JOC
The Journal of Organic Chemistry

VOLUME 67, NUMBER 9 MAY 3, 2002

Articles

Unified Route to the Palmarumycin and Preussomerin Natural Products. Enantioselective Synthesis of (−)-Preussomerin G

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Received October 24, 2001

The total syntheses of eight members of the palmarumycin family have been achieved, with identification of the absolute stereochemistry for three of these natural products. In addition, the ras-farnesyl transferase inhibitor (−)-preussomerin G has been synthesized, achieving the first enantioselective route for accessing this family of natural products. Highlights of the synthetic work include an asymmetric epoxidation of a cyclic enone in excellent yield and enantiomeric excess and a potentially biomimetic oxidative spirocyclization for the introduction of the bis-spiroketal array unique to the preussomerin natural products.

Introduction

The palmarumycins,[1] diepoxins,[2] preussomerins,[3] and related compounds[4] are a structurally remarkable class of natural products isolated from various fungal cultures. They are all graced with a spiro-ketal entity formally derived from 1,8-naphthalenediol and 1,4-naphthoquinone, but at rich and varied oxidation levels. All three classes of fungal metabolites are undoubtedly closely interrelated biosynthetically and may well be derived from a 1,8-naphthalenediol spiroketal with late introduction of the unusual oxygenation patterns. The palmarumycins are exemplified by palmarumycin CP_1 (**1**), C_1 (**2**), C_2 (**3**), and C_{11} (**4**) among greater than 15 other members that show diverse biological effects including antifungal and antibacterial activity.[1] Since our original publication,[5] other routes for the synthesis of several racemic palmarumycins and analogues have been published.[6]

† Imperial College of Science, Technology and Medicine.
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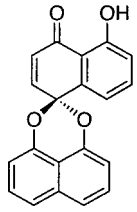
(1) (a) Krohn, K.; Michel, A.; Flörke, U.; Aust, H.-J.; Draeger, S.; Schulz, B. *Liebigs Ann. Chem.* **1994**, 1093. (b) Krohn, K.; Michel, A.; Flörke, U.; Aust, H.-J.; Draeger, S.; Schulz, B. *Liebigs Ann. Chem.* **1994**, 1099. (c) Krohn, K.; Beckmann, K.; Flörke, U.; Aust, H.-J.; Draeger, S.; Schulz, B.; Busemann, S.; Bringmann, G. *Tetrahedron* **1997**, *53*, 3101. (d) Bringmann, G.; Busemann, S.; Krohn, K.; Beckmann, K. *Tetrahedron* **1997**, *53*, 1655. (e) Chu, M.; Patel, G.; Pai, J.-K.; Das, R.; Puar, S. *Bioorg. Med. Chem. Lett.* **1996**, *6*, 579. (e) Krohn, K.; Steingröver, K.; Zsila, F. *Tetrahedron: Asymmetry* **2001**, *12*, 1961. (f) Krohn, K. Natural Products Derived from Naphthalenoid Precursors by Oxidative Dimerization. In *Prog. Chem. Org. Nat. Prod.* (Herz, W., Falk, H., Kirby, G. W., Moore, R. E., Tamm, Ch., Eds.) **2001**, *85*, in press.

(2) (a) Schlingmann, G.; West, R.; Milne, L.; Pearce, C. J.; Carter, G. T. *Tetrahedron Lett.* **1993**, *34*, 7225. (b) Schlingmann, G.; Matile, S.; Berova, N.; Nakanishi, K.; Carter, G. T. *Tetrahedron* **1996**, *52*, 435.

(3) (a) Weber, H. A.; Baezinger, N. C.; Gloer, J. B. *J. Am. Chem. Soc.* **1990**, *112*, 6718. (b) Weber, H. A.; Gloer, J. B. *J. Org. Chem.* **1991**, *56*, 4355. (c) Soman, A. G.; Gloer, J. B.; Koster, B.; Malloch, D. *J. Nat. Prod.* **1999**, *62*, 659. (d) Polishook, J. D.; Dombrowski, A. W.; Tsou, N. N.; Salituro, G. M.; Curotto, J. E. *Mycologia* **1993**, *85*, 62. (e) Singh, S. B.; Zink, D. L.; Liesch, J. M.; Ball, R. G.; Goetz, M. A.; Bolessa, E. A.; Giacobbe, R. A.; Silverman, K. C.; Bills, G. F.; Pelaez, F.; Cascales, C.; Gibbs, J. B.; Lingham, R. B. *J. Org. Chem.* **1994**, *59*, 6296. (f) Krohn, K.; Flörke, U.; John, M.; Root, N.; Steingröver, K.; Aust, H.-J.; Draeger, S.; Schulz, B.; Antus, S.; Simonyi, M.; Zsila, F. *Tetrahedron* **2001**, *57*, 4343.

10.1021/jo0110247 CCC: $22.00
Published on Web 04/03/2002



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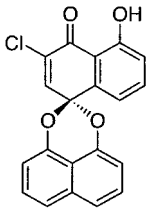

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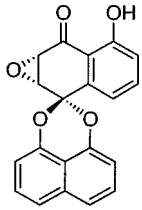

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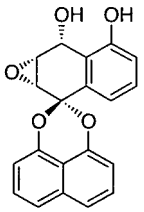

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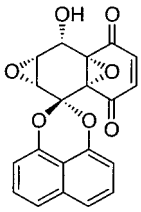

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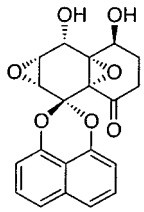

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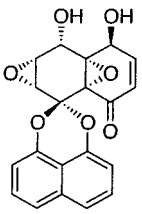

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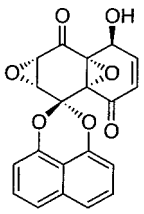

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The diepoxins were first reported in 1993 by Schlingmann and co-workers and are characterized by the bisepoxide functionality on the northern fused decalin rings.[2] Subsequent publications of related products[4] expanded this growing class to greater than 10 members at present. The structures are exemplified by diepoxin φ, also named palmarumycin C_{10} (**5**); diepoxin ζ (**6**), also named Sch 53516, palmarumycin C_{14}, and cladispirone bisepoxide; diepoxin η (**7**), also named Sch 53514 and palmarumycin C_{13}; and diepoxin σ (**8**), also named Sch 49209. The antitumor activity of diepoxin σ (**8**) was first revealed by Chu and co-workers in 1994, with an IC_{50} of 0.75 μm against the invasion of HT 1080 human fibrosarcoma cells.[4e] Wipf et al. have recently reported an elegant formal enantioselective synthesis of diepoxin σ (**8**) using a key enantioselective asymmetric Diels–Alder reaction of *O*-methyl naphthazarin and cyclopentadiene.[7]

The preussomerin family of natural products including preussomerin A (**9**) and D (**10**) were originally isolated from *Preussia isomera* in 1990 by Gloer and co-workers[3a–c] during an investigation into interspecies competition among *coprophilous* (dung-colonizing) fungi. These unusual natural products are characterized by a unique bisketal functionality. Later work by Polishook and co-workers led to the isolation of preussomerins from the endophytic fungus *Harmonerna demtioides*.[3d] Singh et al. isolated preussomerins G (**11**), H, and I (**12**) along with preussomerin D (**10**) from the fermentation broth of an unidentified ceolomycetes fungus.[3e] From the same broth, the deoxypreussomerins B (**3**) and A (**13**), also respectively known as palmarumycins C_2 and CP_2, were also isolated. These were assumed to be biosynthetic precursors of the preussomerins. Singh et al. also showed that preussomerins D (**10**) and G (**11**) had pronounced ras-farnesyl transferase activity and are thus of potential interest in cancer chemotherapy.[3e] Later, Krohn and co-workers isolated a further three-members of the preussomerin family, preussomerins J, K, and L (**14**), and confirmed their absolute configuration by comparison of experimentally determined and calculated CD spectra.[3f]

In 1999, Chi and Heathcock published an elegant synthesis of racemic preussomerin G (**11**) and I (**12**) using a potentially biomimetic construction of the unusual diketal ring system (Scheme 1).[8] Thus, trichloroacetate **15** was hydrolyzed to intermediate **16**, subsequent tautomerization formed bisketal **17** after protonation. The authors depicted the reaction as a two-electron process but did not discuss the mechanism further. The energy difference, determined through ab initio calculations, was found to be in favor of isomer **17** over quinone **16**. The syntheses of preussomerin I (**12**) and G (**11**) were completed from diketal **17** in eight and nine steps, respectively. Later work by Taylor and co-workers described an alternative way of generating the preussomerin nucleus via 2-arylacetal anions.[9]

Results and Discussion

Our initial retrosynthetic plan (Scheme 2) was to proceed via a route that may enable the synthesis of members of the palmarumycin, diepoxin, and laterally the unique preussomerin natural products in enantiopure form all from the same start point, drawing support from the proposed biosynthetic pathway. Thus, acid-catalyzed ketalization of 1,8-naphthalenediol **21** and 5-methoxyte-

(4) (a) Thiergardt, R.; Hug, P.; Rihs, G.; Peter, H. H. *Tetrahedron Lett.* **1994**, *35*, 1043. (b) Thiergardt, R.; Hug, P.; Rihs, G.; Peter, H. H. *Tetrahedron* **1995**, *51*, 733. (c) Chu, M.; Truumees, I.; Patel, M. G.; Gullo, V. P.; Blood, C.; King, I.; Pai, J.-K.; Puar, M. S. *Tetrahedron Lett.* **1994**, *35*, 1343. (d) Petersen, F.; Moerker, T.; Vanzanella, F.; Peter, H. H. *J. Antibiot.* **1994**, *47*, 1098. (e) Chu, M.; Truumees, I.; Patel, M. G.; Gullo, V. P.; Puar, M. S. *J. Org. Chem.* **1994**, *59*, 1222. (f) Chu, M.; Truumees, I.; Patel, M. G.; Blood, C.; Das, P. P.; Puar, M. S. *J. Antibiot.* **1995**, *48*, 329. (g) Sakemi, S.; Inagaki, T.; Kaned, K.; Hirai, H.; Iwata, E.; Sakakibara, T.; Yamauchi, Y.; Norcia, M.; Wondrack, L. M.; Sutcliffe, J. A.; Kojima, N. *J. Antibiot.* **1995**, *48*, 134. (h) Ogishi, H.; Chiba, N.; Mikawa, T.; Sakaki, T.; Miyaji, S.; Sezaki, M. Jpn Pat. JP 01294686 A2, Nov 28, 1989; *Chem. Abstr.* **1990**, *113*, 38906q. (i) McDonald, L. A.; Abbanat, D. R.; Barbieri, L. R.; Bernan, V. S.; Discafani, C. M.; Greenstein, M.; Janota, K.; Korshalla, J. D.; Lassota, P.; Tischler, M.; Carter, G. T. *Tetrahedron Lett.* **1999**, *40*, 2489.

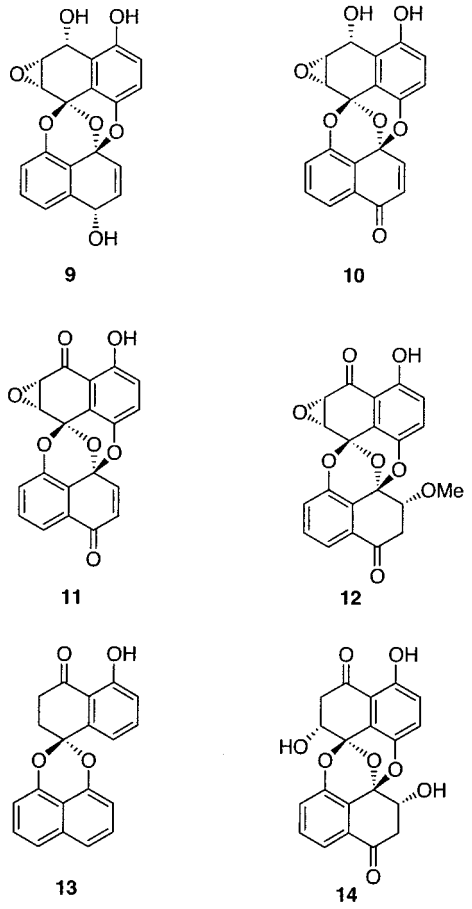
(5) Barrett, A. G. M.; Hamprecht, D.; Meyer, T. *Chem. Commun.* **1998**, 809.

(6) (a) Wipf, P.; Jung, J.-K. *J. Org. Chem.* **1998**, *63*, 3530. (b) Ragot, J. P.; Alcaraz, M.-L.; Taylor, R. J. K. *Tetrahedron Lett.* **1998**, *39*, 4921. (c) Ragot, J. P.; Steeneck, C.; Alcaraz, M.-L.; Taylor, R. J. K. *J. Chem. Soc., Perkin Trans. 1* **1999**, 1073. (d) Coutts, I. G. C.; Allcock, R. W.; Scheeren, H. W. *Tetrahedron Lett.* **2000**, *41*, 9105. (e) Wipf, P.; Jung, J.-K.; Rodríguez, S.; Lazo, J. S. *Tetrahedron* **2001**, *57*, 283. (f) see also Krohn, K.; Beckmann, K.; Aust, H.-J.; Draeger, S.; Schulz, B.; Busemann, S.; Bringmann, G. *Liebigs Ann./Recueil* **1997**, 2531.

(7) Wipf, P.; Jung, J.-K. *J. Org. Chem.* **2000**, *65*, 6319 and references therein.

(8) Chi, S. C.; Heathcock, C. H. *Org. Lett.* **1999**, *1*, 3.

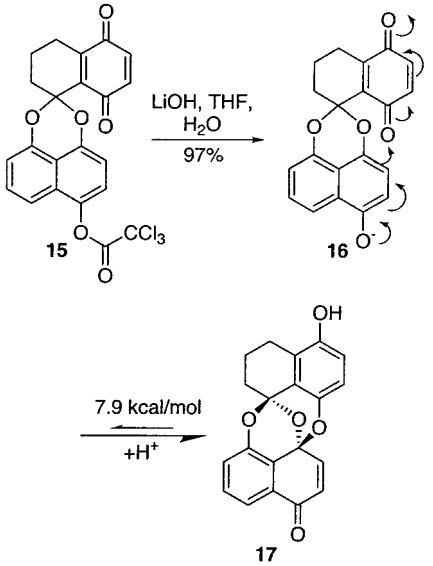
(9) Ragot, J. P.; Prime, M. E.; Archibald, S. J.; Taylor, R. J. K. *Org. Lett.* **2000**, *2*, 1613.



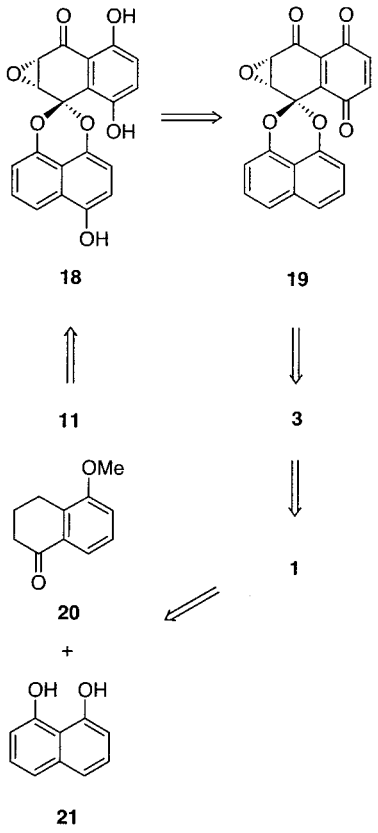
tralone **20** followed by judicious choice of oxidation could form palmarumycin CP_1 (**1**) which could be enantioselectively epoxidized to give palmarumycin C_2 (**3**) before further oxidation to keto-quinone **19**. This intermediate has the potential to undergo selective epoxidation to furnish the diepoxins. Alternatively, quinone **19** could be reduced and further functionalized on the southern naphthalene ring (with creation of a remote ketal chiral center) to give triol **18**, which could be oxidized followed by tautomerization to give preussomerin G (**11**).

The starting point for our synthesis was the preparation of spiroketal **22** by the condensation of 5-methoxy-

Scheme 1



Scheme 2

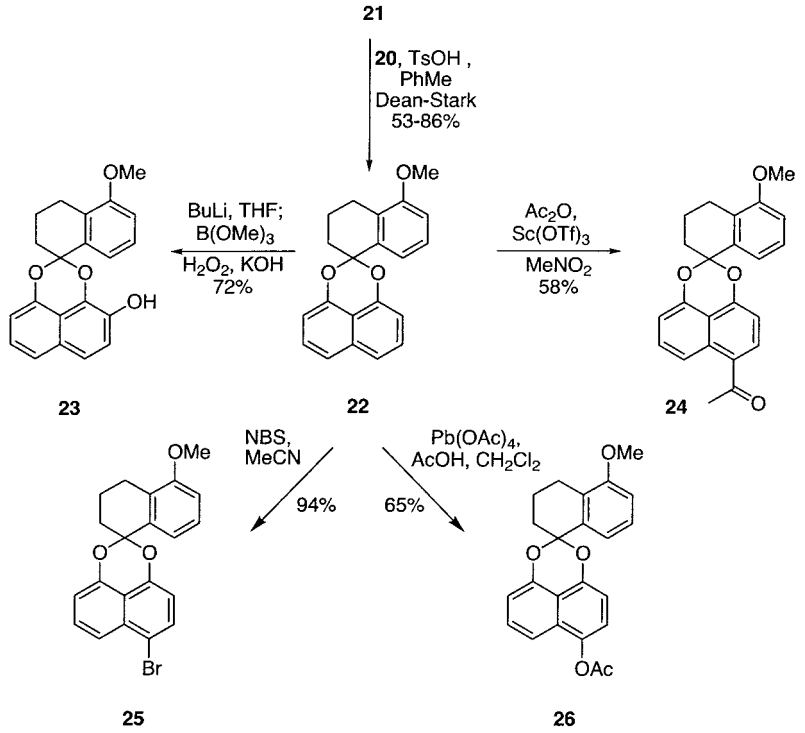


tetralone **20** with 1,8-naphthalenediol **21** under acid catalysis. The reaction proceeded smoothly on a 1 mmol scale under Dean−Stark conditions to give 86% yield of the desired product **22**. Unfortunately, this yield was lowered to 53% on a 125 mmol scale, but was nonetheless reproducible. The structure of spiroketal **22** was confirmed by X-ray crystallography. At this point, we decided to carry out extensive model studies to ascertain a reactivity chart for the palmarumycin core. Interestingly, it turned out that the naphthalene moiety is the preferred site of reaction for a wide range of reagents as exemplified in Scheme 3.

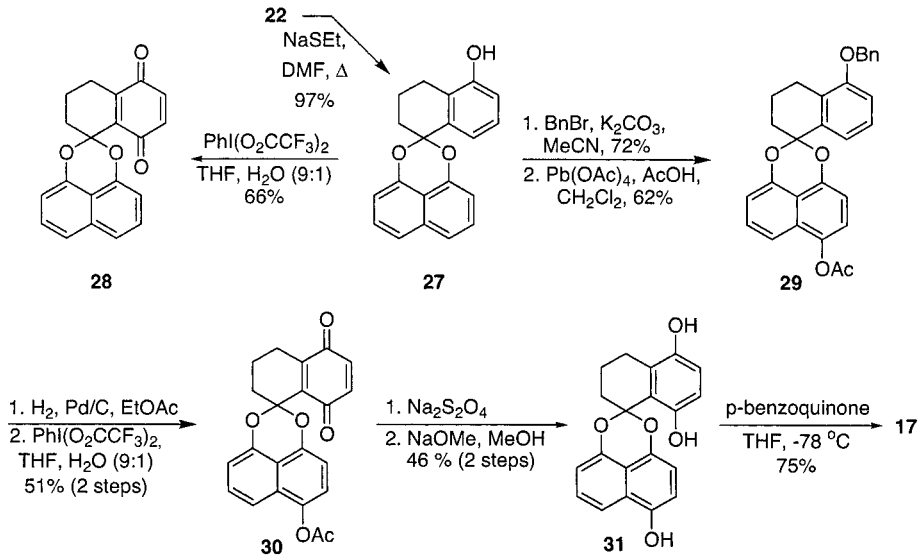
Friedel−Crafts acylation of arene **22** using the conditions of Kobayashi[10] resulted in the smooth conversion to ketone **24**. Reaction of arene **22** with *N*-bromosuccinimide in acetonitrile also proceeded with substitution para to the alkoxy substituent to provide bromide **25**. Acetoxylation of arene **22** using lead tetraacetate in acetic acid and dichloromethane proceeded with similar selectivity to reveal ester **26**.[11] Alternatively ortho-lithiation and trapping with trimethyl borate gave, on oxidative workup, the phenol **23** thereby underscoring the Lewis basic nature of the spiroketal oxygens. However, the northern anisole entity in spiroketal **22** could be selectively oxidized to the corresponding quinone **28** by demethylation to produce phenol **27** followed by hypervalent iodine-mediated oxidation (Scheme 4). Thus, treatment of spiroketal **22** with sodium ethanethiolate (2 equiv) in DMF at reflux gave phenol **27** in an excellent 97% yield. Oxidation using bis-trifluoroacetoxyiodobenzene (2 equiv) in THF and water (9:1) resulted in clean

(10) Kawada, A.; Mitamura, S.; Kobayashi, S. *Synlett* **1994**, 545.
(11) Norman, R. O. C.; Thomas, C. B.; Willson, J. S. *J. Chem. Soc. B* **1971**, 518 and references therein.

Scheme 3



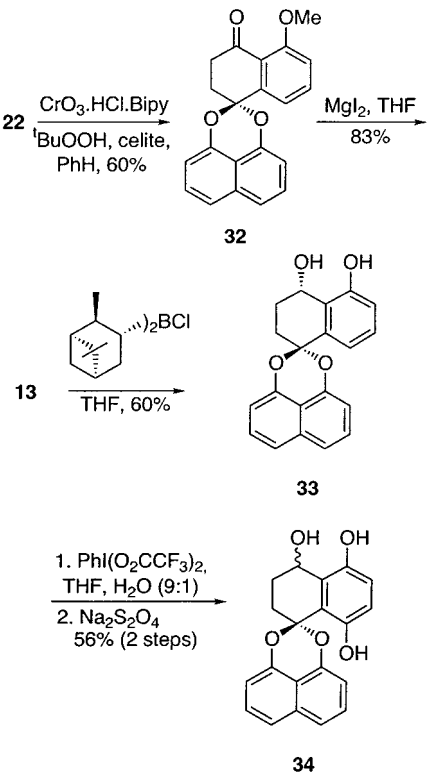
Scheme 4



formation of the corresponding quinone **28**. The choice of solvent was shown to be crucial to the success of the reaction with more polar solvents (e.g., acetonitrile) favoring oxidation of the naphthalene moiety. We speculate that the polar solvent may facilitate stabilization of a SET derived charge tranfer complex with the hypervalent iodine reagent. Switching to the less polar THF as cosolvent may allow a two-electron oxidation process to occur on the phenol ring.

In addition to the investigations of spiroketal oxidation reactions, we decided to carry out model studies to access the preussomerin core. In addition, it was hoped that our studies might also shed some light on the mechanism of the Heathcock cyclization[8] originally tentatively drawn as a two-electron phenolate tautomerization. Thus, phenol **27** was protected as its benzyl ether which was acetoxylated to provide acetate **29**. Benzyl ether hydrogenolysis followed by bis-trifluoroacetoxyiodobenzene mediated oxidation afforded the quinone product **30** in 51% yield over two steps in approximately 90% purity. We hoped that treatment of quinone **30** with aqueous lithium hydroxide**,** according to the procedure of Chi and Heathcock,[8] would provide the preussomerin core. Unfortunately, none of the desired product was formed as judged by analysis of the crude ^{1}H NMR spectrum. The reasons for this may simply be the lower rate of saponification of the acetate versus the trichloroacetate allowing for competitive degradation. Despite this setback, we considered an oxidative route to the preussomerin core and thus quinone **30** was reduced with aqueous dithionite to the unstable hydroquinone. Without further purification, the acetate was subject to Zemplen methanolysis to give triol **31**. We were delighted to find that oxidative cyclization of triol **31** with *p*-benzoquinone at −78 °C in

Scheme 5



dry, degassed THF smoothly formed the preussomerin **17** in 75% yield after purification (Scheme 4). The exact mechanism awaits further study but an SET mechanism seems most likely to be operating.

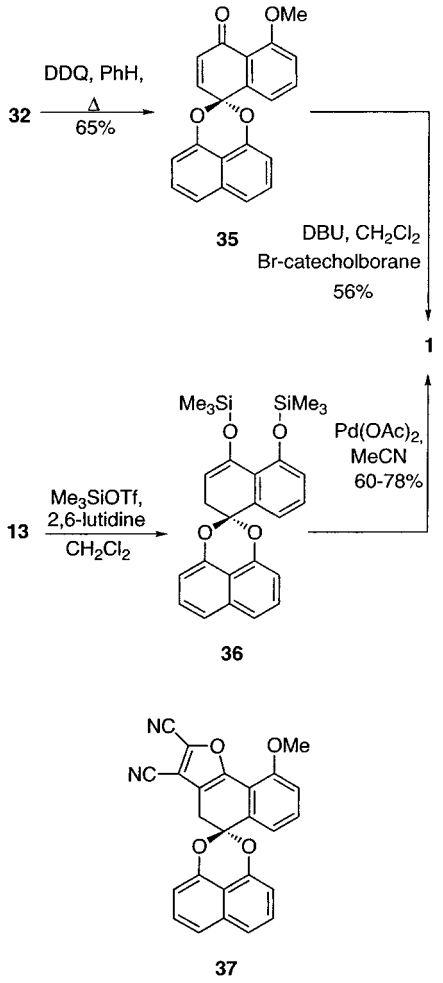
With the early model studies proceeding well, we undertook the syntheses of several palmarumycin natural products en route to the preussomerins. Thus, benzylic oxidation of **22** using catalytic bipyridinium chlorochromate, *tert*-butyl hydroperoxide, and Celite smoothly formed ketone **32** in 60% yield.[12] Many alternative oxidants including the recently published periodinane IBX-mediated oxidation by Nicolaou et al. were much less efficient.[13] Deprotection of the methyl ether was easily achieved by treatment with freshly prepared magnesium iodide in THF at room temperature for 24 h (with care to exclude light) to give palmarumycin CP_2 (**13**). The spectroscopic data for this synthetic material exactly matched that published[1a] and the compound was identical with an authentic sample of palmarumycin CP_2 (**13**) kindly provided by Professor Karsten Krohn. Ketone **13** was converted into CJ-12,371 (**33**) (60% yield, 93% ee) by asymmetric reduction using (+)-*B*-chlorodiisopinocampheylborane (Scheme 5).[14] The enantiomeric excess of alcohol **33** was determined by chiral HPLC while the absolute stereochemistry was determined by comparison of the optical rotation, $[\alpha]^{24}_D$ −42.2 (*c* 0.45, MeOH), with that of the isolated natural product CJ-12,371 (**33**), $[\alpha]^{24}_D$ −46.8 (*c* 0.23, MeOH). It is germane to mention that reduction presumably takes place via intramolecular hydride delivery thereby reversing the absolute stereochemistry of reaction seen with simple alkyl aryl ketones.[14] CJ-12,371 (**33**)[4g] is a DNA−gyrase inhibitor isolated from an unidentified fungus (N983-46). The spectroscopic data of our synthetic material exactly matched those published for the natural product **33**.[4g] Oxidation of CJ-12,371 (**33**) using bis-trifluoroacetoxyiodobenzene in aqueous THF followed by reduction with sodium dithionite gave the corresponding hydroquinone **34** (56%). This substance showed spectroscopic data in full agreement with that published for the natural product CJ-12,372 (**34**).[4g] The synthetic material **34** was found to have undergone racemization presumably through a quinomethide pathway.

To obtain the α,*β*-unsaturated ketone moiety of palmarumycin CP_1 (**1**), ketone **32** was dehydrogenated using DDQ in benzene at reflux followed by O-demethylation of ether **35** using *B*-bromocatecholborane to furnish palmarumycin CP_1 (**1**) in 36% yield over two steps. Although successful on a small scale, the yield dropped substantially on a larger scale. Additionally, the DDQ oxidation reaction gave rise to a second minor product **37** (8%). The structure of this substance was established as the furan **37** by an X-ray crystallographic study. Presumably this product was formed by a SET cycloaddition and subsequent retro-Diels Alder reaction mechanism. Accordingly these problems were circumvented by formation of silyl-enol ether **36** from palmarumycin CP_2 (**13**) using trimethylsilyl trifluoromethanesulfonate and 2,6-lutidine followed by Saegusa oxidation[15] using palladium acetate to form palmarumycin CP_1 (**1**) in an excellent 60−78% yield over a range of reaction scales (Scheme 6). The spectroscopic data for palmarumycin CP_1 (**1**) again accurately matched that published in the paper describing its isolation.[1a] Additionally, the synthetic compound **1** was identical with an authentic sample of the natural product palmarumycin CP_1 (**1**) kindly provided by Professor Karsten Krohn.

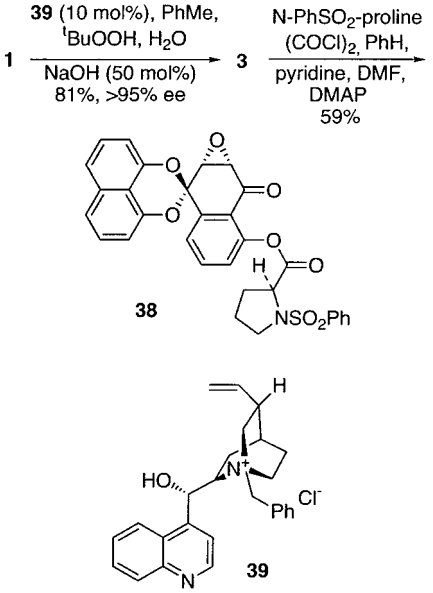
With multigram quantities of synthetic palmarumycin CP_1 (**1**) now in hand, we focused our attention on enantioselective epoxidation of the cyclic enone moiety, a reaction that has been employed with little success historically but for a few exceptions.[16] Our attempts were directed to the use of chiral phase transfer conditions developed by Wynberg and co-workers[16a] and later used by Taylor and co-workers for enantioselective epoxidation of a quinone monoketal (32% yield, 89% ee) in their synthesis of (+)-manumycin.[16b] Accordingly, the epoxidation of palmarumycin CP_1 (**1**) using *N*-benzylcinchoninium chloride **39** (10 mol %) as the chiral phase transfer catalyst proceeded smoothly to provide the desired epoxide **3** in an excellent 81% yield. Furthermore the enantiomeric excess of the product **3** was greater than 95% as determined by chiral HPLC in comparison with the racemic epoxide. The spectroscopic data for the synthetic palmarumycin C_2 (**3**) matched that published for the natural product.[1b] Additionally, our synthetic palmarumycin C_2 (**3**) was identical with an authentic sample of the natural product palmarumycin C_2 (**3**), also named deoxypreussomerin B, kindly provided by Dr. Sheo B. Singh of Merck & Co., Inc. Finally, we have confirmed the structure of our synthetic palmarumycin

(12) Rathore, R.; Saxena, N.; Chandrasekaran, S. *Synth. Commun.* **1986**, *16*, 1493.
(13) Nicolaou, K. C.; Baran, P. S.; Zhong, Y.-L. *J. Am. Chem. Soc.* **2001**, *123*, 3183.
(14) Ramachandran, P. V.; Gong, B.; Brown, H. C. *Tetrahedron Lett.* **1994**, *35*, 2141.
(15) Ito, Y.; Hirao, T.; Saegusa, T. *J. Org. Chem.* **1978**, *43*, 1011.
(16) (a) Wynberg, H. *Top. Stereochem.* **1986**, *16*, 87. (b) Macdonald, G.; Alcaraz, L.; Lewis, N. J.; Taylor, R. J. K. *Tetrahedron Lett.* **1998**, *39*, 5433 and references therein. (c) Arai, S.; Oku, M.; Miura, M.; Shioiri, T. *Synlett* **1998**, 1201.

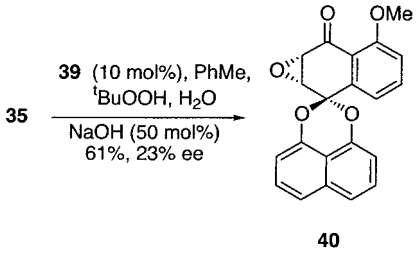
Scheme 6



Scheme 7



Scheme 8



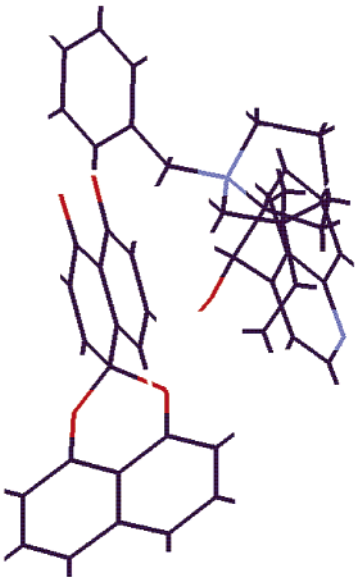
C_2 (**3**) by an X-ray structure determination. The optical rotation of synthetic palmarumycin C_2 (**3**), $[\alpha]^{20}_D$ −300 (*c* 1.00, $CHCl_3$), was in reasonable agreement with the value for the natural product, $[\alpha]^{20}_D$ −341[1b] (*c* 1.00, $CHCl_3$). Synthetic palmarumycin C_2 (**3**) was coupled with *N*-phenylsulfonyl proline to provide the crystalline ester **38** (Scheme 7) the structure of which was confirmed by X-ray crystallography. This unequivocally verified the absolute configuration of palmarumycin C_2 (**3**) as 2(*R*), 3(*S*) and confirmed the stereochemical assignments for palmarumycin C_2 (**3**) by Bringmann et al. which were based upon CD measurements.[1d]

It is also interesting to note that epoxidation of the enone **35** under the same chiral phase transfer reaction conditions resulted in a much slower and less efficient reaction. The epoxide product **40** was isolated in only 61% yield after 9 days reaction but in a much lower (23%) enantiomeric excess (Scheme 8). This result clearly underscores the key role of the phenol moiety in structuring the transition state for the enantioselective hydroperoxide anion addition to the enone (Figure 1). On the basis of these conformational and electronic analyses of the catalyst, two diastereoisomeric pre-transition state complexes **41** and **42** could be formulated through energy minimization calculations.[17] As can be seen for complex **41**, the alcohol motif in the catalyst is hydrogen bonded to one of the spiroketal oxygen atoms while a secondary interaction is formed between the phenoxy−enone moiety and the positively charged ammonium residue, thereby activating the enone system from both ends. Due to the shielding of the two aromatic sidearms, the preferred direction of approach of the oxidant is to the *si* face of the enone. On the other hand, in transition state **42**, the ammonium moiety is orientated away from the enone system and no secondary interaction is possible. The calculated energy difference of 3.9 kcal/mol for the two pre-transition state complexes **41** and **42** are consistent with a highly asymmetric addition of the hydroperoxide anion. It is also noteworthy that epoxidation of palmarumycin CP_1 (**1**) with pseudo-enantiomeric *N*-benzylcinchonidinium chloride proceeded with lower yield (69%) and much lower enantioselecivity (14%). Similar findings were observed by Taylor et al.,[16b] although in their system *N*-benzylcinchonidinium chloride was successful (32% yield, 89% ee) while the pseudo enantiomer *N*-benzylcinchoninium chloride **39** was less effective (15%, 10% ee).

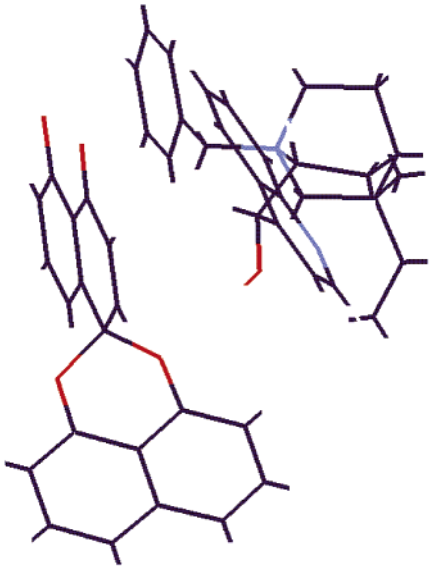
With the key epoxide intermediate, palmarumycin C_2 (**3**), available in ample quantities, the next aim was aromatic substitution of the naphthalene ring concurrent with the creation of a chiral center at the spiro-ketal carbon. Treatment of naphthalene **3** with acetyl nitrate[18] resulted in aromatic substitution to form the nitroarenes **43** and **44** (1:1). Alternatively, bromination using *N*-bromosuccinimide gave bromides **45** and **46** (1:1) (Scheme 9). Contrary to our hope that the epoxide entity in palmarumycin C_2 (**3**) would favor formation of isomers

(17) The minimizations were performed using the Spartan application employing AM1 semiempirical parameters.

(18) Fitzgerald, J. J.; Drysdale, N. E.; Olofson, R. A. *Synth. Commun.* **1992**, *22*, 1807.



Transition State 41: Good Alignment



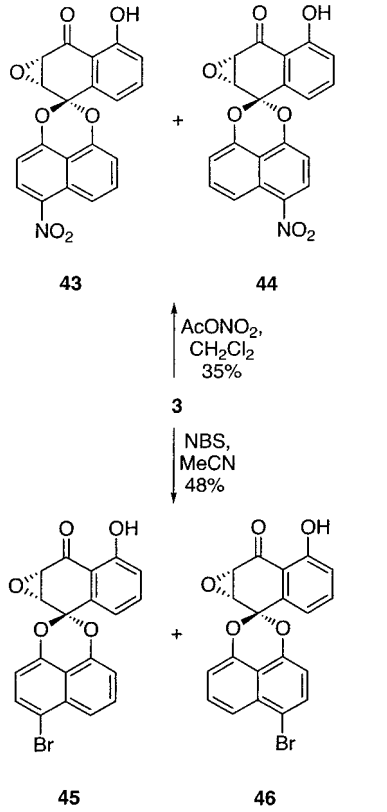
Transition State 42: Poor Alignment

Figure 1.

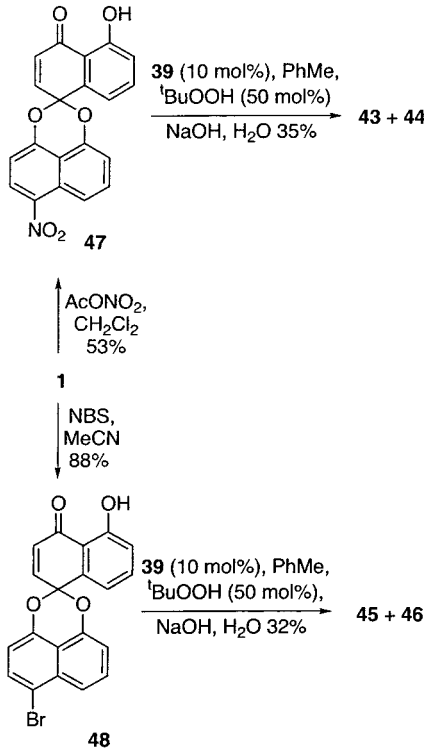
44 and **46** by reducing electron density at the anti-spiroketal oxygen, both nitration and bromination reactions proceeded without any significant diastereoselectivities. In consequence, we attempted a kinetic resolution approach to the naphthalene substitution problem. Thus, palmarumycin CP_1 (**1**) was allowed to react with acetyl nitrate or *N*-bromosuccinimide to form the racemic arenes **47** and **48** respectively in good yield. These products were subjected to the standard asymmetric epoxidation conditions described earlier using only 50 mol % of *tert*-butyl hydroperoxide in the hope that each enantiomer would react at substantially different rates via diastereoisomeric transition states. Unfortunately, although both epoxidation reactions resulted in the required conversions, the products **43**/**44** and **45**/**46** were both isolated as a 1:1 mixture of diastereoisomers (Scheme 10).

At this point, it became apparent that a selective substitution on the naphthalene ring would be difficult without the aid of carefully designed chiral nitration or

Scheme 9

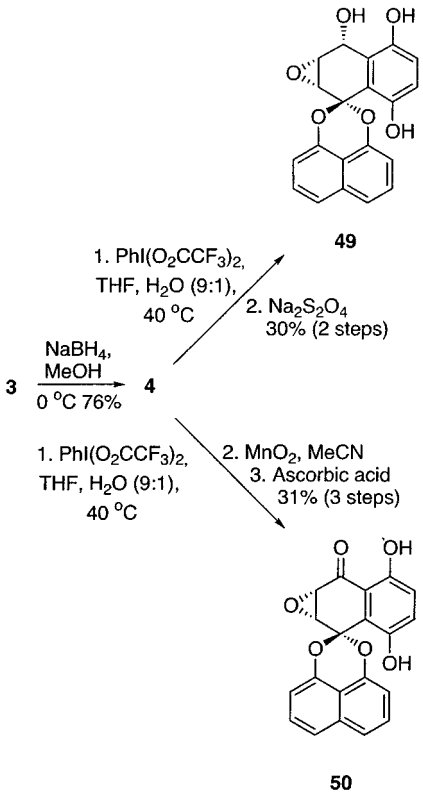


Scheme 10



bromination reagents. Therefore, to access the preussomerin natural products, we faced the necessity of a separation of the diastereoisomers, but single enantiomers, at a late stage of the synthesis. We considered that the extra conformational constriction imposed by the second ketal unit of the preussomerins would allow an easier separation of the two diastereoisomers. The pairs of diastereoisomeric spiroketals **43**/**44** and **45**/**46** were

Scheme 11



both chromatographically homogeneous. However fractional crystallization of the nitroepoxide mixture of **43** and **44** from ethyl acetate and pentane gave crystals of **43** of sufficient quality to permit the determination of an X-ray crystal structure. In addition, the mother liquor was enhanced in the other diastereoisomer **44** as shown by ^{1}H NMR analysis.

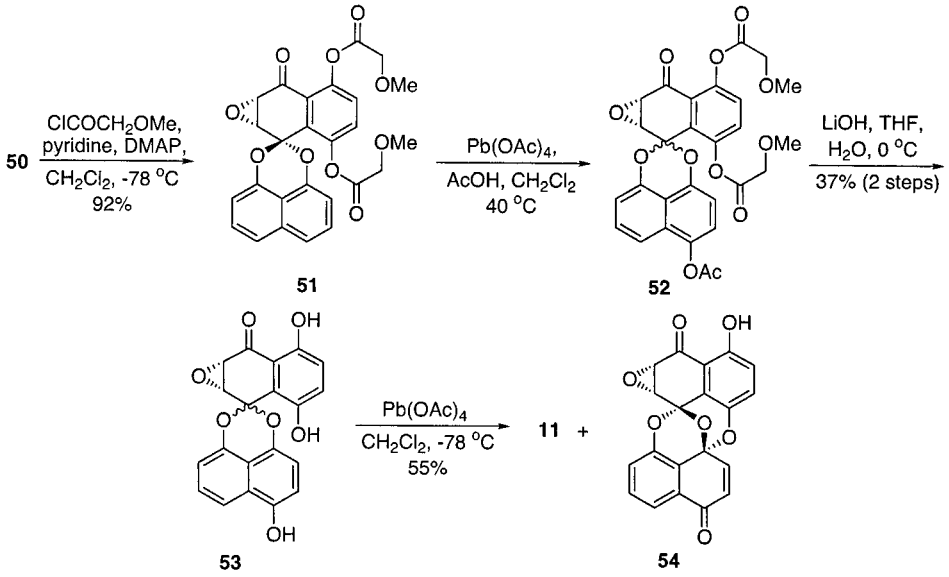
We proceeded to synthesize more advanced members of the palmarumycin family of natural products, and accordingly, palmarumycin C_2 (**3**) was reduced with sodium borohydride in methanol to give palmarumycin C_{11} (**4**) in good yield provided sonication was used prior to hydride addition to aid solubilization of the starting epoxy ketone (Scheme 11). The data for the synthetic palmarumycin C_{11} (**4**) ($[\alpha]^{20}_D$ −155 (*c* 1.00, CH_2Cl_2)) closely matched that reported by Krohn[1b] for the natural product ($[\alpha]^{20}_D$ −153 (*c* 0.24, CH_2Cl_2)). This implies that the absolute configuration of palmarumycin C_{11} (**4**) is unequivocally 2(*R*),3(*R*),4(*R*) and not 2(*S*),3(*S*),4(*S*) as arbitarily drawn in the Krohn paper. Additionally, Chu et al. have reported the isolation of Sch 53823, which was stated to have structure **4**.[1e] Since the reported physical and spectroscopic data for Sch 53823 differ significantly from palmarumycin C_{11} (**4**), this natural product has been incorrectly identified.[6c] Possibly it is the epimeric secondary alcohol. Palmarumycin C_{11} (**4**) was subjected to the standard phenol oxidation procedures to furnish the unstable quinone alcohol, which was used without purification. Reduction with aqueous sodium dithionite furnished palmarumycin C_{12} (**49**) in 30% yield over two steps after purification. The authenticity of synthetic palmarumycin C_{12} (**49**) was confirmed by comparison of the spectral data with that published for the natural product.[1b] In addition, the optical rotation ($[\alpha]^{20}_D$ −165 (*c* 0.26, CH_2Cl_2)) also correlated well with the reported value ($[\alpha]^{20}_D$ −179.6 (*c* 0.20, CH_2Cl_2)),[1b] implying that the absolute configuration of palmarumycin C_{12} (**49**) is unequivocally 2(*R*),3(*R*),4(*R*)[1f] (Scheme 11).

Following hypervalent iodine-mediated oxidation of palmarumycin C_{11} (**4**), the corresponding quinone was further oxidized to the corresponding keto-quinone by reaction with manganese dioxide. Subsequent reduction of the quinone functionality with ascorbic acid gave palmarumycin C_3 (**50**) in 31% yield over three steps (Scheme 11). The spectroscopic data for the synthetic hydroquinone **50** matched that published for naturally occurring palmarumycin C_3 (**50**) although the optical rotation value was found to be lower with the synthetic sample ($[\alpha]^{20}_D$ −246 (*c* 1.00, CH_2Cl_2)) than the natural product ($[\alpha]^{20}_D$ −300 (*c* 1.00, CH_2Cl_2)).[1b] Nonetheless, the absolute configuration of palmarumycin C_3 (**50**) is unequivocally 2(*R*),3(*S*).

Palmarumycin C_3 (**50**) was converted into the corresponding methoxyacetate **51** in excellent yield (92%), and the product **51** was subjected to acetoxylation using lead tetraacetate.[11] The reaction was sluggish compared to earlier studies possibly due to coordination of the lead reagent to the methoxyacetate esters, however this lack of reactivity was overcome by elevation of the reaction temperature to 40 °C. Heating for 24−36 h smoothly formed the desired products **52** as a 1:1 mixture of diastereoisomers as expected. Unfortunately, the northern methoxyacetate unit proved partially labile to silica gel chromatography hampering clean isolation. Therefore, the crude product **52** was simply treated with excess lithium hydroxide in aqueous THF at 0 °C for 90 min to furnish the desired triol **53** as a 1:1 mixture of diastereoisomers in 37% yield over two steps (Scheme 12).

With sufficient quantities of triol **53** in hand, we examined the key oxidative cyclization reaction. We were initially pleased to find that oxidation of triol **53** with *p*-benzoquinone gave small quantities of the desired preussomerin which was identified by analysis of the crude ^{1}H NMR spectrum. However, the yield was low, and elevated temperatures were needed for reaction compared with the model system (Scheme 4). The remaining material was largely recovered triol **53**. Obviously the keto-moiety on the northern hydroquinone unit decelerates the oxidation step consistent with this unit being the site of oxidation and not the southern alkoxyhydroquinone moiety. A range of alternative oxidative cyclization procedures were investigated and we were delighted to find that treatment of triol **53** with lead tetraacetate (1 equiv) at −78 °C for 10 min in dry degassed dichloromethane smoothly formed (−)-preussomerin G (**11**) and (+)-epipreussomerin G (**54**) in an excellent 55% yield as a 1:1 mixture of diastereoisomers (Scheme 12). Furthermore, the conformational rigidity conferred by the extra ring allowed the diastereoisomeric products to be easily separated by chromatography. Synthetic (−)-preussomerin G (**11**) showed spectroscopic data fully matching that reported for the naturally occurring preussomerin G (**11**).[3e] However, the optical rotation for the synthetic material ($[\alpha]_D$ −533 (*c* 0.05, CH_2Cl_2)) was significantly lower than the value reported for the natural product (lit.[3e] $[\alpha]_D$ −688, (*c* 0.66, CH_2Cl_2)).[3e] Since we were concerned that our synthesis may have proceeded with partial racemization, the conversion of synthetic palmarumycin CP_1 (**1**) into preussomerin G (**11**) and epipreussomerin G (**54**) was repeated in the racemic series. Thus epoxidation of palmarumycin CP_1 (**1**) using the DBU-catalyzed addition of *tert*-butyl hy-

Scheme 12



droperoxide gave the racemic epoxide (±)-palmarumycin C_2 (**3**) (83%). Subsequent redox manipulations using exactly the same methods as described in Schemes 11 and 12 gave racemic preussomerin G (±)-(**11**) and epipreussomerin G (±)-**54**. Chiral HPLC confirmed that the synthetic preussomerin G (**11**) was indeed a single enantiomer (t_R 9 min 55 s) and not contaminated by the enantiomer (t_R 9 min). Finally, the synthetic preussomerin G (**11**) was identical with an authentic sample[3f] kindly provided by Professor Karsten Krohn. In our hands this sample of natural preussomerin G (**11**) showed an optical rotation value of $[\alpha]_D$ −567 (*c* 0.68, CH_2Cl_2).

Conclusions

In conclusion, we have developed a unified approach to the palmarumycin and preussomerin natural products culminating in the synthesis of two achiral, one racemic, and five enantiomerically pure members of the palmarumycin family and establishing the absolute configuration in three cases for the first time. In addition we have achieved an enantioselective synthesis of (−)-preussomerin G (**11**), this being the first enantioselective synthesis of the preussomerin class of natural products. These natural products were synthesized utilizing a chiral phase transfer catalyzed epoxidation procedure and a potentially biomimetic oxidative cyclization as the key synthetic steps. We are currently applying the same methodology to the synthesis of additional preussomerins and diepoxins.

Experimental Section

General Procedures. Normal phase HPLC separations were carried out with Unicam Crystal 200 or Alliance Waters 2690 machines using Chiracel OD-H or Chiralpak AD (250 mm × 4.6 mm) columns. The following methods were applied: method A, EtOH/hexane (3:17), flow 0.7 mL/min, 212 nm; method B, EtOH/hexane (1:19), flow 1 mL/min, 224 nm; method C: EtOH/hexane (1:19), flow 0.7 mL/min., 224 nm; method D: EtOH/hexane (1:1), flow 1 mL/min, 215 nm. Analytical and preparative thin-layer chromatography (TLC) was performed on silica gel TLC plates. Visualization was accomplished using UV light or by staining with potassium permanganate or vanillin solutions. Column chromatography was performed under medium pressure using silica gel 60 (230−400 mesh) (eluants are given in parentheses). All reactions were carried out in oven-dried glassware under N_2 atmosphere unless stated otherwise. All reagents were used as supplied. Solvents were distilled prior to use when anhydrous conditions were required: Et_3N, pyridine, DMF, PhH, MeCN, and CH_2Cl_2 were distilled from calcium hydride under nitrogen; THF and Et_2O were distilled from sodium wire and benzophenone while DBU was filtered through a short column of basic alumina. Ac_2O was distilled from phosphorus pentoxide, $B(OMe)_3$ from LiCl. Solutions of *tert*-butyl hydroperoxide in PhMe or PhH were dried by azeotropic removal of the H_2O, and the concentrations were determined by ^1H NMR spectroscopy.

Naphthalene-1,8-diol 21. 1,8-Naphthosultone (24.62 g, 120 mmol), KOH pellets (105.5 g, 1.884 mol), and H_2O (35 mL) were heated to 225 °C under a stream of N_2. A green melt obtained initially was converted into a black tar, and heating was continued for 30 min until the mixture solidified. After cooling to room temperature, the black residue was dissolved in H_2O (1.75 L) and Et_2O (600 mL) and the mixture was acidified with 13% w/w hydrochloric acid (560 mL). The organic layer was separated and the aqueous layer was extracted with Et_2O (2 × 500 mL). The combined organic layers were dried ($MgSO_4$), filtered, and concentrated in vacuo. Chromatography (EtOAc/hexanes, 1:2 to 1:1) gave diol **21** (15.87 g, 83%) as a white solid: mp 140−141 °C (EtOAc/hexanes) (lit.[19] mp 141−142 °C).

(2*H*)-5-Methoxy-2,3-dihydrospiro[naphthalene-1(4*H*),2′-naphtho[1,8-*de*][1,3]dioxine] 22. 5-Methoxytetralone **20** (8.80 g, 50 mmol), $TsOH\cdot H_2O$ (1.90 g, 10.0 mmol), and diol **21** (10.0 g, 62.5 mmol) in PhMe (125 mL) were heated to reflux under N_2 (Dean−Stark with 4 Å molecular sieves). The brown mixture was heated under reflux for 72 h, cooled to room temperature, and rotary evaporated to dryness. The residue was dissolved in Et_2O (500 mL) and saturated aqueous $NaHCO_3$ (200 mL), and the organic layer was dried ($MgSO_4$), filtered, and rotary evaporated. The resulting yellow solid was chromatographed (Et_2O/hexanes, 1:5) to provide spiroketal **22**[20] (8.37 g, 53%) as a slightly yellow solid: mp 155 °C (hexanes/Et_2O); R_f 0.40 (EtOAc/hexanes 1:9); IR (KBr disk) 1604, 1272 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.95 (m, 2H), 2.16 (m, 2H), 2.82 (t, J = 6.6 Hz, 2H), 3.90 (s, 3H), 6.94 (m, 3H), 7.35 (app-t, J = 8.0 Hz, 1H), 7.44−7.58 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.8, 23.1, 30.4, 55.6, 110.6, 109.3, 110.4, 111.3, 119.2, 120.2, 127.1, 127.4, 127.5, 134.2, 136.3, 148.3, 156.7; MS (CI)

(19) Erdmann, H. *Liebigs Ann.* **1888**, *247*, 306.

(20) For the initial report of this compound see ref 5; for subsequent publications see refs 6b and 6c.

m/*z* 319 (M + H)$^+$ *m*/*z* (CI) calcd for $C_{21}H_{19}O_3$ 319.1334, found 319.1344. Anal. Calcd for $C_{21}H_{18}O_3$: C, 79.21; H, 5.70. Found: C, 78.97; H, 5.71. Crystal data for **22**: $C_{21}H_{18}O_3$, $M = 318.4$, monoclinic, $P2_1$ (no. 4), $a = 8.890(1)$ Å, $b = 8.478(1)$ Å, $c = 11.474(1)$ Å, $\beta = 109.27(1)°$, $V = 816.3(1)$ Å^3, $Z = 2$, $D_c = 1.295$ g cm^{-3}, μ(Cu Kα) = 0.69 mm^{-1}, $T = 293$ K, colorless prisms; 1293 independent measured reflections, F^2 refinement, $R_1 = 0.049$, w$R_2 = 0.136$, 1130 independent observed reflections [$|F_o| > 4\sigma(|F_o|)$, $2\theta \leq 120°$], 218 parameters. The absolute structure of **22** could not be determined. CCDC 182476.

(2*H*)-4′-Bromo-5-methoxy-2,3-dihydrospiro[naphthalene-1(4*H*),2′-naphtho[1,8-*de*][1,3]dioxine] 25. Freshly recrystallized NBS (3.91 g, 22 mmol) was added in portions over a period of 30 min to anisole **22** (6.37 g, 20 mmol) in dry MeCN (100 mL). The dark blue solution was maintained at room temperature for 1 h while it turned cloudy. Silica gel (30 g) was added, the mixture was rotary evaporated, and the resulting solid chromatographed (Et_2O/hexanes, 1:1). A dark liquid was collected and then stirred over activated charcoal (5 g) for 30 min. After filtration and evaporation of the solvent, bromide **25** (7.43 g, 94%) was obtained as a white foam: R_f 0.43 (Et_2O/hexanes 3:2); IR (KBr disk) 1605, 1472, 1262 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.90−1.97 (m, 2H), 2.12−2.16 (m, 2H), 2.81−2.85 (m, 2H), 3.90 (s, 3H), 6.84 (d, $J = 8.1$ Hz, 1H), 6.95 (d, $J = 7.9$ Hz, 1H), 7.02 (d, $J = 7.5$ Hz, 1H), 7.39 (app-t, $J = 8.0$ Hz, 1H), 7.50 (d, $J = 8.0$ Hz, 1H), 7.57 (dd, $J = 8.3$, 7.9 Hz, 1H), 7.72 (d, $J = 8.0$ Hz, 1H), 7.81 (d, $J = 8.5$ Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.7, 23.0, 30.3, 55.6, 100.9, 110.2, 110.4, 113.3, 114.5, 119.1, 119.2, 120.0, 127.1, 127.6, 128.8, 130.9, 133.7, 135.9, 148.0, 148.4, 156.7; MS (EI) *m*/*z* 398, 396 (M$^{\bullet+}$), 381, 379, 300; *m*/*z* (EI) calcd for $C_{21}H_{17}{}^{81}BrO_3$ 398.0341, found 398.0342. Anal. Calcd for $C_{21}H_{17}BrO_3$: 63.49; H, 4.31. Found: C, 63.38; H, 4.27.

(2*H*)-4′-Acetyl-5-methoxy-2,3-dihydrospiro[naphthalene-1(4*H*),2′-naphtho[1,8-*de*][1,3]dioxine] 24. Anisole **22** (159 mg, 0.5 mmol) in $MeNO_2$ (2 mL) was added to Ac_2O (229 μL, 2.5 mmol) followed by scandium triflate (49 mg, 0.1 mmol). The color of the reaction mixture changed to brown immediately, and stirring was continued for 10 h. The reaction was terminated by the addition of solid $NaHCO_3$ followed by H_2O (2 mL) and $CHCl_3$ (5 mL). The aqueous layer was separated, extracted with $CHCl_3$ (2 × 5 mL), the extract washed with brine (5 mL) and dried ($MgSO_4$). Chromatography of the brown residue (Et_2O/hexanes, 1:3) gave ketone **24** (104 mg, 58%) as a white solid: mp 195 °C (hexane/EtOH); R_f 0.41 (Et_2O/hexanes 1:1); IR (KBr disk) 1669, 1603 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.96−1.98 (m, 2H), 2.15−2.18 (m, 2H), 2.75 (s, 3H), 2.83 (t, $J = 6.4$ Hz, 2H), 3.90 (s, 3H), 6.94 (d, $J = 8.1$ Hz, 1H), 6.95 (dd, $J = 8.1$, 1.0 Hz, 1H), 7.03 (dd, $J = 7.6$, 1.0 Hz, 1H), 7.37 (t, $J = 8.1$ Hz, 1H), 7.50 (dd, $J = 8.0$, 1.0 Hz, 1H), 7.62 (dd, $J = 7.6$, 7.6 Hz, 1H), 8.10 (d, $J = 7.6$ Hz, 1H), 8.72 (dd, $J = 8.9$, 8.6 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.7, 23.0, 29.2, 30.4, 55.6, 101.1, 108.1, 110.6, 111.6, 113.8, 119.0, 120.0, 127.1, 127.5, 127.6, 130.2, 132.0, 132.9, 135.7, 148.0, 152.6, 156.7, 199.7; MS (CI) *m*/*z* 361 (M + H)$^+$; *m*/*z* (CI) calcd for $C_{23}H_{21}O_4$ 361.1439, found 361.1437. Anal. Calcd for $C_{23}H_{20}O_4$: C, 76.65; H, 5.59. Found: C, 76.69; H, 5.50.

(2*H*)-2′-Hydroxy-5-methoxy-2,3-dihydrospiro[naphthalene-1(4*H*),2′-naphtho[1,8-*de*][1,3]dioxine] 23. *s*-BuLi in hexane (1.3 M; 0.26 mL, 0.33 mmol) was added to anisole **22** (95 mg, 0.30 mmol) in THF (1.2 mL) at −78 °C over 5 min. The resulting brown solution was stirred at this temperature for 1.5 h when $B(OMe)_3$ (54 μL, 0.48 mmol) was added. After being stirred for 1.5 h, the reaction mixture was allowed to warm to room temperature over a period of 30 min. After the mixture was cooled back to −78 °C, aqueous NaOH (2.5 M; 144 μL) and aqueous H_2O_2 (27%; 76 μL) were added, and the mixture was allowed to warm to room temperature and stirred for 90 min. Neutralization with 1 M HCl followed by extraction with Et_2O (3 × 10 mL) gave a yellow organic layer that was dried ($MgSO_4$), filtered, and concentrated. Chromatography (Et_2O/hexanes, 1:3) gave alcohol **23** (72 mg, 72%) as a white solid: mp 164 °C (hexanes); R_f 0.60 (Et_2O/hexanes 1:1); IR (KBr disk) 3349 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.83−1.93 (m, 2H), 2.07−2.11 (m, 2H), 2.80 (t, $J = 6.3$ Hz, 2H), 3.87 (s, 1H), 3.85 (s, 3H), 6.87 (d, $J = 7.4$ Hz, 1H), 6.93 (d, $J = 7.7$ Hz, 1H), 7.21−7.49 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.2, 23.0, 30.5, 55.6, 100.9, 109.8, 110.5, 114.1, 118.1, 119.4, 120.5, 120.8, 124.7, 127.0, 127.6, 128.7, 131.9, 136.0, 138.9, 146.9, 156.7; MS (CI) *m*/*z* 335 (M + H)$^+$, 177; *m*/*z* (CI) calcd for $C_{21}H_{19}O_4$ 335.1283, found 335.1291.

(2*H*)-4′-Acetoxy-5-methoxy-2,3-dihydrospiro[naphthalene-1(4*H*),2′-naphtho[1,8-*de*][1,3]dioxine] 26. CH_2Cl_2 (2 mL) and AcOH (4 mL) were added to spiroketal **22** (80 mg, 0.25 mmol) and $Pb(OAc)_4$ (216 mg, 0.50 mmol), and the mixture was stirred under N_2 for 16 h. The mixture was diluted with EtOAc (20 mL) and saturated aqueous NH_4Cl (10 mL), and the organic layer was separated, dried ($MgSO_4$), and filtered. Chromatography (EtOAc/hexanes, 1:4) gave **26** (61 mg, 65%) as a white solid: mp 144−146 °C (Et_2O); R_f 0.20 (EtOAc/hexanes 1:4); IR (thin film) 1763, 1608, 1201 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.88−1.98 (m, 2H), 2.11−2.17 (m, 2H), 2.46 (s, 3H), 2.81 (t, $J = 6.3$ Hz, 2H), 3.88 (s, 3H), 6.85−7.00 (m, 3H), 7.19 (d, $J = 8.1$ Hz, 1H), 7.35 (app-t, $J = 8.1$ Hz, 1H), 7.42−7.50 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.1, 21.3, 23.4, 30.8, 55.9, 101.3, 109.1, 110.5, 110.8, 114.5, 114.7, 119.5, 119.9, 127.4, 127.7, 127.9, 128.5, 136.5, 140.8, 146.4, 148.9, 157.1, 170.1; MS (CI) *m*/*z* 377 (M + H)$^+$. Anal. Calcd for $C_{23}H_{20}O_5$: C, 73.39; H, 5.36. Found: C, 73.36; H, 5.24.

(2*H*)-5-Hydroxy-2,3-dihydrospiro[naphthalene-1(4*H*),2′-naphtho[1,8-*de*][1,3]dioxine] 27. DMF (5 mL) was added to anisole **22** (318 mg, 1.0 mmol, 1.0 equiv) and NaSEt (168 mg, 2.0 mmol, 2.0 equiv), and the resulting red solution was heated to reflux for 90 min under N_2. After the mixture was cooled to room temperature, H_2O (5 mL) was added, and the reaction mixture was acidified with 1.0 M aqueous HCl. A white solid precipitated out of the orange organic layer. Et_2O (20 mL) was added, the layers were separated, and the aqueous phase was extracted with Et_2O (10 mL). The combined organic layers were washed with brine (10 mL), dried ($MgSO_4$), and rotary evaporated to give a yellow solid that was adsorbed on silica gel (1.5 g). Chromatography (Et_2O/hexanes, 2:1) gave phenol **27** (291 mg, 97%) as a white solid: mp 158 °C (Et_2O/hexane); R_f 0.43 (Et_2O/hexanes, 3:2); IR (KBr disk) 3317, 1632, 1608, 1272 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.00 (m, 2H), 2.17 (m, 2H), 2.82 (t, $J = 6.6$ Hz, 2H), 4.84 (s, 1H), 6.87 (d, $J = 7.3$ Hz, 1H), 6.95 (dd, $J = 6.7$, 0.5 Hz, 2H), 7.35 (app-t, $J = 8.0$ Hz, 1H), 7.41−7.58 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.7, 22.8, 30.4, 100.5, 109.3 113.7, 115.5, 119.8, 120.3, 125.1, 127.2, 127.4, 134.2, 136.8, 148.2, 152.8; MS (CI) *m*/*z* 305 (M + H)$^+$; *m*/*z* (CI) calcd for $C_{20}H_{17}O_3$ 305.1178, found 305.1179. Anal. Calcd for $C_{20}H_{16}O_3$: C, 78.93; H, 5.30. Found: C, 78.73; H, 5.04.

(2*H*)-2,3-Dihydrospiro[naphthalene-1(4*H*),2′-naphtho-[1,8-*de*][1,3]-dioxine]-5,8-dione 28. Phenol **27** (61 mg, 0.2 mmol) was added in small portions over a period of 30 min to $PhI(OCOCF_3)_2$ (181 mg, 0.42 mmol) in THF and H_2O (9:1; 2 mL) at room temperature. After the addition was complete, stirring was continued for a further 20 min, and H_2O (1 mL) and Et_2O (4 mL) were added. The organic layer was separated, washed with brine (1 mL), dried ($MgSO_4$), and concentrated. Chromatography (Et_2O/hexanes, 1:2) gave quinone **28** (42 mg, 66%) as a red solid: mp 85 °C (hexanes); R_f 0.51 (Et_2O/hexanes, 1:1); IR (KBr disk) 1659, 1605 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.83−1.90 (m, 2H), 2.10−2.12 (m, 2H), 2.62 (t, $J = 6.0$ Hz, 2H), 6.72−6.95 (m, 4H), 7.40−7.58 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 17.7, 23.6, 31.8, 98.9, 109.2, 113.0, 120.5, 127.3, 134.3, 135.1, 135.6, 137.9, 146.8, 146.9, 183.5, 187.4; MS (EI) *m*/*z* 318 (M$^{\bullet+}$), 115; *m*/*z* (EI) calcd for $C_{20}H_{15}O_4$ 318.0892, found 318.0906. Anal. Calcd for $C_{20}H_{14}O_4$: C, 75.46; H, 4.43. Found: C, 75.58; H, 4.54.

(2*H*)-5-Benzyloxy-2,3-dihydrospiro[naphthalene-1(4*H*),2′-naphtho[1,8-*de*][1,3]-dioxine]. MeCN (5 mL) followed by $PhCH_2Br$ (59 μL, 0.05 mmol) were added to phenol **27** (150 mg, 0.50 mmol), K_2CO_3 (137 mg, 0.99 mmol), and NaI (10 mg), and the reaction mixture was heated at reflux for 4 h. After rotary evaporation, the residue was dissolved in EtOAc (20 mL) and saturated aqueous $NaHCO_3$ (10 mL), and the organic layer was separated, dried ($MgSO_4$), and filtered. Chromatography (EtOAc/hexanes, 1:15 to 1:9 to 1:4) gave the

title benzyl ether (140 mg, 72%) as a white solid: mp 163−164 °C (Et_2O); R_f 0.60 (EtOAc/hexanes 1:4); IR (thin film) 1606, 1589, 1272 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.89−2.00 (m, 2H), 2.12−2.20 (m, 2H), 2.92 (t, J = 6.3 Hz, 2H), 5.16 (s, 2H), 6.90−7.00 (m, 3H), 7.31−7.55 (m, 11H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.3, 22.8, 29.9, 69.6, 100.1, 108.8, 111.3, 113.2, 119.0, 119.8, 126.5, 126.7, 126.7, 126.9, 127.4, 127.4, 128.1, 133.7, 136.8, 147.8, 155.3; MS (CI) m/z 395 $(M + H)^+$. Anal. Calcd for $C_{27}H_{22}O_3$: C, 82.21; H, 5.62. Found: C, 82.17; H, 5.69.

(2*H*)-4′-Acetoxy-5-benzyloxy-2,3-dihydrospiro[naphthalene-1(4*H*),2′-naphtho[1,8-*de*][1,3]-dioxine] 29. CH_2Cl_2 (2 mL) and AcOH (4 mL) were added to the preceding benzyl ether (140 mg, 0.36 mmol) and $Pb(OAc)_4$ (307 mg, 0.71 mmol), and the mixture was stirred under N_2 for 16 h. The mixture was diluted with EtOAc (20 mL) and saturated aqueous NH_4Cl (10 mL), and the organic layer was separated, dried ($MgSO_4$), and filtered. Chromatography (EtOAc/hexanes, 1:2) gave acetate **29** (100 mg, 62%) as a white solid: mp 193−194 °C (Et_2O); R_f 0.30 (EtOAc/hexanes 1:4); IR (thin film) 1763, 1608, 1201 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.86−1.99 (m, 2H), 2.10−2.17 (m, 2H), 2.45 (s, 3H), 2.88 (t, J = 6.3 Hz, 2H), 5.12 (s, 2H), 6.86−6.97 (m, 3H), 7.17−7.49 (m, 10H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.8, 21.0, 23.3, 30.4, 70.1, 101.0, 108.8, 110.1, 111.9, 114.1, 114.4, 119.3, 119.6, 127.1, 127.1, 127.3, 127.9, 128.0, 128.2, 128.6, 136.2, 137.2, 140.4, 146.1, 148.5, 155.8, 169.8; MS (CI) m/z 453 $(M + H)^+$. Anal. Calcd for $C_{29}H_{24}O_5$: C, 76.98; H, 5.35. Found: C, 76.95; H, 5.29.

(2*H*)-4′-Acetoxy-5-hydroxy-2,3-dihydrospiro[naphthalene-1(4*H*),2′-naphtho[1,8-*de*][1,3]dioxine]. Benzyl ether **29** (100 mg, 0.22 mmol) in EtOAc (5 mL) and 10% Pd/C (20 mg) were hydrogenated at atmospheric pressure for 6 h. The mixture was filtered through Celite and chromatographed (EtOAc/hexanes, 1:4) to give the title phenol (85 mg, 100%) as a white solid: mp 193−194 °C (Et_2O); R_f 0.30 (EtOAc/hexanes 1:2); IR (thin film) 3454, 1744, 1668, 1271 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.82−1.93 (m, 2H), 2.03−2.10 (m, 2H), 2.41 (s, 3H), 2.72 (t, J = 6.3 Hz, 2H), 5.16 (br. s, 1H), 6.71 (d, J = 7.6, 0.9 Hz, 1H), 6.83 (d, J = 8.3 Hz, 1H), 6.90 (dd, J = 6.9, 1.3 Hz, 1H), 7.12−7.19 (m, 2H), 7.34−7.44 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.6, 21.0, 22.8, 30.3, 100.8, 108.8, 110.2, 114.1, 114.4, 115.5, 119.6, 119.6, 125.1, 127.2, 128.2, 136.5, 140.4, 146.0, 148.5, 152.9, 152.9, 169.9; MS (CI) m/z 363 $(M + H)^+$ 233; m/z (CI) calcd for $C_{22}H_{19}O_5$ 363.1232, found 363.1249. Anal. Calcd for $C_{20}H_{18}O_5$: C, 72.92; H, 5.01. Found: C, 72.90; H, 4.94.

(2*H*)-4′-Acetoxy-2,3-dihydrospiro[naphthalene-1(4*H*),2′-naphtho[1,8-*de*][1,3]dioxine]-5,8-dione 30. $PhI(OCOCF_3)_2$ (42.4 mg) in THF and H_2O (9:1; 0.5 mL) was added to the preceding benzyl ether (17 mg, 0.047 mmol) in THF and H_2O (9:1; 1 mL) portionwise over 25 min under N_2, and the red mixture was stirred for 30 min. The mixture was diluted with Et_2O (15 mL) and H_2O (5 mL), and the organic layer was dried ($MgSO_4$), filtered, and rotary evaporated. Chromatography (EtOAc/hexanes, 1:2) gave the quinone **30** (9 mg, 51%) as an orange solid: mp 123−127 °C (Et_2O); R_f 0.30 (EtOAc/hexanes 1:2); IR (thin film) 1764, 1661, 1609, 1202 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.82−1.94 (m, 2H), 2.04−2.16 (m, 2H), 2.46 (s, 3H), 2.63 (t, J = 6.3 Hz, 2H), 6.76−6.88 (m, 3H), 6.93 (d, J = 6.6 Hz, 1H), 7.19 (d, J = 8.2 Hz, 1H), 7.42−7.54 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 17.5, 20.9, 23.5, 31.7, 99.2, 108.6, 109.9, 113.3, 114.5, 115.2, 119.4, 119.7, 128.0, 128.1, 135.0, 137.9, 140.5, 144.6, 147.0, 169.7, 183.3, 187.3; MS (EI) m/z 376 ($M^{\bullet+}$), 334, 43; m/z (CI) calcd for $C_{20}H_{16}O_6$ 376.0947, found 376.0938.

(2*H*)-5,8,4′-Trihydroxy-2,3-dihydrospiro[naphthalene-1(4*H*),2′-naphtho[1,8-*de*][1,3]-dioxine] 31. Quinone **30** (149 mg, 0.40 mmol) in Et_2O (20 mL) was washed with $Na_2S_2O_4$ (390 mg, 2.2 mmol) in H_2O (2 mL) until decolorization was complete. The organic layer was separated, dried ($MgSO_4$), filtered, and rotary evaporated. Chromatography (EtOAc/hexanes, 1:2−1:1) gave an unstable colorless oil. This was dissolved in degassed MeOH (9 mL), treated with NaOMe (33 mg, 6.1 mmol), and stirred for 1 h during which time the mixture turned from yellow to light brown. The mixture was quenched with EtOAc (30 mL) and 1 M HCl, and the organic layer was separated, dried ($MgSO_4$), filtered, and rotary evaporated. Chromatography (EtOAc/hexanes, 1:2) gave triol **31** (61 mg, 46%) as a white solid: mp 228−230 °C dec (Et_2O); R_f 0.15 (EtOAc/hexanes, 1:2); IR (thin film) 3400, 1610, 1265 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.85−1.95 (m, 2H), 2.05−2.18 (m, 2H), 2.75−2.81 (m, 2H), 5.07 (br s, 1H), 5.98 (br s, 1H), 6.79 (app-d, J = 8.5 Hz, 2H), 6.83 (app-d, J = 8.5 Hz, 2H), 7.03 (d, J = 7.6 Hz, 1H), 7.20 (s, 1H), 7.46 (t, J = 8.3 Hz, 1H), 7.81 (d, J = 8.5 Hz, 1H); ^{13}C NMR (75 MHz, acetone-d_6) δ 19.0, 23.9, 31.1, 103.2, 109.4, 110.4, 110.7, 114.8, 115.1, 116.1, 117.0, 121.1, 125.5, 126.4, 126.5, 140.0, 147.6, 147.8, 148.4, 150.2; MS (CI) m/z 337 $(M + H)^+$; m/z (CI) calcd for $C_{20}H_{17}O_5$ 337.1076, found 337.1090. Anal. Calcd for $C_{20}H_{16}O_5$: C, 71.42; H, 4.79. Found: C, 71.51; H, 4.82.

Dideoxypressomerin G 17. *p*-Benzoquinone (2.2 mg, 0.020 mmol) in THF (0.3 mL) was added to triol **31** (5.7 mg, 0.016 mmol) in dry, degassed THF (1.0 mL) at −78 °C under N_2. Following stirring at the same temperature for 30 min, more *p*-benzoquinone (2.2 mg, 0.020 mmol) in THF (0.3 mL) was added and stirring continued for 10 min. Reaction was quenched by addition of 1 M HCl (1 mL), and the mixture was diluted with Et_2O (10 mL). The organic layer was separated, dried ($MgSO_4$), filtered, and rotary evaporated. Preparative TLC (EtOAc/hexanes, 1:2) gave dideoxypressomerin G **17** (4.0 mg, 75%) as a yellow solid: mp 220−223 °C (Et_2O); R_f 0.40 (EtOAc/hexanes 1:2); IR (thin film) 3399, 1677, 1292 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.97−2.24 (m, 2H), 2.40−2.62 (m, 2H), 2.64−2.79 (m, 1H), 2.88−2.99 (m, 1H), 4.42 (br. s, 1H), 6.53 (d, J = 10.2 Hz, 1H), 6.54 (d, J = 8.9 Hz, 1H), 6.69 (d, J = 8.6 Hz, 1H), 7.02 (dd, J = 8.3, 1.0 Hz, 1H), 7.15 (d, J = 9.9 Hz, 1H), 7.35 (app-t, J = 9.9 Hz, 1H), 7.56 (dd, J = 7.6, 1.0 Hz, 1H); MS (CI) m/z 335 $(M + H)^+$, 179; m/z (CI) calcd for $C_{20}H_{15}O_5$ 335.0920, found 335.0919. The spectroscopic data matched those reported by Chi and Heathcock.[8]

5-Methoxy-2,3-dihydrospiro[naphthalene-1(4*H*),2′-naphtho[1,8-*de*][1,3]dioxin]-4-one 32. Spiroketal **22** (5.67 g, 18 mmol, 1.0 equiv), bipyridinium chlorochromate (525 mg, 1.8 mmol, 0.1 equiv), and Celite (2.9 g) were suspended in PhH (70 mL). *tert*-Butyl hydroperoxide in PhH (3 M; 60 mL, 287 mmol, 16 equiv) was added over 5.25 h (syringe pump) under N_2, and the dark mixture was stirred for 16 h and filtered through Celite. HCl (1 M, 50 mL) was added, the layers were shaken vigorously, and the separated organic layer was washed with brine (80 mL) and dried ($MgSO_4$). Silica gel (50 g) was added, and the residue, after rotary evaporation, was chromatographed (EtOAc/hexanes, 2:1) to afford ketone **32**[20] (3.56 g, 60%) as an orange solid: mp 154−156 °C (hexane); R_f 0.28 (Et_2O/hexanes, 4:1); IR (KBr disk) 1681, 1634, 1272 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.49 (t, J = 6.8 Hz, 2H), 2.78 (t, J = 6.8 Hz, 2H), 3.99 (s, 3H), 6.98 (d, J = 7.3 Hz, 2H), 7.14 (d, J = 8.0 Hz, 1H), 7.43−7.68 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 29.4, 35.4, 56.4, 98.9, 109.4, 113.5, 113.6, 117.8, 120.8, 121.0, 127.5, 134.2, 134.9, 142.7, 147.6, 156.7, 195.3; MS (CI) m/z 333 $(M + H)^+$; m/z (CI) calcd for $C_{21}H_{19}O_4$ 333.1126, found 333.1125. Anal. Calcd for $C_{21}H_{18}O_4$: C, 75.89, H, 4.85. Found: C, 75.98; H, 4.88.

Palmarumycin CP_2 13. Et_2O (12.5 mL) and PhH (25 mL) were added to iodine (10.0 g, 39.4 mmol) and Mg turnings (2 g, 83 mmol) under N_2 at 0 °C (caution: exothermic), and the mixture was stirred for 20 min. The mixture was warmed to room temperature and stirred for a further 1.5 h in the dark, after which time the initially brown color had faded. An aliquot of this freshly prepared MgI_2 solution (30.6 mL, 32 mmol, 2.5 equiv) was added to a solution of ketone **32**[20] (4.27 g, 12.7 mmol) in THF (120 mL), and the resulting solution was stirred for 24 h in the dark. The reaction mixture was diluted with 1 M HCl (50 mL) and Et_2O (200 mL). The aqueous layer was separated and extracted with Et_2O (50 mL), and the combined organic layers were dried ($MgSO_4$), filtered, and evaporated to dryness. Chromatography (EtOAc/hexanes, 1:9−1:4) gave palmarumycin CP_2 (**13**) (3.37 g, 83%) as a white solid: mp 171 °C (hexane); R_f 0.40 (EtOAc/hexanes 1:9); IR (KBr disk) 1643, 1608, 1271 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.51 (t, J = 6.8 Hz, 2H), 2.87 (t, J = 6.8 Hz, 2H), 6.98 (d, J = 7.3 Hz, 2H), 7.11 (dd, J = 8.0, 1.0 Hz, 1H), 7.45−7.50 (m, 4H), 7.56 (d, J = 7.8 Hz, 1H), 7.64 (app-t, J = 8.0, 7.8 Hz, 1H) 12.47 (s, 1H); ^{13}C

NMR (75 MHz, $CDCl_3$) δ 29.4, 34.1, 98.4, 109.5, 113.4, 115.4, 116.7, 119.6, 120.9, 127.6, 134.2, 137.2, 141.0, 147.4, 162.5, 203.3; MS (CI) *m/z* 319 $(M + H)^+$, 161; *m/z* (EI) calcd for $C_{20}H_{15}O_4$ 319.0970, found 319.0976. Anal. Calcd for $C_{20}H_{14}O_4$: C, 75.46; H, 4.43. Found: C, 75.76; H, 4.61. The sample of synthetic palmarumycin CP_2 (**13**) was identical in all respects with an authentic sample of the natural product kindly provided by Professor Karsten Krohn.[1a]

CJ-12,371 33. Palmarumycin CP_2 (**13**) (160 mg, 0.50 mmol) in THF (1.5 mL) at −78 °C was added to (+)-*B*-chlorodiisopinocampheylborane (288 mg, 0.90 mmol) in THF (1.5 mL). The red solution was maintained at this temperature for 30 min, allowed to warm to room temperature, and left standing for 18 h. The reaction was terminated by the addition of aqueous hydrogen peroxide (27%; 1.5 mL) and 2 M NaOH (1 mL). After being stirred for 1 h, the reaction mixture was neutralized with 1 M HCl and the aqueous layer separated and extracted with Et_2O (2 × 5 mL). The combined organic layers were washed with brine (2 mL), dried ($MgSO_4$), and rotary evaporated. Chromatography (Et_2O/hexanes, 2:1) gave CJ-12,371 (**33**)[5,21] (96 mg, 60%) as a colorless solid: $[\alpha]^{24}_D$ −42.2 (*c* 0.46, MeOH) (lit.[4g] $[\alpha]^{24}_D$ −46.8 (*c* 0.23, MeOH)); mp 186 °C (CH_2Cl_2); R_f 0.44 (Et_2O/hexanes, 2:1); IR (KBr disk) 3441, 1606, 1257 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.95−2.17 (m, 2H), 2.24−2.33 (m, 1H), 2.39−2.48 (m, 2H), 5.18 (dd, J = 5.9, 8.1 Hz, 1H), 6.94 (2 d, J = 7.1, 6.8 Hz, 2H), 7.04 (dd, J = 7.8, 1.2 Hz, 1H), 7.36−7.63 (m, 6H), 7.97 (s, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 25.9, 28.2, 61.5, 100.5, 109.6 (×2), 113.5, 116.6, 117.9, 120.7 (×2), 126.9, 128.2 (×2), 129.0, 134.3, 136.1, 148.0, 148.3, 155.9; MS (FAB) *m/z* 320 $(M^{+\cdot})$, 303; *m/z* (FAB) calcd for $C_{20}H_{16}O_4$ 320.1049, found 320.1049. Anal. Calcd for $C_{20}H_{16}O_4$: C, 74.99; H, 5.03. Found: C, 75.17; H, 5.01. Chiral HPLC (method A): t_R = 8 min 20 s (CJ-12,371 (**33**)) and t_R = 11 min 22 s ((+)-CJ-12,371); 92% ee. Synthetic CJ-12,371 (**33**) showed spectroscopic data in agreement with that published for the natural product.[4g] Reduction of palmarumycin CP_2 (**13**) (63 mg, 0.0 mmol) in MeOH (1.5 mL) using $NaBH_4$ (23 mg, 0.6 mmol, 3.0 equiv) at 0 °C for 1 h, and workup as above gave racemic CJ-12,371 ((±)-**33**) (60 mg, 94%).

Racemic CJ-12,372 ((±)-34). CJ-12,371 (**33**) (32 mg, 0.1 mmol, 1.0 equiv) in THF and H_2O (9:1, 1 mL) was added dropwise over 30 min to $PhI(OCOCF_3)_2$ (95 mg, 0.22 mmol, 2.2 equiv) in THF and H_2O (9:1, 1 mL) at room temperature. The orange reaction mixture was allowed to stir for 1 h, and then H_2O (2 mL) and Et_2O (4 mL) were added. The red organic layer was separated and washed with a solution of sodium dithionite (87 mg), H_2O (2 mL), and brine (2 mL) and dried ($MgSO_4$). Chromatography (Et_2O/hexanes, 2:1) gave unreacted CJ-12,371 (**33**) (2 mg, 6%) followed by racemic CJ-12,372 ((±)-**34** (19 mg, 56%) as a white solid: mp 178 °C ($CHCl_3$); R_f 0.25 (Et_2O/hexanes 3:1); IR (KBr disk) 3418, 3361, 1605, 1466, 1408, 1266 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.70−2.01 (m, 3H), 2.23−2.34 (m, 1H), 4.93 (s, 1H), 5.08 (br s, 1H), 6.69 (d, J = 8.6, 2.3 Hz, 1H), 6.78 (dd, J = 8.6, 2.3 Hz, 1H), 6.86 (dd, J = 7.6, 1.0 Hz, 1H), 6.91 (dd, J = 7.6, 1.0 Hz, 1H), 7.42−7.55 (m, 4H), 8.41 (d, J = 2.3 Hz, 1H) 9.01 (d, J = 2.3 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 27.3, 28.0, 61.9, 101.5, 109.2, 113.1,-117.2, 117.8, 120.2, 120.9, 127.7, 128.1, 134.3, 148.1, 148.3, 149.7; *m/z* (EI) 318 $(M - H_2O)^{\bullet+}$, 301, 160, 84; *m/z* (EI) calcd for $C_{20}H_{14}O_4$, found 318.0892, found 318.0885.

5-Methoxyspiro[naphthalene-1(4*H*),2′-naphtho[1,8-*de*]-[1,3]dioxin]-4-one 35. PhH (5 mL) was added to ketone **32** (332 mg, 1.0 mmol) and DDQ (272 mg, 1.2 mmol) under N_2. The resulting dark reaction mixture was heated to reflux for 10 h during which time a yellow solid precipitated. After the mixture was cooled to room temperature, silica gel (3 g) was added and the mixture rotary evaporated. Chromatography (Et_2O/hexanes, 2:1) gave enone **35**[20] (213 mg, 65%) as a yellow solid: mp 204 °C (hexane); R_f 0.38 (Et_2O/hexanes, 4:1); IR (KBr disk) 1673, 1642, 1271 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 4.03 (s, 3H), 6.30 (d, J = 10.5 Hz, 1H), 6.86 (d, J = 10.5 Hz, 1H), 6.99 (d, J = 7.5 Hz, 2H), 7.18 (d, J = 8.0 Hz, 1H), 7.42−7.62 (m, 5H), 7.71 (app-t, J = 8.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 56.5, 93.4, 109.8, 113.2, 113.9, 119.0, 120.2, 121.2, 127.6, 132.2, 134.2, 134.9, 135.2, 141.1, 147.4, 160.0, 183.0; MS (CI) *m/z* 331 $(M + H)^+$, 115; *m/z* (CI) calcd for $C_{21}H_{15}O_4$ 331.0970, found 331.0965. Anal. Calcd for $C_{21}H_{14}O_4$: C, 76.36; H, 4.27. Found: C, 76.54; H, 4.24. The minor, less polar furan **37** (32 mg, 8%) was also isolated by chromatography as a crystalline solid: mp 238 °C (Me_2CO/H_2O); R_f 0.52 (Et_2O/hexanes, 2:1); IR (NaCl disk) 2224, 1610, 1411, 1378, 1269, 1055, 752 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.30 (s, 2H), 4.03 (s, 3H), 6.91 (d, J = 7.6 Hz, 2H), 7.13 (dd, J = 8.3, 0.8 Hz, 1H), 7.47 (dd, J = 8.3, 7.6 Hz, 2H), 7.52 (app t, J = 8.2, 7.9 Hz, 1H), 7.56 (d, J = 8.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.9, 56.2, 99.1, 108.4, 109.4, 109.7, 112.9, 113.2, 113.3, 117.5, 118.8, 121.3, 127.6, 129.0, 132,2, 134.2, 135.9, 146.4, 153.4, 155.4; *m/z* (EI) 407 $(M + H)^+$, 406 $(M^{\bullet+})$, 391, 374, 363, 345, 159; *m/z* (EI) calcd for $C_{25}H_{14}O_4N_2$ 406.0953, found 406.0945. Anal. Calcd for $C_{25}H_{14}O_4N_2$: C, 73.89; H, 3.47; N, 6.89. Found: C, 73.70; H, 3.54; N, 6.78. Crystal data for **37**: $C_{25}H_{14}N_2O_4$, M = 406.4, triclinic, $P1$ (no. 1), a = 5.170(1) Å, b = 8.290(1) Å, c = 12.177(1) Å, α = 108.26(1)°, β = 94.11(1)°, γ = 102.12(1)°, V = 479.2(1) Å^3, Z = 1, D_c = 1.408 g cm^{-3}, μ(Cu Kα) = 0.80 mm^{-1}, T = 293 K, colorless blocks; 1620 independent measured reflections, F^2 refinement, R_1 = 0.038, wR_2 = 0.102, 1552 independent observed reflections [$|F_o| > 4\sigma(|F_o|)$, $2\theta \leq 128°$], 281 parameters. The absolute structure of **37** could not be determined. CCDC 182477.

Palmarumycin CP_1 1. Method 1. 2,6-Lutidine (3.21 mL, 27.5 mmol) was added to palmarumycin CP_2 **13** (2.50 g, 7.9 mmol) in dry CH_2Cl_2 (30 mL) at 0 °C followed by the portionwise addition of trimethylsilyl triflate (4.28 mL, 23.6 mmol) every 8 min over 1 h. The mixture was stirred at 0 °C for 1 h and quenched by addition of saturated aqueous $NaHCO_3$ (20 mL). The mixture was diluted with CH_2Cl_2 (30 mL); the organic layer was separated, dried (Na_2SO_4) and evaporated under high vacuum with azeotropic removal of 2,6-lutidine with PhMe (3 × 20 mL); and the residue enol silane **36** was used without further purification. MeCN (80 mL) was added followed by $Pd(OAc)_2$ (1.77 g, 7.86 mmol), and the mixture was stirred under N_2 for 16 h. The mixture was filtered through Celite, which was washed with CH_2Cl_2 (2 × 20 mL), and the combined organic phases were evaporated to dryness. The residue was dissolved in CH_2Cl_2 (120 mL) and washed with saturated aqueous NH_4Cl (30 mL), and the organic layer was dried ($MgSO_4$) and rotary evaporated. Chromatography (CH_2Cl_2/hexanes, 2:1 to CH_2Cl_2) gave palmarumycin CP_1 (**1**)[20] (1.94 g, 78% over both steps) as a yellow solid: mp 172−173 °C (Et_2O); R_f 0.69 (Et_2O/hexanes, 2:1); IR (KBr disk) 1661, 1610, 1268, cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.38 (d, J = 10.6 Hz, 1H), 6.99 (d, J = 7.6 Hz, 2H), 7.04 (d, J = 10.6 Hz, 1H), 7.16 (d, J = 8.4 Hz, 1H), 7.47−7.52 (m, 3H), 7.59 (dd, J = 9.0, 0.5 Hz, 2H), 7.68 (app-t, J = 8.0 Hz, 1H), 12.19 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 92.9, 109.9, 113.0, 113.8, 119.4, 119.7, 121.4, 127.6, 129.8, 134.2, 136.6, 138.8, 139.7, 147.2, 161.9, 188.8; MS (EI) *m/z* 317 $(M + H)^+$, 130, 114, 88; *m/z* (EI) calcd for $C_{20}H_{13}O_4$ 317.0814, found 317.0821. Anal. Calcd for $C_{20}H_{12}O_4$: C, 75.94; H, 3.82. Found: C, 75.94; H, 3.71. The spectroscopic data was identical to that reported previously[1a] and the synthetic palmarumycin CP_1 (**1**) was identical with an authentic sample provided by Professor Karsten Krohn. **Method 2.** *B*-Bromocatecholborane (571 mg, 2.9 mmol) in CH_2Cl_2 (1.0 mL) was added to an ice-cooled solution of ketone **35** (190 mg, 0.58 mmol) and DBU (175 μL, 1.15 mmol) in CH_2Cl_2 (1.4 mL) over a period of 5 min. After the mixture was stirred for 2 min at this temperature, saturated aqueous $NaHCO_3$ (2 mL) was added to the brown reaction mixture, and stirring was continued for another 10 min. Hydrochloric acid (1.0 M) was added to pH 2, and the aqueous layer was extracted with CH_2Cl_2 (3 × 8 mL). The combined organic layers were washed with brine (10 mL), dried ($MgSO_4$), and rotary evaporated. The resulting orange residue was adsorbed on silica gel (250 mg) and chromatographed (Et_2O/hexanes, 1:4) to yield palmarumycin CP_1 (**1**) (101 mg, 56%) as a yellow solid.

Palmarumycin C_2 3. Small-Scale Preparation. *N*-Benzylcinchoninium chloride **39** (8 mg, 0.02 mmol), H_2O (0.1 mL), and *tert*-butyl hydroperoxide in PhMe (3.17 M; 0.12 mL, 0.38 mmol) were added to palmarumycin CP_1 (**1**) (60 mg, 0.19

mmol) in PhMe (1.9 mL) at room temperature followed by the addition of aqueous NaOH (0.11 M; 0.85 mL, 50 mol %). After 8 h, additional oxidant (30 μL, 0.6 equiv) was added, and stirring was continued for 2 h. HCl (1 M, 0.3 mL), CH_2Cl_2 (8 mL), and H_2O (4 mL) were added and both layers shaken vigorously. The separated aqueous layer was extracted with CH_2Cl_2 (2 × 10 mL), and the combined organic extracts were dried ($MgSO_4$). After filtration, silica gel (300 mg) was added and the mixture rotary evaporated and chromatographed (EtOAc/hexanes, 1:4) to give palmarumycin C_2 (**3**) (51 mg, 81%) as a white solid: mp 225 °C (Me_2CO/H_2O); R_f 0.47 (Et_2O/hexane 1:2); $[\alpha]_D$ −300 (*c* 1.00, CH_2Cl_2) (lit.[1b] $[\alpha]_D$ −341 (*c* 1.00, CH_2Cl_2)); IR (KBr disk) 1650, 1611, 1269 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.69 (d, *J* = 4.0 Hz, 1H), 4.11 (d, *J* = 4.0 Hz, 1H), 6.94 (d, *J* = 7.5 Hz, 1H), 7.14 (d, *J* = 8.2 Hz, 1H), 7.20 (d, *J* = 7.3 Hz, 1H), 7.43−7.70 (m, 6H), 11.38 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 53.3, 95.9, 109.3, 110.1, 112.3, 112.8, 119.1, 120.0, 121.3, 121.4, 127.6, 127.8 (2), 134.2, 136.9, 137.6, 146.7, 146.9, 161.9, 196.5; MS (EI) *m*/*z* 332 ($M^{+\cdot}$), 287, 145; *m*/*z* (EI) calcd for $C_{20}H_{12}O_5$ 332.0684, found 332.0685. Anal. Calcd for $C_{20}H_{12}O_5$: C, 72.29; H, 3.64. Found: C, 72.45; H, 3.61. Chiral HPLC (method B): t_R = 8 min 12 s (palmarumycin C_2 (**3**)) and t_R = 9 min 56 s ((+)-palmarumycin C_2). The spectroscopic data were identical to that reported in the literature,[1b] and in addition, the synthetic palmarumycin C_2 (**3**) was identical in all respects with an authentic sample of the natural product, also named deoxypreussomerin A (**3**), kindly provided by Dr. Sheo B. Singh (Merck and Co., Inc.).[3e] **Larger Scale Procedure.** *N*-Benzylcinchoninium chloride **39** (48 mg, 0.12 mmol), H_2O (0.6 mL), and *tert*-butyl hydroperoxide in PhMe (3.17 M; 0.75 mL, 2.3 mmol) were added to palmarumycin CP_1 (**1**) (363 mg, 1.15 mmol) in PhMe (11.4 mL) at room temperature. Aqueous NaOH (0.11 M; 5.1 mL, 50 mol %) was added while the color of the organic layer changed from yellow to orange immediately and the mixture was stirred for 8 h. HCl (1 M) was added (2 mL), and a color change back to yellow was observed. CH_2Cl_2 (50 mL) and H_2O (20 mL) were added, and both layers shaken together vigorously. The separated aqueous layer was extracted with CH_2Cl_2 (2 × 10 mL) and the combined organic extracts were dried ($MgSO_4$), filtered, and rotary evaporated. The crude mixture was triturated with refluxing EtOAc (6 mL) and allowed to cool to room temperature. The mixture was filtered to give palmarumycin C_2 (**3**) (286 mg, 75%) as a yellow solid. The spectroscopic data matched those reported above including optical rotation: $[\alpha]_D$ −302 (*c* 1.00, CH_2Cl_2). Crystal data for **3**: $C_{20}H_{12}O_5$, *M* = 332.3, orthorhombic, $P2_12_12_1$ (no. 19), *a* = 5.245(1) Å, *b* = 13.895(1) Å, *c* = 20.182(1) Å, *V* = 1470.9(3) $Å^3$, *Z* = 4, D_c = 1.501 g cm^{-3}, μ(Cu Kα) = 0.90 mm^{-1}, *T* = 293 K, yellow needles; 1452 independent measured reflections, F^2 refinement, R_1 = 0.046, wR_2 = 0.108, 1216 independent observed reflections [$|F_o| > 4\sigma(|F_o|)$, $2\theta \leq 128°$], 231 parameters. The absolute structure of **3** could not be determined from the X-ray analysis, but was assigned by reference to that of **38**. CCDC 182478.

(±)-Palmarumycin C_2. *tert*-Butyl hydroperoxide in PhMe (3 M; 98 μL, 0.30 mmol,) was added to ice-cooled enone **1** (63 mg, 0.2 mmol) in CH_2Cl_2 (1 mL). After the mixture was stirred for 5 min, DBU in CH_2Cl_2 (0.4 M; 50 μL, 0.02 mmol) was added while the color of the clear solution changed from yellow to orange. The mixture was stirred under ice cooling for 8 h when the reaction was terminated by the addition of a 5% aqueous $Na_2S_2O_5$ (1 mL). After dilution with CH_2Cl_2 (2 mL) and H_2O (2 mL), the layers were separated and the aqueous layer was extracted with CH_2Cl_2 (1 × 5 mL). The combined organic extracts were dried ($MgSO_4$), rotary evaporated, and chromatographed (Et_2O/hexanes, 1:8) to give racemic palmarumycin C_2 ((±)-**3**)[21] (55 mg, 83%) as a yellow solid. The spectroscopic data matched that reported above for the natural enantiomer.

(2*R*,3*S*)-1′a,7′a-Dihydro-6′-methoxyspiro[naphtho[1,8-*de*]-1,3-dioxin-2,2′(7′*H*)-naphth[2,3-*b*]oxiren]-7′-one 40. *N*-Benzylcinchoninium chloride **39** (42 mg, 0.10 mmol), H_2O (1 mL), and *tert*-butyl hydroperoxide in PhMe (3.07 M; 65 μL) were added to enone **35** (33 mg, 0.10 mmol) in PhMe (2 mL). Aqueous NaOH (0.11 M; 0.43 mL) was added while the color of the organic layer changed to orange immediately. After being stirred at room temperature for 9 days, 5% aqueous $Na_2S_2O_5$ (0.5 mL) was added, and the resulting mixture was dissolved in CH_2Cl_2 (10 mL) and H_2O (2 mL). After separation of the layers, the organic extract was washed with brine (3 mL), dried ($MgSO_4$), and filtered. Silica (200 mg) was added and the residue, after rotary evaporation, chromatographed (Et_2O/hexane, 2:1) to provide epoxyketone **40** (102 mg, 61%), which was obtained as a white solid, as well as starting enone **35** (9 mg, 27%). Epoxyenone **40**: $[\alpha]_D$ −67 (*c* 0.28, CH_2Cl_2); mp 187 °C (Et_2O/hexanes); R_f 0.53 (EtOAc/hexane, 1:2); IR (KBr disk) 1670, 1637, 1274 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.72 (d, *J* = 4.4 Hz, 1H), 3.97 (s, 3H), 4.09 (d, *J* = 4.4 Hz, 1H), 6.89 (dd, *J* = 7.1, 1.0 Hz, 1H), 7.14 (d, *J* = 8.1 Hz, 1H), 7.20 (dd, *J* = 7.1, 1.0 Hz, 1H), 7.43 (dd, *J* = 8.2, 7.6 Hz, 1H), 7.48−7.58 (m, 4H), 7.63 (dd, *J* = 8.1, 6.6 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 53.0, 54.1, 56.4, 97.1, 109.3, 109.9, 112.8, 113.9, 118.1, 118.8, 121.1, 121.3, 127.7 (x 2), 134.1, 134.9, 138.1, 146.7, 147.0, 158.9, 191.7; MS (EI) *m*/*z* 347 $(M + H)^+$, 55; *m*/*z* (CI) calcd for $C_{21}H_{14}O_5$ 347.0919, found 347.0934. Anal. Calcd for $C_{21}H_{14}O_5$: C, 72.83; H, 4.07. Found: C, 72.97; H, 4.18; chiral HPLC (method C) t_R = 25 min 11 s and t_R = 27 min 4 s, (23% ee).

(2*R*,3*S*)-7′,7′a-Dihydro-7′-oxospiro[naphtho[1,8-*de*]-1,3-dioxin-2,2′(1′a*H*)-naphth[2,3-*b*]oxiren]-6′-yl 1-(Benzenesulfonyl)pyrrolidine-2(*S*)-carboxylate 38. L-*N*-Phenylsulfonylproline (81 mg, 0.36 mmol) was added to freshly distilled oxalyl chloride (78 μL, 0.9 mmol, 5.0 equiv) in dry PhH (2 mL) under N_2. After the mixture was stirred for 5 min, DMF (microsyringe, 1 drop) was added, resulting in a fierce gas evolution. The clear solution was maintained at room temperature for 30 min and rotary evaporated. PhH (1 mL) was added, and after rotary evaporation, an orange oil was obtained. This was dissolved in CH_2Cl_2 (2 mL) and stirred with pyridine (43 μL, 0.54 mmol) and *N*,*N*-(dimethylamino)pyridine (2 mg). Palmarumycin C_2 (**3**) (63 mg, 0.18 mmol, 1.0 equiv) in CH_2Cl_2 (0.5 mL) was added, and after standing at room temperature for 1 h, the mixture was diluted with CH_2Cl_2 (2 mL) and H_2O (2 mL). The organic phase was successively washed with saturated aqueous $CuSO_4$ (1 mL), H_2O (1 mL), and brine (1 mL) and dried ($MgSO_4$). Filtration, rotary evaporation, and chromatography (Et_2O/hexanes, 2:1) gave ester **38** (62 mg, 59%) as a white solid: mp 171−174 °C (acetone/H_2O); R_f 0.35 (Et_2O/hexanes, 2:1); $[\alpha]_D$ −276 (*c* 0.19, CH_2Cl_2); IR (KBr disk) 1770, 1700, 1447, 1268, cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.84−1.95 (m, 1H), 2.13−2.31 (m, 2H), 2.60−2.71 (m, 1H), 3.38 (dd, *J* = 7.3, 7.2 Hz, 1H), 3.61−3.65 (m, 2H), 3.65 (d, *J* = 4.3 Hz, 1H), 4.55 (d, *J* = 4.3 Hz, 1H), 6.91 (d, *J* = 7.5 Hz, 1H), 7.21 (d, *J* = 7.3 Hz, 1H), 7.41 (d, *J* = 8.2 Hz, 1H), 7.80 (d, *J* = 7.8 Hz, 1H), 7.52−7.66 (m, 7H), 7.76 (t, *J* = 8.0 Hz, 1H), 7.88 (d, *J* = 8.1 Hz, 1H), 7.96 (d, *J* = 7.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.9, 30.3, 48.8, 53.1, 53.8, 60.8, 96.4, 109.4, 110.1, 112.7, 121.3, 121.5, 125.4, 126.2, 127.5, 127.6, 127.7, 129.2 (x 2), 132.9, 134.2, 134.9, 137.7, 138.1, 146.6, 146.9, 149.2, 170.1, 190.9; MS (EI) *m*/*z* 569 $(M + H)^+$, 332, 220; *m*/*z* (EI) calcd for $C_{31}H_{24}NO_8S$ 569.1144, found 569.1134. Crystal data for **38**: $C_{31}H_{23}NO_8S{\cdot}Me_2CO$, *M* = 627.6, monoclinic, $P2_1$ (no. 4), *a* = 11.942(2) Å, *b* = 8.049(1) Å, *c* = 16.425(2) Å, β = 109.84(1)°, *V* = 1485.1(4) $Å^3$, *Z* = 2, D_c = 1.404 g cm^{-3}, μ(Cu Kα) = 1.48 mm^{-1}, *T* = 173 K, colorless platy needles; 2660 independent measured reflections, F^2 refinement, R_1 = 0.047, wR_2 = 0.116, 2388 independent observed reflections [$|F_o| > 4\sigma(|F_o|)$, $2\theta \leq 128°$], 395 parameters. The absolute structure of **38** was determined by a both an *R*-factor test [R_1^+ = 0.0466, R_1^- = 0.0475] and by use of the Flack parameter [x^+ = +0.19(8), x^- = +0.81(8)]. CCDC 182479.

4′-Nitropalmarumycin CP_1 47. $AcONO_2$ in Ac_2O[20] (0.20 mL, 3.16 M, 0.63 mmol, 2.0 equiv) was added to palmarumycin CP_1 (**1**) (100 mg, 0.32 mmol) in MeCN (3 mL) in three portions over 20 min at 0 °C. The mixture was allowed to warm to room temperature, stirred for 14 h, and diluted with Et_2O (20 mL) and saturated aqueous NH_4Cl (10 mL), and the organic layer

(21) This compound has previously been reported as a racemic modification; see ref 6c.

was dried ($MgSO_4$), filtered, and rotary evaporated. Chromatography (EtOAc/hexanes, 1:9−1:4) gave nitroarene **47** (60 mg, 53%) as a yellow solid: mp 195−197 °C dec (Et_2O); R_f 0.20 (EtOAc/hexanes, 1:9); IR (thin film) 1662, 1607, 1273 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.45 (d, J = 10.2 Hz, 1H), 6.99 (d, J = 10.5 Hz, 1H), 7.05 (d, J = 8.6 Hz, 1H), 7.18 (d, J = 7.6 Hz, 1H), 7.20 (d, J = 6.6 Hz, 1H), 7.47 (d, J = 6.6 Hz, 1H), 7.71 (app-t, J = 7.9 Hz, 1H), 7.78 (t, J = 8.3 Hz, 1H), 8.53 (d, J = 8.5 Hz, 1H), 8.58 (d, J = 8.9 Hz, 1H), 12.13 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 93.7, 108.9, 112.1, 112.9, 113.7, 118.6, 119.3, 120.3, 126.9, 128.2, 130.8, 131.9, 136.8, 137.6, 138.1, 139.8, 147.3, 152.6, 162.0, 188.2; MS (CI) m/z 379 ($M + 18^+$, 20), 362 $(M + H)^+$, 317, 49; m/z (CI) calcd for $C_{20}H_{15}N_2O_6$ 379.0930, found 379.0937. Anal. Calcd for $C_{26}H_{11}NO_6$: C, 66.49; H, 3.07, N, 3.88. Found: C, 66.52; H, 2.99; N, 3.82.

4′-Nitropalmarumycin C_2 43 and 44. Method 1. *N*-Benzylcinchoninium chloride **39** (64 mg, 0.15 mmol), H_2O (0.05 mL), and *tert*-butyl hydroperoxide in PhMe (3.16 M; 0.024 mL, 0.076 mmol) was added to enone **47** (53 mg, 0.15 mmol) in PhMe (1.6 mL), followed by aqueous NaOH (0.12 M; 0.34 mL). The mixture was stirred for 14 h at room temperature, quenched with aqueous HCl (1 M; 0.5 mL), and diluted with EtOAc (20 mL) and saturated aqueous NH_4Cl (10 mL). The organic layer was dried ($MgSO_4$), filtered, and rotary evaporated. Chromatography (EtOAc/hexanes, 1:9−1:4) gave recovered enone **47** (30 mg, 55%) followed by a mixture of epoxides **43** and **44** (20 mg, 35%) as a yellow solid as a 1:1 mixture of diastereoisomers: mp 135−137 °C and 172−175 °C dec (EtOAc/hexanes); R_f 0.20 (EtOAc/hexanes, 1:9); $[\alpha]_D$ −245 (c 0.47, $CHCl_3$); IR (thin film) 1659, 1608, 1516, 1414, cm^{-1}; ^{13}C NMR (1:1 mixture of diastereoisomers) (75 MHz, $CDCl_3$) δ 52.9, 53.0, 53.0, 96.9, 108.3, 109.0, 111.5, 112.2, 112.6, 112.7, 118.5, 118.7, 118.8, 120.6, 120.6, 126.9, 128.2, 128.2, 131.9, 132.0, 135.6, 135.6, 137.6, 137.6, 139.8, 140.0, 146.7, 147.1, 151.8, 152.2, 162.0, 195.8, 195.9; MS (CI) m/z 395 $(M + NH_4)^+$, 378 $(M + H)^+$, 52; m/z (CI) calcd for $C_{20}H_{15}N_2O_7$ 395.0879, found 395.0882. Vapor-phase recrystallization using EtOAc and pentane (1:1) over 7 days gave separated diastereoisomer **43** (8 mg, 0.022 mmol, 14%) as yellow crystals. Evaporation of the mother liquor gave a mixture of diastereoisomers **44** and **43** (4:1). Diastereoisomer **43**: ^1H NMR (300 MHz, $CDCl_3$) δ 3.76 (d, J = 3.9 Hz, 1H), 4.10 (d, J = 3.9 Hz, 1H), 6.99 (d, J = 8.6 Hz, 1H), 7.19 (d, J = 8.5 Hz, 1H), 7.39 (d, J = 8.1 Hz, 1H), 7.41 (d, J = 8.0 Hz, 1H), 7.68 (t, J = 8.1 Hz, 1H), 7.84 (dd, J = 8.8, 7.9 Hz, 1H), 8.51 (d, J = 8.6 Hz, 1H), 8.60 (d, J = 8.9 Hz, 1H), 11.35 (s, 1H); $[\alpha]_D$ −181.7 (c 0.60 $CHCl_3$). Crystal data for **43**: $C_{20}H_{11}NO_7$, M = 377.3, monoclinic, $P2_1$ (no. 4), a = 5.066(1) Å, b = 12.601(1) Å, c = 12.298(1) Å, β = 92.55(1)°, V = 784.4(1) Å^3, Z = 2, D_c = 1.598 g cm^{-3}, μ(Cu Kα) = 1.05 mm^{-1}, T = 293 K, yellow plates; 1263 independent measured reflections, F^2 refinement, R_1 = 0.039, wR_2 = 0.098, 1144 independent observed reflections [$|F_o| > 4\sigma(|F_o|)$, $2\theta \leq 128°$], 258 parameters. The absolute structure of **43** could not be determined from the X-ray analysis, but was assigned by reference to those of **38** and **3**. CCDC 182480. Diastereoisomer **44**: ^1H NMR (300 MHz, $CDCl_3$) δ 3.76 (d, J = 3.9 Hz, 1H), 4.10 (d, J = 3.9 Hz, 1H), 7.11 (d, J = 7.8 Hz, 1H), 7.18 (d, J = 8.5 Hz, 1H), 7.26 (d, J = 8.6 Hz, 1H), 7.36 (d, J = 6.7 Hz, 1H), 7.67 (t, J = 8.1 Hz, 1H), 7.75 (dd, J = 8.8, 7.8 Hz, 1H), 8.55 (d, J = 7.4 Hz, 1H), 8.59 (d, J = 7.1 Hz, 1H), 11.36 (s, 1H). **Method 2.** $AcONO_2$ in Ac_2O[20] (3.16 M; 0.023 mL, 1.2 equiv) was added to palmarumycin C_2 (**3**) (20 mg, 0.060 mmol) in CH_2Cl_2 (1 mL) at 0 °C, and the mixture was stirred for 14 h and rotary evaporated. Chromatography (EtOAc/hexanes, 1:9−1:4) gave **43** and **44** (8 mg, 35%) as a 1:1 mixture of diastereoisomers. Spectroscopic data for this sample matched those reported in method 1: $[\alpha]_D$ −240 (c 1.00, $CHCl_3$).

4′-Bromopalmarumycin CP_1 48. *N*-Bromosuccinimide (93 mg, 0.52 mmol, 1.1 equiv) in MeCN (3 mL) was added to palmarumycin CP_1 (**1**) (150 mg, 0.48 mmol) in MeCN (6 mL) in five portions over 40 min. The mixture was stirred for 14 h and evaporated to dryness. Chromatography (EtOAc/hexanes, 1:9−1:4) gave bromide (**48**) (162 mg, 86%) as a yellow solid: mp 180−182 °C dec (Et_2O); R_f 0.55 (EtOAc/hexanes 1:9); IR (thin film) 1661, 1606, 1413 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.39 (d, J = 10.2 Hz, 1H), 6.89 (d, J = 7.9 Hz, 1H), 7.00 (d, J = 10.5 Hz, 1H), 7.08 (d, J = 7.6 Hz, 1H), 7.17 (d, J = 8.3 Hz, 1H), 7.45 (d, J = 7.6 Hz, 1H), 7.62 (t, J = 8.6 Hz, 1H), 7.69 (t, J = 8.3 Hz, 1H), 7.77 (d, J = 8.3 Hz, 1H), 7.89 (d, J = 8.6 Hz, 1H), 12.15 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 93.1, 110.8, 111.1, 113.8, 114.7, 119.4, 119.9, 121.2, 121.4, 129.0, 130.1, 131.1, 132.6, 136.7, 138.4, 139.1, 146.8, 147.3, 161.9, 188.6; MS (EI) m/z 396, 394 ($M^{\bullet+}$), 287; m/z (EI) calcd for $C_{20}H_{11}$-$^{79}BrO_4$ 393.9841, found 393.9837. Anal. Calcd for $C_{20}H_{11}$-Br_1O_4: C, 60.78; H, 2.81. Found: C, 60.86; H, 2.75.

4′-Bromopalmarumycin C_2 45 and 46. Method 1. *N*-Bromosuccinimide (11 mg) in MeCN (0.5 mL) was added to palmarumycin C_2 (**3**) (17 mg, 0.051 mmol) in dry MeCN (1.0 mL) over 1 h at 0 °C. The mixture was stirred for 14 h, silica (50 mg) was added, and the mixture was rotary evaporated. Chromatography (EtOAc/hexanes, 1:9) gave a mixture of the bromides **45** and **46** (10 mg, 48%) as a white solid: mp 173−175 °C and 201−205 °C (Et_2O); R_f 0.50 (EtOAc/hexanes, 1:9); $[\alpha]_D$ −238 (c 1.00, $CHCl_3$); IR (thin film) 1657, 1608, 1264 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.71 (app-d, J = 3.9 Hz, 1H), 4.08 (d, J = 4.0 Hz, 0.5H), 4.08 (d, J = 4.0 Hz, 0.5H), 6.83 (d, J = 8.2 Hz, 0.5H), 7.02 (d, J = 7.6 Hz, 0.5H), 7.10 (d, J = 7.9 Hz, 0.5H), 7.17 (d, J = 8.3 Hz, 1H), 7.29 (d, J = 7.5 Hz, 0.5H), 7.34 (d, J = 1.9 Hz, 0.5H), 7.42 (app-d, J = 7.6 Hz, 1H), 7.57−7.70 (m, 2H), 7.82 (d, J = 7.9 Hz, 0.5H), 7.90 (app-t, J = 8.6 Hz, 1H) 11.37 (app-s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 54.2, 54.3, 97.4, 110.4, 111.3, 111.3, 111.6, 112.1, 112.4, 113.4, 114.6, 115.7, 115.9, 120.1, 120.2, 121.2, 121.4, 122.3, 122.4, 122.6, 128.8, 128.9, 130.1, 130.2, 132.2, 132.4, 133.7, 137.6, 138.8, 147.4, 147.7, 147.8, 148.2, 163.0, 197.4; MS (EI) m/z 412, 410 ($M^{+\cdot}$), 145; m/z (EI) calcd for $C_{20}H_{11}{}^{79}BrO_5$ 409.9790, found 409.9797. Anal. Calcd for $C_{20}H_{11}BrO_5$: C, 58.42; H, 2.70. Found: C, 58.36; H, 2.80. **Method 2.** *N*-Benzylcinchoninium chloride **39** (2 mg) and *tert*-butyl hydroperoxide in PhMe (3.19 M; 12 μL, 0.038 mmol) were added to bromoketone **48** (30 mg, 0.076 mmol) in PhMe (0.8 mL), followed by aqueous NaOH (0.11 M; 0.17 mL, 0.5 equiv). The mixture stirred for 14 h at room temperature, quenched by the addition of aqueous HCl (1 M; 0.5 mL). The mixture was diluted with EtOAc (20 mL) and saturated aqueous NH_4Cl (10 mL). The organic layer was dried ($MgSO_4$), filtered, and rotary evaporated. Chromatography (EtOAc/hexanes, 1:20 to 1:9) gave bromides **45** and **46** (10 mg, 32%) as a yellow solid as a 1:1 mixture of diastereoisomers along with recovered **48** (18 mg, 60%). The spectroscopic data for this sample matched those in method 1: $[\alpha]_D$ −235 (c 1.00, $CHCl_3$).

Palmarumycin C_{11} 4. Palmarumycin C_2 (**3**) (504 mg, 1.52 mmol) in dry MeOH (31 mL) under N_2 was sonicated for 2 min followed by the addition of $NaBH_4$ (57 mg, 1.52 mmol) at 0 °C. After being stirred for 10 min at this temperature, the clear colorless solution was quenched by addition of saturated aqueous NH_4Cl (10 mL) and EtOAc (10 mL), and the mixture was warmed to room temperature. HCl (1 M, 5 mL) was added to dissolve the precipitate, and EtOAc (10 mL) was added. The organic layer was separated and was again washed with 1 M HCl (10 mL) followed by drying ($MgSO_4$), filtration, and evaporation. Chromatography (preadsorbed on silica with CH_2Cl_2) (EtOAc/hexanes, 1:2) gave palmarumycin C_{11} (**4**) (386 mg, 76%) as a white solid: mp 220−225 °C ($CHCl_3$); R_f 0.25 (EtOAc/hexanes, 1:2); $[\alpha]_D$ −155 (c 1.00, CH_2Cl_2), (lit.[1b] $[\alpha]_D$ −153 (c 0.24, CH_2Cl_2)); IR (KBr disk) 3491, 1670, 1270 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.02 (br d, J = 11.5 Hz, 1H), 3.76 (dd, J = 4.4, 2.7 Hz, 1H), 3.89 (d, J = 4.3 Hz, 1H), 5.46 (dd, J = 11.4, 2.6 Hz, 1H), 6.93 (d, J = 7.3 Hz, 1H), 7.07 (dd, J = 6.8, 2.4 Hz, 1H), 7.15 (d, J = 7.3 Hz, 1H), 7.35 (app-t, J = 7.9, 7.7 Hz, 1H), 7.39 (dd, J = 7.6, 2.4 Hz, 1H), 7.43 (app-t, J = 8.3, 7.6 Hz, 1H), 7.50 (app-t, J = 8.3, 7.4 Hz, 1H), 7.51−7.63 (m, 2H), 8.26 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 52.8, 54.2, 66.2, 96.6, 109.0, 109.9, 112.8, 118.5, 118.9, 119.3, 120.9, 121.0, 127.4, 127.7, 130.5, 132.0, 134.1, 147.2, 147.3, 156.5; MS (CI) m/z 334 $(M + H)^+$, 316, 287, 114; m/z (CI) calcd for $C_{20}H_{15}O_5$ 335.0919, found 335.0932. Anal. Calcd for $C_{20}H_{14}O_5$: C, 71.85; H, 4.22. Found: C, 71.62; H, 4.27. The spectroscopic data for synthetic palmarumycin C_{11} (**4**) closely matched those reported by Krohn for the natural product.[1b] Reduction of

racemic palmarumycin C_2 (±)-**2** in the same way gave racemic palmarumycin C_{11} ((±)-**4**)[21] (74%).

Palmarumycin C_{12} 49. $PhI(OCOCF_3)_2$ (76 mg, 0.18 mmol) was added to palmarumycin C_{11} (**4**) (27 mg, 0.080 mmol) in THF and H_2O (9:1; 1.6 mL) under N_2 over a period of 20 min. The temperature of the mixture was maintained between 25 and 30 °C while the color of the reaction mixture changed to orange. Two further aliquots of the oxidant (2 × 15 mg, 2 × 0.32 mmol) were added after 2 and 3 h, and the reaction was terminated 1 h after the last addition. H_2O (1 mL) and Et_2O (3 mL) were added, and the separated organic layer washed with aqueous sodium dithionite (2 mL of 70 mg $Na_2S_2O_4$ in 4 mL H_2O) followed by brine (2 mL) and drying ($MgSO_4$). Chromatography (EtOAc/hexanes, 1:2) gave palmarumycin C_{12} (**49**) (9 mg, 30%) as well as unreacted palmarumycin C_{11} (**4**) (3 mg, 11%). Palmarumycin C_{12} (**49**): mp 199−201 °C (CH_2Cl_2); R_f 0.34 (Et_2O/hexanes 2:1); $[\alpha]_D$ −165 (*c* 0.26, CH_2Cl_2); IR (KBr disk) 3484, 3447, 1585, 1266, cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.04 (d, J = 11.5 Hz, 1H), 3.74 (dd, J = 4.3, 4.2 Hz, 1H), 3.85 (d, J = 4.4 Hz, 1H), 5.38 (dd, J = 11.5, 2.9 Hz, 1H), 6.89 (s, 1H), 6.98 (d, J = 8.9 Hz, 1H), 7.03 (d, J = 8.9 Hz, 1H), 7.05 (d, J = 7.3 Hz, 1H), 7.23 (d, J = 7.5 Hz, 1H), 7.50 (dd, J = 8.3, 7.6 Hz, 1H), 7.52 (d, J = 8.2 Hz, 1H), 7.58 (d, J = 8.3 Hz, 1H), 7.52−7.64 (dd, J = 8.2, 6.9 Hz, 1H), 7.80 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 52.7, 54.2, 66.1, 99.0, 110.2, 110.9, 113.1, 115.2, 118.9, 120.1, 120.9, 121.5, 122.4, 127.6, 127.7, 134.1, 145.7, 146.9, 149.8, 150.0; MS (EI) *m*/*z* 350 ($M^{+\cdot}$), 332, 316, 160; *m*/*z* (EI) calcd for $C_{20}H_{14}O_6$ 350.0790, found 350.0775. Spectroscopic data for synthetic palmarumycin C_{12} (**49**) were in excellent agreement for those published for the natural product **49**.[1b]

Palmarumycin C_3 50. $PhI(OCOCF_3)_2$ (322 mg, 0.75 mmol) in THF and water (9:1; 2.8 mL) was added to palmarumycin C_{11} (**4**) (125 mg, 0.37 mmol) in THF and H_2O (9:1; 5.5 mL) over 1 min at 40 °C, and stirring was continued at the same temperature for 4 h. The mixture was diluted with EtOAc (25 mL) and saturated aqueous $NaHCO_3$ (10 mL). The organic layer was separated, dried ($MgSO_4$), filtered, and rotary evaporated, and the residue was dissolved in MeCN (15 mL). MnO_2 (619 mg) was added followed by a second portion (311 mg) after a 30 min delay. Stirring was continued for a further 1 h when the mixture was filtered through Celite and washed with MeCN (2 × 5 mL). Ascorbic acid (153 mg) was added to the mixture with stirring until the red solution changed to pale yellow. Rotary evaporation and chromatography (EtOAc/hexanes, 1:4) gave palmarumycin C_3 (**50**) (40 mg, 31% over three steps) as a yellow solid: mp 210−215 °C ($CHCl_3$/hexanes); R_f 0.51 (Et_2O/hexanes, 2:1); $[\alpha]_D$ −246 (*c* 0.62, $CHCl_3$) (lit.[1b] $[\alpha]_D$ −300 (*c* 1.0, CH_2Cl_2)); IR (KBr disk) 3479, 1655, 1611, 1266, cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.66 (d, J = 4.0 Hz, 1H), 4.06 (d, J = 4.0 Hz, 1H), 7.06 (d, J = 7.1 Hz, 1H), 7.14 (d, J = 9.2 Hz, 1H), 7.28 (d, J = 7.0 Hz, 1H), 7.32 (d, J = 9.2 Hz, 1H), 7.38 (s, 1H), 7.52 (app-t, J = 8.3, 7.6 Hz, 1H), 7.57 (app-t, J = 8.3, 7.6 Hz, 1H), 7.64 (d, J = 8.0 Hz, 1H), 7.70 (d, J = 8.1 Hz, 1H), 11.50 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 52.7, 53.2, 99.0, 110.4, 111.3 (×2), 113.1, 116.1, 121.8, 122.5, 122.9, 127.7, 128.0, 129.8, 134.2, 145.1, 146.6, 149.3, 157.2, 195.7; MS (EI) *m*/*z* 348 ($M^{\bullet+}$), 303, 215; *m*/*z* (EI) calcd for $C_{20}H_{12}O_6$ 348.0633, found 348.0631. The spectroscopic data for synthetic palmarumycin C_3 (**50**) matched that reported for the natural product.[1b] Reaction of racemic palmarumycin C_{11} ((±)-**4**) in the same way gave racemic palmarumycin C_3 ((±)-**50**) (30%).

Palmarumycin C_3 Di(2-methoxyacetate) 51. Pyridine (189 μL) and 2-methoxyacetyl chloride (117 uL, 1.28 mmol) were added to palmarumycin C_3 (**50**) (90 mg, 0.26 mmol) and 4-*N*,*N*-(dimethylamino)pyridine (1 mg) in CH_2Cl_2 (5 mL) at −78 °C under N_2, and the mixture was stirred for 3 h. The mixture was quenched with of 1 M HCl (5 mL) and CH_2Cl_2 (10 mL), and the organic layer was separated, dried ($MgSO_4$), filtered, and rotary evaporated. Excess 2-methoxyacetyl chloride was removed by azeotrope with PhMe (2 × 5 mL). The residue was triturated with Et_2O (1.5 mL) at reflux and filtered to give diester **51** (117 mg, 92%) as a white solid: mp 170−173 °C (Et_2O); R_f 0.10 (EtOAc/hexanes, 1:2); $[\alpha]_D$ −166 (*c* 0.57, $CHCl_3$); IR (thin film) 1785, 1702, 1113 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.08 (s, 3H), 3.60 (s, 3H), 3.63 (d, J = 17.0 Hz, 1H), 3.63 (d, J = 4.0 Hz, 1H), 3.81 (d, J = 17.0 Hz, 1H), 3.99 (d, J = 4.0 Hz, 1H), 4.41 (s, 2H), 7.00 (d, J = 7.6 Hz, 1H), 7.11 (d, J = 7.6 Hz, 1H), 7.36 (d, J = 8.9 Hz, 1H), 7.40−7.61 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 53.2, 54.1, 59.2, 59.7, 69.0, 69.6, 95.7, 109.6, 109.8, 112.0, 121.5, 121.5, 122.9, 127.3, 127.8, 127.8, 129.3, 131.4, 134.2, 145.9, 145.9, 147.0, 147.1, 168.2, 168.9, 189.6; MS (CI) *m*/*z* 510, $(M + NH_4)^+$. Anal. Calcd for $C_{26}H_{20}O_{10}$: C, 63.42; H, 4.09. Found: C, 63.51; H, 4.08. Protection of racemic palmarumycin C_3 ((±)-**50**) in the same way gave racemic diester ((±)-**51**) (96%).

4′-Hydroxypalmarumycin C_3 53. Dry CH_2Cl_2 (3.5 mL) and AcOH (3.5 mL) were added to diester **51** (117 mg, 0.24 mmol) and $Pb(OAc)_4$ (212 mg, 0.48 mmol) under N_2. The mixture was heated to 40 °C for 40 h and rotary evaporated, and AcOH was removed by azeotrope with PhMe (2 × 5 mL). The residue was dissolved in CH_2Cl_2 (20 mL) and saturated aqueous NH_4Cl (10 mL), and the organic layer was separated, dried ($MgSO_4$), filtered, and rotary evaporated. LiOH (100 mg, 2.38 mmol) in degassed H_2O (2.34 mL) was added to the crude product **52** in dry THF (11.7 mL) at 0 °C, and the mixture was stirred for 1.5 h. The reaction was quenched with saturated aqueous NH_4Cl (10 mL) and EtOAc (20 mL), and the organic layer was separated. The aqueous layer was re-extracted with EtOAc (10 mL), and the combined organic layers were dried ($MgSO_4$), filtered, and rotary evaporated. Chromatography (EtOAc/hexanes, 1:2) gave triol **53** (32 mg, 37% over two steps) as a yellow solid: mp 200−205 °C dec (Et_2O); R_f 0.20 (EtOAc/hexanes, 1:2); $[\alpha]_D$ −230 (*c* 0.50, $CHCl_3$); IR (thin film) 3472, 1653, 1613 cm^{-1}; ^1H NMR (300 MHz, acetone-d_6) δ 3.63 (app-d, J = 4.0 Hz, 1H), 3.64 (d, J = 4.0 Hz, 0.5H), 4.03 (app-d, J = 4.0 Hz, 1H), 6.72−7.07 (m, 4H), 7.17−7.26 (m, 1H), 7.34−7.45 (m, 1H), 7.74−7.80 (m, 1H), 7.92 (app-d, J = 8.3 Hz, 0.5H), 8.85 (s, 0.5H), 8.92 (s, 0.5H), 11.38 (s, 0.5H), 11.40 (s, 0.5H); ^{13}C NMR (75 MHz, acetone-d_6) δ 55.3, 54.5, 54.7, 98.9, 110.4, 110.6, 111.2, 111.5, 112.1, 112.9, 115.2, 117.6, 118.0, 119.4, 122.9, 123.0, 126.4, 127.6, 127.7, 130.9, 140.7, 147.7, 149.6, 150.9, 157.9, 198.1; MS (CI) *m*/*z* 365 $(M + H)^+$; *m*/*z* (CI) calcd for $C_{20}H_{13}O_7$ 365.0661, found 365.0665. Anal. Calcd for $C_{20}H_{12}O_7$: C, 65.94; H, 3.32. Found: C, 66.00; H, 3.20. Reaction of racemic diester (±)-**51** in the same way gave racemic triol (±)-**53** (35%).

Preussomerin G 11 and Epipreussomerin G 54. $Pb(OAc)_4$ (12.2 mg, 0.028 mmol) in dry CH_2Cl_2 (1 mL) was added to triol **53** (10.0 mg, 0.028 mmol) in dry CH_2Cl_2 (8 mL) at −78 °C under N_2 and the mixture stirred for 10 min. The mixture was quenched with saturated aqueous NH_4Cl (10 mL) and CH_2Cl_2 (20 mL), and the organic layer was separated. The aqueous layer was re-extracted with CH_2Cl_2 (10 mL), and the combined organic layers were dried ($MgSO_4$), filtered, and rotary evaporated. Chromatography (EtOAc/hexanes, 1:2) gave preussomerin G (**11**) and epipreussomerin G (**54**) (5.5 mg, 0.015 mmol, 55%) as a yellow solid. Further chromatography (EtOAc/hexanes, 1:4) gave (−)-preussomerin G (**11**) (2.5 mg, 25%) followed by epipreussomerin G (**54**) (2.5 mg, 25%) both as yellow solids. **Preussomerin G (11).** An analytical sample was prepared by trituration of this sample with hot Et_2O and pentane (1:5; 1 mL): mp 210−213 °C (Et_2O/pentane) (lit.[3e] mp 222−225 °C dec); R_f 0.20 (EtOAc/hexanes, 1:4); $[\alpha]_D$ −533 (*c* 0.05, CH_2Cl_2; IR (thin film) 3382, 3352, 1678, 1661, 1467 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.86 (d, J = 4.0 Hz, 1H), 4.25 (d, J = 4.0 Hz, 1H), 6.59 (d, J = 10.0 Hz, 1H), 6.96 (d, J = 9.0 Hz, 1H), 7.04−7.08 (m, 2H), 7.24 (d, J = 10 Hz, 1H), 7.43 (app-t, J = 8.0 Hz, 1H), 7.65 (d, J = 7.6 Hz, 1H), 10.22 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 52.1, 53.6, 89.9, 93.8, 109.7, 115.1, 120.5, 120.6, 120.8, 121.2, 126.7, 129.8, 131.1, 133.5, 140.7, 143.3, 148.6, 156.0, 183.7, 195.4; UV λ_{max} ($CHCl_3$) 373 (ϵ 3.3 × 10^4), 272 (6.0 × 10^3), 241 (9.0 × 10^3) nm; MS (CI) *m*/*z* 363 $(M + H)^+$, 191, 174, 52; *m*/*z* (CI) calcd for $C_{20}H_{11}O_7$ 363.0505, found 363.0516. Chiral HPLC (method D): t_R = 9 min and t_R = 11 min ((−)-preussomerin G (**11**); (>95% ee)). The spectroscopic data for synthetic preussomerin G (**11**) matched that reported for the natural product[3e] and the sample was identical with authentic samples of preussomerin G (**11**) provided by Profes-

sor Karsten Krohn and Dr. Sheo B. Singh (Merck and Co. Inc.). Oxidation of racemic triol (±)-**53** in the same way gave racemic preussomerin G (±)-**11** (20%). **Epipreussomerin G (54).** An analytical sample was prepared by trituration of this sample with hot Et_2O (1 mL): mp 173−174 °C (Et_2O); R_f 0.15 (EtOAc/hexanes, 1:4); $[\alpha]_D = +285$ (*c* 0.05, CH_2Cl_2); IR (thin film) 3644, 1680, 1650, 1473, cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.80 (d, $J = 3.0$ Hz, 1H), 4.12 (d, $J = 3.0$ Hz, 1H), 6.60 (d, $J = 10.0$ Hz, 1H), 6.95 (d, $J = 9.0$ Hz, 1H), 7.04 (d, $J = 9.0$ Hz, 1H), 7.14 (d, $J = 10.0$ Hz, 1H), 7.18 (d, $J = 8.5$ Hz, 1H), 7.43 (app-d, $J = 8.0$ Hz, 1H), 7.62 (d, $J = 7.5$ Hz, 1H), 11.02 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 53.0, 59.0, 89.8, 89.8, 112.0, 118.3, 120.3, 120.5, 121.2, 121.3, 127.3, 129.2, 131.0, 133.6, 140.0, 142.6, 148.4, 157.8, 183.5, 191.9; MS (CI) *m*/*z* 363 $(M + H)^+$, 190, 174, 161, 52; *m*/*z* (CI) calcd for $C_{20}H_{11}O_7$ 363.0505, found 363.0509.

Acknowledgment. We thank GlaxoSmithKline for most generous support of our research, for the Glaxo endowment (to A.G.M.B.), and for the HPLC analysis of synthetic preussomerin G (**11**) and synthetic racemic preussomerin G (±)-**11** kindly carried out by Gregory D. Jonas; the Wolfson Foundation for establishing the Wolfson Centre for Organic Chemistry in Medicinal Science at Imperial College; Professor Karsten Krohn for authentic samples of palmarumycins CP_1 (**1**), CP_2 (**13**), C_{12} (**49**), and preussomerin G (**11**); and Dr. Sheo B. Singh and Merck and Co., Inc., for authentic samples of palmarumycin C_2 (deoxypreussomerin B (**3**)) and preussomerin G (**11**).

Supporting Information Available: X-ray crystallographic data for **3**, **22**, **37**, **38**, and **43**; ^1H and ^{13}C NMR spectra for palmarumycin CP_1 (**1**), palmarumycin C_2 (**3**), palmarumycin C_{11}(**4**), palmarumycin CP_2 (**13**), (−)-preussomerin G (**11**), CJ,12−371 (**33**), (±)-CJ,12−372 (**34**), palmarumycin C_{12} (**49**), and palmarumycin C_3 (**50**); and ^1H NMR spectra for phenol **23**, quinone **30**, ester **38**, nitro arenes **43**/**44**, and epipreussomerin G (**54**). This material is available free of charge via the Internet at http://pubs.acs.org.

JO0110247