am. Chem. Soc.* **1955**, *77*, 5068. Eschenmoser, A.; Ruzicka, L.; Jeger, O; Arigoni, D. *Helv. Chim. Acta* **1955**, *38*, 1890. For reviews which discuss other examples of cationic polyene cyclizations obeying this principle see: Harding, K. E. *Bioorg. Chem.* **1973**, *2*, 248. Johnson, W. S. *Ibid.* **1976**, *5*, 51.

(11) See Cross, A. D.; Harrison, I. T. *J. Am. Chem. Soc.* **1963**, *85*, 3223 for a discussion of cyano group shielding and deshielding effects. (b) See also Lombardi, P.; Cookson, R. C.; Weber, H. P; Renold, W.; Hauser, A.; Schulte-Elte, K. H.; Willholm, B.; Thommen, W.; Ohloff, G. *Helv. Chim. Acta* **1976**, *59*, 1158 for assignments of the epimeric norbromo acetylenes corresponding to nitriles **11d** and **11d′**.

(12) Faulkner, D. J. *Phytochemistry* **1976**, *15*, 1992.

biguous assignment of stereochemistry at C-8 for these two substances was not possible. Therefore each alcohol was converted by formal dehydration into the corresponding vinyl derivative and only one of these, of course, was identical with the natural substance, **15**. These transformations were initially effected by formation of the *p*-toluenesulfonates **19** and **20**, displacement with sodium phenyl selenoate to give the selenides **21** and **22**, and oxidative elimination to **15** and its C-8 epimer **25**. The overall yields for these net dehydrations (43% for both **17** and **18**) were substantially improved by the independent reaction of alcohols **17** and **18** with *o*-nitrophenyl selenocyanate and tri-*n*-butylphosphine[13] to give the arylselenides **23** (crystalline) and **24** (oil) which, upon room temperature oxidation, spontaneously eliminated *o*-nitrophenylselenenic acid to provide **15** (85% from **17**) and **25** (93% from **18**), respectively. The identity of spectral data for synthetic **15** with that from the natural sample[12,14] allowed for the complete assignment of stereochemistry in compounds **17**–**24**. The synthesis of 3β-bromo-8-epicaparrapi oxide proceeded in seven steps and 12% overall yield and involved one chromatographic separation.

In summary, the mercuric trifluoroacetate mediated brominative cyclization leads to improved yields of lactones (**1** and **4**), allows for the generation of bicyclic bromo ethers (**11** and **14**) from substrate alcohols (**10**) which apparently do not cyclize under previously used conditions, and is the key reaction in this synthesis of *dl*-3β-bromo-8-epicaparrapi oxide (**15**). Further applications of this method to problems in the area of marine natural product synthesis are under investigation.

Experimental Section

General. Melting points were determined on a Kofler hot stage and are uncorrected. Elemental analyses were performed by M-H-W Laboratories, Phoenix, Arizona. Column chromatography was carried out under pressure on silica gel H for TLC (EM 7736, Type 60) using a modification of the short column chromatography technique.[15] Infrared spectra were recorded on a Perkin-Elmer 237 instrument, nuclear magnetic resonance spectra were obtained on Varian HFT-80 and XL-100 instruments in the Fourier transform mode, and mass spectra were determined on AEI MS-30 (electron impact, EI) and Finnigan 4000 (chemical ionization, CI) instruments.

Preparation of Bromo Lactone 1 from Homogeranic Acid. Homogeranic acid[4] (1.70 g, 9.34 mmol) was dissolved in 15 mL of CH_3NO_2 and treated under a nitrogen atmosphere at room temperature with a solution of mercuric trifluoroacetate ($Hg(TFA)_2$, 4.38 g, 10.3 mmol) in 10 mL of CH_3NO_2. After stirring the solution for 40 min the crude trifluoroacetate **2** could be isolated if desired by dilution with H_2O, extraction with CH_2Cl_2, drying ($MgSO_4$), and removal of solvent to leave a crude sample of an oily brown solid: IR ($CHCl_3$) 1770, 1690, 1180 cm^{-1}; NMR ($CDCl_3$) δ 1.13 (s, 6 H), 1.39 (s, 3 H), 1.4–2.6 (m), 2.86 (br dd, J = 12, 5 Hz, 1 H). The crude solution of **2** in CH_3NO_2 was poured into 170 mL of saturated KBr solution and stirred with thorough mixing in the dark at room temperature for 5 days. Extraction with CH_2Cl_2, drying ($MgSO_4$), and solvent removal left the crude bromomercuri lactone **3** as a brown solid (3.34 g, 7.24 mmol, 78%). A portion was recrystallized from CH_2Cl_2 (1×) and acetone (1×) to leave a white powder: mp 144–151 °C; IR ($CHCl_3$) 1780 cm^{-1}; NMR ($CDCl_3$) δ 1.13 (s, 6 H), 1.39 (s, 3 H), 1.5–2.55 (m), 2.67 (br dd, J = 12, 5 Hz, 1 H); MS (EI) m/e (%) [464 (4)] × 10, [463 (3)] × 10, [462 (2)] × 10, [461 (5)] × 10, [460 (2)] × 10, [459 (2)] × 10, 181 (100). Crude **3** (3.34 g, 7.24 mmol) was dissolved in 24 mL of pyridine, purged with O_2, and treated in the dark at room temperature with an O_2 saturated solution of LiBr (1.26 g, 14.5 mmol) and Br_2 (1.28 g, 7.97 mmol) in 19 mL of pyridine. After 20 h the reaction mixture was diluted with Et_2O, washed with 2 N HCl (4×), water, saturated $NaHCO_3$, and brine, dried ($MgSO_4$), and concentrated to leave a crude oil (1.32 g) which was chromatographed on silica gel (80 g, 5:1 hexanes/EtOAc) to give crystalline bromo lactone **1** (485 mg, 20% from homogeranic acid) with spectral properties identical with those previously reported.[4] On a 0.5-g scale reaction a 33% overall yield was obtained. No evidence for the presence of epimeric bromo lactone **4** was found.

Preparation of Bromo Lactone 4 from 3. The bromomercuri lactone **3** (200 mg, 0.434 mmol), which had been triturated with EtOAc to effect partial purification, was dissolved in 1.5 mL of dry pyridine and placed in a 0.5 × 26 cm Pyrex tube. A solution of Br_2 (25 μL, 0.48 mmol) in 1.8 mL of pyridine was added rapidly via syringe to effect efficient mixing immediately after the tube had been placed in the center of a Rayonet photochemical reactor, mounted with 300-nm wavelength bulbs. After being irradiated for 10 min the mixture was diluted with CH_2Cl_2, washed with 2 N HCl (2×), water, and brine, dried ($MgSO_4$), and concentrated to leave the axial bromo lactone **4** as a yellow solid (107 mg, 0.412 mmol, 96% from **3**, 38% from homogeranic acid). NMR analysis of the crude product showed no evidence for the epimeric bromo lactone **1**. Recrystallization from hexanes/EtOAc (4×) gave an analytical sample: mp 114–118 °C; IR ($CHCl_3$) 1775 cm^{-1}; NMR ($CDCl_3$) δ 1.11 (s, 6 H), 1.37 (s, 3 H), 1.8–2.8 (m, 7 H), 4.24 (dd, J = 3.3 Hz, 1 H); MS (CI, NH_3) 280 and 278 ($M + NH_4^+$). Anal. Calcd for $C_{11}H_{17}BrO_2$: C, 50.59; H, 6.56; Br, 30.60. Found: C, 50.65; H, 6.80; Br, 30.53.

Preparation of Trans Diol 7 from Trans Lactone 6. A 2:1 mixture[4] of trans lactone **6** and cis lactone **9** (300 mg, 1.65 mmol) was dissolved in 20 mL of dry THF and added slowly to $LiAlH_4$ (115 mg, 3.28 mmol) under N_2. This mixture was stirred for 11 h at room temperature, quenched with 120 μL of H_2O, 120 μL of 10% NaOH, and 350 μL of H_2O, diluted with Et_2O, filtered, washed with brine, dried ($MgSO_4$), and concentrated to leave 254 mg of a mixture of diols **7** and **8** which were purified by chromatography on silica gel (25 g, EtOAc; TLC: R_f(**7**) 0.7, R_f(**8**) 0.2 in 1:1 hexanes/EtOAc) to give crystalline **7** (135 mg, 66%), which was recrystallized (3× hexanes/EtOAc) to give an analytical sample: mp 102–103 °C; IR (KBr) 3250, 1385, 1370, 1030 cm^{-1}; NMR ($CDCl_3$) δ 0.82, 0.93, 1.22 (3 s, 3 CH_3), 1.2–1.9 (m, 8 H), 3.0 (br s, 2 H), 3.32–3.92 (m, 2 H); MS (CI, NH_3) m/e (%) 204 (5, $M + NH_4^+$), 186 (100, $M + NH_4^+ - H_2O$), 169 (100, $M + H^+ - H_2O$); MS (EI) 171 (1), 168 (1), 153 (9), 109 (46), 71 (89), 69 (42), 43 (100). Anal. Calcd for $C_{11}H_{22}O_2$: C, 70.92; H, 11.90. Found: C, 70.70; H, 12.15.

Preparation of Trans Diol 7 from Bromo Lactones 1 and 4. In separate experiments lactones **1** (72 mg, 0.28 mmol) and **4** (92 mg, 0.35 mmol) in 1 mL of dry THF were added to a preformed solution of sodium (70 mg, 3.0 mmol and 81 mg, 3.5 mmol, respectively) in 5 mL of liquid NH_3. The reaction mixtures were allowed to reflux for 55 min and were quenched with 0.5 mL of absolute EtOH. The NH_3 was evaporated, saturated NH_4Cl was added, the mixtures were extracted with CH_2Cl_2, and the organic layers were dried ($MgSO_4$) and concentrated to leave crude (>90% pure by NMR) diol **7** (29 mg, 51% from **1** and 38 mg, 58% from **4**), the NMR spectra of which were identical with that of authentic **7** described above.

Preparation of Cis Diol 8 from Cis Lactone 9. The pure cis lactone **9**[4] (124 mg, 0.681 mmol) was reduced with $LiAlH_4$ (50 mg, 1.4 mmol) by the same procedure described above for the reduction of **6** to **7** to afford crystalline diol **8** (119 mg, 94%), which was recrystallized (3×, hexanes/EtOAc) to give an analytical sample: mp 100.5–101.5 °C; IR (KBr) 3250, 1385, 1370, 1040 cm^{-1}; NMR ($CDCl_3$) δ 0.89, 0.99, 1.17 (3 s, 3 CH_3), 1.25–1.95 (m, 8 H), 3.61 (br t, J = 7 Hz, 2 H); MS (EI) m/e (%) 186 (1), 171 (8), 168 (7), 153 (32), 127 (83), 109 (98), 83 (66), 71 (100), 69 (76), 43 (79). Anal. Calcd for $C_{11}H_{22}O_2$: C, 70.92; H, 11.90. Found: C, 70.86; H, 12.16.

Preparation of Substrates 10a–10f. Compound **10a**[16] was prepared as a 3:1 mixture of *E* and *Z* isomers by $LiAlH_4$ reduction of geranylacetic acid, compounds **10b–10f** were prepared from (*E*)-geranylacetone[17] by $NaBH_4$ reduction (**10b**),[18] methyllithium

(13) Grieco, P. A.; Gilman, S.; Nishizawa, M. *J. Org. Chem.* **1976**, *41*, 1485.

(14) The original spectra were kindly provided by Professor D. John Faulkner for comparison purposes.

(15) Hunt, B. J.; Rigby, W. *Chem. Ind. (London)* **1967**, 1868.

(16) Chang, C.-F.; Tamura, S. *Agric. Biol. Chem.* **1972**, *36*, 2405.

addition (**10c**),[19] Reformatsky reaction with methyl bromoacetate (**10e**),[20] and vinylmagnesium bromide addition (**10f**, nerolidol). Cyanohydrin **10d**[21] was prepared[22] by adding (*E*)-geranylacetone (587 mg, 3.02 mmol) in 2 mL of CH_3NO_2 to a solution of 10 mg of ZnI_2 and trimethylsilyl cyanide (Me_3SiCN; 449 mg, 4.54 mmol) in 4 mL of CH_3NO_2 at room temperature. After 30 min (under similar conditions a reaction run in CD_3NO_2 and monitored by NMR analysis was over within 5 min) the solvent and excess Me_3SiCN were removed under reduced pressure to leave a crude trimethylsilylcyanohydrin (864 mg, 2.94 mmol, 98%): NMR (CD_3NO_2) δ 0.29 (s, 9 H), 1.66 (s, 3 H), 1.7 (br s, 9 H), 1.9–2.5 (m, 8 H), 5.15 (br m, 2 H), and 0.13 (residual Me_3SiCN). This crude oil (864 mg, 98%) was dissolved in 20 mL of dioxane and 5 mL of 0.5 N HCl was added. The solution was stirred at room temperature for 40 min, diluted with H_2O, and extracted with Et_2O. The combined extracts were washed with H_2O and brine, dried ($MgSO_4$), and concentrated to afford the cyanohydrin **10d** as a pale yellow oil (637 mg, 2.86 mmol, 95%): IR (neat) 3430, 2240 (w) cm^{-1}; NMR ($CDCl_3$) δ 1.60 (s, 6 H), 1.68 (br s, 6 H), 1.8–2.5 (m, 8 H), 5.09 (br q, 2 H).

General Procedure for Cyclization of Alcohols 10 to Organomercuric Trifluoroacetates 12 and Bromides 13. A solution (0.5 M) of alcohol **10** in dry CH_3NO_2 was treated with a solution (0.5 M) of mercuric trifluoroacetate (1.1 equiv) in dry CH_3NO_2 at room temperature. After about 10 min the mixture was added to saturated aqueous KBr (7 volume excess) in the dark and stirred rapidly overnight. The resulting heterogeneous mixture was extracted with CH_2Cl_2 (3×) and the extracts were dried ($MgSO_4$) and concentrated to leave crude **13**. This could if necessary be partially purified by trituration with pentane or EtOAc or crystallization from CH_2Cl_2 or acetone. If desired the crude trifluoroacetates **12** could be isolated by removal of CH_3NO_2 before KBr treatment. (The material containing **12a** and **13a** was actually obtained as a mixture of cis- and trans-fused rings because the precursor alcohol **10a** was a mixture of *E* and *Z* olefins.) The samples containing **12b**, **12d**, and **12e** and **13b**, **13d**, and **13e** were nearly 1:1 mixtures of epimers at C_8. The NMR ($CDCl_3$) spectra of crude **12** and **13** exhibited the appropriate number of methyl resonances and the axial methine proton on the mercury-bearing carbon routinely moved upfield by about 0.2–0.3 ppm upon exchanging the trifluoroacetate (**12**) to bromide (**13**). Appropriate clusters of peaks corresponding to ($M + H^+$) or ($M + NH_4^+$) were observed in the mass spectrum (CI, CH_4 or NH_3) for each of the mixtures of bromides **13**. The IR ($CHCl_3$) spectra of crude **12** characteristically showed absorptions of 1780 (m) and 1680 (s) cm^{-1} while those of **13** lacked absorption in the carbonyl region.

13c ($R^1 = R^2 = CH_3$). The crude product (1.03 g) from reaction of **10c** (689 mg, 3.28 mmol) as outlined above was purified by short-column chromatography on silica gel (15 g, 5:1 hexanes/EtOAc) to provide an as yet unidentified nonpolar olefin [230 mg, 1.11 mmol, 39%, mol wt 208 by MS (CI)] and **13c** (657 mg, 1.34 mmol, 41%) as a white powder: mp 159–169 °C; IR ($CHCl_3$) 2970, 2940, 2860, 1460, 1445, 1390, 1380, 1375, 1370, 1125, 1065, 980, 965, 935, 905, 840 cm^{-1}; NMR ($CDCl_3$) δ 0.98, 1.09, 1.16, 1.25, 1.31 (5 s, 5 CH_3), 1.2–2.2 (m, 9 H), 2.80 (dd, *J* = 10, 8 Hz, 1 H); MS (EI) *m/e* (%) 478 (1), 477 (8), 476 (4), 475 (10), 474 (6), 473 (7), 472 (3), 471 (2), 209 (18), 69 (100); MS (EI, CH_4) cluster at 487–495 ($M + H^+$). Further elution with pure EtOAc led to recovery of unidentifiable, polar, colored material (121 mg).

Conversion of 13 to Equatorial Bromides 11. The bromomercuri ether **13** was dissolved in dry pyridine (0.5 M) and the solution was saturated with O_2. A solution of bromine (1.1 equiv) and LiBr (1.1 equiv) in dry pyridine (0.5 M) also saturated with O_2 was added and the mixture was stirred in the dark overnight. The solution was diluted with Et_2O, washed with 2 N HCl (4×), H_2O, saturated $NaHCO_3$, and brine, dried ($MgSO_4$), and concentrated to leave the crude bromides **11**, which were chromatographed on silica gel (19:1 hexanes/EtOAc).

***trans*-11a and *cis*-11a.** *trans*-**11a** (19% from **10a**) as a colorless oil: IR (neat) 2950, 2860, 1455, 1390, 1375, 1215, 1150, 1085, 980, 880, 810, 765, 695 cm^{-1}; NMR ($CDCl_3$) δ 0.86, 1.05, 1.27 (3 s, 3 CH_3), 1.3–2.3 (m, 9 H), 3.6 (m, 2 H), 3.93 (m, ABX, 1 H); MS (EI) *m/e* (%) 262 (4), 260 (4), 247 (96), 245 (100), 165 (41), 139 (47), 98 (41). A small sample was further purified by molecular distillation [150 °C (1 mmHg)]. Anal. Calcd for $C_{12}H_{21}BrO$: C, 55.18; H, 8.10; Br, 30.59. Found: C, 54.97; H, 8.24; Br, 30.59. *cis*-**11a** (6% from **10a**) as a colorless oil: IR (neat) 2960, 2930, 2860, 1465, 1440, 1385, 1375, 1360, 1270, 1220, 1095, 1085, 1055, 1010, 975, 940, 885, 860 cm^{-1}; NMR ($CDCl_3$) δ 1.17, 1.19, 1.35 (3 s, 3 CH_3), 1.3–2.3 (m, 9 H), 3.65 (m, 2 H), 4.18 (m, 1 H); MS (EI) *m/e* (%) 262 (1), 260 (1), 247 (97), 245 (100), 180 (13), 165 (35), 139 (41), 111 (25), 98 (28); exact mass calcd ($C_{12}H_{21}{}^{79}BrO$) 260.0775, found 260.0746.

11b and 11b′. **11b′** (12% from **10b**) as a colorless oil: IR (neat) 2970, 2940, 2860, 1455, 1390, 1375, 1155, 1135, 1095, 1075, 1035, 1000, 955, 935, 875, 765, 695 cm^{-1}; NMR ($CDCl_3$) δ 0.86 (s, 3 H), 1.04 (s, 3 H), 1.07 (d, *J* = 7 Hz, 3 H), 1.26 (s, 3 H), 1.1–2.3 (m, 9 H), 3.64 (br m, 1 H, $W_{1/2} \approx 18$ Hz), 3.94 (m, ABX, 1 H); MS (EI) *m/e* (%) 276 (2), 274 (2), 261 (39), 259 (38), 194 (18), 179 (28), 112 (42), 69 (100); mol wt calcd ($C_{13}H_{23}{}^{79}BrO$) 274.0932, found 274.0921. **11b** (16% from **10b**) as a colorless oil: IR (neat) 2950, 2930, 2870, 1460, 1390, 1375, 1220, 1155, 1135, 1110, 1080, 1000, 960, 940, 870, 775, 695 cm^{-1}; NMR ($CDCl_3$) δ 0.93 (s, 3 H), 1.06 (s, 3 H), 1.14 (d, *J* = 7 Hz, 3 H), 1.26 (s, 3 H), 1.3–2.2 (m, 9 H), 3.94 (m, 2 H, $W_{1/2} < 12$ Hz); MS (EI) *m/e* (%) 276 (2), 274 (3), 261 (96), 259 (100), 153 (61), 123 (50), 69 (62); exact mass ($M^+ - CH_3$) calcd ($C_{12}H_{20}{}^{81}BrO$) 261.0678, found 261.0693.

11c (26% from **10c**) as a colorless oil: IR (neat) 2970, 2950, 2870, 1460, 1390, 1380, 1375, 1360, 1230, 1140, 1120, 1075, 985, 935, 870, 830, 765, 690 cm^{-1}; NMR ($CDCl_3$) δ 0.89, 1.07, 1.16, 1.25, 1.30 (5 s, 5 CH_3), 1.4–2.3 (m, 9 H), 3.95 (m, ABX, 1 H); MS (EI) *m/e* (%) 275 (22), 273 (22), 175 (28), 69 (74), 43 (100); MS (CI, CH_4) 291, 289 ($M + H^+$). Anal. Calcd for $C_{14}H_{25}BrO$: C, 58.13; H, 8.71; Br 27.63. Found: C, 58.22; H, 8.63; Br, 27.81.

11d and 11d′. **11d′** (14% from **10d**) as a crystalline solid which was sublimed [90 °C (0.5 mm)] to provide an analytical sample: mp 110.5–111.5 °C; IR (KBr) 2980, 2950, 2870, 2225 (w), 1475, 1460, 1440, 1390, 1380, 1375, 1185, 1155, 1100, 1075, 970, 880, 840, 775, 705 cm^{-1}; NMR ($CDCl_3$) δ 0.90, 1.07, 1.55, 1.57 (4 s, 4 CH_3), 1.2–2.3 (m, 9 H), 3.88 (m, ABX, 1 H); MS (EI) *m/e* (%) 301 (2), 299 (1), 286 (90), 284 (100), 259 (16), 257 (17), 220 (4), 204 (41). Anal. Calcd for $C_{14}H_{22}BrNO$: C, 56.00; H, 7.39; Br, 26.62; N, 4.66. Found: C, 55.96; H, 7.24; Br, 26.83; N, 4.55. **11d** (11% from **10d**) as a crystalline solid which was recrystallized from hexanes to give an analytical sample: mp 96.5–97.5 °C; IR ($CHCl_3$) 2980, 2880, 1460, 1395, 1380, 1150, 1125, 1105, 1080, 1010, 970, 880 cm^{-1}; NMR ($CDCl_3$) δ 0.96, 1.08, 1.23, 1.53 (4 s, 4 CH_3), 1.4–2.3 (m, 9 H), 3.97 (m, ABX, 1 H); MS (EI) *m/e* (%) 286 (90), 284 (100), 259 (14), 257 (9), 256 (19), 254 (15), 220 (3), 204 (52), 175 (41), 135 (49), 109 (52), 43 (57). Anal. Calcd for $C_{14}H_{22}BrNO$: C, 56.00; H, 7.39; Br, 26.62; N, 4.66. Found: C, 56.04; H, 7.34; Br, 26.79; N, 4.54.

11e and 11e′. The purified mixture of **11e** and **11e′** had the following properties: IR (neat) 1735, 1390, 1380 cm^{-1}; NMR ($CDCl_3$) δ 0.88 (s), 1.06 (s), 1.25 (s), 1.28 (br s), 1.34 (s), 1.3–2.3 (m), 2.40 (AB), 2.62 (AB), 3.61 (s), 3.93 (m, ABX); MS (EI) *m/e* (%) 333 (31), 331 (31), 275 (25), 273 (29), 175 (32), 135 (40), 69 (40), 43 (100), 41 (49); exact mass ($M^+ - CH_3$) calcd ($C_{15}H_{24}{}^{79}BrO_3$) 331.0908, found 331.0912; MS (CI, CH_4) 349, 347 ($M + H^+$).

Conversion of 13 to Axial Bromides 14. The bromomercuri ether **13** was dissolved in dry pyridine (0.5 M) in a Pyrex tube and a solution of bromine in pyridine (1.1 equiv, 0.5 M) was rapidly added via syringe to effect efficient mixing. The solution was immediately exposed to 300-nm irradiation in a Rayonet reactor for 10 min and worked up as for the other bromination reactions to leave crude product mixtures which were carefully chromatographed on silica gel (19:1 hexanes/EtOAc).

14b and 14b′. The yields of **14b** and **14b′** (colorless oils) were somewhat diminished because of accompanying formation of epimers **11b** and **11b′** as a result of poor initial mixing. The order

(17) Although commerical (Pfaltz and Bauer) and gratis (kindly provided by Givaudan Corp.) samples of "geranylacetone" were purported to consist of >95% of the *E* isomer, they were in fact ~2:1 mixtures of *E*/*Z* isomers and were carefully fractionated by spinning band distillation.

(18) Sarma, A. S.; Banerjee, S. *Indian J. Chem.* **1970**, *8*, 665.

(19) Ushakovia, I. B.; Rozenberg, L. M.; Genekh, I. S.; Sanin, P. I. *Neftekhimiya* **1968**, *8*, 651; *Chem. Abstr.* **1969**, *70*, 28303v.

(20) Svishchuk, A. A.; Basalkevich, E. D.; Vysotskii, N. N. *Ukr. Khim. Zh. (Russ. Ed.)* **1975**, *41*, 216; *Chem. Abstr.* **1975**, *83*, 10446c.

(21) Weichet, J.; Leiner, J.; Simek, A.; Capek, A. Czechoslovakian Patent 131 154, 1969; *Chem. Abstr.* **1970**, *72*, P132032h.

(22) Gassman, P. G; Talley, J. J. *Tetrahedron Lett.* **1978**, 3773.

of elution was **11b'** (4%), **14b'** (10%), **14b** (12%), and **11b** (8% from **10b**). **14b'**: IR (neat) 2950, 2870, 1455, 1395, 1375, 1210, 1090, 1040, 960, 930, 875, 850, 690 cm^{-1}; NMR ($CDCl_3$) δ 0.94 (s, 3 H), 1.04 (s, 3 H), 1.13 (d, J = 7 Hz, 3 H), 1.27 (s, 3 H), 1.3–2.3 (m, 9 H), 3.67 (m, 1 H, $W_{1/2}$ = 20 Hz), 4.22 (br dd, J = 3, 3 Hz); MS (EI) m/e (%) 276 (2), 274 (3), 261 (100), 259 (100), 195 (5), 179 (21), 153 (20), 123 (43), 112 (36), 69 (40), 55 (30), 43 (71); mol wt calcd ($C_{13}H_{23}{}^{79}BrO$) 274.0932, found 274.0939. **14b**: IR (neat) 2980, 2950, 2870, 1455, 1390, 1380, 1210, 1080, 965, 695 cm^{-1}; NMR ($CDCl_3$) δ 1.01 (s, 3 H), 1.04 (s, 3 H), 1.13 (d, J = 7 Hz, 3 H), 1.25 (s, 3 H), 1.3–2.3 (m, 9 H), 3.99 (m, 1 H, $W_{1/2}$ = 14 Hz), 4.21 (br dd, J = 3, 3 Hz, 1 H); MS (EI) m/e (%) 276 (2), 274 (1), 261 (38), 259 (46), 179 (23), 153 (33), 112 (76), 69 (48), 55 (45), 43 (100); exact mass ($M^+ - CH_3$) calcd ($C_{12}H_{20}{}^{81}BrO$) 261.0678, found 261.0679.

14c (21% from **10c**) as an oily solid which was sublimed [50 °C (1 mm)] to give an analytical sample: mp 63–64.5 °C; IR (thin film) 2970, 2950, 2870, 1455, 1390, 1380, 1375, 1210, 1140, 1110, 975, 705 cm^{-1}; NMR ($CDCl_3$) δ 0.96, 1.05, 1.19, 1.25, 1.29 (5 s, 5 CH_3), 1.3–2.3 (m, 9 H), 4.21 (br dd, J = 3, 3 Hz, 1 H); MS (EI) m/e (%) 275 (80), 273 (80), 257 (13), 255 (12), 175 (72), 167 (100), 149 (97), 126 (85), 69 (88), 43 (72); MS (CI, CH_4) 291, 289 ($M + H^+$). Anal. Calcd for $C_{14}H_{25}BrO$: C, 58.13; H, 8.71; Br, 27.63. Found: C, 57.89; H, 8.63; Br, 27.64.

Preparation of 17 and 18 from 11e and 11e'. A crude mixture of esters **11e** and **11e'** (1.82 g, 5.24 mmol) was dissolved in 50 mL of dry THF, cooled to 0 °C under N_2, and treated with diisobutylaluminum hydride (31 mL of 1.0 M solution in hexanes). After 15 min 5 mL of absolute MeOH was carefully added, and the mixture was poured into 150 mL of 0.5 N HCl and stirred at room temperature for 40 min. Extraction with Et_2O, washing the combined extracts with saturated $NaHCO_3$ and brine, drying ($MgSO_4$), and solvent removal left a crude oil (1.59 g) which was chromatographed on silica gel (160 g, 3:1 hexanes/EtOAc) to give alcohol **18** (502 mg, 1.57 mmol, 22% from **10e**) as a colorless oil: IR (neat) 3425, 2950, 2870, 1460, 1390, 1380, 1140, 1120, 1080, 1040, 1000, 940, 875, 775, 695 cm^{-1}; NMR ($CDCl_3$) δ 0.88 (s, 3 H), 1.07 (s, 3 H), 1.30 (s, 6 H), 1.2–2.3 (m, 12 H), 3.75 (m, 2 H), 3.91 (m, ABX, 1 H); MS (EI) m/e (%) 305 (18), 303 (18), 287 (4), 285 (3), 275 (55), 273 (56), 257 (13), 255 (13), 175 (66), 135 (100), 43 (77), exact mass ($M^+ - CH_3$) calcd ($C_{14}H_{24}{}^{81}BrO$) 305.0939, found 305.0942; MS (CI, CH_4) 321, 319 ($M + H^+$). Compound **18** was followed by **17** (499 mg, 1.56 mmol, 22% from **10e**) as a colorless oil: IR (neat) 3350, 2950, 2870, 1450, 1390, 1375, 1215, 1145, 1100, 1080, 995, 935, 875, 770, 695 cm^{-1}; NMR ($CDCl_3$) δ 0.92 (s, 3 H), 1.03 (s, 3 H), 1.21 (s, 3 H), 1.32 (s, 3 H), 1.3–2.2 (m, 12 H), 3.75 (m, 2 H), 3.95 (m, ABX, 1 H); MS (EI) m/e (%) 305 (16), 303 (17), 287 (5), 285 (4), 275 (100), 273 (100), 257 (36), 255 (37), 175 (99), 135 (88), exact mass ($M^+ - CH_2CH_2OH$) calcd ($C_{13}H_{22}{}^{81}BrO$) 275.0834, found 275.0853; MS (CI, CH_4) 321, 319 ($M + H^+$).

Preparation of Phenyl Selenides 21 and 22 via Toluenesulfonates 19 and 20. Alcohol **17** (100 mg, 0.313 mmol) was dissolved in 1 mL of dry pyridine, treated with TsCl (120 mg, 0.627 mmol), stirred overnight under N_2 at room temperature, and poured into ice water. Extraction with Et_2O, washing of the extracts with 2 N HCl (3×), saturated $NaHCO_3$, and brine, drying ($MgSO_4$), and concentration left crude **19** (105 mg, 71%): IR (neat) 3000, 2970, 2940, 2860, 1600, 1460, 1390, 1375, 1360, 1180, 955, 815, 775, 660 cm^{-1}; NMR ($CDCl_3$) δ 0.86 (s, 3 H), 1.05 (s, 6 H), 1.16 (s, 3 H), 1.1–2.3 (m, 11 H), 2.44 (br s, 3 H), 3.90 (m, ABX, 1 H), 4.13 (t, J = 7 Hz, 2 H), 7.30 (d, J = 8 Hz, 2 H), 7.75 (d, J = 8 Hz, 2 H); MS (EI) m/e (%) 459 (3), 457 (2), 287 (28), 285 (29), 275 (82), 273 (78), 257 (32), 255 (33), 175 (100), 135 (62), exact mass ($M^+ - CH_3$) calcd ($C_{21}H_{30}{}^{79}BrO_4S$) 457.1048, found 457.1051; MS (CI, CH_4) 475, 473 ($M + H^+$). The crude toluenesulfonate **19** (62 mg, 0.131 mmol) was added to a solution of PhSeNa (from 50 mg of PhSeSePh and 12 mg of $NaBH_4$ in 2 mL of absolute EtOH) and stirred under N_2 at room temperature for 4 h. Dilution with saturated NH_4Cl, extraction with Et_2O, washing of the extracts with brine, drying ($MgSO_4$), and solvent removal left a crude oil which was purified by preparative TLC on silica gel (0.5 × 200 × 200 mm, 19:1 hexanes/EtOAc elution) to give selenide **21** (43 mg, 0.094 mmol, 72%) as a colorless oil: IR (neat) 3050, 2950, 2860, 1580, 1480, 1460, 1390, 1375, 1215, 1130, 1075, 980, 940, 875, 735, 690 cm^{-1}; NMR ($CDCl_3$) δ 0.85, 1.04, 1.10, 1.20 (4 s, 4 CH_3), 1.2–2.3 (m, 11 H), 2.92 (m, 2 H), 3.92 (m, ABX, 1 H), 7.15–7.55 (m, 5 H); MS (EI) m/e (%) 462 (1), 461 (1), 460 (5), 459 (2), 458 (7), 457 (1), 456 (3), 455 (1), 454 (1), 275 (59), 273 (60), 257 (25), 255 (26), 193 (33), 175 (85), 149 (43), 135 (62), 129 (80), 43 (100); mol wt calcd ($C_{21}H_{31}{}^{81}BrO^{80}Se$) 460.0702, found 460.0734.

By a procedure identical with the one above, alcohol **18** (124 mg, 0.326 mmol) was converted into the solid toluenesulfonate **20** (93 mg, 0.20 mmol, 60%), which was recrystallized from hexanes/EtOAc to give an analytical sample: mp 109.5–112 °C; IR ($CHCl_3$) 3050, 2950, 2870, 1595, 1460, 1390, 1380, 1360, 1175, 1110, 1075, 950 cm^{-1}; NMR ($CDCl_3$) δ 0.85, 1.03, 1.18, 1.23 (4 s, 4 CH_3), 1.2–2.3 (m, 11 H), 2.45 (br s, 3 H), 3.87 (m, ABX, 1 H), 4.18 (t, J = 7 Hz, 2 H), 7.32 (d, J = 8 Hz, 2 H), 7.77 (d, J = 8 Hz, 2 H); MS (EI) m/e (%) 459 (42), 457 (33), 287 (47), 285 (38), 275 (68), 273 (81), 175 (100), 135 (94). Anal. Calcd for $C_{22}H_{33}BrO_4S$: C, 55.81; H, 7.03; Br, 16.88. Found: C, 55.85; H, 7.05; Br, 16.91. Compound **20** (140 mg, 0.296 mmol) was then converted into the selenide **22** (110 mg, 0.240 mmol, 81%, after preparative TLC) as a colorless oil: IR (neat) 3050, 2950, 2860, 1580, 1480, 1460, 1390, 1380, 1225, 1145, 1120, 1075, 1000, 840, 735, 690 cm^{-1}; NMR ($CDCl_3$) δ 0.82, 1.04, 1.20, 1.28 (4 s, 4 CH_3), 1.2–2.3 (m, 11 H), 2.45 (m, 2 H), 3.91 (m, ABX, 1 H), 7.15–7.50 (m, 5 H); MS (EI) m/e (%) 461 (1), 460 (3), 459 (1), 458 (4), 457 (1), 456 (2), 455 (1), 454 (1), 275 (39), 273 (42), 257 (18), 255 (19), 175 (58), 135 (45), 43 (100); mol wt calcd ($C_{21}H_{31}{}^{79}BrO^{80}Se$) 458.0723, found 458.0735.

Preparation of *dl*-3β-Bromo-8-epicaparrapi Oxide (15) from Phenyl Selenide 21. The selenide **21** (34 mg, 0.074 mmol) was dissolved in 1 mL of 7:3 MeOH/H_2O, $NaIO_4$ (23 mg, 0.105 mmol) was added, and the reaction mixture was stirred at room temperature for 2.5 h. $CHCl_3$ (10 mL) and saturated $NaHCO_3$ (10 mL) were added, the layers were separated, the organic portion was washed with brine and dried ($MgSO_4$), and the chloroform solution was heated briefly to reflux. Solvent removal left a crude oil (30 mg) which was purified by preparative TLC on silica gel (0.5 × 200 × 200 mm, 10:1 hexanes/EtOAc) to leave pure **15** (19 mg, 0.063 mmol, 85%) as a colorless oil whose spectral data matched those of the natural sample:[12,14] IR (neat) 3070, 3000, 2980, 2940, 1640, 1460, 1390, 1375, 1150, 1100, 1080, 1010, 975, 910, 840, 690 cm^{-1}; NMR ($CDCl_3$) δ 0.84, 1.06, 1.12, 1.25 (4 s, 4 CH_3), 1.2–2.4 (m, 9 H), 3.94 (m, ABX, 1 H), 4.89 (dd, J = 11, 2 Hz, 1 H), 4.95 (dd, J = 18, 2 Hz, 1 H), 5.97 (dd, J = 18, 11 Hz, 1 H); MS (EI) m/e (%) 302 (1), 300 (1), 287 (48), 285 (49), 275 (3), 273 (3), 81 (95), 43 (100).

Preparation of *dl*-3β-Bromo-8-caparrapi Oxide (25) from Phenyl Selenide 22. Selenide **22** (102 mg, 0.223 mmol) in 10 mL of $CHCl_3$ was treated with 75 μL of 40% CH_3CO_3H. After 10 min at room temperature the solution was washed with saturated $NaHCO_3$, refluxed for 1.5 h, washed again with $NaHCO_3$, dried ($MgSO_4$), and concentrated to give crude **25** (60 mg, 89% >90% purity by NMR).

Preparation of *o*-Nitrophenyl Selenides 23 and 24 from 17 and 18. Alcohol **17** (170 mg, 0.533 mmol) in 3 mL of dry THF was treated with *o*-$NO_2PhSeCN$ (170 mg, 0.746 mmol) and (n-Bu)$_3$P (151 mg, 0.746 mmol). After stirring for 3 h at room temperature the solvent was removed and the crude residue was chromatographed on silica gel (30 g, 6:1 hexanes/EtOAc) to give bright yellow crystals of **23** (251 mg, 0.501 mmol, 94%) which were recrystallized from hexanes/EtOAc to give an analytical sample: mp 120.5–122 °C; IR ($CHCl_3$) 2990, 2950, 2860, 1590, 1565, 1505, 1460, 1390, 1375, 1330, 1305, 1145, 1070, 1035, 980, 940, 875, 850 cm^{-1}; NMR ($CDCl_3$) δ 0.90, 1.07, 1.23, 1.31 (4 s, 4 CH_3), 1.2–2.3 (m, 11 H), 2.95 (m, 2 H), 3.94 (m, ABX, 1 H), 7.30 (m, 1 H), 7.50 (m, 2 H), 8.25 (d, J = 8 Hz, 1 H); MS (EI) m/e (%) 505 (<1), 503 (<1), 275 (16), 273 (16), 257 (7), 255 (7), 193 (16), 175 (35), 135 (32), 43 (100). Anal. Calcd for $C_{21}H_{30}BrNO_3Se$: C, 50.11; H, 6.01; Br, 15.88; N, 2.78. Found: C, 50.12; H, 5.92; Br, 15.90; N, 2.66.

By an analogous procedure alcohol **18** (310 mg, 0.972 mmol) was converted into the selenide **24** (489 mg, 0.972 mmol, 100%) as a yellow oil which could not be crystallized: IR (neat) 3030, 2970, 2890, 1595, 1575, 1520, 1460, 1400, 1380, 1340, 1315, 1155, 1130, 1105, 1085, 1045, 860, 795, 735, 700 cm^{-1}; NMR ($CDCl_3$) δ 0.89, 1.08, 1.27, 1.32 (4 s, 4 CH_3), 1.2–2.3 (m, 11 H), 2.95 (br t, J = 7 Hz, 2 H), 3.94 (m, ABX, 1 H), 7.42 (m, 3 H), 8.23 (dd, J = 8, 2 Hz, 1 H); MS (EI) m/e (%) 505 (1), 503 (1), 275 (45), 273

(44), 257 (22), 255 (19), 195 (100), 177 (96), 175 (65), 135 (33); mol wt calcd ($C_{21}H_{30}{}^{81}BrNO_3{}^{80}Se$) 505.0554, found 505.0483.

Preparation of *dl*-3β-Bromo-8-epicaparrapi Oxide (15) from 23. Selenide **23** (87 mg, 0.174 mmol) in 3 mL of THF was added to a solution of $NaIO_4$ (45 mg, 0.208 mmol) in 3 mL of 7:3 absolute MeOH/H_2O and stirred at room temperature for 20 h. Et_2O and saturated $NaHCO_3$ were added, the Et_2O layer was washed with brine, dried ($MgSO_4$), and concentrated to give **15** (47 mg, 0.156 mmol, 90%, >95% pure by NMR).

Preparation of *dl*-3β-Bromo-8-caparrapi Oxide (25) from 24. By a procedure analogous to that above, selenide **24** (250 mg, 0.497 mmol) was converted into **25** (139 mg, 0.462 mmol, 93%), which was purified by preparative TLC on silica gel (2 × 200 × 200 mm, 19:1 hexanes/EtOAc) to give pure **25** (116 mg, 0.388 mmol, 78%) as a colorless oil: IR (neat) 3060, 2950, 2860, 1640, 1460, 1390, 1375. 1145, 1110, 1075, 990, 915, 870, 840, 775, 690 cm^{-1}; NMR ($CDCl_3$) δ 0.89, 1.01, 1.26, 1.31 (4 s, 4 CH_3), 1.3–2.3 (m, 9 H), 3.91 (m, ABX, 1 H), 4.87 (dd, J = 11, 2 Hz, 1 H), 5.07 (dd, J = 18, 2 Hz, 1 H), 5.83 (dd, J = 11, 18 Hz, 1 H); MS (EI) m/e (%) 287 (4), 285 (4), 275 (17), 273 (17), 257 (8), 255 (9), 175 (38), 135 (42), 43 (100); exact mass ($M^+ - CH_3$) calcd ($C_{14}H_{22}{}^{79}BrO$) 285.0853, found 285.0871; MS (CI, CH_4) 303, 301 ($M + H^+$).

Acknowledgment. This research was supported by funds provided by the Research Corporation, a DuPont Young Faculty Award, an Institutional Research Grant from the American Cancer Society, and the Graduate School, University of Minnesota. The NMR instrument was purchased through NSF departmental instrumentation grant number CHE 76-05167.

Registry No. 1, 71041-54-8; 2, 71041-55-9; 3, 71041-56-0; 4, 71041-57-1; 6, 71075-17-7; 7, 71041-58-2; 8, 64532-88-3; 9, 19432-10-1; (*E*)-10a, 67858-88-2; (*Z*)-10a, 71041-59-3; 10b, 29665-88-1; 10c, 71041-60-6; 10d, 71041-61-7; 10e, 71041-62-8; 10f, 2211-29-2; *cis*-11a, 71041-63-9; *trans*-11a, 71041-64-0; 11b, 71041-65-1; 11b′, 71041-66-2; 11c, 71041-67-3; 11d, 71041-68-4; 11d′, 71041-69-5; 11e, 71041-70-8; 11e′, 71041-71-9; *cis*-12a, 71041-72-0; *trans*-12a, 71041-73-1; 12b, 71041-74-2; 12b′, 71041-75-3; 12d, 71041-76-4; 12d′, 71041-77-5; 12e, 71041-78-6; 12e′, 71041-79-7; *cis*-13a, 71041-80-0; *trans*-13a, 71041-81-1; 13b, 71041-82-2; 13b′, 71041-83-3; 13c, 71041-84-4; 13d, 71041-85-5; 13d′, 71041-86-6; 13e, 71041-87-7; 13e′, 71041-88-8; 14b, 71041-89-9; 14b′, 71041-90-2; 14c, 71041-91-3; 15, 71075-18-8; 17, 71041-92-4; 18, 71041-93-5; 19, 71041-94-6; 20, 71050-11-8; 21, 71041-95-7; 22, 71041-96-8; 23, 71041-97-9; 24, 71075-19-9; 25, 71075-20-2; homogeranic acid, 459-85-8; mercuric trifluoroacetate, 13257-51-7; geranyl acetic acid, 5579-63-5; (*E*)-geranylacetone, 3796-70-1; trimethylsilyl cyanide, 7677-24-9; TsCl, 98-59-9; *o*-$NO_2PhSeCN$, 51694-22-5.

Mercury Salt Catalyzed Nitration of Benzene Derivatives

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Received May 8, 1979

The isomer distributions and product yields have been determined for the mercuric acetate catalyzed nitration of 1,2- and 1,3-dimethylbenzenes, 1,1′-biphenyl, (1,1-dimethylethyl)benzene, the halobenzenes, and methoxybenzene. In most instances, the mercury salt catalyzed reaction exerts a strong influence on the reaction rate and on the product distribution. The isomer distributions are effectively controlled in the reactions of the hydrocarbons. Moreover, the side-chain substitution and ipso reaction products are suppressed in the catalyzed nitration of 1,2-dimethylbenzene. The halobenzenes undergo mercury(II)-catalyzed nitration, but the reactions are slow. The nitration of the mercurated methoxybenzenes produces 15% 2- and 85% 4-nitromethoxybenzene in 90% yield. However, the catalytic reaction has not been successfully accomplished. All the experimental results are in accord with the view that the mercuration reaction is the rate- and product-determining process in this nitration reaction.

Mercuration is the rate-determining and product-determining step in the mercuric acetate catalyzed nitration of methylbenzene[1-3] (eq 1). The subsequent nitroso-

$$C_6H_5CH_3 + Hg(OAc)_2 \rightarrow CH_3C_6H_4Hg(OAc) + HOAc \quad (1)$$

demercuration and oxidation reactions occur rapidly[3] (eq 2 and 3). Thus, the isomer distribution obtained in the

$$CH_3C_6H_4HgOAc + NO^+ \rightarrow CH_3C_6H_4NO + HgOAc^+ \quad (2)$$

$$CH_3C_6H_4NO + HNO_3 \rightarrow CH_3C_6H_4NO_2 + HNO_2 \quad (3)$$

catalyzed nitration of methylbenzene reflects the isomer distribution obtained in the initial mercuration reaction. Inasmuch as mercuration and uncatalyzed nitration yield different product distributions, the mercury acetate catalyzed nitration provides a method for the control of the isomer distribution. We have examined the merit of this approach by the study of the isomer distributions for the catalyzed nitration of eight other benzene derivatives.

Results and Discussion

The xylenes, (1,1-dimethylethyl)benzene, 1,1′-biphenyl, the halobenzenes, and methoxybenzene were examined in the course of this work. The results for mercuration, uncatalyzed nitration, and catalyzed nitration are summarized in Table I.

The mercuric acetate catalyzed nitration of 1,2-dimethylbenzene proceeds smoothly to give the isomeric products in 75% yield in 2 h. The isomer distribution obtained in the catalyzed reaction is very similar to the isomer distribution obtained in the mercuration reaction and significantly different from the isomer distribution obtained in the nitration reaction under comparable conditions. More importantly, the array of byproducts, including aldehydes, esters, and benzylic nitration products

(1) T. Osawa, T. Yoshida, and K. Namba, *Kogyo Kayaku*, **27**, 162 (1966).
(2) H. Komoto, F. Hayano, T. Takami, and S. Yamato, *J. Polym. Sci., Polym. Chem. Ed.*, **9**, 2983 (1971).
(3) L. M. Stock and T. L. Wright, *J. Org. Chem.*, **42**, 2875 (1977).
(4) H. C. Brown and C. W. McGary, Jr., *J. Am. Chem. Soc.*, **77**, 2306 (1955).
(5) H. C. Brown and M. Dubeck, *J. Am. Chem. Soc.*, **81**, 5608 (1959).
(6) H. C. Brown and G. Goldman, *J. Am. Chem. Soc.*, **84**, 1650 (1962).
(7) L. M. Stock and H. C. Brown, *Adv. Phys. Org. Chem.*, **1**, 35 (1963).

0022-3263/79/1944-3467$01.00/0