Studies on Mercury(II)-Mediated Opening of Bi- and Tercyclopropane Arrays

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The first examples of the mercury(II)-mediated ring opening of bicyclopropane and tercyclopropane arrays have been investigated. The presence of an adjacent cyclopropyl group dramatically increased the rate of the mercury-mediated opening of the first cyclopropane in a cyclopropane array. In contrast to the mercury-mediated ring opening of monocyclopropanes which usually undergo a concerted ring-opening mechanism, electrophilic openings of cyclopropane arrays occurred through a stabilized, free carbocation. Excellent regio- and stereoselectivities were observed in the mercury-mediated intramolecular openings of the second cyclopropanes in the cyclopropane arrays, giving rise to the formation of enantiomerically pure, highly substituted tetrahydrofurans.

Introduction

FR-900848 (**1**), which was isolated from the fermentation broth of *Streptoverticillium fervens* by Yoshida and co-workers at Fujisawa in 1990,[1] shows potent, selective activity against filamentous fungi such as *Aspergillus niger*, *Mucor rouxianus*, *Aureobasidium pullulans*, and various *Trichophyton* sp., etc. In contrast it is essentially inactive against nonfilamentous fungi including *Candida albicans* and Gram-positive and -negative bacteria. Another structurally related cholesteryl ester transfer protein inhibitor U-106305 (**2**) was recently isolated by Upjohn scientists from the fermentation broth of *Streptomyces* sp. UC 11136.[2] U-106305 (**2**) is a potent *in vitro* inhibitor of the cholesteryl ester transfer protein (CETP) reaction, thus being of potential application in the prevention of arteriosclerosis.[3] These compounds are structurally remarkable as they contain a quartercyclopropane array and a quinquecyclopropane array, respectively (Figure 1). We have recently reported the total syntheses of FR-900848 and U-106305.[4−6] During the studies of the total syntheses and the structural assignments of these cyclopropane array-containing natural products, we have developed an efficient, bidirectional approach to the enantioselective synthesis of cyclopropane arrays such as **3**−**8** (Figure 2).[7]

Although the electrophilic carbon−carbon bond cleavage in cyclopropanes has been subjected to considerable investigation and speculation, no systematic study on the

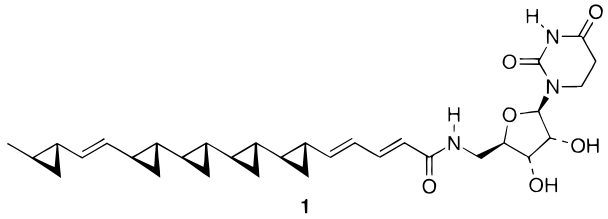

Figure 1.

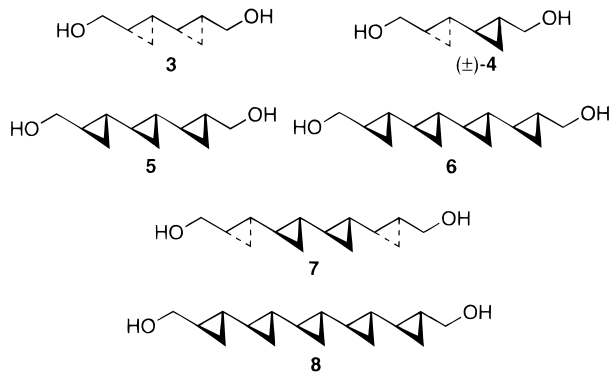

Figure 2.

cleavage of multiple cyclopropane arrays has been reported.[8−10] In this paper we report our studies on the

[⊗] Abstract published in *Advance ACS Abstracts,* June 15, 1997.

(1) Yoshida, M.; Ezaki, M.; Hashimoto, M.; Yamashita, M.; Shigematsu, N.; Okuhara, M.; Hotikoshi, K. *J. Antibiot.* **1990**, *18*, 748.

(2) Kuo, M. S.; Zielinski, R. J.; Cialdella, J. I.; Marschke, C. K.; Dupuis, M. J.; Li, G. P.; Kloosterman, D. A.; Spilman, C. H.; Marshall, V. P. *J. Am. Chem. Soc.* **1995**, *117*, 10629.

(3) For recent review, see: Yalpani, M. *Chem. Ind.* **1996**, 85.

(4) (a) Barrett, A. G. M.; Kasdorf, K. *Chem. Commun.* **1996**, 325. (b) Barrett, A. G. M.; Kasdorf, K. *J. Am. Chem. Soc.* **1996**, *118*, 11030.

(5) Barrett, A. G. M.; Hamprecht, D.; White, A. J. P.; Williams, D. J. *J. Am. Chem. Soc.* **1996**, *118*, 7863.

(6) For a second total synthesis of FR-900848, see: (a) Falck, J. R.; Mekonnen, B.; Yu, J.; Lai, J. Y. *J. Am. Chem. Soc.* **1996**, *118*, 6096. For a second total synthesis of U-106305, see: (b) Charette, A. B.; Helene, L. *J. Am. Chem. Soc.* **1996**, *118*, 10327.

(7) (a) Barrett, A. G. M.; Kasdorf, K.; Williams, D. J. *J. Chem. Soc., Chem. Commun.* **1994**, 1781. (b) Barrett, A. G. M.; Tustin, G. J. *J. Chem. Soc., Chem. Commun.* **1995**, 355. (c) Barrett, A. G. M.; Doubleday, W. W.; Kasdorf, K.; Tustin, G.; White, A. J. P.; Williams, D. J. *J. Chem. Soc., Chem. Commun.* **1995**, 407. (d) Barrett, A. G. M.; Kasdorf, K.; White, A. J. P.; Williams, D. J. *J. Chem. Soc., Chem. Commun.* **1995**, 649. (e) Barrett, A. G. M.; Doubleday, W. W.; Tustin, G. *Tetrahedron* **1996**, *52*, 15325.

(8) For reviews on cleavage of cyclopropanes, see: (a) Preston, P. M.; Tennant, G. *Chem. Rev.* **1972**, *72*, 627. (b) DePuy, C. H. *Top. Curr. Chem.* **1973**, *40*, 73. (c) Gibson, D. H.; DePuy, C. H. *Chem. Rev.* **1974**, *74*, 605. (d) Crabtree, R. H. *Chem. Rev.* **1985**, *85*, 245. (e) Rappoport, Z., Ed. *The Chemistry of the Cyclopropyl Group*, Parts 1 and 2; J. Wiley and Sons: London, 1987.

(9) For examples in mercury-induced ring opening of cyclopropanes, see: (a) Lukina, R.; Gladshetein, M. *Dokl. Akad. Nauk SSSR* **1950**, *71*, 65. (b) DePuy, C. H.; MsGuirk, R. H. *J. Am. Chem. Soc.* **1973**, *95*, 2366. (c) Collum, D. B.; Mohamadi, F.; Hallock, J. S. *J. Am. Chem. Soc.* **1983**, *105*, 6882. (d) Collum, D. B.; Still, W. C.; Mohamadi, F. *J. Am. Chem. Soc.* **1986**, *108*, 2094. (e) Lambert, J. B.; Chelius, E. C.; Bible, R. H., Jr.; Hajdu, E. *J. Am. Chem. Soc.* **1991**, *113*, 1331. (f) Kocovsky, P.; Srogl, J.; Pour, M.; Gogoll, A. *J. Am. Chem. Soc.* **1994**, *116*, 186. (g) Kocovsky, P.; Grech, J. M.; Mitchell, W. *J. Org. Chem.* **1995**, *60*, 1482.

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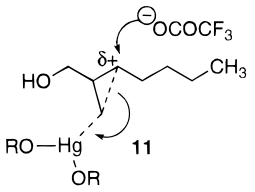
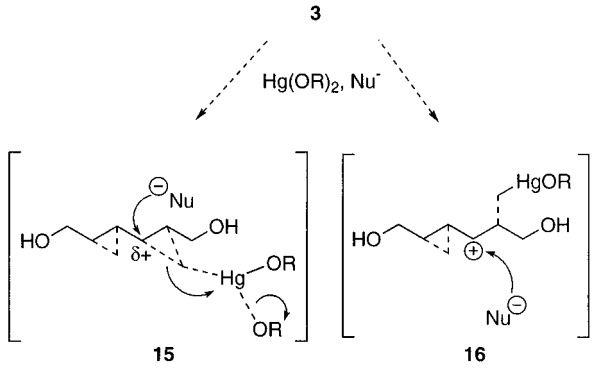


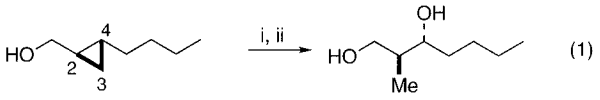
Figure 3.

Scheme 1. Possible Reaction Pathways of the Mercury-Mediated Opening of Bicyclopropanedimethanol 3



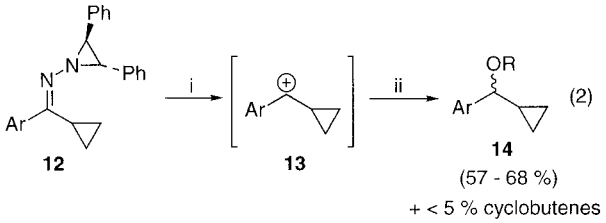
mercury-mediated opening of the bicyclopropane arrays (**3** and **4**) and tercyclopropane array (**5**).

Mercury-mediated opening of monocyclopropanes are well-documented and are known to occur with high regio- and stereoselectivity.[9] For example, when cyclopropane **9** was allowed to react with mercuric trifluoroacetate ($Hg(OCOCF_3)_2$) followed by addition of sodium chloride and a reductive workup ($LiAlH_4$, THF), the cyclopropane was cleaved regioselectively (at C_3-C_4 only) and stereoselectively (inversion−retention at C_4 = 45:1), eq 1.[9d] The regioselectivity of the electrophilic opening of cyclopropane can be explained by the fact that bond C_3-C_4 is the most electron-rich bond in the cyclopropane as both bonds C_2-C_3 and C_2-C_4 are relatively electron poor due to the inductive effect of the neighboring electron-withdrawing group (CH_2OH). The high level of stereoselectivity can be explained by a concerted mechanism in which bond breaking (C_3-C_4) and bond forming (C−HgOR and $C-OCOCF_3$) occur at almost the same time (Figure 3).



i. $Hg(OCOCF_3)_2$, CH_2Cl_2, 25 °C; NaCl; ii $LiAlH_4$, THF, 0 °C

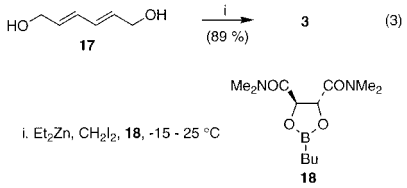
It is well-known that a cyclopropyl group is uncommonly efficient at stablizing a positive charge generated on an adjacent carbon atom.[11a] A recent report by Kirmse and co-workers showed that a cyclopropyl group can stabilize an adjacent carbocation and the rate of trapping of the cyclopropylcarbinyl cation by an external nucleophile is much faster than the rate of rearrangement to form cyclobutenes (eq 2).[11b] In an electrophilic ring opening of a cyclopropane array such as bicyclopropane **3** (Scheme 1), formation of free carbocation **16** (that can be stabilized by the adjacent cyclopropyl group) may be a more favorable pathway than the usual concerted ring opening which proceeds through the intermediate **15**.



i. hυ, ROH; ii. ROH

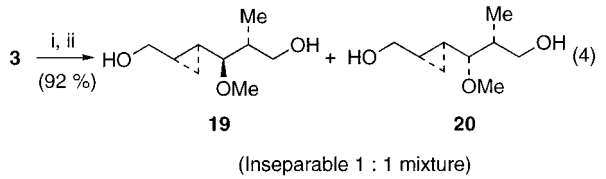
Results and Discussion

Bicyclopropanedimethanol **3** was prepared from muconidiol **17** *via* the Charette cyclopropanation[12] in the presence of the chiral auxiliary **18** (eq 3).[7b] When the



i. Et_2Zn, CH_2I_2, **18**, -15 - 25 °C

bicyclopropanedimethanol **3** was allowed to react with 2 equiv of mercuric trifluoroacetate ($Hg(OCOCF_3)_2$) in methanol at room temperature, the starting material was consumed within 20 min. Addition of solid NaCl followed by reductive demercuration with $LiAlH_4$ in THF at 0 °C afforded a 1:1 inseparable mixture of stereoisomers (eq 4). When benzyl alcohol (BnOH) was used instead of MeOH as the solvent (and as the nucleophile), mercury-mediated opening of the bicyclopropanedimethanol **3** resulted in a 1:1.2 separable mixture of organomercurial chlorides (Scheme 2). Once again this ring-opening reaction was complete within 20 min. Reductive demercuration of the organomercurial chlorides **21** and **22** provided the monocyclopropanes **23** and **24** in good yields.



i. $Hg(OCOCF_3)_2$, MeOH, 25 °C; NaCl; ii. $LiAlH_4$, THF, 0 °C

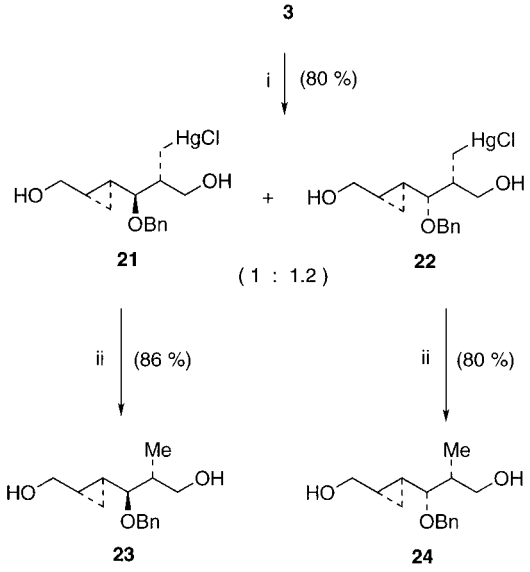
Very little change in the stereoselectivity was observed on using various mercury salts ($Hg(OCOCF_3)_2$, $Hg(OAc)_2$, $Hg(NO_3)_2$, and $Hg(OClO_3)_2$) or using a cosolvent (DME,

(10) For representative examples of opening of cyclopropanes by metals other than mercury, see the follow. Thallium: (a) Kocovsky, P.; Pour, M.; Gogoll, A. Hanus, V.; Smrcina, M. *J. Am. Chem. Soc.* **1990**, *112*, 6735. (b) Kocovsky, P.; Srogl, J.; Pour, M.; Gogoll, A. *J. Am. Chem. Soc.* **1994**, *116*, 186. Palladium: (c) Bäckvall, J. E.; Björkman, E. E.; Pettersson, L.; Siegbahn, P.; Strich, A. *J. Am. Chem. Soc.* **1985**, *107*, 7408. (d) Blomberg, M. R. A.; Siegbahn, P. E. M.; Bäckvall, J. E. *J. Am. Chem. Soc.* **1987**, *109*, 4405. Platinum: (e) Ikura, K.; Kambe, N.; Sonoda, N. *J. Am. Chem. Soc.* **1992**, *114*, 1520. (f) Stewart, F. F.; Neilsen, W. D.; Ekeland, R. E.; Larsen, R. D.; Jennings, P. W. *Organometallics* **1993**, *12*, 4858. Rhodium: (g) Gassman, P. G.; Bonser, S. M. *Tetrahedron Lett.* **1983**, *24*, 3431. Iridium: (h) Campbell, W. H.; Jennings, P. W. *Organometallics* **1983**, *2*, 1460.

(11) (a) Hart, H.; Law, P. A. *J. Am. Chem. Soc.* **1964**, *86*, 1957. (b) Kirmse, W.; Krzossa, B.; Steenken, S. *J. Am. Chem. Soc.* **1996**, *118*, 7473. (c) For a review on rearrangements and eliminations of cyclopropylcarbinyl cations, see: Olah, G. A.; Reddy, V. P.; Prakash, G. K. S. *Chem. Rev.* **1992**, *92*, 69.

(12) Charette, A. B.; Juteau, H. *J. Am. Chem. Soc.* **1994**, *116*, 2651.

Scheme 2. Mercury-Mediated Opening of Bicyclopropanedimethanol 3



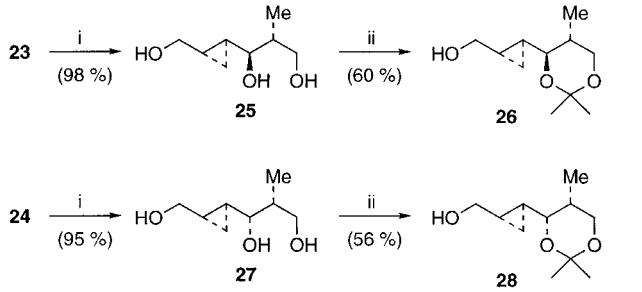
i. $Hg(OCOCF_3)_2$, BnOH, 25 °C; NaCl; ii. $LiAlH_4$, THF, 0 °C

CH_2Cl_2, THF, toluene, and CCl_4). The stereoselectivity varied from 1:1 to 1:1.5 in slight favor of isomer **22**. The yields of the ring-opening reactions remained high (65−85%) with the use of different mercury salts but decreased dramatically to 40−50% when a nonpolar cosolvent was used. In all these cases, the ring-opening reaction was complete within 20 min. Lowering the temperature of the mercury-induced ring-opening reaction led to a slight increase in stereoselectivity, eventually giving a 1.5:1 ratio in favor of isomer **21** at −30 °C albeit at a slower rate of reaction. At 0 °C, the ring-opening reaction was complete in 20 min, −20 °C required 2.5 h and −30 °C required 12 h. Very little reaction was observed when the reaction temperature was reduced further.

The rate of these mercury-mediated openings of the bicyclopropanedimethanol **3** was much faster than the ring opening of normal monocyclopropanes under similar reaction conditions. Mercury-mediated opening of monocyclopropanes usually requires 18 h to 5 days for the reactions to go to completion.[9] The rapid ring opening of the first cyclopropane in a bicyclopropane array as well as the unusual random formation of the two stereoisomers can be explained by the formation of the stabilized cyclopropylcarbinyl cation as suggested previously in Scheme 1. Thus, the rate of the first cyclopropane ring opening was enhanced by an adjacent cyclopropyl group, and instead of undergoing the usual concerted electrophilic ring-opening pathway (as in a normal monocyclopropane, Figure 3), a stabilized, free carbocation was formed which explained the lack of stereoselectivity in the formation of the ether residue.

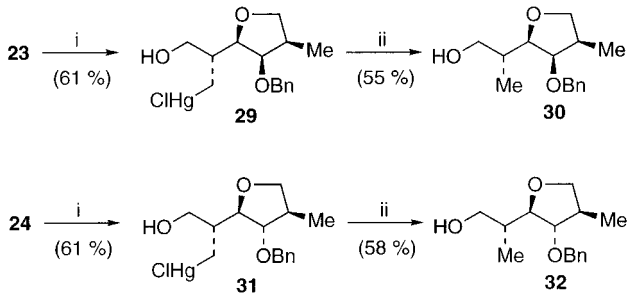
The regiochemistry of the mercury-mediated ring opening was confirmed by high-field NMR studies (HETCOR and HCOSY experiments). The stereochemistries of **23** and **24** were assigned by converting to the corresponding acetonides **26** and **28** and comparison of the coupling constants.[13] Thus, hydrogenolysis of **23** and **24** afforded triols **25** and **27**. Formation of the acetonides **26** and **28** was achieved by treating triols **25** and **27** using 1 equiv of 2,2-dimethoxypropane with a catalytic amount of pyridinium *p*-toluenesulfonate in DMF (Scheme 3). As

Scheme 3. Formation of Acetonides 26 and 28



i. H_2, 10% Pd/C, EtOH; ii. $Me_2C(OMe)_2$, pyridinium *p*-toluenesulfonate, DMF

Scheme 4. Mercury-Mediated Intramolecular Openings of 23 and 24



i. $Hg(OCOCF_3)_2$, CH_2Cl_2, 25 °C; NaCl; ii. $LiAlH_4$, THF, 0 °C

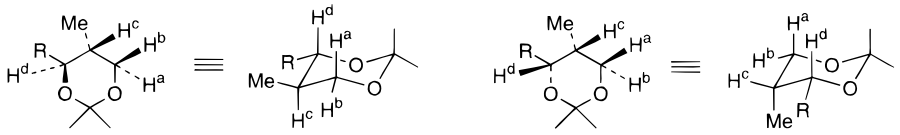
shown in Table 1, these *anti* and *syn* acetonides **26** and **28** showed a great difference in the coupling constants and these values matched perfectly with those reported in the literature.[13]

When the monocyclopropanes **23** and **24** were allowed to react with 2 equiv of $Hg(OCOCF_3)_2$ in CH_2Cl_2 at room temperature, intramolecular ring openings occurred to provide tetrahydrofurans **29** and **31** (Scheme 4). Reductive demercuration of **29** and **31** with $LiAlH_4$ afforded the highly substituted tetrahydrofurans **30** and **32**. The ring opening of the second cyclopropanes (i.e., the remaining cyclopropanes in **23** and **24**) required a much longer time (48 h) to go to completion as compared with the rate of opening of the first cyclopropanes, even though the second ring-opening reactions were intramolecular processes. As expected from literature precedent,[9c] these intramolecular ring-opening reactions were highly regio- and stereoselective, generating single regio- and stereoisomers **29** and **31** with inversion of configuration at the carbon attacked by the internal nucleophile. Formation of the other regioisomers such as **33**/**34** with a six-membered ring instead of a five-membered ring and the other stereoisomers such as **35**/**36** with retention of configuration at the carbon attacked by the internal nucleophile were not observed in these cases (Figure 4).

The structure and stereochemistry of the tetrahydrofurans **30** and **32** were assigned by high-field NMR studies (HETCOR, HCOSY, and NOE experiments), Table 2. These data from NOE studies agreed with the previous stereochemistry assignments of the OBn groups in the first cyclopropane ring openings (**23** and **24**) as determined by the coupling constants of the acetonides **26** and **28** (Scheme 3 and Table 1).

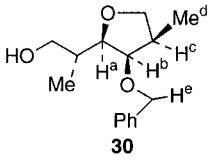
(13) The assignments of these types of *anti* and *syn* 1,3-diols by comparing the coupling constants of the corresponding acetonides have been used widely in the literature. For an excellent example, see: Evans, D. A.; Chapman, K. T.; Carreira, E. M. *J. Am. Chem. Soc.* **1988**, *110*, 3560.

Table 1. Coupling Constants from Acetonides Derived from Triols 25 and 27

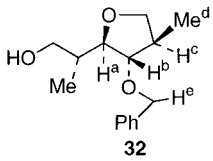


	26, R =  R = ^{i}Pr[13]		**28**, R =  R = ^{i}Pr[13]	
J_{ab}	11.5 Hz	11.4 Hz	J_{ab}	11.5 Hz	11.4 Hz
J_{ac}	11.5 Hz	11.1 Hz	J_{ac}	1.6 Hz	1.7 Hz
J_{bc}	5.1 Hz	5.0 Hz	J_{bc}	2.9 Hz	2.8 Hz
J_{cd}	9.8 Hz	10.1 Hz	J_{cd}	2.6 Hz	2.3 Hz

Table 2. NOE Studies of Tetrahydrofurans 30 and 32

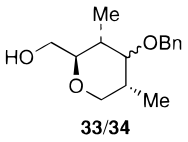


30

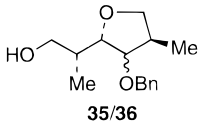


32

Irradiation at	Enhancement at **30**		Enhancement at **32**	
H^b	H^a 8%		H^a trace	
H^c	H^a 4%	H^b 5%	H^a 3%	H^b trace
Me^d	H^b 2%	H^e 4%	H^b 5%	H^e 2%



33/34



35/36

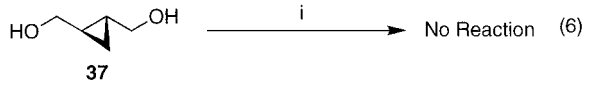
Figure 4.

When the monocyclopropane **24** was treated with $Hg(OCOCF_3)_2$ in MeOH instead of CH_2Cl_2, only the intramolecular ring-opened product (**31**) was isolated and no intermolecular ring-opened product(s) with MeOH was observed. When the monocyclopropane-containing acetonide **28** was submitted to the usual mercury-mediated ring-opening conditions, no reaction was observed even after 7 days (eq 5). On the basis of these results and the

28 → (i) → No Reaction (5)

i. $Hg(OCOCF_3)_2$, MeOH, 25 °C, 7 days

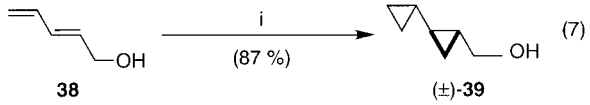
studies on the first and the second ring openings (*vide infra*), several features of the mercury-mediated ring opening of the cyclopropane array bicyclopropanedimethanol **3** can be concluded: (i) the presence of the cyclopropyl group enhances the rate of the mercury-mediated ring opening of the first cyclopropane; (ii) the first cyclopropane ring opening in a bicyclopropanedimethanol is probably *via* a free carbocation and this cation is stabilized by the adjacent cyclopropyl group but the rate of rearrangement of this cyclopropylcarbinyl cation is much slower than trapping with an external nucleophile (MeOH or BnOH) and therefore no rearrangement products were detected; (iii) once the first cyclopropane has been opened up, the remaining cyclopropane became "deactivated" by the two adjacent electron-withdrawing CH_2OR groups and did not undergo rapid intermolecular ring opening. This is supported by that fact that the monocyclopropane-containing acetonide **28** as well as the monocyclopropanedimethanol **37**[5] did not undergo ring opening (eqs 5 and 6).



37 → (i) → No Reaction (6)

i. $Hg(OCOCF_3)_2$, MeOH, 25 °C, 10 days

In order to further confirm the above conclusions, bicyclopropane **39** and cyclopropane **43** were synthesized and their mercury-mediated ring openings were studied and compared. Dicyclopropanation of the *trans*-penta-2,4-dien-1-ol (**38**)[14] with diethylzinc and diiodomethane provided the desired racemic bicyclopropane **39** (87%) (eq 7). Cyclopropane **43** was prepared in three steps from 2-methylpropanal *via* Wadsworth−Emmons olefination,[15] DIBAL-H reduction of the resulting α,β-unsaturated ester, and cyclopropanation (Scheme 5).



38 → (i), (87 %) → (±)-**39** (7)

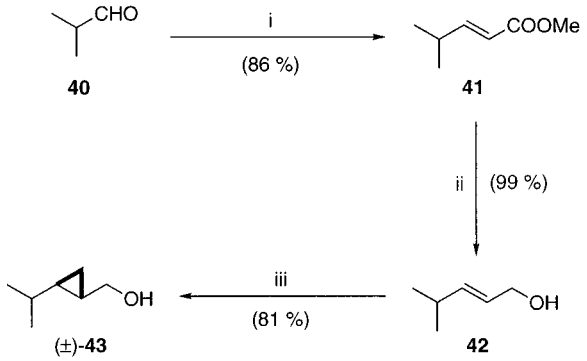
i. Et_2Zn, CH_2I_2, CH_2Cl_2, -20 - 25 °C

As expected, when the bicyclopropane **39** was allowed to react with $Hg(OCOCF_3)_2$ in MeOH, the starting material was consumed within 15 min. Under the same conditions, monocyclopropane **43** required 10 days for the reaction to go to completion. Thus, the cyclopropyl group did show a significant enhancement on the rate of ring opening. As expected from literature precedent,[9d] high stereoselectivity (with inversion at the carbon attacked by the nucleophile, MeOH) was observed in the ring opening of **43**. Indeed, only one single diastereomer was

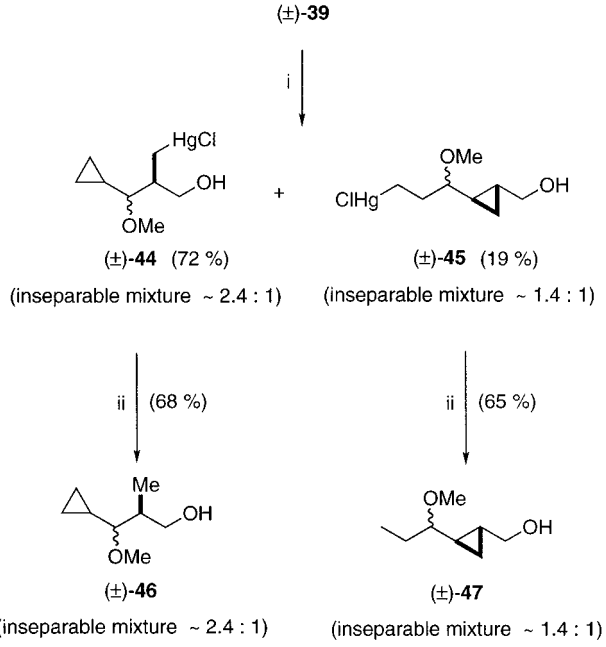
(14) Alker, D.; Ollis, W. D.; Shahriari-Zavareh, H. *J. Chem. Soc., Perkin Trans. 1* **1990**, 1637.

(15) (a) Wadsworth, W. S. *Org. React.* **1977**, *25*, 73. (b) Maryanoff, B. E.; Reitz, A. B. *Chem. Rev.* **1989**, *89*, 863.

Scheme 5. Synthesis of Cyclopropane 43

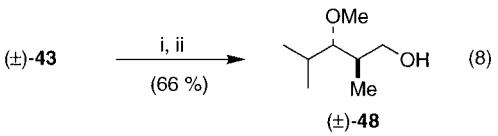


Scheme 6. Mercury-Mediated Opening of Bicyclopropane 39



i. $Hg(OCOCF_3)_2$, MeOH, 25 °C; NaCl; ii. $LiAlH_4$, THF, 0 °C

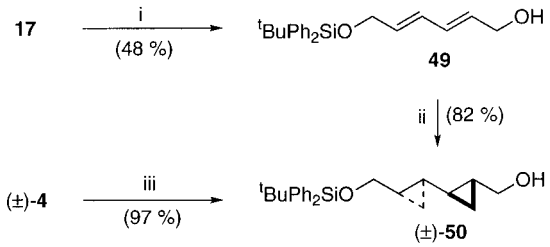
isolated from this reaction (eq 8). In case of the mercury-mediated ring opening of the bicyclopropane **39**, a mixture of regioisomers as well as stereoisomers was obtained (Scheme 6). Thus, a carbocation intermediate must have been formed in order to give such a low stereoselectivity as compared to the high stereoselectivity of the ring opening of **43**.



i. $Hg(OCOCF_3)_2$, MeOH, 25 °C; NaCl; ii. $LiAlH_4$, THF, 0 °C

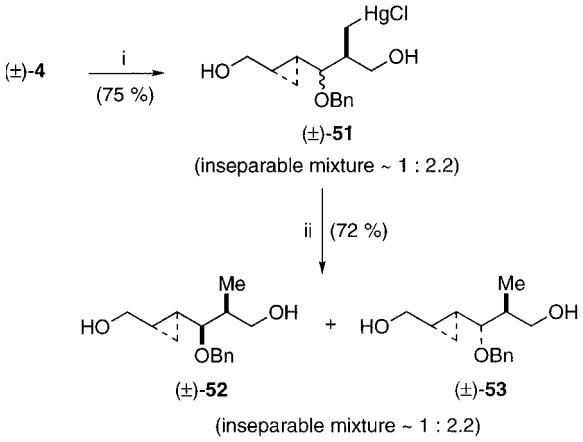
It would be interesting to see if there is any difference between the *syn*-bicyclopropanedimethanol (**3**) and the *anti*-bicyclopropanedimethanol (**4**) in the rate and in the stereoselectivity of the mercury-mediated ring-opening reaction. Thus, the racemic *anti*-bicyclopropanedimethanol (**4**) was synthesized based on the methodology previously developed in our group[7b] (Scheme 7) and the mercury-mediated ring-opening reaction was studied (Scheme 8). When the *anti*-bicyclopropanedimethanol (**4**)

Scheme 7. Synthesis of Bicyclopropanedimethanol 4



i. $^tBuPh_2SiCl$, imidazole, DMF, 12 h; ii. Et_2Zn, CH_2I_2, CH_2Cl_2, -20 °C, 16 h; iii. TBAF, THF, 2 h.

Scheme 8. Mercury-Mediated Opening of Bicyclopropanedimethanol 4

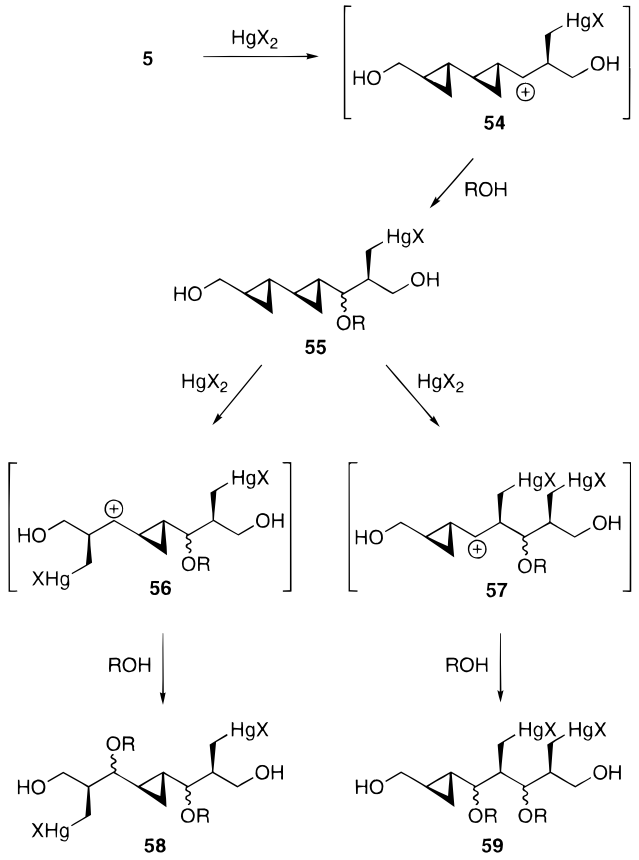


i. $Hg(OCOCF_3)_2$, BnOH, 25 °C; NaCl; ii. $LiAlH_4$, THF, 0 °C

was allowed to react with $Hg(OCOCF_3)_2$ (2 equiv), the starting material was once again consumed within 20 min and addition of sodium chloride afforded a 1:2.2 inseparable mixture of **51** (which also contained trace amount of rearrangement products). Reductive demercuration of **51** with $LiAlH_4$ afforded **52** and **53** in good yields.

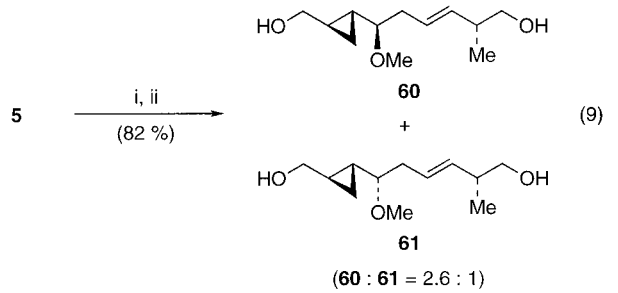
After study of the mercury-mediated ring opening in the bicyclopropane array systems, we continued our studies on the tercyclopropane array system. Thus, the enantiomerically pure tercyclopropanedimethanol **5** was prepared from the readily available *trans*-butene-1,4-diol in four steps as previously described in our total synthesis of U-106305.[5] Based on the results on the bicyclopropane arrays systems, *vide infra*, one would expect that a double ring opening of the tercyclopropanedimethanol **5** should occur and these ring-opening reactions should be very fast as these cyclopropanes are "activated" by an adjacent cyclopropane (Scheme 9). Thus, opening of the first cyclopropane in the tercyclopropane array would lead to the formation of the cyclopropylcarbinyl cation **54** which is stabilized by an adjacent cyclopropyl group. Trapping of this cation with ROH would provide the bicyclopropane **55**. This bicyclopropane should undergo rapid opening again to provide cyclopropylcarbinyl cations **56** and **57**, both of which are stabilized by a neighboring cyclopropane. Trapping of these cations with ROH would lead to the formation of the monocyclopropanes **58** and **59**. One would also expect that the reaction should stop at this stage as the remaining cyclopropanes in these monocyclopropanes **58** and **59** would be "deactivated" by the two neighboring electron-withdrawing groups (CHOR)

Scheme 9. Possible Products in the Mercury-Mediated Opening of Tercyclopropanedimethanol 5



as we observed previously in the cases of cyclopropanes **28** and **37** (eqs 5 and 6). Surprisingly, adducts **58** and **59** were not the products that we obtained in the mercury-mediated ring opening of tercyclopropane **5**.

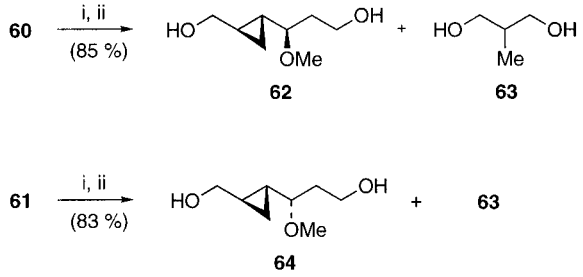
When the tercyclopropanedimethanol **5** was allowed to react with 3 equiv of $Hg(OCOCF_3)_2$ in MeOH at room temperature, the starting material was consumed within 20 min. Addition of sodium chloride followed by reductive demercuration with $LiAlH_4$ afforded a separable mixture of stereoisomers **60** and **61** as the only isolated products in good yield (eq 9). The structures of **60** and **61** were determined by high-field NMR studies (HETCOR and HCOSY experiments), and the stereochemistry of the OMe groups was determined by NOE studies of the corresponding tetrahydrofuran derivatives (**66** and **67**) as described below.



i. $Hg(OCOCF_3)_2$, MeOH, 25 °C; NaCl; ii. $LiAlH_4$, THF, 0 °C

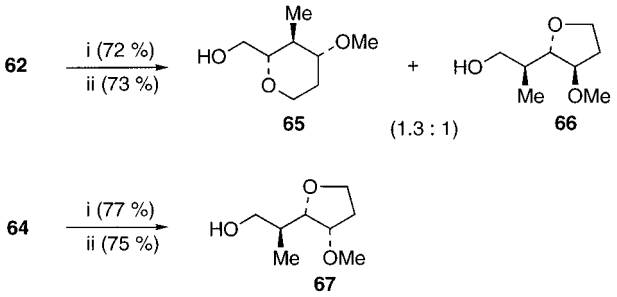
Ozonolysis of **60** followed by a reductive workup with $NaBH_4$ afforded the cyclopropane **62** and 2-methylpropane-1,3-diol (**63**) (Scheme 10). Similarly, the cyclopropane **64** was also obtained from ozonolysis of **61**. Surprisingly, unlike the cases with cyclopropanes **23** and **24** (Scheme 4) which showed excellent regioselectivity giving only the tetrahydrofuran ring-opened products, the mercury-mediated intramolecular ring opening of cyclopropane **62** afforded a 1.3:1 mixture of two regioisomers, the tetrahydropyran **65** and the tetrahydrofuran **66** (Scheme 11). When cyclopropane **64** was allowed to react with $Hg(OCOCF_3)_2$ under similar conditions, only one regioisomer, the tetrahydrofuran **67**, was formed. At this stage, we do not have a good explanation to account for the fact that mercury-mediated intramolecular ring opening of cyclopropanes **23**, **24** (Scheme 4), and **64** (Scheme 11) gave only one regioisomer while under the same reaction conditions cyclopropane **62** afforded two regioisomers (Scheme 4). But it is clear that, in all cases, only the products with inversion of configuration at the carbon attacked by the internal nucleophile were formed. The structures and the stereochemistry of tetrahydropyran **65** and tetrahydrofurans **66** and **67** were assigned on the basis of high-field NMR studies (HETCOR, HCOSY, and NOE experiments).

Scheme 10. Ozonolysis of 60 and 61



i. O_3, $MeOH/CH_2Cl_2$, -78 °C; ii. $NaBH_4$, -78 - 25 °C

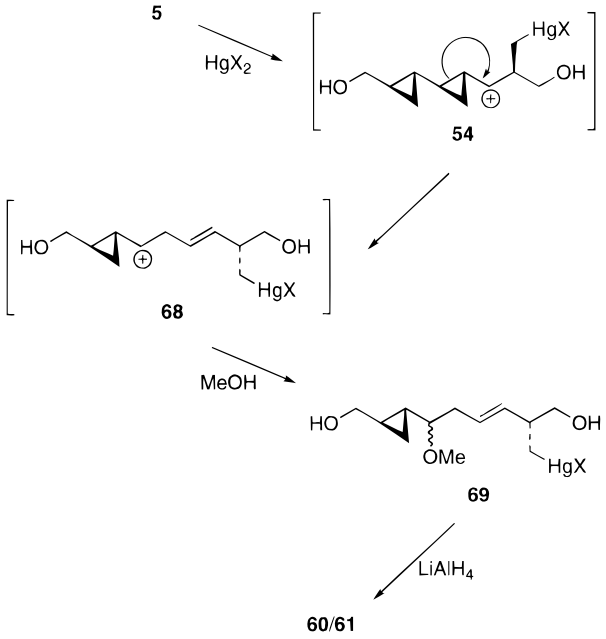
Scheme 11. Mercury-Mediated Intramolecular Opening of 62 and 64



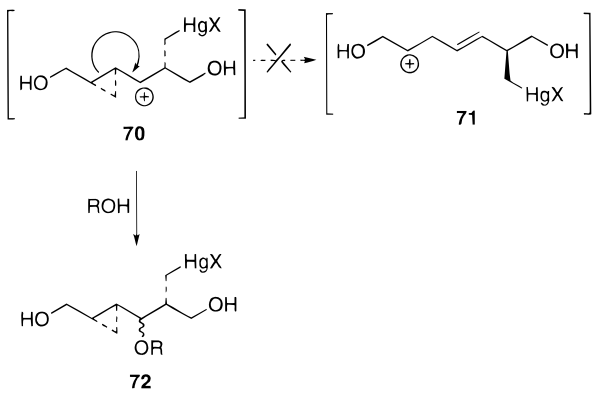
i. $Hg(OCOCF_3)_2$, CH_2Cl_2, 25 °C; NaCl; ii. $LiAlH_4$, THF, 0 °C

A proposed mechanism for the formation of **60** and **61** in the mercury-mediated ring-opening reaction of tercyclopropane **5** is shown in Scheme 12. Similar to the cases with the bicyclopropane arrays, the first cyclopropane in the tercyclopropane array **5** is cleaved regioselectively to give **54** as the resulting free carbocation is stabilized by the adjacent cyclopropyl group. This cation then undergoes rapid rearrangement to give another cyclopropyl-stabilized cation **68**. Trapping of cation **68** with MeOH followed by addition of NaCl and a reductive demercuration will lead to the formation of the observed products **60** and **61**. The rate of the rearrangement of the cyclopropylcarbinyl cation **54** (**54** → **68**, Scheme 12) must be much faster than the rate of trapping of **54** with an external nucleophile (**54** → **55**, Scheme 9) in order to provide the observed products **60** and **61**. This type of

Scheme 12. Proposed Mechanism of the Mercury-Mediated Ring Opening of Tercyclopropanedimethanol 5



Scheme 13. Rearrangement of Cyclopropylcarbinyl Cation 70



rearrangement (**54** → **68**) was not observed in the bicyclopropane array systems. This is probably because this type of rearrangement would lead to the formation of a destabilized cation (**71**) as this cation would be next to an adjacent electron-withdrawing group (CH_2OH), Scheme 13. Thus, trapping of the cyclopropylcarbinyl cation **70** with ROH to provide the monocyclopropane **72** would be the preferable process.

Conclusion

We have demonstrated the first examples of mercury(II)-mediated ring opening of bi- and tercyclopropane arrays. The presence of an adjacent cyclopropyl group dramatically increased the rate of the mercury-mediated opening of the first cyclopropane in a cyclopropane array. In contrast to the mercury-mediated ring opening of monocyclopropanes which usually undergoes a concerted ring-opening mechanism, electrophilic openings of cyclopropane arrays occurred through a stabilized, free carbocation. Excellent regio- and stereoselectivities were observed in the mercury-mediated intramolecular openings of the second cyclopropanes in the cyclopropane arrays, giving rise to the formation of enantiomerically pure, highly substituted tetrahydrofurans. Studies on the ring-opening reactions of the higher order cyclopropane arrays such as the quartercyclopropane arrays **6** and **7**, and the quinquecyclopropane array such as **8** (Figure 2), as well as further investigation on the intramolecular ring openings of these cyclopropane arrays are now in progress within our laboratories.

Experimental Section

General. All reactions were carried out in an atmosphere of dry nitrogen at ambient temperature unless otherwise stated. Standard column chromatography was carried out on BDH silica gel 60, 230−400 mesh ASTM, using flash chromatography techniques (eluants are given in parentheses).[16] Analytical thin-layer chromatography (TLC) was performed on Merck precoated silica gel 60 F_{254} plates. All glassware was flame dried under an inert atmosphere of dry nitrogen. Hexanes refers to bp 40−60 °C redistilled petroleum. Solvents were purified by distillation under N_2 from CaH_2 (CH_2Cl_2, DMF, Et_3N, pyridine); Ph_2CO-Na, diethyl ether (Et_2O); Ph_2CO−K, tetrahydrofuran (THF); Mg and I_2, methanol (MeOH). Bicyclopropanedimethanol **3**,[4a] tercyclopropanedimethanol **5**,[5] monocyclopropanedimethanol **37**,[5] *anti*-bicyclopropane **50**,[7b,e] mucondiol **17**,[7b] and *trans*-penta-2,4-dienyl-1-ol **38**[14] were prepared as described in the literature. All other reagents were obtained from commercial sources and used without further purification.

Mercury-Mediated Ring Opening of (1*S*,3*R*,4*R*,6*S*)-1,6-Bis(hydroxymethyl)bicyclopropane (3) with MeOH as Nucleophile. $Hg(O_2CCF_3)_2$ (360 mg, 0.844 mmol, 2 equiv) was added to bicyclopropane **3** (57.8 mg, 0.406 mmol) in anhydrous MeOH (4.5 mL). The mixture was stirred at room temperature for 20 min when TLC indicated that all starting material was consumed. After the solution was stirred for an additional 40 min, solid NaCl (3 g) was added and the mixture was stirred vigorously for 3 h. Excess NaCl was removed by filtration, and the solids were washed with MeOH. Rotary evaporation gave an oil which was dissolved in THF (25 mL), and $LiAlH_4$ (840 mg, 22.1 mmol) was added at 0 °C under N_2. After being stirred at 0 °C for 5 h, the mixture was diluted with Et_2O, a minimal amount of water and potassium sodium tartrate were added at 0 °C, and the solution was stirred for 1 h. The mixture was filtered through silica and washed with MeOH/Et_2O (1:1), rotary evaporated, and chromatographed (EtOAc:hexanes 0:1, 1:9, 1:3, 1:1, 3:1, 1:0) to provide an inseparable 1:1 mixture of the products **19** and **20** as a colorless viscous oil (65.1 mg, 0.374 mmol, 92%). These diastereomeric diols were separated by conversion to the corresponding diester derivative (4-biphenylcarbonyl chloride (2.5 equiv), DMAP (0.1 equiv), Et_3N (5 equiv), CH_2Cl_2, 25 °C, 2 h), separation of these diesters by flash column chromatography (diester of **19**, R_f 0.57 (Et_2O:hexanes = 1:1); diester of **20** R_f 0.49 (Et_2O:hexanes = 1:1)), followed by DIBAL-H reduction (DIBAL-H (5 equiv), CH_2Cl_2, −78 °C, 2 h) of the separated diesters to provide pure samples of **19** and **20** both as colorless oils for characterization.

(1*S*,3*S*)-3-(Hydroxymethyl)-1-[(1*S*, 2*R*)-3-hydroxy-1-methoxy-2-methylprop-1-yl]cyclopropane (19): R_f 0.22 (EtOAc); $[\alpha]^{25}_D$ = +30.8 (*c* = 1.29, MeOH); IR ($CHCl_3$) 3065 (m), 3431 (br s), 1054 (s) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 3.70 (dd, 1H, *J* = 10.8, 4.0 Hz), 3.57 (dd, 1H, *J* = 10.8, 6.4 Hz), 3.54 (dd, 1H, *J* = 11.4, 6.6 Hz), 3.46 (dd, 1H, *J* = 11.4, 7.1 Hz), 3.43 (s, 3H), 2.90 (br s, 1H), 2.60 (dd, 1H, *J* = 8.8, 5.8 Hz), 2.40 (br s, 1H), 1.92 (m, 1H), 1.18 (m, 1H), 0.99 (d, 3H, *J* = 7.1 Hz), 0.77 (m, 1H), 0.46 (dt, 1H, *J* = 8.6, 5.1 Hz), 0.39 (dt, 1H, *J* = 8.6, 5.2 Hz); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 89.1, 66.6, 66.6, 58.0, 40.6, 20.4, 19.2, 14.5, 7.1; MS (CI, NH_3) *m*/*z* 192 $[M + NH_4]^+$, 175 $[M + H]^+$, 160, 143, 130, 125, 115, calcd for $C_9H_{22}NO_3$ ($[M + NH_4]^+$) 192.1600, found 192.1595. Anal. Calcd for $C_9H_{18}O_3$: C, 62.04; H, 10.41. Found: C, 62.24; H, 10.19.

(1*S*,3*S*)-3-(Hydroxymethyl)-1-[(1*R*,2*R*)-3-hydroxy-1-methoxy-2-methylprop-1-yl]cyclopropane (20): R_f 0.22

(16) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.

(EtOAc); $[\alpha]^{25}_D = +4.1$ ($c = 4.06$, MeOH); IR ($CHCl_3$) 3065 (m), 3401 (br s), 1079 (s), 1014 (s) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 3.67 (d, 2H, $J = 5.4$ Hz), 3.62 (dd, 1H, $J = 11.1$, 6.3 Hz), 3.40 (s, 3H), 3.36 (dd, 1H, $J = 11.1$, 7.4 Hz), 2.65 (dd, 1H, $J = 8.8$, 4.1 Hz), 2.53 (br s, 2H), 1.99 (m, 1H), 1.00 (d, 3H, $J = 7.2$ Hz), 0.92 (m, 1H), 0.83 (m, 1H), 0.66 (dt, 1H, $J = 8.3$, 5.0 Hz), 0.61 (dt, 1H, $J = 8.3$, 5.0 Hz); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 87.1, 65.9, 65.4, 56.6, 39.1, 17.5, 16.6, 12.2, 9.3; MS (CI, NH_3) m/z 192 $[M + NH_4]^+$, 175 $[M + H]^+$, 160, 143, 130, 125, 115, calcd for $C_9H_{22}NO_3$ ($[M + NH_4]^+$) 192.1600, found 192.1590. Anal. Calcd for $C_9H_{18}O_3$: C, 62.04; H, 10.41. Found: C, 62.16; H, 10.19.

Mercury-Mediated Ring Opening of (1*S*,3*R*,4*R*,6*S*)-1,6-Bis(hydroxymethyl)bicyclopropane (3) with BnOH as Nucleophile. $Hg(O_2CCF_3)_2$ (12.0 g, 28.1 mmol, 2 equiv) was added to bicyclopropane **3** (2.00 g, 14.1 mmol) in benzyl alcohol (140 mL). The mixture was stirred at room temperature for 30 min when TLC indicated that all starting material was consumed. After the solution was stirred for an addition 30 min, solid NaCl (100 g) was added and the reaction mixture was stirred vigorously for 3 h. Excess NaCl was removed by filtration, and the solids were washed with diethyl ether. Rotary evaporation and chromatography (EtOAc:hexanes 0:1, 1:9, 1:3, 2:3, 4:1, 1:0) gave products **21** (2.48 g, 36%) and **22** (2.98 g, 44%) both as colorless viscous oils.

(1*S*,3*S*)-1-[(1*S*,2*R*)-2-[(Chloromercurio)methyl]-3-hydroxy-1-(phenylmethoxy)prop-1-yl]-3-(hydroxymethyl-)cyclopropane (21): R_f 0.37 (EtOAc); $[\alpha]^{25}_D = +2.8$ ($c = 1.51$, MeOH); IR ($CHCl_3$) 3605 (m), 3437 (br s), 1070 (s), 1013 (s) cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.29 (m, 5H), 4.77 (d_{AB}, 1H, $J = 11.7$ Hz), 4.50 (d_{AB}, 1H, $J = 11.7$ Hz), 3.89 (dd, 1H, $J = 11.0$, 4.9 Hz), 3.56 (m, 2H), 3.41 (dd, 1H, 11.2, 7.0 Hz), 2.83 (dd, 1H, $J = 8.7$, 3.5 Hz), 2.27 (m, 1H), 1.77 (d_{AB}, 1H, $J = 12.0$, 6.2 Hz), 1.67 (d_{AB}d, 1H, $J = 12.0$, 5.6 Hz), 1.52 (br s, 2H), 1.17 (m, 1H), 0.83 (m, 1H), 0.44 (dt, 1H, $J = 8.7$, 5.1 Hz), 0.32 (dt, 1H, $J = 8.7$, 5.3 Hz); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 137.8, 128.7, 128.2, 128.1, 84.5, 71.6, 66.0, 64.3, 44.2, 28.2, 21.0, 18.7, 6.4; MS (CI, NH_3) m/z 504 $[M + NH_4]^+$, 468 $[M - H_2O]^+$, 451 $[M - Cl]^-$, 396, 379, 360, 231, 191, 108, 91, calcd for $C_{15}H_{25}NO_3HgCl$ ($[M + NH_4]^+$) 504.1229, found 504.1266.

(1*S*,3*S*)-1-[(1*R*,2*R*)-2-[(Chloromercurio)methyl]-3-hydroxy-1-(phenylmethoxy)prop-1-yl]-3-(hydroxymethyl-)cyclopropane (22): R_f 0.23 (EtOAc); $[\alpha]^{25}_D = -11.7$ ($c = 1.06$, MeOH); IR ($CHCl_3$) 3603 (m), 3428 (br s), 1066 (s), 1014 (s) cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.27 (m, 5H), 4.64 (d_{AB}, 1H, $J = 11.8$ Hz), 4.45 (d_{AB}, 1H, $J = 11.8$), 3.64 (dd, 2H, $J = 10.8$, 5.5 Hz), 3.52 (dd, 1H, $J = 10.7$, 5.8 Hz), 3.32 (dd, 1H, $J = 10.9$, 7.2 Hz), 2.93 (dd, 1H, $J = 8.6$, 3.4 Hz), 2.35 (m, 1H), 1.97 (dd, 1H, $J = 12.2$, 5.2 Hz), 1.71 (dd, 1H, $J = 12.2$, 4.4 Hz), 1.57 (br s, 2H), 0.84 (m, 2H), 0.67 (m, 2H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 137.9, 128.6, 128.1, 128.0, 82.6, 71.2, 66.3, 66.1, 44.6, 25.5, 18.9, 16.8, 11.1; MS (CI, NH_3) m/z 504 $[M + NH_4]^+$, 468 $[M - H_2O]^+$, 451 $[M - Cl]^+$, 396, 379, 360, 231, 191, 108, 91, calcd for $C_{15}H_{25}NO_3HgCl$ ($[M + NH_4]^+$) 504.1229, found 504.1266.

(1*S*,3*S*)-3-(Hydroxymethyl)-1-[(1*S*,2*R*)-3-hydroxy-2-methyl-1-(phenylmethoxy)prop-1-yl]cyclopropane (23). Organomercurial diol **21** (2.48 g, 5.11 mmol) in THF (150 mL) was added *via* cannula to $LiAlH_4$ (2.10 g, 55.3 mmol) in THF (170 mL) at 0 °C under N_2. The mixture was stirred at 0 °C for 3 h and diluted with Et_2O, a minimal amount of water and potassium sodium tartrate were added at 0 °C, and the mixture was stirred for 30 min. The mixture was filtered through silica and washed with MeOH/Et_2O (1:4). Rotary evaporation and chromatography (EtOAc:hexanes 0:1, 1:9, 1:3, 1:1, 3:1, 1:0) gave the product **23** (1.10 g, 4.39 mmol, 86%) as a colorless viscous oil: R_f 0.41 (EtOAc); $[\alpha]^{25}_D = +16.7$ ($c = 1.35$, MeOH); IR ($CHCl_3$) 3603 (m), 3480 (br s), 1069 (s), 1018 (s) cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.26 (m, 5H), 4.74 (d_{AB}, 1H, $J = 11.5$ Hz), 4.47 (d_{AB}, 1H, $J = 11.5$ Hz), 3.71 (dd, 1H, $J = 10.9$, 3.9 Hz), 3.55 (dd, 1H, $J = 10.9$, 6.0 Hz), 3.49 (dd, 1H, $J = 11.2$, 6.6 Hz), 3.40 (dd, 1H, $J = 11.2$, 7.0 Hz), 2.79 (dd, 1H, $J = 8.7$, 5.5 Hz), 1.90 (m, 1H), 1.80 (br s, 1H), 1.15 (m, 1H), 0.98 (d, 3H, $J = 7.1$ Hz), 0.84 (m, 1H), 0.38 (m, 2H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 138.4, 128.5, 127.7(2), 86.3, 71.6, 66.3, 66.0, 40.4, 20.4, 19.3, 14.5, 6.9; MS (CI, NH_3) m/z 268 $[M + NH_4]^+$, 251 $[M + H]^+$, 233 $[M - H_2O + H]^+$, 191, 160, 143, 130, 125, 108, calcd for $C_{15}H_{23}O_3$ ($[M + H]^+$) 251.1647, found 251.1664. Anal. Calcd for $C_{15}H_{22}O_3$: C, 71.97; H, 8.86. Found: C, 71.99; H, 8.78.

(1*S*,3*S*)-3-(Hydroxymethyl)-1-[(1*R*,2*R*)-3-hydroxy-2-methyl-1-(phenylmethoxy)prop-1-yl]cyclopropane (24). Organomercurial diol **22** (2.98 g, 6.14 mmol) in THF (180 mL) was added to $LiAlH_4$ (2.55 g, 67.1 mmol) in THF (200 mL) at 0 °C under N_2, and the mixture was stirred at 0 °C for 3 h. The mixture was diluted with Et_2O, a minimal amount of water and potassium sodium tartrate were added at 0 °C, and the mixture was stirred for 30 min. The mixture was filtered through silica and washed with MeOH/Et_2O (1:4). Rotary evaporation and chromatography (EtOAc:hexanes 0:1, 1:9, 1:3, 1:1, 3:1, 1:0) gave the product **24** (1.23 g, 4.91 mmol, 80%) as a colorless viscous oil: R_f 0.34 (EtOAc); $[\alpha]^{25}_D = +8.2$ ($c = 0.18$, MeOH); IR ($CHCl_3$) 3612 (m), 3445 (br s), 1069 (s), 1019 (s) cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.26 (m, 5H), 4.69 (d_{AB}, 1H, $J = 11.7$ Hz), 4.45 (d_{AB}, 1H, $J = 11.7$ Hz), 3.62 (m, 2H), 3.53 (dd, 1H, $J = 11.1$, 6.0 Hz), 3.34 (dd, 1H, $J = 11.1$, 6.8 Hz), 2.85 (dd, 1H, $J = 8.3$, 3.9 Hz), 2.40 (br s, 1H), 1.99 (m, 1H), 1.58 (br s, 1H), 0.98 (d, 3H, $J = 7.1$ Hz), 0.87 (m, 2H), 0.59 (m, 2H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 138.7, 128.4, 127.6(2), 84.9, 70.9, 66.4, 66.0, 39.9, 18.2, 17.3, 12.5, 10.0; MS (CI, NH_3) m/z 268 $[M + NH_4]^+$, 251 $[M + H]^+$, 233 $[M - H_2O + H]^+$, 191, 160, 143, 130, 125, 108, calcd for $C_{15}H_{23}O_3$ ($[M + H]^+$) 251.1647, found 251.1662. Anal. Calcd for $C_{15}H_{22}O_3$: C, 71.97; H, 8.86. Found: C, 71.95; H, 8.94.

(1*S*,3*S*)-1-[(1*S*,2*R*)-1,3-Dihydroxy-2-methylprop-1-yl]-3-(hydroxymethyl)cyclopropane (25). H_2(g) was attached to a flask containing diol **23** (20.1 mg, 79.9 μmol) and Pd/C (10%, 5.0 mg) in absolute EtOH (0.75 mL), and the mixture was stirred for 12 h. Chromatography (EtOAc:EtOH 1:0, 1:9) gave the product **25** (12.6 mg, 78.7 μmol, 98%) as a colorless viscous oil: R_f 0.21 (EtOH:EtOAc = 1:9); $[\alpha]^{25}_D = +10.5$ ($c = 2.29$, MeOH); IR (film) 3303 (br s), 1088 (s), 1038 (s) cm^{-1}; ^1H NMR (CD_3OD, 300 MHz) δ 3.57 (dd, 1H, $J = 10.7$, 6.0 Hz), 3.43 (dd, 1H, $J = 10.7$, 6.2 Hz), 3.32 (m, 2H), 2.82 (dd, 1H, $J = 8.5$, 6.4 Hz), 1.73 (m, 1H), 0.90 (dm, 4H, $J = 7.0$ Hz), 0.71 (m, 1H), 0.42 (m, 2H); ^{13}C NMR (CD_3OD, 75.5 MHz) δ 76.9, 65.2, 64.7, 42.0, 20.7, 17.8, 12.2, 7.8; MS (CI, NH_3) m/z 178 $[M + NH_4]^+$, 160, 143, 130, 125, 112, calcd for $C_8H_{20}NO_3$ ($[M + NH_4]^+$): 178.1443, found 178.1440.

(1*S*,3*S*)-3-(Hydroxymethyl)-1-[(1*S*,2*R*)-2-methyl-1,3-*O*-(1-methylethylidene)-1,3-dihydroxyprop-1-yl]cyclopropane (26). 2,2-Dimethoxypropane (1 equiv, 25.0 μL, 0.205 mmol) was added to triol **25** (32.9 mg, 0.205 mmol) and pyridinium *p*-toluenesulfonate (5.0 mg) in DMF (2 mL) at 0 °C. The mixture was stirred at room temperature for 24 h. Saturated $NaHCO_3$ solution was added, and the aqueous layer was extracted into Et_2O (5×). The organic layer was washed with brine and dried (Na_2SO_4). Rotary evaporation and chromatography (EtOAc:hexanes 0:1, 1:9, 1:3, 1:1, 3:1, 1:0) gave the product **26** (24.7 mg, 0.123 mmol, 60%) as a colorless viscous oil: R_f 0.32 (EtOAc); $[\alpha]^{25}_D = +1.8$ ($c = 1.06$, MeOH); IR (film) 3400 (br s), 1098 (m), 1057 (m), 1011 (m) cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 3.68 (dd, 1H, $J = 11.7$, 5.1 Hz), 3.55 (dd, 1H, $J = 10.9$, 6.6 Hz), 3.47 (t, 1H, $J = 11.5$ Hz), 3.37 (dd, 1H, $J = 11.0$, 7.5 Hz), 2.80 (dd, 1H, $J = 9.8$, 8.2 Hz), 2.19 (br s, 1H), 1.83 (m, 1H), 1.39 (s, 3H), 1.38 (s, 3H), 1.04 (m, 1H), 0.85 (d, 3H, $J = 6.7$ Hz), 0.76 (m, 1H), 0.60 (m, 2H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 98.3, 78.3, 66.4, 66.1, 35.9, 29.8, 20.8, 19.0, 18.0, 12.9, 8.7; MS (CI, NH_3) m/z 218 $[M + NH_4]^+$, 201 $[M + H]^+$, 185, 160, 143, 130, 125, 95, calcd for $C_{11}H_{24}NO_3$ ($[M + NH_4]^+$) 218.17562, found 218.17596; calcd for $C_{11}H_{21}O_3$ ($[M + H]^+$) 201.1491, found 201.1493.

(1*S*,3*S*)-1-[(1*R*,2*R*)-1,3-Dihydroxy-2-methylprop-1-yl]-3-(hydroxymethyl)cyclopropane (27). H_2(g) was attached to a flask containing diol **24** (18.5 mg, 0.0739 mmol) and Pd/C (10%, 5.0 mg) in absolute EtOH (0.75 mL), and the mixture was stirred for 12 h. Chromatography (EtOAc:EtOH 1:0, 1:9) gave the product **27** (11.2 mg, 0.0699 mmol, 95%) as a colorless viscous oil: R_f 0.24 (EtOH:EtOAc = 1:9); $[\alpha]^{25}_D = +4.3$ ($c = 0.31$, MeOH); IR (film) 3330 (br s), 1088 (s), 1036 (s) cm^{-1}; ^1H NMR (CD_3OD, 300 MHz) δ 3.66 (dd, 1H, $J = 10.7$, 6.6 Hz), 3.51 (dd, 1H, $J = 10.7$, 6.0 Hz), 3.43 (m, 2H), 2.99 (dd, 1H, J

= 8.4, 4.6 Hz), 1.84 (m, 1H), 1.01 (dm, 4H, J = 6.9 Hz), 0.94 (m, 1H), 0.58 (m, 1H), 0.48 (m, 1H); ^{13}C NMR (CD_3OD, 75.5 MHz) δ 75.9, 64.9, 64.5, 41.5, 20.8, 18.5, 10.9, 7.7; MS (CI, NH_3) m/z 178 $[M + NH_4]^+$, 160, 143, 130, 125, 112, calcd for $C_8H_{20}NO_3$ ($[M + NH_4]^+$) 178.1443, found 178.1434.

(1*S*,3*S*)-3-(Hydroxymethyl)-1-[(1*R*,2*R*)-2-methyl-1,3-*O*-(1-methylethylidene)-1,3-dihydroxyprop-1-yl]cyclopropane (28). 2,2-Dimethoxypropane (1 equiv, 44.0 μL, 0.362 mmol) was added to triol **27** (58.0 mg, 0.362 mmol) and pyridinium *p*-toluenesulfonate (8.0 mg) in DMF (3.5 mL) at 0 °C. The mixture was stirred at room temperture for 24 h. Saturated $NaHCO_3$ solution was added, and the aqueous layer was extracted into Et_2O (5×). The organic layer was washed with brine and dried (Na_2SO_4). Rotary evaporation and chromatography (EtOAc:hexanes 0:1, 1:9, 1:3, 1:1, 3:1, 1:0) gave the product **28** (40.6 mg, 0.203 mmol, 56%) as a colorless viscous oil: R_f 0.39 (EtOAc); $[\alpha]^{25}_D = +26.3$ (c = 1.37, MeOH); IR (film) 3401 (br s), 1097 (m), 1058 (m), 1011 (m) cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 4.05 (dd, 1H, J = 11.5, 2.9 Hz), 3.59 (dd, 1H, J = 11.5, 1.6 Hz), 3.49 (m, 2H), 3.23 (dd, 1H, J = 8.2, 2.6 Hz), 1.59 (m, 1H), 1.57 (br s, 1H), 1.42 (s, 3H), 1.39 (s, 3H), 1.19 (d, 3H, J = 7.0 Hz), 0.93 (m, 1H), 0.88 (m, 1H), 0.60 (m, 2H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 98.6, 75.5, 66.7, 66.4, 32.3, 29.6, 19.4, 19.1, 17.5, 11.5, 9.7; MS (CI, NH_3) m/z 218 $[M + NH_4]^+$, 201 $[M + H]^+$, 185, 160, 143, 130, 125, 95, calcd for $C_{11}H_{24}NO_3$ ($[M + NH_4]^+$): 218.1756, found 218.1750; calcd for $C_{11}H_{21}O_3$ ($[M + H]^+$) 201.1491, found 201.1491.

(2*R*,3*R*,4*R*)-2-[(1*R*)-2-Hydroxy-1-methylethyl]-4-methyl-3-(phenylmethoxy)tetrahydrofuran (30). $Hg(O_2CCF_3)_2$ (682 mg, 1.60 mmol, 2 equiv) was added to cyclopropane **23** (195 mg, 0.779 mmol) in CH_2Cl_2 (8 mL). The mixture was stirred at room temperature for 48 h, and TLC indicated that all starting material was consumed. Solid NaCl (5.0 g) was added, and the mixture was stirred vigorously for 3 h. The mixture was filtered through silica (washed with EtOAc: hexanes 0:1, 1:9, 1:3 discarded; EtOAc:hexanes 1:1, 1:0 collected), and rotary evaporation gave crude product **29** (229 mg, 0.472 mmol, 61%). This crude product was dissolved in THF (28 mL), and $LiAlH_4$ (180 mg, 4.73 mmol) was added at 0 °C under N_2. The mixture was allowed to stir at 0 °C for 3 h and diluted with Et_2O, a minimal amount of water and potassium sodium tartrate were added at 0 °C, and the solution was stirred for 30 min. The mixture was filtered through silica and washed with MeOH/Et_2O (1:4). Rotary evaporation and chromatography (EtOAc:hexanes 0:1, 1:9, 1:4, 1:3, 2:3) gave the product **30** (64.7 mg, 0.258 mmol, 55%) as a colorless viscous oil: R_f 0.24 (EtOAc); $[\alpha]^{25}_D = -25.8$ (c = 0.59, MeOH); IR (film) 3447 (br s), 1104 (s), 1042 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.35 (m, 5H), 4.73 (d_{AB}, 1H, J = 11.3 Hz), 4.54 (d_{AB}, 1H, J = 11.3 Hz), 3.94 (t, 1H, J = 8.0 Hz), 3.86 (t, 1H, J = 3.5 Hz), 3.70 (dd, 1H, J = 9.8, 3.1 Hz), 3.62−3.57 (m, 3H), 3.26 (dd, 1H, J = 7.9, 3.6 Hz), 2.40 (m, 1H), 2.27 (m, 1H), 1.14 (d, 3H, J = 6.8 Hz), 0.74 (d, 3H, J = 6.8 Hz); ^{13}C NMR ($CDCl_3$, 100.58 MHz) δ 138.2, 128.4, 127.7, 127.7, 89.6, 81.5, 74.4, 72.9, 68.2, 39.2, 34.6, 13.7, 11.0; MS (CI, NH_3) m/z 268 $[M + NH_4]^+$, 251 $[M + H]^+$, 118, 108, 91, calcd for $C_{15}H_{23}O_3$ ($[M + H]^+$) 251.1647, found 251.1640. Anal. Calcd for $C_{15}H_{22}O_3$: C, 71.97; H, 8.86. Found: C, 71.94; H, 8.81.

(2*R*,3*S*,4*R*)-2-[(1*R*)-2-Hydroxy-1-methyleth-1-yl]-4-methyl-3-(phenylmethoxy)tetrahydrofuran (32). $Hg(O_2CCF_3)_2$ (682 mg, 1.60 mmol, 2 equiv) was added to cyclopropane **24** (200 mg, 0.799 mmol) in CH_2Cl_2 (8 mL). The mixture was stirred at room temperature for 48 h, and TLC indicated that all starting material was consumed. Solid NaCl (5.0 g) was added, and the mixture was stirred vigorously for 3 h. The mixture was filtered through silica (washed with EtOAc: hexanes 0:1, 1:9, 1:3 discarded; EtOAc:hexanes 1:1, 1:0 collected), and rotary evaporation gave crude product **31** (235 mg, 0.485 mmol, 61%). This crude product was dissolved in THF (28 mL), and $LiAlH_4$ (183.1 mg, 4.82 mmol) was added at 0 °C under N_2. The mixture was allowed to stir at 0 °C for 3 h and diluted with Et_2O, a minimal amount of water and potassium sodium tartrate were added at 0 °C, and the mixtured was stirred for 30 min. The mixture was filtered through silica and washed with MeOH/Et_2O (1:4). Rotary evaporation and chromatography (EtOAc:hexanes 0:1, 1:9, 1:4, 1:3, 2:3) gave the product **32** (70.4 mg, 0.281 mmol, 58%) as a colorless viscous oil: R_f 0.33 (EtOAc); $[\alpha]^{25}_D = +24.1$ (c = 0.16, MeOH); IR (film) 3445 (br s), 1075 (s), 1029 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.34 (m, 5H), 4.60 (d_{AB}, 1H, J = 11.5 Hz), 4.48 (d_{AB}, 1H, J = 11.5 Hz), 3.96 (dd, 1H, J = 8.7, 6.0 Hz), 3.65 (t, 1H, J = 4.5 Hz), 3.62−3.57 (m, 3H), 3.49 (dd, 1H, J = 4.5, 2.3 Hz), 3.12 (m, 1H), 2.34 (m, 1H), 1.88 (m, 1H), 1.10 (d, 3H, J = 7.3 Hz), 0.89 (d, 3H, J = 6.9 Hz); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 137.8, 128.5, 127.8, 127.8, 90.2, 89.7, 73.6, 71.6, 68.0, 39.3, 38.6, 18.2, 13.2; MS (CI, NH_3) m/z 268 $[M + NH_4]^+$, 251 $[M + H]^+$, 118, 108, 91, calcd for $C_{15}H_{23}O_3$ ($[M + H]^+$) 251.1647, found 251.1642. Anal. Calcd for $C_{15}H_{22}O_3$: C, 71.97; H, 8.86. Found: C, 71.77; H, 8.70.

(1*R,3*S**)-1-(Hydroxymethyl)bicyclopropane (39).** Et_2Zn (neat, 2.10 mL, 20.5 mmol, 6 equiv) was added slowly to CH_2Cl_2 (22 mL) when CH_2I_2 (1.70 mL, 21.1 mmol, 6 equiv) was added dropwise at −20 °C. The mixture was allowed to stir for 15 min at −15 °C before a solution of *trans*-penta-2,4-dien-1-ol (**38**)[14] (290 mg, 3.45 mmol) in CH_2Cl_2 (13 mL) was added *via* cannula at −20 °C. The mixture was stirred at −10 °C for 2 h and at room temperature for 12 h. The mixture was quenched with saturated NH_4Cl solution at 0 °C followed by addition of 0.5 M HCl. The product was extracted into CH_2Cl_2 (4×), and the organic layer was washed with a saturated $NaHCO_3$ solution and brine and dried (Na_2SO_4). Rotary evaporation at ∼50 mmHg/room temperature and chromatography (EtOAc:hexanes 0:1, 1:4, 1:1) gave the product **39** (337 mg, 3.01 mmol, 87%) as a colorless oil: R_f 0.25 (Et_2O: hexanes = 1:1); IR (film) 3446 (br s), 3206 (br s), 1035 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.43 (m, 2H), 1.44 (br s, 1H), 0.87 (m, 2H), 0.74 (m, 1H), 0.42−0.30 (m, 4H), 0.06 (m, 2H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 67.09, 19.4, 18.9, 11.89, 8.0, 3.2, 2.9; MS (CI, NH_3) m/z 130 $[M + NH_4]^+$, 112, 95, calcd for $C_7H_{16}NO$ ($[M + NH_4]^+$) 130.1232, found 130.1231.

Methyl *trans*-4-Methyl-2-pentenoate (41). $(EtO)_2P(O)CH_2COOMe$ (23.0 mL, 125 mmol) was added dropwise to pentane-washed NaH (2.95 g, 123 mmol) in benzene (150 mL), and the mixture was stirred at room temperature for 45 min. Isobutyraldehyde (**40**) (10.0 mL, 110 mmol) was added, and the mixture was allowed to stir at 70 °C for 2.5 h. After the reaction was quenched with water (50 mL), the aqueous layer was extracted with Et_2O (4×), and the combined ethers layer were washed with brine and dried ($MgSO_4$). After removal of the solvent (at 760 mmHg), the crude product was purified by distillation (first at 125 °C/760 mmHg to remove trace of the *cis* isomer (<100 mg) and at 100 °C/150 mmHg for the *trans* isomer) to afford the product **41** as a colorless oil (12.0 g, 86%). Spectral data were in accord with those reported in the literature.[17]

***trans*-4-Methyl-2-penten-1-ol (42).** DIBAL-H (1 M in hexanes, 140 mL, 140 mmol) was added to ester **41** (6.10 g, 47.6 mmol) in CH_2Cl_2 (200 mL) at −78 °C. The mixture was stirred at −78 °C for 1 h and quenched with saturated NH_4Cl solution and 1 M HCl at 0 °C. The aqueous layer was extracted with CH_2Cl_2 (4×), and the combined organic layers were washed with brine and dried (Na_2SO_4). After removal of the solvent at ∼80 mmHg/room temperature, the crude product was purified by distillation (55−65 °C/10−15 mmHg) to afford the product **42** as a colorless oil (4.70 g, 46.9 mmol, 99%). Spectral data were in accord with those reported in the literature.[18]

(1*S,3*R**)-1-(Hydroxymethyl)-3-isopropylcyclopropane (43).** Et_2Zn (neat, 6.10 mL, 59.5 mmol, 3 equiv) was added slowly to CH_2Cl_2 (80 mL) when CH_2I_2 (4.80 mL, 59.5 mmol, 3 equiv) was added dropwise at −20 °C. The mixture was allowed to stir for 15 min at −15 °C before a solution of **42** (2.00 g, 20.0 mmol) in CH_2Cl_2 (80 mL) was added *via* cannula at −20 °C. The mixture was stirred at −20 °C for 2 h and at room temperature for 12 h. The mixture was quenched with saturated NH_4Cl solution at 0 °C followed by addition of 0.5 M HCl. The product was extracted into CH_2Cl_2

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(4×), and the organic layer was washed with a saturated $NaHCO_3$ solution and brine and dried (Na_2SO_4). Rotary evaporation at ~80 mmHg/room temperature and chromatography (EtOAc:hexanes 0:1, 1:4, 1:1) gave the product **43** (1.84 g, 16.1 mmol, 81%, containing ~3% of the *cis* isomer) as a colorless oil. Spectral data were in accord with those reported in the literature.[19]

Mercury-Induced Ring Opening of Bicyclopropane 39. $Hg(O_2CCF_3)_2$ (380 mg, 0.891 mmol, 2 equiv) was added to bicyclopropane **39** (50.0 mg, 0.446 mmol) in methanol (4.5 mL). The mixture was stirred at room temperature for 15 min, and TLC indicated that all starting material was consumed. After the solution was stirred for an addition 30 min, solid NaCl (2.5 g) was added and the mixture was stirred vigorously for 3 h. Excess NaCl was removed by filtration, and the solids were washed with MeOH/Et_2O (1:4). Rotary evaporation and chromatography (EtOAc:hexanes 0:1, 1:4, 1:1) gave the products **44** (122 mg, 0.321 mmol, 72%, dr ~2.4:1) and **45** (32.1 mg, 0.085 mmol, 19%, dr ~1.4:1) both as colorless viscous oils.

(2*S,3*R**/*S**)-2-[(Chloromercurio)methyl]-3-cyclopropyl-3-methoxy-1-propanol (44):** R_f 0.34 (EtOAc:hexanes = 1:1); IR (film) 3399 (br s), 1086 (s), 1028 (m) cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 3.94 (dd, 1H, J = 11.1, 4.5 Hz), 3.57 (m, 1H), 3.39 (s, 3H), 2.42 (dd, 1H, J = 8.9, 3.1 Hz), 2.32 (m, 1H), 2.15 (br s, 1H), 1.78 (m, 2H), 0.79 (m, 1H), 0.72 (m, 1H), 0.44 (m, 2H), 0.00 (m, 1H); minor isomer showed resolved peaks at δ 3.67 (dd, 1H, J = 10.7, 5.0 Hz), 3.41 (s, 3H), 2.64 (dd, 1H, J = 8.6, 3.1 Hz); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 89.1, 64.3, 57.7, 43.8, 28.4, 12.1, 5.8, 0.3; minor isomer showed resolved peaks at δ 86.2, 67.1, 56.9, 44.1, 24.2, 12.0, 6.4, −0.2; MS (CI, NH_3) m/z 398 $[M + NH_4]^+$, 396 $[M + NH_4]^+$, 362, 360, 145, 130, 85, calcd for $C_8H_{19}NO_2ClHg$ ($[M + NH_4]^+$) 398.0811 and 396.0788, found 398.0813 and 396.0797.

(1*R,3*R**)-1-[3-(Chloromercurio)-1(*R**/*S**)-methoxypropn-1-yl]-3-(hydroxymethyl)cyclopropane (45):** R_f 0.18 (EtOAc:hexanes = 1:1); IR (film) 3399 (br s), 1083 (s), 1041 (s), 1018 (s) cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 3.48 (m, 2H), 3.37 (s, 3H), 2.48 (m, 1H), 2.10−1.60 (m, 4H), 0.77 (m, 1H), 0.64 (m, 2H), 0.38 (m, 1H); minor isomer showed resolved peaks at δ 3.40 (s, 3H), 0.25 (m, 1H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) major isomer δ 84.1, 66.2, 56.8, 33.1, 24.4, 19.8, 16.6, 5.7; minor isomer δ 84.2, 66.1, 56.9, 32.8, 24.3, 21.5, 19.7, 10.8; MS (CI, NH_3) m/z 398 $[M + NH_4]^+$, 396 $[M + NH_4]^+$, 362, 330, 162, 130, 115, 71, calcd for $C_8H_{19}NO_2ClHg$ ($[M + NH_4]^+$) 398.0811 and 396.0788, found 398.0806 and 396.0786.

(2*S,3*R**/*S**)-3-Cyclopropyl-3-methoxy-2-methyl-1-propanol (46).** $LiAlH_4$ (96.0 mg, 2.53 mmol) was added to **44** (120 mg, 0.317 mmol, dr ~2.4:1) in THF (15 mL) at 0 °C under N_2, and the mixture was stirred at 0 °C for 3 h. The mixture was diluted with Et_2O, a minimal amount of water and potassium sodium tartrate were added at 0 °C, and the mixture was stirred for 30 min. The product was extracted into Et_2O (×4), and the organic layer was washed with brine and dried (Na_2SO_4). Rotary evaporation at ~80 mmHg/room temperature and chromatography (EtOAc:hexanes 0:1, 1:9, 1:4, 1:1, 4:1) gave the products **46** (30.9 mg, 0.214 mmol, 68%, dr ~2.4:1) as a colorless oil: R_f 0.43 (Et_2O:hexanes = 4:1); IR (film) 3393 (br s), 1091 (s), 1028 (s) cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 3.61 (m, 1H), 3.46 (m, 1H), 3.313 (s, 3H), 2.84 (t, 1H, J = 5.4 Hz), 2.38 (dd, 1H, J = 8.9, 5.9 Hz), 1.83 (m, 1H), 0.89 (d, 3H, J = 7.1 Hz), 0.76 (m, 1H), 0.54 (m, 1H), 0.37 (m, 1H), 0.28 (m, 1H), 0.00 (m, 1H); minor isomer showed resolved peaks at δ 3.308 (s, 3H), 2.64 (t, 1H, J = 5.2 Hz), 2.50 (dd, 1H, J = 8.9, 3.2 Hz), 0.88 (d, 3H, J = 7.1 Hz); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 90.3, 66.7, 57.3, 40.3, 14.4, 12.8, 4.2, 1.2; minor isomer showed resolved peaks at δ 88.7, 57.2, 39.2, 11.7, 11.2, 4.9, 0.3; MS (CI, NH_3) m/z 162 $[M + NH_4]^+$, 145 $[M + H]^+$, 130, 112, 95, 85, calcd for $C_8H_{20}NO_2$ ($[M + NH_4]^+$): 162.1494, found 162.1490.

(1*R,3*R**)-3-(Hydroxymethyl)-1-[1(*R**/*S**)-methoxyprop-1-yl]cyclopropane (47).** $LiAlH_4$ (40.0 mg, 1.05 mmol) was added to **45** (50.2 mg, 0.132 mmol, dr ~1.4:1) in THF (6 mL) at 0 °C under N_2, and the mixture was stirred at 0 °C for 3 h. The mixture was diluted with Et_2O, a minimal amount of water and potassium sodium tartrate were added at 0 °C, and the mixture was stirred for 30 min. The product was extracted into Et_2O (×4), and the organic layer was washed with brine and dried (Na_2SO_4). Rotary evaporation at ~80 mmHg/room temperature and chromatography (EtOAc:hexanes 0:1, 1:9, 1:4, 1:1, 4:1) gave the products **47** (12.4 mg, 0.086 mmol, 65%, dr ~1.4:1) as a colorless oil: R_f 0.28 (Et_2O:hexanes = 4:1); IR (film) 3381 (br s), 1102 (s), 1080 (s), 1052 (s) cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 3.44 (m, 2H), 3.31 (s, 3H), 2.45 (m, 1H), 1.55 (m, 2H), 1.49 (br s, 1H), 0.89 (t, 3H, J = 7.4 Hz), 0.82 (m, 1H), 0.70−0.27 (m, 3H); minor isomer showed resolved peaks at δ 3.33 (s, 3H), 1.72 (br s, 1H), 0.88 (t, 3H, J = 7.5 Hz); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 85.0, 66.5, 56.7, 27.6, 20.2, 17.5, 9.9, 6.6; minor isomer showed resolved peaks at δ 85.3, 56.8, 27.4, 20.4, 9.7, 9.5; MS (CI, NH_3) m/z 162 $[M + NH_4]^+$, 145 $[M + H]^+$, 130, 115, 95, 71, calcd for $C_8H_{20}NO_2$ ($[M + NH_4]^+$) 162.1494, found 162.1494.

(2*R,3*S**)-2,4-Dimethyl-3-methoxy-1-pentanol (48).** $Hg(O_2CCF_3)_2$ (750 mg, 1.76 mmol, 2 equiv) was added to **43** (100 mg, 0.876 mmol) in MeOH (9 mL). The mixture was stirred at room temperature and was monitored by TLC. After 10 days, solid NaCl (2.5 g) was added and the mixture was stirred vigorously for 3 h. Excess NaCl and mercury salts were removed by filtration through silica (eluted with EtOAc:hexanes = 1:1). The residue oil was dissolved in THF (20 mL) and was added to $LiAlH_4$ (266 mg, 7.00 mmol) in THF (20 mL) at 0 °C under N_2. After being stirred for 3 h at 0 °C, the mixture was diluted with Et_2O, a minimal amount of water and potassium sodium tartrate were added at 0 °C, and the mixture was stirred for 30 min. The product was extracted into Et_2O (×5), and the organic layer was washed with brine and dried (Na_2SO_4). Rotary evaporation and chromatography (EtOAc:hexanes 0:1, 1:9, 1:4) gave the product **48** (84.5 mg, 0.587 mmol, 66%) as a colorless oil: R_f 0.21 (EtOAc:hexanes = 1:3); IR (film) 3392 (br s), 1087 (s), 1035 (s) cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 3.64 (m, 1H), 3.57 (m, 1H), 3.44 (s, 3H), 2.86 (t, 1H, J = 5.5 Hz), 2.81 (dd, 1H, J = 6.3, 5.3 Hz), 1.87−1.77 (m, 2H), 0.92 (m, 9H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 92.6, 66.3, 61.5, 37.1, 31.0, 20.1, 17.3, 15.5; MS (CI, NH_3) m/z 164 $[M + NH_4]^+$, 147 $[M + H]^+$, 99, 87, calcd for $C_8H_{19}O_2$ ($[M + H]^+$) 147.1385, found 147.1385.

(1*R,3*S**,4*R**,6*S**)-1,6-Bis(hydroxymethyl)bicyclopropane (4).** TBAF (1 M in THF, contain 5% water) was added to a solution of **50**[7b,e] (201 mg, 0.528 mmol) in THF (0.5 mL) at room temperature. The mixture was stirred at room temperature for 2 h and was quenched with MeOH (1 mL). Rotary evaporation and chromatography (EtOAc:hexanes 1:4, 1:1, 1:0) gave the product **4** (72.8 mg, 0.512 mmol, 97%) as a colorless oil. Recrystallization from EtOAc at 0 °C afforded white crystals: mp 29−30 °C; R_f 0.18 (EtOAc); IR (KBr) 3306 (br s), 1031 (s), 1015 (s) cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 3.48 (m, 2H), 3.35 (m, 2H), 2.12 (br s, 2H), 0.91−0.77 (m, 4H), 0.33 (t, 4H, J = 6.7 Hz); ^{13}C NMR ($CDCl_3$, 75.47 MHz) δ 66.7, 19.4, 18.1, 8.46; MS (CI, NH_3) m/z 160 $[M + NH_4]^+$, 142 $[M + NH_4 - H_2O]^+$, 125, 107, 83, calcd for $C_8H_{18}NO_2$ ($[M + NH_4]^+$) 160.1338, found 160.1341.

Mercury-Induced Ring Opening of *anti*-Bicyclopropanedimethanol (4). $Hg(O_2CCF_3)_2$ (391 mg, 0.917 mmol, 2 equiv) was added to cyclopropanedimethanol **4** (65.0 mg, 0.457 mmol) in BnOH (5 mL). The mixture was stirred at room temperature for 20 min, and TLC indicated that all starting material was consumed. Solid NaCl (2.5 g) was added, and the mixture was stirred vigorously for 3 h. The mixture was filtered through silica (washed with EtOAc:hexanes 0:1, 1:9, 1:3 discarded; EtOAc:hexanes 1:1, 1:0 collected), and rotary evaporation gave crude product **51** (166 mg, 0.343 mmol, 75%). This residue was dissolved in THF (25 mL), and $LiAlH_4$ (180 mg, 4.74 mmol) was added at 0 °C under N_2. The mixture was allowed to stir at 0 °C for 2 h and diluted with Et_2O, a minimal amount of water and potassium sodium tartrate were added at 0 °C, and the solution was stirred for 30 min. The mixture was filtered through silica and washed with MeOH/Et_2O (1:4). Rotary evaporation and chromatography (EtOAc:hexanes 0:1, 1:9, 1:3, 2:3, 4:1, 1:0) gave two combined fractions (82.4 mg, 72% and **52**:**53** ~1:2.2): the first fraction contained

(19) (a) Lillien, I.; Doughty, R. A. *J. Org. Chem.* **1968**, *33*, 3841. (b) Lillien, I.; Handloser, L. *J. Am. Chem. Soc.* **1971**, *93*, 1682.

65% **52**, 25% **53**, and 10% of nonidentified rearranged products and the second fraction contained 85% **53** and 15% **52** as determined by ^{1}H NMR.

(1*S,3*S**)-3-(Hydroxymethyl)-1-[(1*S**,2*S**)-3-hydroxy-2-methyl-1-(phenylmethoxy)prop-1-yl]cyclopropane (52):** R_f 0.38 (EtOAc); IR (film) 3368 (br s), 1041 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.13 (m, 5H), 4.58 (d_{AB}, 1H, J = 11.8 Hz), 4.37 (d_{AB}, 1H, J = 11.8 Hz), 3.57−3.23 (m, 4H), 2.79 (dd, 1H, J = 8.5, 3.3 Hz), 1.81 (m, 1H), 1.00 (m, 1H), 0.83 (d, 3H, J = 7.2 Hz), 0.69 (m, 1H), 0.27 (m, 1H), 0.19 (m, 1H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 138.7, 128.5, 127.7, 127.6, 84.2, 71.5, 66.4, 66.2, 39.3, 20.8, 17.9, 11.8, 6.2; MS (CI, NH_3) *m*/*z* 268 $[M + NH_4]^+$, 251 $[M + H]^+$, 191, 160, 143, 130, 125, 108, 91, calcd for $C_{15}H_{23}O_3$ ($[M + H]^+$) 251.1647, found 251.1652.

(1*S,3*S**)-3-(Hydroxymethyl)-1-[(1*R**,2*S**)-3-hydroxy-2-methyl-1-(phenylmethoxy)prop-1-yl]cyclopropane (53):** R_f 0.34 (EtOAc); IR (film) 3368 (br s), 1040 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.25 (m, 5H), 4.73 (d_{AB}, 1H, J = 11.6 Hz), 4.43 (d_{AB}, 1H, J = 11.6 Hz), 3.72 (dd, 1H, J = 10.7, 6.8 Hz), 3.63 (m, 2H), 3.24 (dd, 1H, J = 11.1, 7.6 Hz), 2.74 (dd, 1H, J = 8.6, 4.7 Hz), 2.47 (br s, 1H), 2.27 (br s, 1H), 1.98 (m, 1H), 0.96 (d, 3H, J = 7.1Hz), 0.87 (m, 2H), 0.58 (m, 2H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 138.7, 128.4, 127.6(2), 86.0, 71.2, 66.5, 65.7, 40.1, 19.7, 17.5, 14.6, 10.5; MS (CI, NH_3) *m*/*z* 268 $[M + NH_4]^+$, 251 $[M + H]^+$, 233, 191, 160, 143, 125, 95, 91, calcd for $C_{15}H_{23}O_3$ ($[M + H]^+$) 251.1647, found 251.1653.

Mercury-Induced Ring Opening of Tercyclopropanedimethanol 5. $Hg(O_2CCF_3)_2$ (5.06 g, 11.9 mmol, 3 equiv) was added to tercyclopropanedimethanol **5** (720 mg, 3.95 mmol) in MeOH (50 mL). The mixture was stirred at room temperature for 20 min, and TLC indicated that all starting material was consumed. The mixture was allowed to stir for an additional 2 h. Solid NaCl (12 g) was added, and the mixture was stirred vigorously for 3 h. The mixture was filtered through silica (eluted with EtOAc), and rotary evaporation gave a crude product as a viscous oil. This residue was filtered through silica again (washed with EtOAc:hexanes 0:1, 1:9, 1:3 discarded; EtOAc:hexanes 1:1, 1:0 collected), and rotary evaporation gave a gummy white solid residue. The residue was dissolved in THF (40 mL) and was added *via* cannula to a suspension of $LiAlH_4$ (1.50 g, 39.5 mmol, 10 equiv) in THF (40 mL) at 0 °C under N_2. The mixture was allowed to stir at 0 °C for 3 h and diluted with Et_2O, a minimal amount of water and potassium sodium tartrate were added at 0 °C, and the solution was stirred for 30 min. The mixture was filtered through silica and washed with MeOH/Et_2O (1:5). Rotary evaporation and chromatography (EtOAc:hexanes 0:1, 1:9, 1:4, 2:3, 3:2, 4:1, 1:0) gave a partially separable mixture of products **60** and **61** both as colorless viscous oils (695 mg, 3.24 mmol, 82%). The first fraction contained 90% **60** and 10% **61**, the second fraction contained 69% **60** and 31% **61**, and the third fraction contained 85% **61** and 15% **60** as determined by ^{1}H NMR.

(1*R*,3*R*)-3-(Hydroxymethyl)-1-[(1*R*,5*R*)-6-hydroxy-1-methoxy-5-methylhex-3(*E*)-en-1-yl]cyclopropane (60): R_f 0.17 (EtOAc); IR (film) 3391 (br s), 1096 (s), 1035 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 5.60 (ddd, 1 H, J = 15.4, 7.9, 6.7 Hz), 5.33 (dd, 1H, J = 15.4, 8.1 Hz), 3.62 (dd, 1H, J = 11.3, 6.0 Hz), 3.51 (dd, 1H, J = 10.5, 5.0 Hz), 3.37 (s, 3H), 3.32 (dd, 1H, J = 10.5, 4.7 Hz), 3.27 (dd, 1H, J = 11.3, 7.5 Hz), 2.60 (dt, 1H, J = 8.6, 5.5 Hz), 2.42−2.28 (m, 5H), 0.96 (d, 3H, J = 6.8 Hz), 0.87 (m, 1H), 0.74 (m, 1H), 0.62 (dt, 1H, J = 8.3, 5.0 Hz), 0.56 (dt, 1H, J = 8.3, 5.0 Hz); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 135.3, 127.6, 83.7, 67.2, 66.1, 56.6, 39.8, 38.0, 20.0, 17.3, 16.5, 9.9; MS (CI, NH_3) *m*/*z* 232 $[M + NH_4]^+$, 215 $[M + H]^+$, 200, 165, 115, 71, calcd for $C_{12}H_{26}NO_3$ ($[M + NH_4]^+$) 232.1913, found 232.1907. Anal. Calcd for $C_{12}H_{22}O_3$: C, 67.26; H, 10.35. Found: C, 67.37; H, 10.06.

(1*R*,3*R*)-3-(Hydroxymethyl)-1-[(1*S*,5*R*)-6-hydroxy-1-methoxy-5-methylhex-3(*E*)-en-1-yl]cyclopropane (61): R_f 0.13 (EtOAc); IR (film) 3370 (br s), 1095 (m), 1033 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 5.56 (dt, 1H, J = 15.4, 7.0 Hz), 5.34 (dd, 1H, J = 15.4, 7.4 Hz), 3.51−3.32 (m, 4H), 3.37 (s, 3H), 2.70 (br s, 2H), 2.62 (dt, 1H, J = 8.3, 5.6 Hz), 2.36−2.27 (m, 3H), 1.12 (m, 1H), 0.97 (d, 3H, J = 6.8 Hz), 0.73 (m, 1H), 0.37 (m, 2H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 135.1, 127.2, 83.7, 67.2, 66.1, 56.8, 39.7, 37.6, 20.3(2), 16.5, 6.6; MS (CI, NH_3) *m*/*z* 232 $[M + NH_4]^+$, 215 $[M + H]^+$, 200, 165, 115, 71, calcd for $C_{12}H_{26}NO_3$ ($[M + NH_4]^+$) 232.1913, found 232.1905. Anal. Calcd for $C_{12}H_{22}O_3$: C, 67.26; H, 10.35. Found: C, 67.53; H, 10.07.

(1*R*,3*R*)-3-(Hydroxymethyl)-1-[(1*R*)-3-hydroxy-1-methoxyprop-1-yl]cyclopropane (62). Ozone was passed through a solution containing diol **60** (200 mg, 0.933 mmol) in MeOH (0.5 mL) and CH_2Cl_2 (2.5 mL) at −78 °C. TLC indicated that all the starting material was consumed in 5 min. $NaBH_4$ (500 mg, 13.2 mmol) was added at −78 °C, and the mixture was stirred at 0 °C for 1 h and at room temperature for 1 h. The mixture was quenched with MeOH at 0 °C, a few drops of water were added, and the mixture was filtered through silica (MeOH). Rotary evaporation and chromatography (EtOAc: hexanes 0:1, 1:3, 1:1, 4:1, 1:0, EtOH:EtOAc 1:9) gave the product **62** (127 mg, 0.794 mmol, 85%) as a colorless viscous oil: R_f 0.23 (EtOH:EtOAc = 1:9); $[\alpha]^{25}_D$ = +1.8 (c = 0.73, MeOH); IR (film) 3353 (br s), 1206 (s), 1142 (s), 1077 (s), 1040 (s), 1016 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.81 (m, 2H), 3.71 (dd, 1H, J = 11.3, 5.7 Hz), 3.62 (br s, 2H), 3.39 (s, 3H), 3.18 (dd, 1H, J = 11.2, 8.1 Hz), 2.72 (m, 1H), 1.88 (m, 2H), 0.84 (m, 2H), 0.65 (m, 2H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 83.7, 66.2, 59.9, 56.6, 36.7, 20.6, 17.0, 10.4; MS (CI, NH_3) *m*/*z* 178 $[M + NH_4]^+$, 161 $[M + H]^+$, 146, 129, 115, 101, 71, calcd for $C_8H_{17}O_3$ ($[M + H]^+$) 161.1178, found 161.1184. Anal. Calcd for $C_8H_{16}O_3$: C, 59.98; H, 10.07. Found: C, 59.94; H, 10.25.

(1*R*,3*R*)-3-(Hydroxymethyl)-1-[(1*S*)-3-hydroxy-1-methoxyprop-1-yl]cyclopropane (64). Ozone was passed through a solution containing diol **61** (100 mg, 0.467 mmol) in MeOH (0.25 mL) and CH_2Cl_2 (1.25 mL) at −78 °C. TLC indicated that all the starting material was consumed in 5 min. $NaBH_4$ (250 mg, 6.61 mmol) was added at −78 °C, and the mixture was stirred at 0 °C for 1 h and at room temperature for 1 h. The mixture was quenched with MeOH at 0 °C, a few drops of water were added, and the mixture was filtered through silica (MeOH). Rotary evaporation and chromatography (EtOAc:hexanes 0:1, 1:3, 1:1, 4:1, 1:0, EtOH:EtOAc 1:9) gave the product **64** (62.1 mg, 0.388 mmol, 83%) as a colorless viscous oil: R_f 0.23 (EtOH:EtOAc = 1:9); $[\alpha]^{25}_D$ = +4.5 (c = 0.65, MeOH); IR (film) 3354 (br s), 1206 (s), 1142 (s), 1078 (s), 1041 (s), 1015 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.76 (m, 2H), 3.56 (dd, 1H, J = 11.2, 6.5 Hz), 3.43 (s, 3H), 3.40 (m, 1H), 2.92 (br s, 2H), 2.82 (m, 2H), 1.84 (m, 2H), 1.20 (m, 1H), 0.77 (m, 1H), 0.43 (dt, 1H, J = 8.8, 4.9 Hz), 0.33 (dt, 1H, J = 8.4, 5.1 Hz); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 83.8, 66.0, 60.6, 56.8, 36.7, 21.0, 20.3, 5.9; MS (CI, NH_3) *m*/*z* 178 $[M + NH_4]^+$, 161 $[M + H]^+$, 146, 129, 115, 101, 71, calcd for $C_8H_{17}O_3$ ($[M + H]^+$) 161.1178, found 161.1183.

Mercury-Induced Intramolecular Ring Opening of Cyclopropane 62. $Hg(O_2CCF_3)_2$ (546 mg, 1.28 mmol, 2 equiv) was added to cyclopropane **62** (103 mg, 0.640 mmol) in CH_2Cl_2 (6.5 mL). The mixture was stirred at room temperature for 48 h, and TLC indicated that all starting material was consumed. Solid NaCl (4.0 g) was added, and the mixture was stirred vigorously for 3 h and filtered through silica (EtOAc: hexanes 0:1, 1:9, 1:3 discarded; EtOAc:hexanes 1:1, 1:0 collected). Rotary evaporation gave a crude product (182 mg, 0.461 mmol, 72%) as a viscous oil which was dissolved in THF (25 mL), and $LiAlH_4$ (175 mg, 4.61 mmol, 10 equiv) was added at 0 °C under N_2. The mixture was allowed to stir at 0 °C for 3 h and diluted with Et_2O, a minimal amount of water and potassium sodium tartrate were added at 0 °C, and the solution was stirred for 30 min. The mixture was filtered through silica and washed with MeOH/Et_2O (1:4). Rotary evaporation and chromatography (EtOAc:hexanes 0:1, 1:9, 1:4, 2:3, 3:2, 4:1, 1:0) gave products **65** (30.5 mg, 0.190 mmol, 41%) and **66** (23.4 mg, 0.146 mmol, 32%) both as colorless viscous oils.

(2*S*,3*R*,4*R*)-2-(Hydroxymethyl)-4-methoxy-3-methyltetrahydropyran (65): R_f 0.29 (EtOAc); $[\alpha]^{25}_D$ = −55.4 (c = 0.50, MeOH); IR (film) 3452 (br s), 1095 (s), 1067 (m), 1042 (m) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 4.07 (ddd, 1H, J = 11.7, 4.9, 1.8 Hz), 3.75 (dd, 1H, J = 11.6, 2.6 Hz), 3.55 (dd, 1H, J = 11.6, 6.9 Hz), 3.44 (ddd, 1H, J = 12.7, 11.7, 2.1 Hz), 3.35 (s, 3H), 3.07 (ddd, 1H, J = 9.8, 6.9, 2.6 Hz), 2.90 (ddd, 1H, J = 10.5,

10.3, 4.6 Hz), 2.24 (br s, 1H), 2.04 (ddt, 1H, J = 12.8, 4.6, 1.8 Hz), 1.52−1.42 (m, 2H), 0.93 (d, 3H, J = 6.5 Hz); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 82.0, 81.8, 65.8, 63.8, 56.1, 38.38, 30.9, 12.6; MS (CI, NH_3) m/z 178 $[M + NH_4]^+$, 161 $[M + H]^+$, 129, 114, 97, 71, 58, calcd for $C_8H_{17}O_3$ ($[M + H]^+$) 161.1178, found 161.1180.

(2*S*,3*R*)-2-[(1*S*)-2-Hydroxy-1-methyleth-1-yl]-3-methoxytetrahydrofuran (66): R_f 0.34 (EtOAc); $[\alpha]^{25}_D$ = −66.9 (c = 0.34, MeOH); IR (film) 3434 (br s), 1113 (s), 1065 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.96 (ddd, 1H, J = 8.4, 7.2, 4.1 Hz), 3.82 (dd, 1H, J = 15.7, 8.4 Hz), 3.71 (dt, 1H, J = 5.4, 3.3 Hz), 3.65−3.60 (m, 3H), 3.32 (s, 3H), 3.18 (br s, 1H), 1.96 (m, 2H), 1.73 (m, 1H), 0.90 (d, 3H, J = 6.9 Hz); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 89.2, 84.4, 67.7, 66.9, 56.7, 38.2, 31.4, 13.3; MS (CI, NH_3) m/z 178 $[M + NH_4]^+$, 161 $[M + H]^+$, 128, 101, 72, calcd for $C_8H_{17}O_3$ ($[M + H]^+$) 161.1178, found 161.1169.

(2*S*,3*S*)-2-[(1*S*)-2-Hydroxy-1-methyleth-1-yl]-3-methoxytetrahydrofuran (67). $Hg(O_2CCF_3)_2$ (268 mg, 0.628 mmol, 2 equiv) was added to cyclopropane **64** (50.3 mg, 0.314 mmol) in CH_2Cl_2 (3 mL). The mixture was stirred at room temperature for 48 h, and TLC indicated that all starting material was consumed. Solid NaCl (2.0 g) was added, the mixture was stirred vigorously for 3 h and filtered through silica (EtOAc: hexanes 0:1, 1:9, 1:3 discarded; EtOAc:hexanes 1:1, 1:0 collected). Rotary evaporation gave a crude product (95.5 mg, 0.242 mmol, 77%) as a viscous oil which was dissolved in THF (13 mL), and $LiAlH_4$ (92.8 mg, 2.44 mmol, 10 equiv) was added at 0 °C under N_2. The mixture was allowed to stir at 0 °C for 3 h and diluted with Et_2O, a minimal amount of water and potassium sodium tartrate were added at 0 °C, and the solution was stirred for 30 min. The mixture was filtered through silica and washed with MeOH/Et_2O (1:4). Rotary evaporation and chromatography (EtOAc:hexanes 0:1, 1:9, 1:4, 2:3, 3:2, 4:1, 1:0) gave the product **67** (29.1 mg, 0.182 mmol, 75%) as a colorless viscous oil: R_f 0.31 (EtOAc); $[\alpha]^{25}_D$ = +58.7 (c = 1.19, MeOH); IR (film) 3447 (br s), 1130 (s), 1067 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.98 (dd, 1H, J = 15.8, 8.2 Hz), 3.82−3.77 (m, 2H), 3.58 (m, 2H), 3.44 (dd, 1H, J = 9.6, 3.4 Hz), 3.29 (s, 3H), 3.20 (br s, 1H), 2.15 (m, 1H), 2.06 (dddd, 1H, J = 13.0, 7.4, 4.1, 1.0 Hz), 1.89 (m, 1H), 0.83 (d, 3H, J = 6.8 Hz); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 88.1, 80.7, 68.1, 66.5, 56.6, 34.4, 30.2, 13.5; MS (CI, NH_3) m/z 178 $[M + NH_4]^+$, 161 $[M + H]^+$, 128, 101, 72, calcd for $C_8H_{17}O_3$ ($[M + H]^+$) 161.1178, found 161.1174.

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Supporting Information Available: ^{1}H and ^{13}C NMR spectra of **4**, **19**−**28**, **30**, **32**, **39**, **44**−**48**, **52**, **53**, **60**−**62**, and **64**−**67** (34 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from ACS; see any current masthead page for ordering information.

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