# Transformations of Quinic Acid. Asymmetric Synthesis and Absolute Configuration of Mycosporin I and Mycosporin-gly

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D-(−)-Quinic acid (**1**) was converted to the fungal metabolites mycosporin I (**2**) and mycosporin-gly (**13**) via the iminophosphorane **64**. The latter was prepared in 10 steps from **1** using oxidative bromination of quinide **33** to furnish **41**. Reduction of the γ-lactone, followed by protection of the 1,2-diol, was accompanied by migration of the benzoyl group to yield **43**. The latter was oxidized to **47** which underwent displacement by sulfinate to give **59**. O-Methylation, followed by reduction of the benzoate, afforded **61**. Oxidation of **61** produced **62** which was converted to β-azido enone **63**. Treatment of **63** with triphenylphosphine gave crystalline **64**. An aza-Wittig reaction of **64** with glyoxylate and reduction of the resultant imine yielded **68** which, after deprotection, afforded **13**. Analogous coupling of **64** with diethyl ketomalonate and subsequent reduction of the ester groups led to **2**. Mycosporin I and mycosporin-gly are shown by this sequence to possess *S* absolute configuration.

(1*R*,3*R*,4*R*,5*R*)-1,3,4,5-Tetrahydroxycyclohexane-1-carboxylic acid, (D-(−)-quinic acid, **1**), occupies a prominent position among primary metabolites originating from D-glucose. Its location on a pathway which intersects the shikimate route at 5-dehydroquinate[1] lends **1** particular significance in the context of metabolic processes leading to aromatic systems. However, while the importance of **1** as a ubiquitous natural product is widely recognized,[2] its role as a biogenetic precursor to more highly elaborated secondary metabolites is less well defined,[3] and a firm connection between quinic acid and cyclitol derivatives such as the mycosporins (**2**–**12**) has yet to be made. Nevertheless, the abundance of **1** in the chiral pool, along with the fact that it is available from nature in a state of very high optical purity, has made it an attractive starting material for asymmetric synthesis.[4] In fact, several applications of quinic acid in total synthesis have been reported[5] and extensive investigations of its chemical properties have been described.[6] We recognized an opportunity to extend these studies in devising a synthetic entry to the mycosporins, the nucleus of which bears a close structural resemblance to **1**. At the outset of this work no information on the absolute configuration of the mycosporins was available, and it was hoped that a synthesis from **1** would settle this important issue.

Mycosporins, originally named P 310s, were first observed by Leach in the mycelia of species of *Fungi imperfecti* which responded to irradiation by near-UV light.[7] Subsequently, these substances were shown to be widespread in fungi, occurring exclusively in the sexual spores of sporulating mycelia.[8] Numerous attempts to define a role for mycosporins in light-induced reproductive processes of various fungi have led to conflicting results. Some groups have claimed sporogenic activity[7cd,9] while others have failed to confirm this property.[10] The conclusion reached in a careful study by Tan and Epton,[11] and supported in later work by others,[12] is that mycosporins are no more than photoprotective devices, serving to filter solar radiation in the 290–320 nm region which is fungicidal during the reproductive phase. However, a recent study by Dehorter[13] has shown that addition of mycosporins to dark-grown cultures of *Nectria galligena* induces sporulation and a concomitant decrease in sterol content, strongly suggesting that mycosporins also play a hormonal role in sexual morphogenesis in this organism. Regardless of whether mycosporins are chemical signals which initiate fungal reproduction[14] or are simply sunscreens, their chemistry has been given only cursory examination.

The structures of the first mycosporins were deduced in 1976. Mycosporins I and III, isolated from the basidiomycete *Stereum hirsutum*, were shown to possess structures **2** and **3**, respectively,[15,16] and shortly thereafter the structure of mycosporin II was assigned as **4**.[17] Subsequently, the hydrolyzed form of **4**, mycosporin glutamicol (**5**),[18,19] was found to be widespread in fungi,

[⊗] Abstract published in *Advance ACS Abstracts,* May 1, 1995.

(1) Haslam, E. *Shikimic Acid. Metabolism and Metabolites*; Wiley: New York, 1974; p 3.

(2) Bohm, B. A. *Chem. Rev.* **1965**, *65*, 435.

(3) Boudet, A. *Compt. Rend.* **1969**, *269D*, 1966.

(4) Hanessian, S. *Total Synthesis of Natural Products: The 'Chiron' Approach*; Pergamon: Oxford, UK, 1983; p 206.

(5) For a recent example, see White, J. D.; Toske, S. G.; Yakura, T. *Synlett* **1994**, 591.

(6) Haslam, E. *Shikimic Acid. Metabolism and Metabolites*; Wiley: New York, 1974; p 64.

(7) (a) Leach, C. M. *Phytopathology* **1964**, *54*, 1434, 1435. (b) Leach, C. M.; Trione, E. J. *Plant. Physiol.* **1965**, *40*, 808. (c) Leach, C. M. *Can. J. Bot.* **1965**, *43*, 185. (d) Leach, C. M. *Mycologia* **1965**, *57*, 291.

(8) Arpin, N.; Bouillant, M. L. The Fungal Spore: Morphogenetics Controls, Proceedings of 111th International Fungal Spore Symposium, Gwatt, 1980, Turian, G.; Hohl, H. R., Eds.; Academic Press, London, 1981; p 435.

(9) (a) Trione, E. J.; Leach, C. M.; Mutch, J. T. *Nature* **1966**, *212*, 163. (b) Trione, E. J.; Leach, C. M. *Phytopathology* **1969**, *59*, 1077. (c) Dehorter, B. *Can. J. Bot.* **1976**, *54*, 600. (d) Dehorter, B.; Bernillon, J. *Can. J. Bot.* **1983**, *61*, 1435.

(10) (a) Vargas, J. M., Jr.; Wilcoxson, R. D. *Phytopathology* **1969**, *59*, 1706. (b) Moyer, B. G.; Leath, K. T. *Can. J. Bot.* **1976**, *54*, 1839. (c) Van den Ende, G.; Cornelis, J. J. *Neth. J. Plant. Pathol.* **1970**, *76*, 183.

(11) (a) Tan, K. K.; Epton, H. A. S. *Trans. Br. Mycol. Soc.* **1973**, *61*, 145. (b) Tan, K. K.; Epton, H. A. S. *Trans. Br. Mycol. Soc.* **1974**, *63*, 157.

(12) (a) Brook, P. J. *New Zealand J. Bot.* **1981**, *19*, 299. (b) Young, H.; Patterson, V. J. *Phytochemistry* **1982**, *21*, 1075.

(13) Dehorter, B.; Brocquet, M. F.; Lacoste, L.; Alais, J.; Lablache-Combier, A.; Maquestiau, A.; Van Harverbeke, Y.; Flammang, R.; Mispreuve, H. *Phytochemistry* **1980**, *19*, 2311.

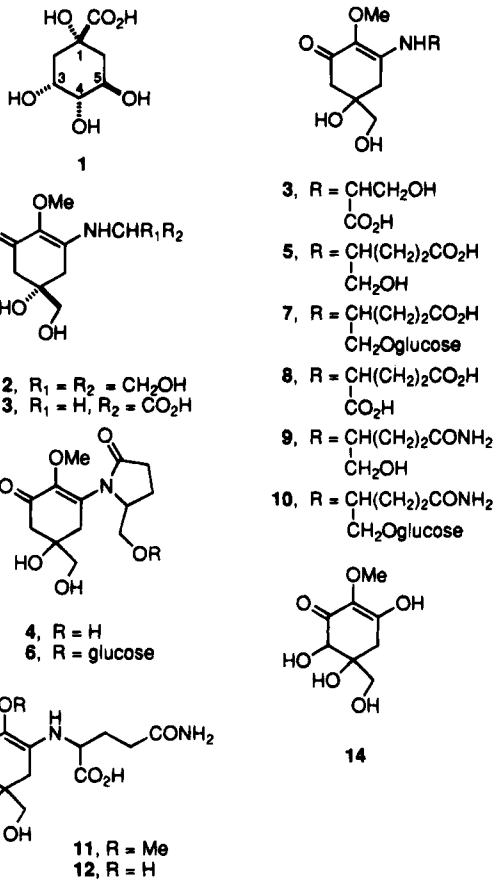
(14) Pittet, J.-L.; Bourguignon, B.; Arpin, N. *Physiol. Plant.* **1983**, *57*, 565.

(15) Favre-Bonvin, J.; Arpin, N.; Brevard, C. *Can. J. Chem.* **1976**, *54*, 1105.

(16) Arpin, N.; Favre-Bonvin, J.; Thivend, S. C. R. *Acad. Sci. Paris D* **1976**, 997.

0022-3263/95/1960-3600$09.00/0 

and glucosides **6** and **7** of **4** and **5**, respectively, were also isolated.[18,20] Other members of this family now include mycosporin-glu (**8**),[12b] mycosporin glutaminol (**9**) and its glucoside **10**,[21] mycosporin glutamine (**11**),[22] and the desmethyl derivative of **11**, normycosporin-gln (**12**).[23] The last is believed to be a biogenetic precursor of other mycosporins; methylation followed by reduction of the amino acid side chain and glucosylation leads to a stable glucoside which can be stored within the spore.[24]




Mycosporin-gly (**13**) was the first member of the family to be isolated from a nonfungal source. Its presence in the coral *Palythoa tuberculosa* along with palytoxin was first reported by Hirata.[25] A large number of imine derivatives of mycosporins ("iminomycosporins") have since been extracted from marine plants and animals,[26] along with the interesting substance gadusol (**14**).[27]

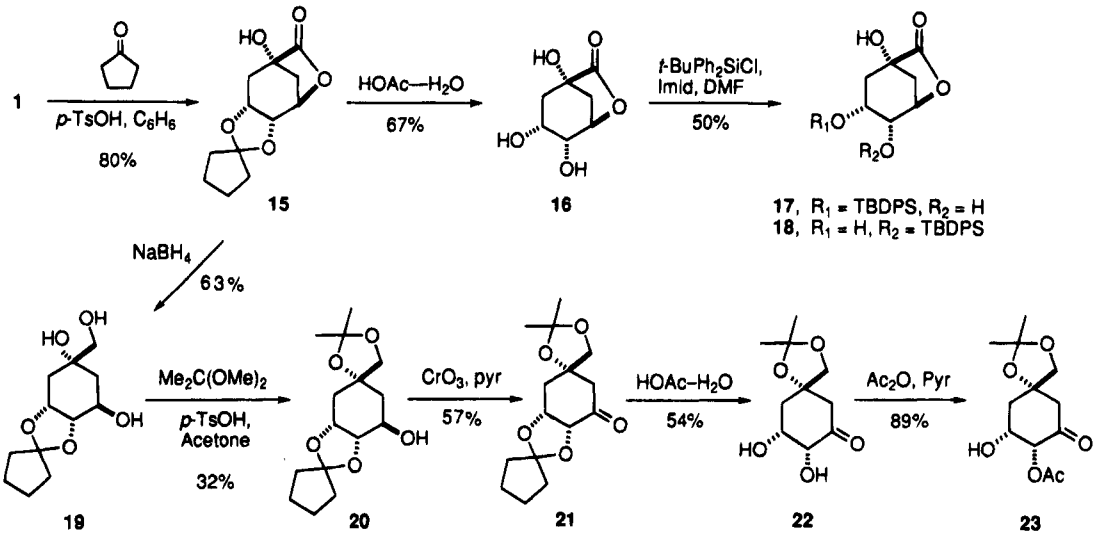
Aside from their instability toward hydrolysis, which leads to a meso cyclohexane-1,3-dione structure, the most noteworthy feature of the chemistry of mycosporins is their facile transformation to a benzenoid system.[25] The accompanying erasure of the stereochemical signature of the mycosporins probably explains why their absolute configuration has remained unknown. We now describe details of a study which began as an inquiry into the chemistry of quinic acid and which culminated in asymmetric syntheses of mycosporin I (**2**) and mycosporin-gly (**13**).[28] These syntheses establish that **2** and **12** possess *S* configuration.

Two operating principles guided our plans. First, potential meso intermediates were to be avoided if the chirality of **1** was to be preserved en route to the mycosporins. This required that a distinction between the functionality at C3 and C5 be carefully maintained throughout any sequence of transformations. It was also recognized that progressive elevation of the oxidation level of **1** toward that of the mycosporins increases the propensity for aromatization, and it was clearly essential to avoid sensitive intermediates or harsh reagents which could accelerate this unwanted outcome.[29] Initial attempts to separate the reactivity of functional groups present in **1** focused on quinide (**16**), easily prepared by hydrolysis of cyclopentylidene ketal **15** (Scheme 1). The latter was obtained by a procedure analogous to that used to acquire the corresponding cyclohexylidene derivative.[30,31] Unfortunately, little selectivity was observed in reactions of the axial and equatorial hydroxyl groups of **16**. For example, with *tert*-butyldiphenylsilyl chloride, **16** gave a 3:2 mixture of **17** and **18**, respectively. This unsatisfactory outcome forced us to adopt a different tactic which hinged on selective ketalization of triol **19**, obtained by reduction of **15** with sodium borohydride.[30] Treatment of **19** with 2,2-dimethoxypropane under carefully controlled conditions gave **20** accompanied by the diacetonide which was formed by exchange of the cyclopentylidene ketal. Oxidation of **20** afforded ketone **21**, from which the cyclopentylidene ketal could be removed by selective hydrolysis. The C8 hydroxyl group of dihydroxy ketone **22** could be selectively acetylated, but attempts to further transform acetate **23** without aromatization were unsuccessful.

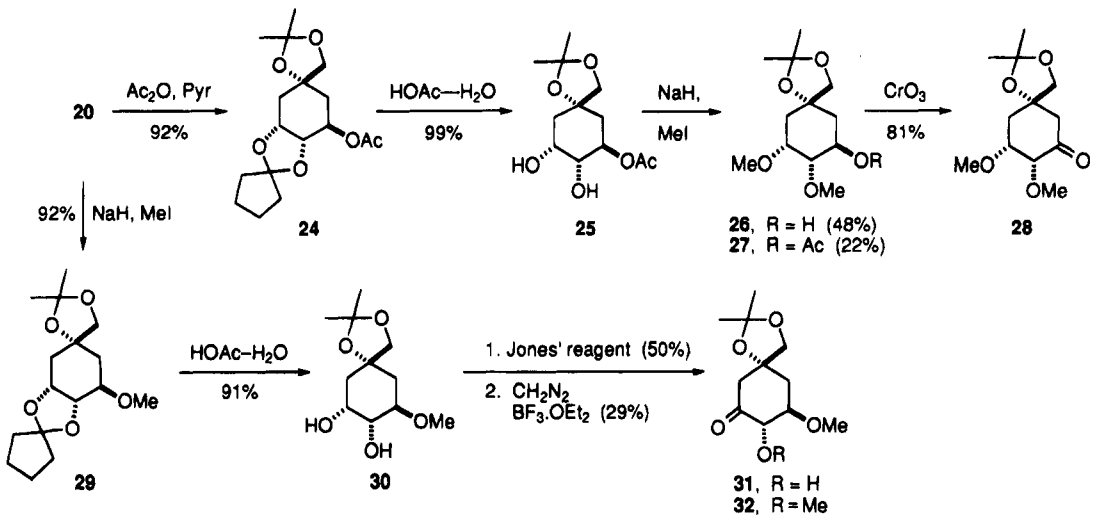
In an alternative sequence (Scheme 2) departing from **20**, the secondary alcohol was acetylated and the cyclopentylidene ketal **24** was hydrolyzed to give diol **25** in high yield. However, methylation of **25** under basic conditions resulted in concomitant cleavage of the acetate and led to a mixture of **26** and **27**, whereas exposure of **25** to methyl triflate destroyed the acetonide. Oxidation

(17) Arpin, N.; Favre-Bonvin, J.; Thivend, S. *Tetrahedron Lett.* **1977**, *10*, 819.
(18) Favre-Bonvin, J.; Bouillant, M.-L.; Lunel, M. C.; Bernillon, J. L.; Pittet, J.-L.; Arpin, N. *Planta Med.* **1980**, *39*, 196.
(19) Fayret, J.; Bernillon, J.; Bouillant, M.-L.; Favre-Bonvin, J.; Arpin, N. *Phytochemistry* **1981**, *20*, 2709.
(20) Bouillant, M.-L.; Pittet, J.-L.; Bernillon, J.; Favre-Bonvin, J.; Arpin, N. *Phytochemistry* **1981**, *20*, 2705.
(21) Pittet, J.-L.; Bouillant, M.-L.; Bernillon, J.; Arpin, N.; Favre-Bonvin, J. *Tetrahedron Lett.* **1983**, *24*, 65.
(22) Bernillon, J.; Bouillant, M.-L.; Pittet, J.-L.; Favre-Bonvin, J.; Arpin, N. *Phytochemistry* **1984**, *23*, 1083.
(23) Lunel, M.-C.; Arpin, N.; Favre-Bonvin, J. *Tetrahedron Lett.* **1980**, *21*, 4715.
(24) Pittet, J. L.; Letoublon, R.; Frot-Coutaz, J.; Arpin, N. *Planta* **1983**, *159*, 159.
(25) Ito, S.; Hirata, Y. *Tetrahedron Lett.* **1977**, 2429.
(26) (a) Takano, S.; Uemura, D.; Hirata, Y. *Tetrahedron Lett.* **1978**, 2299. (b) Furusaki, A.; Matsumoto, T.; Tsujino, I.; Sekikawa, I. *Bull. Chem. Soc. Jpn.* **1980**, *53*, 319. (c) Takano, S.; Uemura, D.; Hirata, Y. *Tetrahedron Lett.* **1978**, 4909. (d) Hirata, Y.; Uemura, D.; Ueda, K.; Takano S. *Pure Appl. Chem.* **1979**, *51*, 1875. (e) Uemura, D.; Katayama, C.; Wada, A.; Hirata, Y. *Chem. Lett.* **1980**, 755. (f) Tsujino, I.; Yabe, K.; Sekikawa, I. *Botanica Marina* **1980**, *23*, 65. (g) Tsujino, I.; Yabe, K.; Sekikawa, I.; Hamanaka, N. *Tetrahedron Lett.* **1978**, 1401. (h) Takano, S.; Nakanishi, A.; Uemura, D.; Hirata, Y. *Chem. Lett.* **1979**, 419. (i) Chioccara, F.; Misuraca, G.; Novellino, E.; Prota, G. *Tetrahedron Lett.* **1979**, 3181. (j) Kobayashi, J.; Nakamura, H.; Hirata, Y. *Tetrahedron Lett.* **1981**, *22*, 3001. (k) Nakamura, H.; Kobayashi, J.; Hirata, Y. *Chem. Lett.* **1981**, 1413. (l) Nakamura, H.; Kobayashi, J.; Hirata, Y. J. *Chromatography* **1982**, *250*, 113.
(27) (a) Chioccara, F.; Gala, A. D.; DeRosa, M.; Novellino, E.; Prota, G. *Bull. Soc. Chim. Belg.* **1980**, *89*, 1101. (b) Grant, P. T.; Plack, P. A.; Thomson, R. H. *Tetrahedron Lett.* **1980**, *21*, 4043. (c) Plack, P. A.; Fraser, N. W.; Grant, P. T.; Middleton, C.; Mitchell, A.I.; Thomson, R. H. *Biochem. J.* **1981**, *199*, 741.
(28) Preliminary communication: White, J. D.; Cammack, J. H.; Sakuma, K. *J. Am. Chem. Soc.* **1989**, *111*, 8970.
(29) An earlier route to the mycosporins which foundered on this obstacle is described in Ruppert, J. F. Ph.D. Thesis, Oregon State University, 1977.
(30) Mercier, D.; Leboul, J.; Cleophax, J.; Gero, S. D. *Carbohydr. Res.* **1971**, *20*, 299.
(31) De Pooter, H.; De Brucker, J.; Van Sumere, C. F. *Bull. Soc. Chim. Belg.* **1975**, *84*, 835.

**Scheme 1**



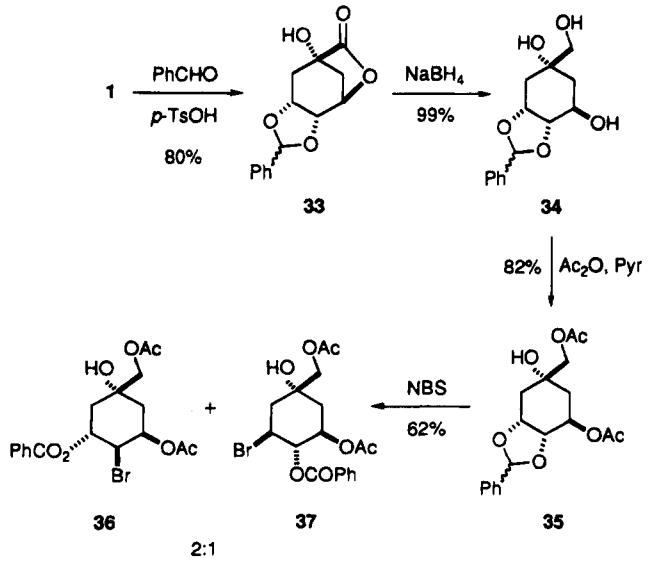

**Scheme 2**




of **26** gave **28**, but this ketone was too sensitive toward further transformations which would advance it in the direction of the mycosporins. A variation of this sequence in which **20** was methylated to yield **29** initially appeared more promising since the latter could be cleanly hydrolyzed to diol **30**. Oxidation of **30** gave an unstable substance identified as **31** after conversion to dimethoxyketone **32**, but attempts to continue the oxidation process from **31** to the level of an α-diketone resulted only in aromatization.

Our failure to find a means for reaching the oxidation state of the mycosporins from **16**, together with difficulties associated with the purification of **20** formed in the ketalization of **19**, prompted a search for a new route from quinic acid which would avoid the need for differential protection of pairs of 1,2-diols. A convenient solution to this problem, shown in Scheme 3, was found in the treatment of **1** with benzaldehyde which afforded the benzylidene quinide **33** as a mixture of stereoisomers at the acetal carbon. As with **15**, sodium borohydride efficiently reduced lactone **33** to triol **34**. The latter was acetylated to give diacetate **35** accompanied by a trace of the triacetate. Application to **35** of a protocol developed by Hanessian,[32] in which *O*-benzylidene acetals of

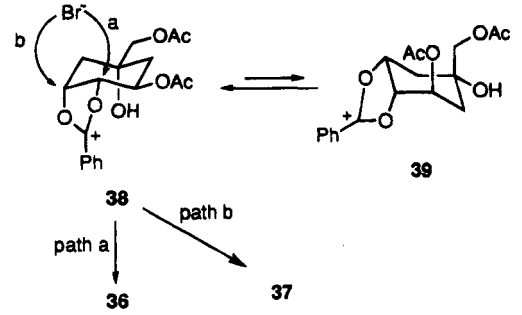
**Scheme 3**



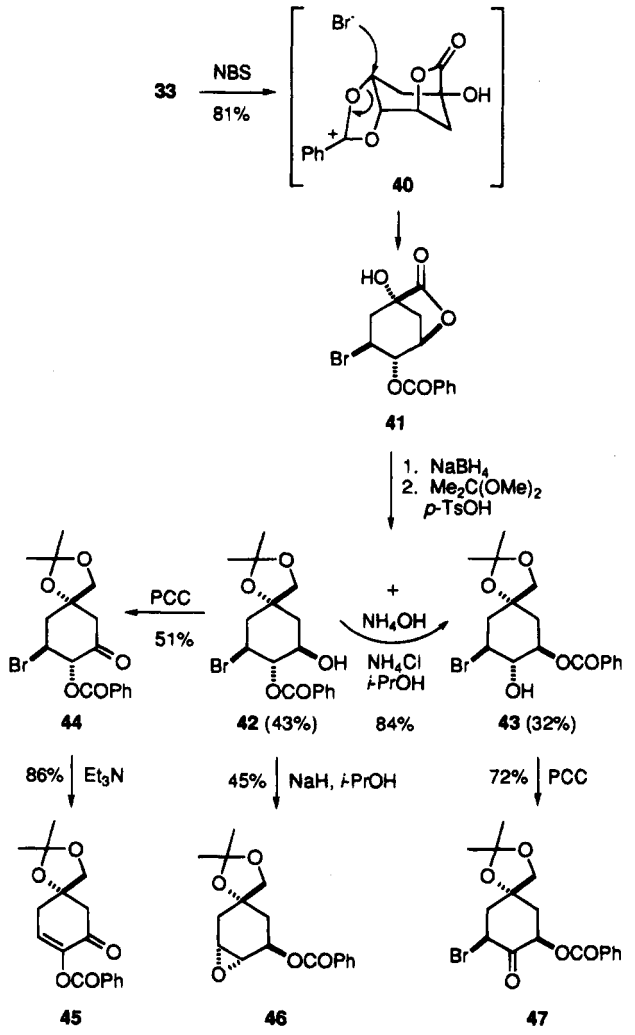

sugars are reacted with *N*-bromosuccinimide to yield bromo benzoates, led to a 2:1 mixture of **36** and **37**, respectively. The structures of **36** and **37** could be assigned unequivocably from their $^1$H NMR spectra. The poor regioselectivity observed in this reaction is probably

(32) Hanessian, S.; Plessas, N. R. *J. Org. Chem.* **1969**, *34*, 1035, 1045, 1053.

**Scheme 4**

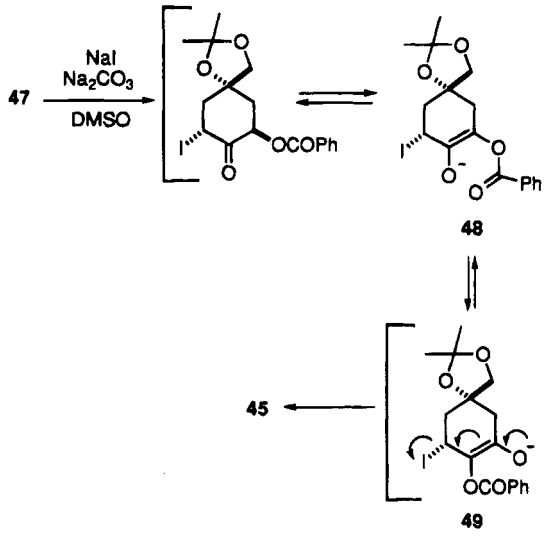



**Scheme 5**




due to alternate modes of attack by bromide on conformer **38** (paths a and b, Scheme 4), ring inversion to give **39** being disfavored due to 1,3-diaxial interactions in this conformer. Since **33** is constrained to a single conformation by the bridging $\gamma$-lactone (and therefore would be expected to yield a single regioisomer in opening of the benzylidene ring), this acetal was treated with *N*-bromosuccinimide to give exclusively the product **41** from axial attack on the intermediate cation **40** (Scheme 5). Exposure of **41** to sodium borohydride, followed by acetonide formation, resulted in a mixture of **42** and **43**, the latter presumably arising from intramolecular transesterification after reduction to yield the sterically less hindered benzoate. The major alcohol **42** was oxidized to **44**, but attempts to displace the bromo substituent in this ketone with amines such as glycine methyl ester were unsuccessful. Instead, elimination to the $\alpha,\beta$-unsaturated ketone **45** was the predominant pathway. Further treatment of this material with basic reagents in the hope of removing the benzoate or effecting conjugate addition led only to aromatized products.

**Scheme 6**




In the belief that **43** would afford a more tractable substrate for reaching the oxidation level of the mycosporins, several attempts were made to promote the transesterification of **42**. Although sodium hydride did indeed result in transfer of the benzoate to the C5 hydroxyl group, this was followed by elimination of the resulting *trans*-bromohydrin to yield epoxide **46**. Milder conditions employing ammonium hydroxide and ammonium chloride in 2-propanol solved this problem, and **43** was then carried forward to **47** by oxidation.

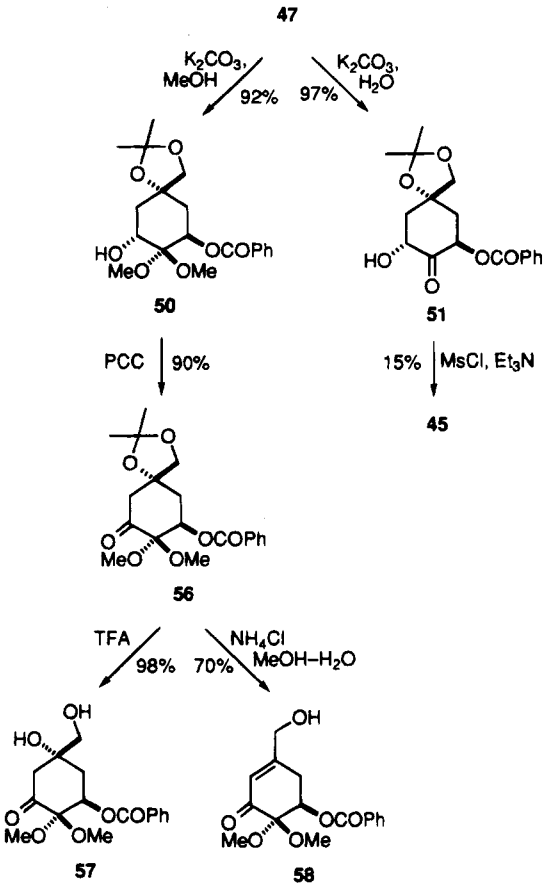
$\alpha$-Bromo ketone **47** appeared to be an ideal substrate on which to focus further synthetic studies since not only would this system offer less opportunity for elimination but it could, in principle, undergo oxidation directly to an $\alpha$-diketone in the presence of dimethyl sulfoxide and a base.[33] For those bromo ketones where displacement of halide is slow, in situ replacement by iodine has been shown to provide a more compliant candidate for oxidation.[34] In the case of **47**, however, another surprise awaited us, for treatment of this compound with sodium iodide in dimethyl sulfoxide containing sodium carbonate gave exclusively the $\alpha,\beta$-unsaturated ketone **45**. An explanation for this unexpected result is shown in Scheme 6 and can be found in the reverse migration of the benzoyl group via enolate **48**. This leads to enolate **49** which then expels iodide. Enone **45** is not formed unless sodium iodide is present, suggesting that it is the final elimination from **49** which drives this process forward.

Having failed to effect oxidation at C3 of **47** we turned our attention to the functional group at C5 with the aim of saponifying the benzoate and oxidizing the resultant hydroxy ketone. Here again a surprise was in store, since methanolic potassium carbonate did not furnish the product of ester cleavage but instead gave the dimethyl ketal **50** (Scheme 7). The $^1$H NMR spectrum of **50** confirmed that the hydroxyl substituent was axial ($J_{H-H}$ = 4,6 Hz). A clue to the pathway by which this substance had been produced lay in the observation that replace-

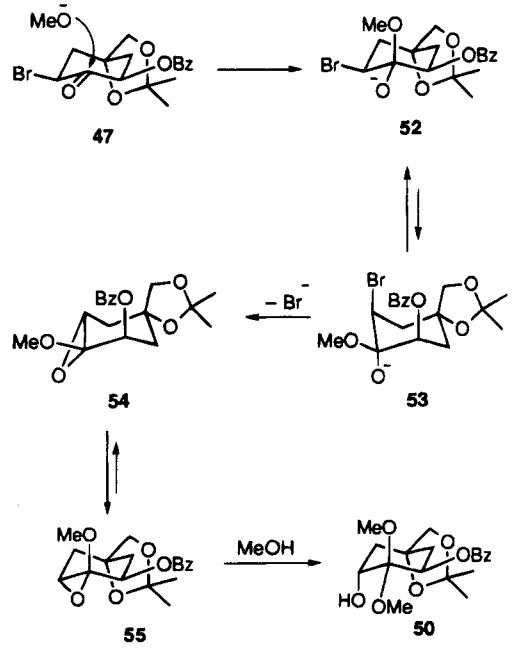
(33) (a) Iacona, R. N.; Rowland, A. T.; Nace, H. R. *J. Org. Chem.* **1964**, *29*, 3495. (b) Nace, H. R.; Iacona, R. N. *J. Org. Chem.* **1964**, *29*, 3498.

(34) Bauer, D. P.; Macomber, R. S. *J. Org. Chem.* **1975**, *40*, 1990.

**Scheme 7**



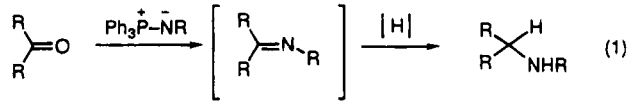

**Scheme 8**

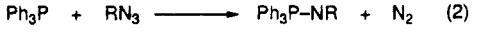



ment of the bromine substituent by a hydroxyl group had occurred with clean inversion. Subsequently, it was discovered that treatment of **47** with aqueous potassium carbonate results in an even more efficient conversion to α-hydroxy ketone **51**. The formation of **50** is consistent with axial attack by methoxide at the ketone carbonyl of **47** in the more stable conformation shown in Scheme 8. In order to accommodate trans diaxial elimination, however, tetrahedral intermediate **52** must undergo chair–chair conversion to **53**. Epoxide **54** would revert to the more stable conformer **55** before opening in diaxial fashion to **50**. An analogous mechanism can be envisioned for formation of **51** with the modification that the intermediate hydroxy epoxide would probably collapse directly to product.

The ready availablility of **51** raised hopes that it would be possible to oxidize this substance to an α-diketone and enter the mycosporin manifold from this point. Unfortunately, all efforts along these lines were unsuccessful, and attempts to displace the hydroxyl group of **51** via its mesylate led to **45** as the only isolable product. Ketal **50**, on the other hand, was smoothly oxidized to the crystalline ketone **56** and, with a substance now at the oxidation level of the mycosporin nucleus, it was hoped that either elimination of methanol or hydrolysis of the ketal moiety would allow entry to the natural system. Unfortunately, neither of these options could be reduced to practice. Treatment of **56** with trifluoroacetic acid resulted in quantitative cleavage of the acetonide to yield **57** in which the ketal remained intact, whereas ammonium chloride promoted clean elimination of **56** to **58**.

It was clear from these results that a different plan was needed for attaining the β-enaminone structure of the mycosporins from **47**, and a new approach was initiated which introduced the amino acid side chain into the mycosporin nucleus via an aza-Wittig reaction. The latter, sometimes designated as a Staudinger reaction,[35] has seen limited application to the synthesis of complex structures,[36] although in combination with reduction of the intermediate imine (eq 1) it offers convenient access to sensitive secondary amines.[37] With this tactic in mind, the focus shifted to acquisition of an appropriate iminophosphorane, for which a general method of preparation is available in the reaction of triphenylphosphine with an azide (eq 2).[38]




A pivotal observation made during studies on bromo ketone **47** was that clean displacement of the bromine substituent could be effected with phenylsulfinate in dimethylformamide without the complications seen with previous transformations of this substance (Scheme 9). Keto sulfone **59** was shown by X-ray crystallographic analysis[44] to have retained configuration during this substitution, a consequence of the facile enolization of **59** which allows the sulfonyl group to assume a more stable equatorial orientation after displacement. Advantage was taken of this enolization by reacting **59** with diazomethane, which resulted in quantitative O-methylation to give **60**. Reduction of the benzoate afforded **61** which was oxidized to ketone **62**. The latter, not surprisingly, proved to be unstable, readily undergoing elimination to a benzenoid system. Nevertheless, it was possible

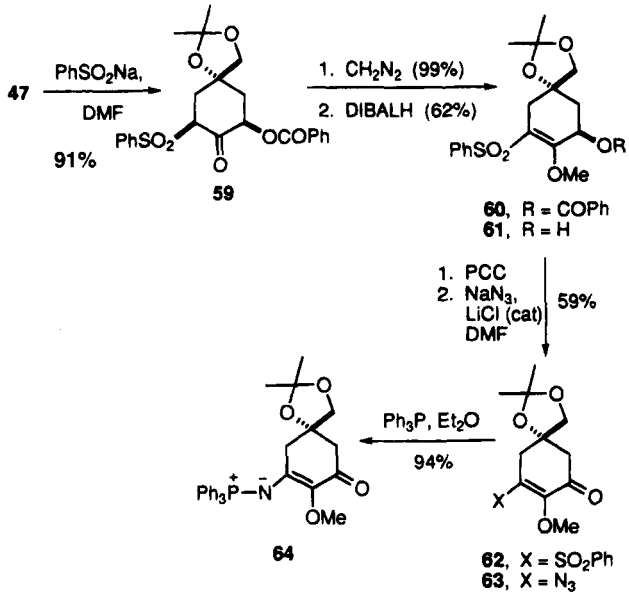
(35) Golobov, Y. G.; Zhmurova, I. N.; Kasukhin, L. F. *Tetrahedron* **1981**, *37*, 437.

(36) *Inter alia* Ackrell, J.; Galeazzi, E.; Muchowski, J. M.; Tökés, L. *Can. J. Chem.* **1979**, *57*, 2696. Lambert, P. H.; Vaultier, M.; Carrié, R. *J. Chem. Soc. Chem. Commun.* **1982**, 1224. Pilard, S.; Vaultier, M. *Tetrahedron Lett.* **1984**, *25*, 1555.

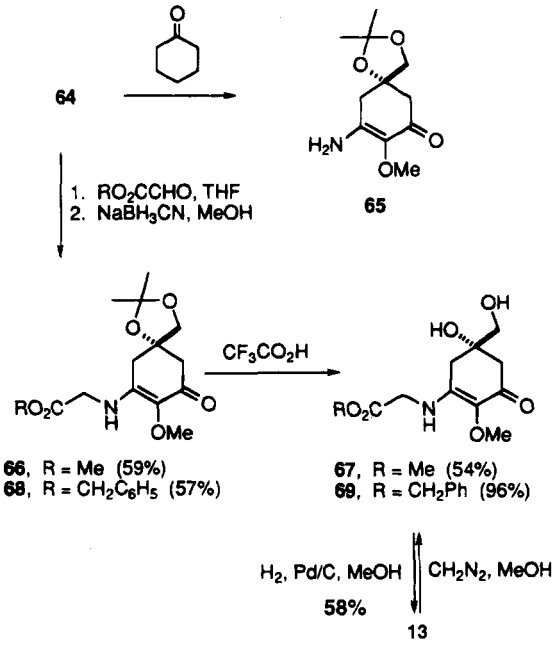
(37) For an elegant, intramolecular example, applied to a synthesis of (+)-croomine, see Williams, D. R.; Brown, D. L.; Benbow, J. W. *J. Am. Chem. Soc.* **1989**, *111*, 1923.

(38) Staudinger, H.; Hauser, E. *Helv. Chim. Acta* **1921**, *4*, 861.

**Scheme 9**



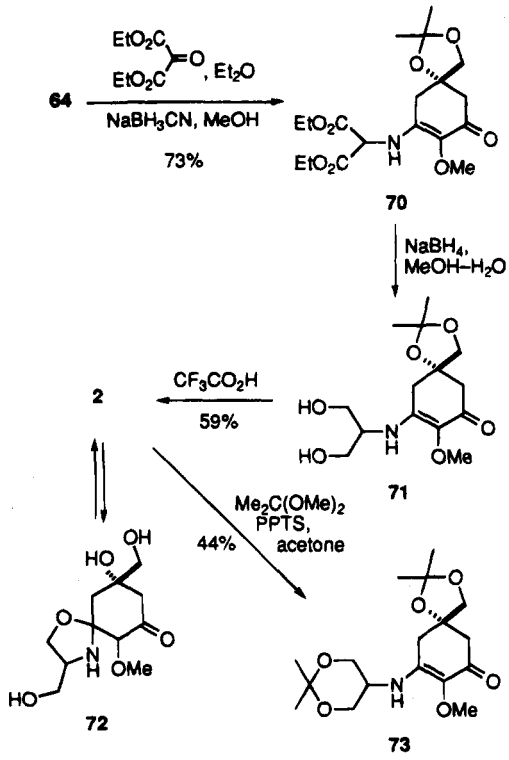

**Scheme 10**




to replace the sulfonyl group of **62** with azide under carefully controlled conditions, and exposure of the resulting vinylogous acyl azide **63** to triphenylphosphine led in high yield to the stable, crystalline iminophosphorane **64**.

With **64** available in quantity from **1**, an ideal point for launching a final attack on members of the mycosporin family seemed to be at hand. First experiments, however, were not encouraging. An attempted aza-Wittig reaction of **64** with cyclohexanone gave enaminone **65** rather than the expected imine (Scheme 10), and although the latter could, in principle, be used for attaching the mycosporin side chain, efforts to alkylate this enaminone, for example with methyl bromoacetate, were unsuccessful. As with resonance-stabilized carbon ylides, iminophosphorane **64** does not condense with less reactive ketones. Fortunately, aldehydes were more responsive, and treatment of **64** with methyl glyoxylate, followed by in situ reduction of the intermediate aldimine with sodium cyanoborohydride, afforded **66** in good yield.

**Scheme 11**



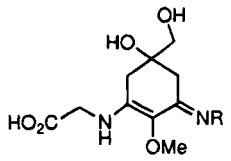

Removal of the acetonide protection from **66** with trifluoroacetic acid yielded mycosporin-gly methyl ester (**67**). The latter was also prepared by esterification of natural mycosporin-gly (**13**) with diazomethane, and a firm correlation between synthetic and naturally derived materials, including optical rotation,[25] was made at this point. However, it proved impossible to saponify either **66** or **67** without compromising the cyclohexenone nucleus of these structures, and for a route to mycosporin-gly itself we were forced to retreat to **64**.

With the secure knowledge that the enaminone moiety of mycosporins was resistant to hydrogenation, **64** was subjected to reductive condensation with benzyl glyoxylate[39] to furnish **68**. After cleavage of the acetonide, hydrogenolysis of benzyl ester **69** afforded synthetic mycosporin-gly (**13**) with spectral properties in good agreement with those recorded for the natural substance.[25]

The most direct route to mycosporin I (**2**) from **64** appeared to be through an aza-Wittig reaction with 2,2-dimethyl-1,3-dioxan-5-one[40] but, as with cyclohexanone, all attempts to effect coupling with this ketone went unrewarded. Fortunately, the more electrophilic keto group of diethyl oxomalonate did react with **64**, and in situ reduction of the resulting ketimine produced the expected enaminone **70** in good yield (Scheme 11). Reduction of the α-amino ester functions of **70** to diol **71** with sodium borohydride proceeded uneventfully,[41] and subsequent cleavage of the acetonide furnished **2** which was identical in its chromatographic behavior and by spectral comparison with a sample of natural mycosporin I.[15] However, discrepancies were noted in the measured optical rotations for synthetic and natural **2** which were traced to mutarotation of this substance caused by

(39) Jung, M. E.; Shishido, K.; Davis, L. H. *J. Org. Chem.* **1982**, *47*, 891.
(40) Araki, Y.; Nagasawa, J.; Ishido, Y. *J. Chem. Soc. Perkin Trans. 1* **1981**, 12.
(41) Seki, H.; Koga, K.; Matsuo, H.; Ohki, S.; Matsuo, I.; Yamada, S. *Chem. Pharm. Bull. Jpn.* **1965**, *13*, 995.

cyclization to spirooxazolidine **72**. The conversion of both synthetic and natural mycosporin I to the same bis(acetonide) **73** permitted unambiguous confirmation of the structure and absolute configuration of **2**. Finally, several attempts were made to condense **66**, **67**, and certain synthetic intermediates along the routes to **2** and **13** with various amines in the hope of extending this approach toward iminomycosporins such as palythine (**74**)[26a] and asterina-330 (**75**).[26k] All of these efforts met with failure, the most frequent outcome being aromatization.



**74**, R = H
**75**, R = $CH_2CH_2OH$

The fact that mycosporin I (**2**) and mycosporin-gly (**13**) are shown by this work to possess *S* configuration implies that, if they have their biosynthetic origin in quinic acid (**1**) as proposed,[42] it is the C5 hydroxyl substituent of **1** which is oxidized *in vivo* to a keto group. It follows that the amino acid side chain of these mycosporins is attached at C3 by a mechanism which does not involve a meso intermediate. If the biosynthetic pathway to mycosporins passes through the well-known 3-dehydroquinate, Schiff base formation by condensation of an amino acid at C3 would parallel the initial step in the proposed enzymatic route to 3-dehydroshikimate.[43] In the case of mycosporins, however, formation of the amino acid conjugate is not followed by loss of a proton from C2. Rather, subsequent oxidation occurs at C5.

## Experimental Section

Preparative thin layer chromatography (TLC) was carried out on precoated plates (silica gel 60 F-254, layer thickness (2 mm) manufactured by E. Merck). For column chromatography silica gel 60 (230–400 mesh ASTM) manufactured by E. Merck was used. Elemental analyses were performed by Desert Analytics, Tucson, AZ.

**(1*S*,3*R*,4*R*,5*R*)-3,4-*O*-Cyclopentylidene-1,3,4-trihydroxy-6-oxabicyclo[3.2.1]octan-7-one (15).** A solution of **1** (25.00 g, 0.13 mol), *p*-toluenesulfonic acid (0.11 g, 0.60 mmol), and cyclopentanone (200 mL, 190 g, 2.26 mol) in benzene (250 mL) was stirred under reflux for 20 h with water removal via a Dean–Stark trap. After the solution had cooled to room temperature, sodium bicarbonate (0.15 g, 1.78 mmol) was added, and the mixture was stirred vigorously for 15 min. The mixture was filtered through a bed of charcoal, and the filtrate was evaporated to leave a residue which was dissolved in methylene chloride. The solution was boiled with decolorizing carbon, filtered, and evaporated to give a solid which was recrystallized from benzene. Treatment of the mother liquor with decolorizing carbon, followed by filtration, evaporation, and crystallization of the residual solid from benzene provided additional product, yielding a total of 25.20 g (80%) of **15**: mp 139–141 °C; $[\alpha]^{20}_D$ −38° (*c* 2.3, $CHCl_3$); IR (KBr) 3450, 1780 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) δ 4.67 (1H, dd, *J* = 3, 6 Hz), 4.25 (2H, m), 3.05 (1H, s), 2.62 (1H, d, *J* = 12 Hz), 2.25 (3H, m), 1.8 (2H, m), 1.65 (6H, s); MS *m*/*z* 240 ($M^+$). Anal. Calcd for $C_{12}H_{16}O_5$: C, 59.99; H, 6.71. Found: C, 60.01; H, 6.72.

**(1*S*,3*R*,4*R*,5*R*)-1,3,4-Trihydroxy-6-oxabicyclo[3.2.1]octan-7-one (16).** A solution of **15** (800 mg, 3.30 mmol) in 80% aqueous acetic acid (20 mL) was stirred at room temperature for 24 h and then at 55 °C for a further 24 h. Removal of the solvent as an azeotrope with cyclohexane left a residue which was purified by chromatography on silica, with a large volume of ethyl acetate as eluant, to give 390 mg (67%) of **16** which was further purified by sublimation: mp 180–186 °C; $[\alpha]^{20}_D$ −28.1° (*c* 0.44, MeOH); IR (KBr) 3325, 1790 $cm^{-1}$; $^1H$ NMR ($d_6$-DMSO) δ 6.19 (1H, s), 5.50 (1H, d, *J* = 4 Hz), 5.12 (1H, d, *J* = 7 Hz), 4.80 (1H, t, *J* = 5 Hz), 4.14 (1H, dt, *J* = 4, 5 Hz), 3.85 (1H, m), 2.65 (1H, d, *J* = 11 Hz), 2.52 (1H, dd, *J* = 2, 5 Hz), 2.20 (1H, d, *J* = 2 Hz), 2.12 (1H, d, *J* = 11 Hz); $^{13}C$ NMR ($d_6$-DMSO) δ 177.5, 75.8, 71.4, 65.4, 65.1, 39.2, 36.6; MS *m*/*z* 156 ($M^+$ − 18). Anal. Calcd for $C_7H_{10}O_5$: C, 48.27; H, 5.80. Found: C, 48.28; H, 5.83.

**(1*R*,3*R*,4*S*,5*R*)-3-[(*tert*-Butyldiphenylsilyl)oxy]-1,4-dihydroxy-6-oxabicylo[3.2.1]octan-7-one (17) and (1*S*,3*R*,4*R*,-5*R*)-4-[(*tert*-Butyldiphenylsilyl)oxy]-1,3-dihydroxy-6-oxabicyclo[3.2.1]octan-7-one (18).** A solution of *tert*-butyldiphenylsilyl chloride (0.26 g, 1.0 mmol) in dimethylformamide (2 mL) was added dropwise to a solution of **16** (174 mg, 1.0 mmol) and imidazole (170 mg, 2.5 mmol) in dimethylformamide (1.5 mL). The mixture was stirred for 1.5 h, and the solvent was removed under vacuum. The residual oily mixture was separated by chromatography on silica, with 10% ether in methylene chloride as eluant, to yield 122 mg (30%) of the less polar **17** followed by 85 mg (20%) of **18**, both as oils.

**17**: $[\alpha]^{20}_D$ −51.8° (*c* 0.52, $CHCl_3$); IR (neat) 3450, 1790 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) δ 7.45 (10H, m), 4.73 (1H, dd, *J* = 5, 4 Hz), 3.85 (2H, m), 3.10 (1H, s), 3.00 (1H, s), 2.60 (1H, d, *J* = 11 Hz), 2.25 (1H, dd, *J* = 6, 3 Hz), 1.90 (2H, m), 1.10 (9H, s); MS *m*/*z* 355 ($M^+$ − 57).

**18**: $[\alpha]^{20}_D$ −24.3° (*c* 0.18, $CHCl_3$); IR (neat) 3450, 1795 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) δ 7.50 (10H, m), 4.15 (2H, m), 3.70 (1H, m), 3.50 (1H, bs), 2.56 (1H, d, *J* = 11 Hz), 2.10 (4H, m), 1.10 (9H, s); MS *m*/*z* 355 ($M^+$ − 57); HRMS *m*/*z* 355.102 ($M^+$ − 57, calcd for $C_{19}H_{19}O_5Si$ 355.100).

**(1*R*,2*S*,3*R*,5*R*)-1,2-*O*-Cyclopentylidene-1,2,3,5-tetrahydroxy-5-(hydroxymethyl)cyclohexane (19).** A solution of **15** (0.88 g, 3.70 mmol) in ethanol (20 mL) was stirred at room temperature with sodium borohydride (0.88 g, 23 mmol) for 20 h. Saturated, aqueous sodium chloride (20 mL) was added, and the mixture was stirred for an additional 12 h. The mixture was extracted with chloroform (5 × 30 mL), and the combined extracts were dried (sodium sulfate) and concentrated to give crude **19** as a yellow oil. Crystallization from ethyl acetate–ethanol yielded 563 mg (63%) of **19** as a colorless solid: mp 93–94 °C; $[\alpha]^{20}_D$ −42.3° (*c* 4.68, $CH_3OH$); IR (KBr) 3350 $cm^{-1}$; $^1H$ NMR ($d_6$-DMSO) δ 5.20–4.90 (1H, m), 4.50 (1H, m), 4.30 (1H, s), 4.10 (3H, m), 3.50 (2H, bs), 2.00 (12H, m); HRMS *m*/*z* 244.129 ($M^+$), calcd for $C_{12}H_{20}O_5$ 244.131.

**(5*R*,7*R*,8*S*,9*R*)-8,9-*O*-Cyclopentylidene-7,8,9-trihydroxy-2,2-dimethyl-1,3-dioxaspiro[4.5]decane (20).** A solution of **19** (76 mg, 0.31 mmol), *p*-toluenesulfonic acid (2 mg), 2,2-dimethoxypropane (1.0 mL, 0.85 g, 8.0 mmol), and acetone (2.5 mL) in methylene chloride (1 mL) was heated to reflux and immediately allowed to cool to room temperature. The mixture was stirred with solid sodium bicarbonate and filtered. Removal of the solvent left an oil which was purified by HPLC, using ethyl acetate as eluant, to yield 28 mg (32%) of **20**: $[\alpha]^{20}_D$ −14.7° (*c* 0.15, $CHCl_3$); IR (neat) 3500 $cm^{-1}$; $^1H$ NMR ($CCl_4$) δ 4.10 (2H, m), 3.75 (3H, m), 3.00 (1H, s), 1.85 (4H, m), 1.60 (8H, m), 1.30 (6H, s); MS *m*/*z* 284 ($M^+$), 269 ($M^+$ − 15); HRMS *m*/*z* 284.161 ($M^+$), calcd for $C_{15}H_{24}O_5$ 284.162.

There was also isolated 23 mg (29%) of a bis(acetonide): $[\alpha]^{20}_D$ −23.0° (*c* 0.33, $CHCl_3$); IR ($CHCl_3$) 3450 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) δ 4.40–3.80 (3H, m), 3.75 (1H, s), 3.73 (1H, s), 2.00 (4H, m), 1.50 (3H, s), 1.38 (6H, s), 1.34 (3H, s); MS *m*/*z* 243 ($M^+$ − 15); HRMS *m*/*z* 243.121 ($M^+$ − 15), calcd for $C_{12}H_{19}O_5$ 243.123.

**(5*S*,8*R*,9*R*)-8,9-*O*-Cyclopentylidene-8,9-dihydroxy-2,2-dimethyl-1,3-dioxaspiro[4.5]decan-7-one (21).** Pyridinium chlorochromate (2.43 g, 11.24 mmol) was suspended in methylene chloride (15 mL), and a solution of **20** (799 mg, 2.80

(42) Favre-Bonvin, J.; Bernillon, J.; Salin, N.; Arpin, N. *Phytochemistry* **1987**, *26*, 2509.
(43) Walsh, C. *Enzymatic Reaction Mechanisms*; Freeman: San Francisco, 1979; p 555.
(44) The author has deposited atomic coordinates for this structure with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK.

mmol) in methylene chloride (6 mL) was added rapidly at room temperature. After 9 h the black mixture was diluted with ether, and the solvent was decanted. The residual black solid was washed with ether, and the combined ethereal washings were filtered through a pad of silica on Florisil. Evaporation of the solvent at reduced pressure left 450 mg (57%) of pure **21**: mp 105–107 °C; $[\alpha]^{20}_D$ −49.5° (*c* 1.83, $CHCl_3$); IR (KBr) 1720 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) δ 4.48 (1H, m), 4.25 (1H, d, *J* = 7 Hz), 3.80 (2H, s), 2.67 (1H, d, *J* = 1 Hz), 2.60 (1H, s), 2.25 (2H, m), 2.10–1.60 (8H, m), 1.40 (6H, s); MS *m/z* 282 ($M^+$), 267 ($M^+$ − 15); HRMS *m/z* 282.147 ($M^+$), calcd for $C_{15}H_{22}O_5$ 282.147. Anal. Calcd for $C_{15}H_{22}O_5$: C, 63.81; H, 7.85. Found: C, 63.66; H, 7.89.

**(5*S*,8*R*,9*R*)-8,9-Dihydroxy-2,2-dimethyl-1,3-dioxaspiro-[4.5]decan-7-one (22).** A solution of **21** (302 mg, 1.07 mmol) in 80% aqueous acetic acid (20 mL) was set aside at 0 °C for 1 week. Solvent evaporation under vacuum at room temperature left a residue which was chromatographed on silica, with ethyl acetate as eluant, to give 124 mg (54%) of **22**: IR ($CHCl_3$) 3500, 1735 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) δ 4.40 (1H, m), 4.20 (1H, m), 3.87 (2H, s), 3.47 (1H, bs), 3.35 (1H, bs), 2.70 (2H, m), 2.45–2.10 (2H, m), 1.45 (6H, s). This substance was unstable and was used promptly for the next reaction.

**(5*S*,8*R*,9*R*)-8-Acetoxy-9-hydroxy-2,2-dimethyl-1,3-dioxaspiro[4.5]decan-7-one (23).** To a solution of **22** (378 mg, 1.75 mmol) and pyridine (1 mL) in methylene chloride (6 mL) at 0 °C was added acetic anhydride (357 mg, 3.5 mmol). After 3 h a further quantity of acetic anhydride (127 mg, 1.25 mmol) was added and the stirred mixture was allowed to warm to room temperature. After 5 h the mixture was evaporated to dryness under vacuum while maintaining the temperature at *ca.* 25 °C, and the residue was taken up in ethyl acetate. The solution was filtered through a short column of Florisil, and the solvent was evaporated. The residue was chromatographed on silica, with methylene chloride–ethyl acetate as eluant, to give 400 mg (89%) of **23**: IR (neat) 3480, 1730 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) δ 5.30 (1H, d, *J* = 4 Hz), 4.51 (1H, q, *J* = 5 Hz), 3.98 (2H, s), 3.91 (1H, m), 2.80 (3H, m), 2.27 (3H, s), 2.20 (1H, m), 1.42 (6H, s). Anal. Calcd for $C_{12}H_{18}O_6$: C, 55.81; H, 7.02. Found: C, 55.77; H, 6.94.

**(5*S*,7*R*,8*R*,9*R*)-8,9-*O*-Cyclopentylidene-7-acetoxy-8,9-dihydroxy-2,2-dimethyl-1,3-dioxaspiro[4.5]decane (24).** A solution of **20** (155 mg, 0.55 mmol) in methylene chloride (2 mL) was added to a solution of acetic anhydride (2 mL) in pyridine (5 mL) at 0 °C and the mixture was stirred for 6 h. The mixture was concentrated to *ca.* 0.5 mL, the residual oil was taken up in carbon tetrachloride, and the mixture was filtered. Evaporation of the solvent left a semisolid which was crystallized from hexane–methylene chloride to give 165 mg (92%) of **24**: mp 59–61 °C; IR (neat) 1740 $cm^{-1}$; $^1H$ NMR ($CCl_4$) δ 5.14 (1H, m), 4.10 (1H, q, *J* = 5 Hz), 3.76 (1H, t, *J* = 5 Hz), 3.62 (2H, s), 2.02 (3H, s), 2.01 (2H, m), 1.90 (4H, m), 1.65 (6H, m), 1.33 (6H, s); MS *m/z* 326 ($M^+$); HRMS *m/z* 326.172, calcd for $C_{17}H_{26}O_6$ 326.173. Anal. Calcd for $C_{17}H_{26}O_6$: C, 62.56; H, 8.03. Found: C, 62.58; H, 7.77.

**(5*S*,7*R*,8*R*,9*R*)-7-Acetoxy-8,9-dihydroxy-2,2-dimethyl-1,3-dioxaspiro[4.5]decane (25).** A solution of **24** (202 mg, 0.62 mmol) in 80% aqueous acetic acid (10 mL) was allowed to stand for 10 h at 0 °C. The solvent was evaporated under vacuum while maintaining the temperature at *ca.* 25 °C to give 160 mg (99%) of virtually pure **25**: IR (neat) 3450, 1735 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) δ 5.33 (1H, dt, *J* = 6, 8 Hz), 4.1–3.4 (6H, m), 2.10 (3H, s), 2.05 (2H, m), 1.80 (2H, m), 1.43 (6H, s). This compound was unstable and was used without further purification.

**(5*S*,7*R*,8*S*,9*R*)-9-Hydroxy-7,8-dimethoxy-2,2-dimethyl-1,3-dioxaspiro[4.5]decane (26) and (5*R*,7*R*,8*S*,9*R*)-9-Acetoxy-7,8-dimethoxy-2,2-dimethyl-1,3-dioxaspiro[4.5]decane (27).** To a solution of **25** (900 mg, 3.46 mmol) and methyl iodide (6 mL) in tetrahydrofuran (20 mL) at room temperature was added sodium hydride (189 mg, 4 mmol, 50% dispersion in mineral oil) in several portions. After 6 h an additional quantity of sodium hydride (189 mg, 4 mmol) was added, and the mixture was stirred for 12 h. Solid ammonium chloride (1 g) was added, and the mixture was poured into ether. The separated ethereal solution was washed with saturated, aqueous sodium chloride and dried (sodium sulfate). Solvent evaporation afforded an oil which was chromatographed on silica, with methylene chloride in ethyl acetate as eluant, to afford 221 mg (22%) of **27** followed by 391 mg (46%) of **26**. Both of these compounds were unstable, and the latter was immediately oxidized to **28** as described below.

**(5*S*,8*R*,9*R*)-8,9-Dimethoxy-2,2-dimethyl-1,3-dioxaspiro-[4.5]decan-7-one (28).** To a stirred solution of pyridine (237 mg, 3.0 mmol) in methylene chloride (5 mL) at 0 °C was added chromium trioxide (150 mg, 1.5 mmol). After 5 min the mixture was allowed to warm to room temperature, and a solution of **26** (57 mg, 0.23 mmol) in methylene chloride (3 mL) was added. The mixture was stirred for 15 min and was filtered through Celite. The filtrate was concentrated at reduced pressure, and the residue was chromatographed on a short column of Florisil, with methylene chloride as eluant, to afford 46 mg (82%) of **28** which was crystallized from ether: mp 101–103 °C; IR (KBr) 1725 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) δ 3.83 (2H, s), 3.9–3.6 (2H, m), 3.51 (3H, s), 3.48 (3H, s), 2.70 (1H, d, *J* = 14 Hz), 2.56 (1H, d, *J* = 14 Hz), 1.90 (2H, m), 1.33 (6H, s); MS *m/z* 229 ($M^+$ − 15). Anal. Calcd for $C_{12}H_{20}O_5$: C, 59.00; H, 8.25. Found: C, 58.94; H, 8.03.

**(5*R*,7*R*,8*S*,9*R*)-8,9-*O*-Cyclopentylidene-8,9-dihydroxy-7-methoxy-2,2-dimethyl-1,3-dioxaspiro[4.5]decane (29).** To a stirred solution of **20** (0.99 g, 3.49 mmol) in tetrahydrofuran (20 mL) was added sodium hydride (200 mg, 4.16 mmol, 50% dispersion in mineral oil), and the mixture was stirred at room temperature for 3 h. An excess of aqueous ammonium chloride was added, and the mixture was extracted with ethyl acetate. The extract was dried (magnesium sulfate), and the solvent was removed to leave an oil which was chromatographed on silica, with hexane–ethyl acetate as eluant, to yield 0.95 g (92%) of **29**: IR (neat) 1100 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) δ 4.06 (1H, q, *J* = 5 Hz), 3.81 (1H, t, *J* = 5 Hz), 3.64 (2H, s), 3.55 (1H, m), 3.38 (3H, s), 2.02–1.60 (12H), 1.32 (6H, s); HRMS *m/z* 298.179, calcd for $C_{16}H_{26}O_5$ 298.178. Anal. Calcd for $C_{16}H_{26}O_5$: C, 64.41; H, 8.78. Found: C, 64.32; H, 8.91.

**(5*S*,7*R*,8*R*,9*R*)-8,9-Dihydroxy-7-methoxy-2,2-dimethyl-1,3-dioxaspiro[4.5]decane (30).** A solution of **29** (0.62 g, 2.0 mmol) in 80% aqueous acetic acid (15 mL) was allowed to stand at 0 °C for 12 h, and the solvent was removed under vacuum at 0 °C. The residue was chromatographed on silica, with hexane–ethyl acetate as eluant, to afford 0.42 g (86%) of **30**: IR (neat) 3430 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) δ 4.25–3.30 (5H, m), 3.82 (2H, s), 3.46 (3H, s), 2.40–1.70 (4H, m), 1.44 (6H, s); HRMS *m/z* 232.131, calcd for $C_{11}H_{20}O_5$ 232.131.

**(5*R*,8*S*,9*R*)-8-Hydroxy-9-methoxy-2,2-dimethyl-1,3-dioxaspiro[4.5]decan-7-one (31).** To a stirred solution of **30** (0.38 g, 1.69 mmol) in acetone (30 mL) at 0 °C was added a slight excess of Jones reagent (*ca.* 1 M), and the mixture was stirred for 30 min. A large excess of solid sodium bicarbonate was added to the mixture which was stirred for 15 min and filtered. The solvent was removed, and the residue was triturated with ether. The ethereal solution was dried (magnesium sulfate) and filtered through Celite. Removal of the solvent gave 0.19 g (50%) of **31**: IR ($CHCl_3$) 3450, 1705, 1195 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) δ 4.15 (1H, d, *J* = 9 Hz), 3.84–3.40 (3H, m), 3.58 (3H, s), 2.65 (2H, m), 2.48–1.65 (2H, m), 1.40 (6H, s); HRMS *m/z* 215.091($M^+$ − 15), calcd for $C_{10}H_{15}O_5$ 215.092. This substance was unstable and rapidly decomposed.

**(5*R*,8*S*,9*R*)-8,9-Dimethoxy-2,2-dimethyl-1,3-dioxaspiro-[4.5]decan-7-one (32).** To a solution of **31** (40 mg, 0.17 mmol) in ether (5 mL) at 0 °C was added a drop of boron trifluoride–diethyl etherate followed by an excess of diazomethane in ether. The mixture was allowed to stand overnight at 0 °C, after which the yellow color had disappeared. Evaporation of the solvent and preparative thin layer chromatography of the residue on silica, with ethyl acetate–hexane (4:1) as eluant, gave 12 mg (29%) of **32** as an amorphous solid: mp 113–114 °C; $^1H$ NMR ($CDCl_3$) δ 3.84 (2H, s), 3.78–3.38 (2H, m), 3.51 (3H, s), 3.48 (3H, s), 2.80–1.80 (4H, m), 1.40 (6H, s); MS *m/z* 244 ($M^+$), 229. Anal. Calcd for $C_{12}H_{20}O_5$: C, 59.00; H, 8.25. Found: C, 58.76; H, 8.04.

**(1*S*,3*R*,4*R*,5*R*)-3,4-*O*-Benzylidene-1,3,4-trihydroxy-6-oxabicyclo[3.2.1]octan-7-one (33).** A suspension of **1** (5.01 g, 0.026 mol) in benzene (100 mL) and benzaldehyde (20 mL) containing a catalytic amount of *p*-toluenesulfonic acid was refluxed for 20 h with water removal via a Dean–Stark trap.

The resulting solution was cooled to room temperature and was washed with saturated, aqueous sodium bisulfite. The benzaldehyde–sulfite addition product formed a colloidal precipitate which was dissolved by addition of water. The organic layer was repeatedly washed with aqueous sodium bisulfite until most of the benzaldehyde had been removed and was then washed with saturated, aqueous sodium bicarbonate and dried (sodium sulfate). The solvent was evaporated to leave 5.48 g (80%) of **33** as a mixture of two diastereomers. An analytical sample was prepared by chromatography on silica, with ethyl acetate as eluant: IR (neat) 3475, 1790 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 7.80 (2H, m), 7.50 (3H, m), 6.18 (0.3H, s), 5.18 (0.7H, s), 4.75 (1H, m), 4.45 (2H, m), 3.70 (1H, bs), 2.75 (1H, d, $J$ = 12 Hz), 2.40 (3H, m); MS $m/z$ 262 ($M^+$), 261 ($M^+ - 1$); HRMS $m/z$ 262.084 ($M^+$, calcd for $C_{14}H_{14}O_5$ 262.084). Anal. Calcd for $C_{14}H_{14}O_5$: C, 64.12; H, 5.38. C, 63.88; H, 5.26.

**(1*R*,2*S*,3*R*,5*R*)-1,2-*O*-Benzylidene-1,2,3,5-tetrahydroxy-5-(hydroxymethyl)cyclohexane (34).** A solution of **33** (4.40 g, 16.8 mmol) and sodium borohydride (4.12 g, 108 mmol) in ethanol (120 mL) was stirred at room temperature for 24 h. Saturated, aqueous sodium chloride (80 mL) was added and stirring was continued for a further 18 h. The mixture was extracted with ethyl acetate, and the extract was dried (sodium sulfate). Filtration and solvent evaporation afforded crude **34** as an extremely hygroscopic, amorphous solid. Chromatography on silica, with 10% methanol in methylene chloride as eluant, gave 4.40 g (99%) of **34**: IR (neat) 3600–3200 $cm^{-1}$; MS $m/z$ 266 ($M^+$), 248 ($M^+ - 18$). Further characterization of **34** was abandoned due to its hygroscopic nature.

**(1*R*,2*R*,3*R*,5*S*)-3-Acetoxy-5-(acetoxymethyl)-1,2-*O*-benzylidene-1,2,5-trihydroxycyclohexane (35).** A solution of **34** (1.07 g, 4.01 mmol) in pyridine (25 mL) and acetic anhydride (10 mL) was stirred at room temperature for 20 h. The mixture was filtered, and most of the solvent was evaporated. Residual pyridine was removed via azeotropic distillation with benzene, and the residue was dissolved in methylene chloride and filtered again. Solvent evaporation left an oil which was purified by chromatography on silica, with ether as eluant, to give 1.15 g (82%) of **35**: IR ($CCl_4$) 3525, 1740 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 7.35 (5H, m), 6.23 (0.3H, s), 5.83 (0.7H, s), 5.35 (1H, m), 4.43 (1H, m), 4.27 (1H, m), 3.95 (2H, s), 3.05 (0.3H, s), 2.85 (0.7H, s), 2.50–1.80 (4H, m), 2.10 (3H, s), 2.00 (3H, s); MS $m/z$ 350 ($M^+$); HRMS $m/z$ 350.1374 ($M^+$, calcd for $C_{18}H_{22}O_7$ 350.1366). Anal. Calcd for $C_{18}H_{22}O_7$: C, 61.71; H, 6.33. Found: C, 61.82; H, 6.41.

**(1*R*,2*R*,3*R*,5*R*)-1-Acetoxy-5-(acetoxymethyl)-3-(benzoyloxy)-2-bromo-5-hydroxycyclohexane (36) and (1*R*,2*S*,3*S*,5*R*)-1-Acetoxy-5-(acetoxymethyl)-2-(benzoyloxy)-3-bromo-5-hydroxycyclohexane (37).** A suspension of **35** (263 mg, 0.75 mmol), *N*-bromosuccinimide (138 mg, 0.78 mmol), and a catalytic amount of benzoyl peroxide in carbon tetrachloride (25 mL) was stirred at reflux for 20 min, during which the mixture became yellow and solid succinimide floated to the surface. The mixture was cooled to room temperature and filtered, and the solvent was removed under vacuum. Purification of the residual oil was carried out by chromatography on silica, with ether as eluant, to give 130 mg (40%) of the less polar **36** followed by 73 mg (22%) of **37**.

**36**: $[\alpha]^{20}_D$ −38.4° (*c* 0.49, $CHCl_3$); IR ($CHCl_3$) 3450, 1730 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 8.00 (2H, m), 7.45 (3H, m), 5.50 (2H, m), 4.58 (1H, t, $J$ = 4 Hz), 4.00 (2H, s), 2.75 (1H, s), 2.50–1.80 (4H, m), 2.09 (3H, s), 2.08 (3H, s); MS $m/z$ 357 and 355 ($M^+ - 73$). Anal. Calcd for $C_{18}H_{21}BrO_7$: C, 50.36; H, 4.94; Br, 18.61. Found: C, 49.96; H, 4.74; Br, 18.28.

**37**: IR ($CCl_4$) 3500, 1740 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 8.00 (2H, m), 7.45 (3H, m), 5.40 (2H, m), 4.35 (1H, m), 3.97 (2H, s), 2.70–1.90 (4H, m), 2.10 (3H, s), 1.86 (3H, s); MS $m/z$ 431 and 429 ($M^+ + 1$), 413 and 411 ($M^+ - 17$).

**(1*R*,3*S*,4*S*,5*R*)-4-(Benzoyloxy)-3-bromo-1-hydroxy-6-oxabicyclo[3.2.1]octan-7-one (41).** To a solution of **33** (2.27 g, 8.65 mmol) in carbon tetrachloride (150 mL) was added *N*-bromosuccinimide (1.70 g, 9.54 mmol) and benzoyl peroxide (54 mg, 0.22 mmol). The mixture was refluxed for 1 h, during which it turned yellow, and solid succinimide floated to the surface. After the mixture had cooled, it was filtered and the solvent was evaporated. The residue was chromatographed on silica, with 20% ether in methylene chloride as eluant, to give a solid which was crystallized from ethyl acetate–hexane to yield 2.38 g (81%) of **41**: mp 145–147 °C; $[\alpha]^{20}_D$ +78.0° (*c* 0.12, $CHCl_3$); IR ($CHCl_3$) 3500, 1800, 1725 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 7.95 (2H, m), 7.70–7.30 (3H, m), 5.60 (1H, d, $J$ = 4 Hz), 4.95 (1H, m), 4.45 (1H, m), 3.40 (1H, s), 2.95–2.30 (4H, m); MS $m/z$ 343 and 341 ($M^+ + 1$). Anal. Calcd for $C_{14}H_{13}O_5Br$: C, 49.28; H, 3.85; Br, 23.42. Found: C, 49.35; H, 3.85; Br, 23.17.

**(5*R*,7*R*,8*S*,9*S*)-8-(Benzoyloxy)-9-bromo-7-hydroxy-2,2-dimethyl-1,3 dioxaspiro[4,5]decane (42) and (5*R*,7*R*,8*S*,9*S*)-7-(Benzoyloxy)-9-bromo-8-hydroxy-2,2-dimethyl-1,3-dioxaspiro[4,5]decane (43).** To a solution of **41** (650 mg, 1.90 mmol) in 2-propanol (20 mL) was added sodium borohydride (81.6 mg, 2.16 mmol), and the mixture was stirred at room temperature for 4 h. Saturated, aqueous ammonium chloride was added, followed by water, to dissolve the precipitate which had formed. The mixture was extracted with ethyl acetate, and the extract was dried (sodium sulfate). Filtration and solvent evaporation left a residue to which was added acetone (10 mL), 2,2-dimethoxypropane (10 mL), and a catalytic amount of *p*-toluenesulfonic acid. The solution was heated at reflux for 1 h, allowed to cool, and filtered through a short column of silica. Solvent evaporation left a mixture containing two products which were separated by chromatography on silica, with 10% ether in methylene chloride as eluant, to give 317 mg (43%) of the more polar **42** and 238 mg (32%) of **43**.

**42**: $[\alpha]^{20}_D$ +27.6° (*c* 0.50, $CHCl_3$); IR ($CHCl_3$) 3500, 1720 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 8.05 (2H, m), 7.50 (3H, m), 5.20 (1H, dd, $J$ = 10, 12 Hz), 4.35 (1H, m), 4.02 (1H, m), 3.80 (2H, s), 2.70–1.60 (5H, m), 1.40 (6H, s); MS $m/z$ 387 and 385 ($M^+ + 1$). Anal. Calcd for $C_{17}H_{21}BrO_5$: C, 52.99; H, 5.50; Br, 20.74. Found: C, 53.00; H, 5.35; Br, 20.45.

**43**: $[\alpha]^{20}_D$ +15.3° (*c* 0.50, $CHCl_3$); IR ($CHCl_3$) 3600, 1720 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 8.02 (2H, m), 7.45 (3H, m), 5.30 (1H, m), 4.50–3.90 (2H, m), 3.80 (2H, s), 2.67 (1H, d, $J$ = 3 Hz), 2.50–1.50 (4H, m), 1.45 (3H, s), 1.42 (3H, s); MS $m/z$ 387 and 385 ($M^+ + 1$), 371 and 369 ($M^+ - 15$); HRMS $m/z$ 371.030 ($M^+ - 15$, calcd for $C_{16}H_{18}BrO_5$ 371.032).

A solution of **42** (275 mg, 0.71 mmol) in 2-propanol (5 mL) containing saturated, aqueous ammonium chloride (2.5 mL) and saturated, aqueous ammonium hydroxide (0.25 mL) was stirred at room temperature for 17 h. The solvent was evaporated and the residue was chromatographed as described above to yield 230 mg (84%) of **43**.

**(5*R*,8*S*,9*S*)-8-(Benzoyloxy)-9-bromo-2,2-dimethyl-1,3-dioxaspiro[4,5]decan-7-one (44).** A solution of **42** (33.0 mg, 0.086 mmol) in methylene chloride (5 mL) containing pyridinium chlorochromate (93.6 mg, 0.43 mmol) was stirred at room temperature for 24 h. Water was added, and the mixture was extracted with methylene chloride. The organic layer was dried (sodium sulfate) and filtered, and the solvent was evaporated. Chromatography of the residue on silica, with 2% ether in methylene chloride as eluant, gave 16.6 mg (51%) of **44**: IR ($CHCl_3$) 1750, 1730 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 8.07 (2H, m), 7.45 (3H, m), 5.52 (1H, d, $J$ = 11 Hz), 4.55 (1H, td, $J$ = 5, 11 Hz), 3.88 (1H, s), 3.86 (1H, s), 2.60 (4H, m), 1.40 (3H, s), 1.36 (3H, s); MS $m/z$ 385 and 383 ($M^+ + 1$), 384 and 382 ($M^+$), 369 and 367 ($M^+ - 15$); HRMS $m/z$ 367.018 ($M^+ - 15$, calcd for $C_{16}H_{16}BrO_5$ 367.018).

**(5*S*)-8-(Benzoyloxy)-2,2-dimethyl-1,3-dioxaspiro[4.5]-dec-8-en-7-one (45). A. From 44.** To a solution of **44** (215 mg, 0.56 mmol) in methylene chloride (3.5 mL) at room temperature was added triethylamine (0.2 mL). After 3.5 h the reaction mixture was washed with 5% aqueous hydrochloric acid and diluted with methylene chloride. The separated organic layer was washed with 5% aqueous sodium bicarbonate and water and was dried (sodium sulfate). Filtration through silica, followed by evaporation of the solvent, left a solid which was crystallized from ether to give 146 mg (86%) of **45**: mp 124–125 °C; $[\alpha]^{20}_D$ −7.2° (*c* 0.22, $CHCl_3$); IR ($CHCl_3$) 1745, 1710 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 8.10 (2H, m), 7.63–7.46 (3H, m), 6.65 (1H, t, $J$ = 5 Hz), 3.97 (1H, d, $J$ = 9 Hz), 3.93 (1H, d, $J$ = 9 Hz), 2.95 (1H, d, $J$ = 16 Hz), 2.89–2.76 (3H, m), 1.43 (3H, s), 1.42 (3H, s); $^{13}C$ NMR ($CDCl_3$) $\delta$ 203.7, 178.2, 135.6, 122.9, 121.2, 119.8, 118.5, 117.9, 99.7, 70.1, 62.8, 38.4, 25.7, 16.4, 16.2; MS $m/z$ 302 ($M^+$), 287 ($M^+ - 15$); HRMS $m/z$

302.115 ($M^+$, calcd for $C_{17}H_{18}O_5$ 302.115). Anal. Calcd for $C_{17}H_{18}O_5$: C, 67.54; H, 6.00. Found: C, 67.49; H, 5.88.

**B. From 51.** A solution of **51** (35.5 mg, 0.11 mmol), methanesulfonyl chloride (0.017 mL, 0.22 mmol), and triethylamine (0.077 mL, 0.55 mmol) in methylene chloride (2 mL) was stirred at room temperature for 0.5 h. Saturated, aqueous sodium bicarbonate (2 mL) was added, and the mixture was extracted with methylene chloride. The extract was dried (sodium sulfate), and the solvent was evaporated to leave a residue which was purified by preparative layer chromatography. Elution with 10% ether in methylene chloride gave 5 mg (15%) of **45** whose spectral properties were identical with those of material prepared by method A.

**(1*R*,3*S*,5*R*,6*R*)-5-(Benzoyloxy)-2′,2′-dimethylspiro(1′,3′-dioxolane-4′,3-[7]oxabicyclo[4.1.0]heptane) (46).** A catalytic amount of sodium hydride was added to a solution of **42** (38.0 mg, 0.099 mmol) in 2-propanol (5 mL) at room temperature, and the reaction was quenched after 1 min with saturated, aqueous ammonium chloride. The mixture was extracted with ether and the extract was dried (sodium sulfate). Filtration and removal of the solvent left an oily residue which was purified by chromatography on silica, with 2% ether in methylene chloride as eluant, to give 13.5 mg (45%) of **46**: $[\alpha]^{20}_D$ +115.5° (*c* 0.35, $CHCl_3$); IR ($CHCl_3$) 1730 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 8.00 (2H, m), 7.50 (3H, m), 5.67 (1H, m), 3.97 (1H, d, $J$ = 9 Hz), 3.72 (1H, d, $J$ = 9 Hz), 3.22 (2H, s), 2.50−1.55 (4H, m), 1.45 (3H, s), 1.30 (3H, s); MS $m/z$ 289 ($M^+$ − 15); HRMS $m/z$ 289.107 ($M^+$ − 15, calcd for $C_{16}H_{17}O_5$ 289.108). Anal. Calcd for $C_{17}H_{20}O_5$: C, 67.09; H, 6.62. Found: C, 66.97; H, 6.64.

**(5*R*,7*R*,9*S*)-7-(Benzoyloxy)-9-bromo-2,2-dimethyl-1,3-dioxaspiro[4.5]decan-8-one (47).** A solution of **43** (1.13 g, 2.90 mmol) in methylene chloride (22 mL) was added to a suspension of pyridinium chlorochromate (3.15 g, 14.6 mmol) in methylene chloride (8 mL). The mixture was refluxed for 11 h, cooled, and quenched with water. The mixture was extracted with methylene chloride, and the combined extracts were filtered through a short column of silica and dried (sodium sulfate). The solvent was removed to leave a residue which was purified by chromatography on silica, with 5% ether in methylene chloride as eluant, to afford 804 mg (72%) of **47**: $[\alpha]^{20}_D$ +33.0° (*c* 0.22, $CHCl_3$); IR ($CHCl_3$) 1760, 1730 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 8.02 (2H, m), 7.45 (3H, m), 5.82 (1H, dd, $J$ = 7, 14 Hz), 5.07 (1H, dd, $J$ = 6, 14 Hz), 3.87 (2H, s), 2.65 (2H, m), 2.50 (2H, dd, $J$ = 10, 12 Hz), 1.50 (6H, s); MS $m/z$ 385 and 383 ($M^+$ + 1), 384 and 382 ($M^+$), 369 and 367 ($M^+$ − 15). Anal. Calcd for $C_{17}H_{19}BrO_5$: C, 53.27; H, 5.01; Br, 20.85. Found: C, 53.00; H, 4.93; Br, 20.56.

**(5*S*,7*R*,9*R*)-7-(Benzoyloxy)-9-hydroxy-8,8-dimethoxy-2,2-dimethyl-1,3-dioxaspiro[4.5]decane (50).** To a solution of **47** (242 mg, 0.63 mmol) in anhydrous methanol (20 mL) at −78 °C was added solid potassium carbonate (89 mg, 0.64 mmol), and the mixture was allowed to warm to 0 °C over 4 h. Pyridinium *p*-toluenesulfonate (315 mg, 1.25 mmol) was added to the pink solution, which caused the color to fade, and the mixture was warmed to room temperature and diluted with ethyl acetate (30 mL). The solution was evaporated to a volume of *ca.* 20 mL and was washed with saturated, aqueous sodium bicarbonate ,and water. The separated organic layer was dried by azeotropic distillation with benzene, and the solvent was removed to leave crude **50**. Chromatography of this material on silica, with 10% ether in methylene chloride as eluant, gave 211 mg (92%) of **50**: $[\alpha]^{20}_D$ +18.9° (*c* 0.45, $CHCl_3$); IR ($CHCl_3$) 3550, 1720 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 8.01 (2H, m), 7.60−7.43 (3H, m), 5.65 (1H, dd, $J$ = 4, 10 Hz), 4.08 (1H, dd, $J$ = 4, 6 Hz), 3.88 (1H, d, $J$ = 9 Hz), 3.78 (1H, d, $J$ = 9 Hz), 3.47 (3H, s), 3.40 (3H, s), 2.28−1.89 (4H, m), 1.44 (6H, s); $^{13}C$ NMR ($CDCl_3$) $\delta$ 165.4, 133.1, 130.4, 129.7 (×2), 128.5 (×2), 109.9, 99.0, 81.2, 74.0, 71.1, 70.3, 50.5, 49.6, 38.2, 37.9, 27.1, 26.9; MS $m/z$ 366 ($M^+$), 348 ($M^+$ − 18); HRMS $m/z$ 366.166 ($M^+$, calcd for $C_{19}H_{26}O_7$ 366.168). Anal. Calcd for $C_{19}H_{26}O_7$: C, 62.27; H, 7.17. Found: C, 61.86; H, 7.05.

**(5*S*,7*R*,9*R*)-7-(Benzoyloxy)-9-hydroxy-2,2-dimethyl-1,3-dioxaspiro[4.5]decan-8-one (51).** To a solution of **47** (773 mg, 2.01 mmol) in a 2:1 mixture of tetrahydrofuran and water (150 mL) at 0 °C was added solid potassium carbonate (280 mg, 2.02 mmol), and the mixture was allowed to warm to room temperature during 4 h. Partial evaporation of the solvent left an aqueous layer which was extracted with ether. Evaporation of the ether followed by crystallization of the residual solid from ether gave 625 mg (97%) of **51**: mp 84−87 °C; $[\alpha]^{20}_D$ −7.4° (*c* 0.4, $CHCl_3$); IR (KBr) 3350, 1720 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 7.98 (2H, m), 7.40 (3H, m), 5.92 (1H, dd, $J$ = 5, 9 Hz), 4.30 (1H, t, $J$ = 6 Hz), 3.97 (1H, s), 3.95 (1H, s), 2.60−2.00 (4H, m), 1.45 (6H, s); MS $m/z$ 320 ($M^+$), 305 ($M^+$ − 15), 277 ($M^+$ − 43); HRMS $m/z$ 305.104 ($M^+$ − 15, calcd for $C_{16}H_{17}O_6$ 305.103). This substance decomposed at room temperature or upon attempted chromatography.

**(5*R*,7*R*)-7-(Benzoyloxy)-8,8-dimethoxy-2,2-dimethyl-1,3-dioxaspiro[4.5]decan-9-one (56).** To a solution of **50** (28.1 mg, 0.077 mmol) in methylene chloride (25 mL) were added pyridinium chlorochromate (42.5 mg, 0.197 mmol) and sodium acetate (6.0 mg, 0.07 mmol, 1 equiv), and the mixture was stirred at room temperature for 24 h. Ether was added and the supernatant was decanted. The black residue was washed with ether, and the combined organic solutions were filtered through a short column of silica. Evaporation of the solvent and chromatography of the residue on silica, with 5% ether in methylene chloride as eluant, gave 25.2 mg (90%) of **56**: mp 99−102 °C; $[\alpha]^{20}_D$ +71.6° (*c* 2.11, $CHCl_3$); IR ($CHCl_3$) 1730, 1720 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 7.92 (2H, dd, $J$ = 1, 8 Hz), 7.61−7.43 (3H, m), 5.67 (1H, dd, $J$ = 3, 4 Hz), 3.94 (1H, d, $J$ = 9 Hz), 3.56 (1H, dd, $J$ = 1, 9 Hz,), 3.29 (3H, s), 3.28 (3H, s), 2.98 (1H, dd, $J$ = 1, 12 Hz), 2.86 (1H, dd, $J$ = 2, 13 Hz), 2.78 (1H, dd, $J$ = 3, 15 Hz), 2.23 (1H, ddd, $J$ = 2, 4, 15 Hz), 1.42 (3H, s), 1.28 (3H, s); $^{13}C$ NMR ($CDCl_3$) $\delta$ 201.7, 164.8, 133.7, 129.7, 128.9, 128.6, 108.9, 99.2, 81.0, 73.6, 69.2, 50.6, 50.2, 49.4, 37.0, 27.6, 26.0; MS $m/z$ 364 ($M^+$), 349 ($M^+$ − 15); HRMS $m/z$ 364.153 ($M^+$, calcd for $C_{19}H_{24}O_7$ 364.152). Anal. Calcd for $C_{19}H_{24}O_7$: C, 62.63; H, 6.64. Found: C, 62.66; H, 6.59.

**(3*R*,5*R*)-3-(Benzoyloxy)-5-hydroxy-5-(hydroxymethyl)-2,2-dimethoxycyclohexanone (57).** To a solution of **56** (14.2 mg, 0.039 mmol) in chloroform (1 mL) at 0 °C was added 50% aqueous trifluoroacetic acid (0.5 mL). After 1 min the solvent was evaporated to leave a moist solid which was dried by removal of water as a benzene azeotrope. Crystallization of the solid from methylene chloride−hexane gave 12.7 mg (98%) of **57**: mp 148−150 °C; $[\alpha]^{20}_D$ −17.4° (*c* 0.5, $CH_3OH$); IR ($CHCl_3$) 3500, 1720 $cm^{-1}$; $^1H$ NMR ($d_6$-acetone) $\delta$ 8.02 (2H, m), 7.64−7.50 (3H, m), 5.65 (1H, dd, $J$ = 10, 4 Hz), 3.51 (1H, s), 3.48 (1H, s), 3.43 (3H, s), 3.36 (3H, s), 2.99 (1H, d, $J$ = 13 Hz), 2.85 (3H, bs), 2.45-2.37 (2H, m); $^{13}C$ NMR ($d_6$-acetone) $\delta$ 202.2, 165.1, 133.6, 129.8, 129.4, 128.6, 99.8, 73.5, 70.9, 68.7, 51.1, 50.3, 47.9, 35.9; MS $m/z$ 324 ($M^+$), 306 ($M^+$ − 18); HRMS $m/z$ 324.120 ($M^+$, calcd for $C_{16}H_{20}O_7$ 324.121). Anal. Calcd for $C_{16}H_{20}O_7$: C, 59.25; H, 6.22. Found: C, 59.41; H, 6.06.

**(5*R*)-5-(Benzoyloxy)-3-(hydroxymethyl)-6,6-dimethoxy-2-cyclohexenone (58).** A solution of **56** (2.3 mg, 0.01 mmol) in methanol (3 mL) containing saturated, aqueous ammonium chloride was stirred at room temperature for 3.5 d. The methanol was evaporated, and the residue was extracted with ether. The ethereal extract was washed with water and dried (sodium sulfate). Removal of the solvent, followed by chromatography of the residue on silica, with ether as eluant, gave 1.4 mg (70%) of **58**: IR ($CHCl_3$) 3525, 1720, 1695 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 7.87 (2H, m), 7.40 (3H, m), 6.21 (1H, m), 5.75 (1H, dd, $J$ = 3, 4 Hz), 4.22 (2H, bs), 3.30 (3H, s), 3.22 (3H, s), 2.85 (1H, m), 2.63 (1H, m), 2.35 (1H, m); MS $m/z$ 306 ($M^+$), 275 (M − 31), 274 (M − 32); HRMS $m/z$ 306.109 ($M^+$, calcd for $C_{16}H_{18}O_6$ 306.110).

**(5*R*,7*R*,9*S*)-7-(Benzoyloxy)-2,2-dimethyl-9-(phenylsulfonyl)-1,3-dioxaspiro[4.5]decan-8-one (59).** A mixture of **47** (650 mg, 1.69 mmol) and sodium benzenesulfinate (418 mg, 2.54 mmol) in dimethylformamide (8 mL) was stirred for 15 h at room temperature. The solution was extracted with methylene chloride, and the extract was washed with water, dried (magnesium sulfate), and concentrated in vacuo. Purification of the residue by chromatography on silica, with ether in hexane (1:1) as eluant, gave 685 mg (91%) of pure **59**. Recrystallization from ether afforded colorless needles: mp 169−172 °C; $[\alpha]^{20}_D$ +28.1° (*c* 1.12, $CHCl_3$); IR (KBr) 2989, 2880, 1744, 1722, 1450, 1307, 1276, 1146 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 8.05 (2H, d, $J$ = 8 Hz), 8.00 (2H, d, $J$ = 8 Hz), 7.63 (1H, dd, $J$

= 8, 8 Hz), 7.54 (3H, dd, $J$ = 8, 8 Hz), 7.43 (2H, dd, $J$ = 8, 8 Hz), 5.71 (1H, dd, $J$ = 13, 7 Hz), 4.55 (1H, dd, $J$ = 13, 5 Hz), 3.98 (1H, d, $J$ = 9 Hz), 3.91 (1H, d, $J$ = 9 Hz), 2.81 (1H, ddd, $J$ = 13, 5, 4 Hz), 2.46 (1H, ddd, $J$ = 13, 7, 3 Hz), 2.24 (1H, dd, $J$ = 13, 1 Hz), 2.14 (1H, dd, $J$ = 13, 1 Hz), 1.25 (3H, s), 1.22 (3H, s); $^{13}$C NMR ($CDCl_3$) $\delta$ 194.9, 164.9, 138.0, 134.0, 133.4, 129.8, 129.6, 128.9, 128.4, 111.2, 78.1, 73.4, 73.0, 66.9, 41.4, 36.5, 27.0, 26.9; MS $m/z$ 445 ($M^+$ + 1), 444 ($M^+$), 429, 105; HRMS $m/z$ 444.1241 ($M^+$), calcd for $C_{23}H_{24}O_7S$ 444.1243. Anal. Calcd for $C_{23}H_{24}O_7S$: C, 62.15; H, 5.44. Found: C, 62.29; H, 5.40.

**(5*R*,7*R*)-7-(Benzoyloxy)-8-methoxy-2,2-dimethyl-9-(phenylsulfonyl)-1,3-dioxaspiro[4.5]dec-8-ene (60).** To a solution of **59** (92.8 mg, 0.209 mmol) in ether–ethyl acetate (2:1, 15 mL) at 0 °C was added dropwise ethereal diazomethane (10 mL). The yellow solution was stirred for 1 h and then gradually allowed to warm to room temperature. Stirring was continued for 15 h, and the mixture was evaporated under reduced pressure. The residue was purified by chromatography on silica, with ethyl acetate in hexane (1:1) as eluant, to give 94.4 mg (99%) of **60** as a colorless glass: mp 58–59 °C; $[\alpha]^{20}_D$ +72.5° ($c$ 1.40, $CHCl_3$); IR (KBr) 2986, 2943, 1722, 1642, 1305, 1265, 1147, 1084 cm$^{-1}$; $^1$H NMR ($CDCl_3$) $\delta$ 7.97 (2H, d, $J$ = 8 Hz), 7.94 (2H, d, $J$ = 9 Hz), 7.63–7.59 (2H, m), 7.53 (2H, dd, $J$ = 8, 7 Hz), 7.46 (2H, d, $J$ = 8 Hz), 5.97 (1H, t, $J$ = 5 Hz), 3.99 (1H, d, $J$ = 9 Hz), 3.78 (1H, d, $J$ = 9 Hz), 3.37 (3H, s), 3.04 (1H, d, $J$ = 17 Hz), 2.73 (1H, d, $J$ = 17 Hz), 2.40 (1H, dd, $J$ = 14, 5 Hz), 1.99 (1H, dd, $J$ = 14, 4 Hz), 1.47 (3H, s), 1.34 (3H, s); $^{13}$C NMR ($CDCl_3$) $\delta$ 165.1, 156.0, 142.2, 133.8, 133.0, 129.8, 128.8, 128.7, 128.6, 127.7, 122.8, 109.7, 77.9, 72.7, 65.5, 56.6, 38.1, 35.2, 27.5, 26.6; MS $m/z$ 443 ($M^+$ – 15), 336, 137, 125, 105, 77; HRMS $m/z$ 458.1399, calcd for $C_{24}H_{26}O_7S$ 458.1399. Anal. Calcd for $C_{24}H_{26}O_7S$: C, 62.87; H, 5.72. Found: C, 62.97; H, 5.75.

**(5*R*,7*R*)-7-Hydroxy-8-methoxy-2,2-dimethyl-9-(phenylsulfonyl)-1,3-dioxaspiro[4.5]dec-8-ene (61).** To a solution of **60** (59 mg, 0.129 mmol) in methylene chloride (3.0 mL) at 0 °C was added dropwise diisobutylaluminum hydride (1 M solution in hexane, 0.52 mL, 0.52 mmol), and the mixture was stirred for 3 h. The mixture was diluted with methylene chloride (5 mL), washed with 0.5 N hydrochloric acid, saturated sodium bicarbonate, and brine, and was dried (magnesium sulfate). Removal of the solvent and purification of the residue by chromatography on silica, with ethyl acetate in hexane (1:1) as eluant, afforded 28.2 mg (62%) of **61** as a colorless glass: mp 45–50 °C; $[\alpha]^{20}_D$ +93.9° ($c$ 1.01, $CHCl_3$); IR (KBr) 3458, 1636, 1301, 1288, 1142 cm$^{-1}$; $^1$H NMR ($CDCl_3$) $\delta$ 7.90 (2H, d, $J$ = 8 Hz), 7.59 (1H, t, $J$ = 8 Hz), 7.51 (2H, dd, $J$ = 8, 8 Hz), 4.59 (1H, t, $J$ = 6 Hz), 3.87 (1H, d, $J$ = 9 Hz), 3.83 (1H, d, $J$ = 9 Hz), 3.56 (3H, s), 2.82 (1H, d, $J$ = 17 Hz), 2.71 (1H, d, $J$ = 17 Hz), 2.26 (1H, dd, $J$ = 13, 5 Hz), 1.82 (1H, dd, $J$ = 13, 6 Hz), 1.43 (3H, s), 1.37 (3H, s); $^{13}$C NMR ($CDCl_3$) $\delta$ 160.0, 142.3, 132.9, 128.6, 127.5, 119.2, 109.4, 78.2, 72.8, 63.6, 56.6, 41.1, 35.4, 27.2, 26.8; MS $m/z$ 354 ($M^+$), 339, 247, 240, 219, 125, 123, 115, 99, 95, 77; HRMS $m/z$ 354.1137 ($M^+$), calcd for $C_{17}H_{22}O_6S$ 354.1137.

**(5*R*)-8-Methoxy-2,2-dimethyl-9-(phenylsulfonyl)-1,3-dioxaspiro[4.5]dec-8-en-7-one (62).** A mixture of **61** (121 mg, 0.342 mmol), sodium acetate (28 mg, 0.34 mmol), and pyridinium chlorochromate (221 mg, 1.03 mmol) in methylene chloride (5 mL) was stirred for 13 h at room temperature. The mixture was diluted with methylene chloride and was washed with water, dried (magnesium sulfate), and concentrated in vacuo. Purification of the residue by preparative thin layer chromatography, with ethyl acetate in hexane (1:1) as eluant, gave 71 mg (59%) of **62** as a colorless oil: $[\alpha]^{20}_D$ –9.1° ($c$ 3.55, $CHCl_3$); IR (neat) 2988, 1704, 1616, 1449, 1373, 1322, 1308, 1448, 1083 cm$^{-1}$; $^1$H NMR ($CDCl_3$) $\delta$ 7.94 (2H, d, $J$ = 7 Hz), 7.63 (1H, d, $J$ = 7 Hz), 7.54 (2H, dd, $J$ = 7, 7 Hz), 3.80 (1H, d, $J$ = 9 Hz), 3.79 (1H, d, $J$ = 9 Hz), 3.67 (3H, s), 3.18 (1H, dd, $J$ = 18, 1 Hz), 3.04 (1H, d, $J$ = 18 Hz), 2.78 (1H, dd, $J$ = 16, 1 Hz), 2.65 (1H, d, $J$ = 16 Hz), 1.37 (3H, s), 1.33 (3H, s); $^{13}$C NMR ($CDCl_3$) $\delta$ 192.6, 151.9, 140.7, 138.6, 133.8, 128.9, 128.0, 110.7, 79.4, 72.8, 60.4, 49.2, 36.3, 26.9, 26.7; MS $m/z$ 354 ($M^+$ + 2), 353 ($M^+$ + 1), 352 ($M^+$), 294, 277, 211, 154, 153, 125; HRMS $m/z$ 352.0980 ($M^+$), calcd for $C_{17}H_{20}O_6S$ 352.0981. Anal. Calcd for $C_{17}H_{20}O_6S$: C, 57.94; H, 5.72. Found: C, 58.19; H, 5.77.

**(5*S*)-9-Azido-8-methoxy-2,2-dimethyl-1,3-dioxaspiro[4.5]dec-8-en-7-one (63).** A mixture of **61** (189 mg, 0.53 mmol), pyridinium chlorochromate (346 mg, 1.60 mmol), and sodium acetate (44 mg, 0.53 mmol) in methylene chloride (20 mL) was stirred for 15 h at room temperature. The mixture was extracted with methylene chloride, and the extract was washed with water, dried (magnesium sulfate), and concentrated in vacuo. The resulting crude ketone **62** (174 mg), sodium azide (172 mg, 2.65 mmol), and lithium chloride (2.0 mg, 0.05 mmol) were dissolved in dimethylformamide (6 mL), and the solution was stirred for 5 h at room temperature. The mixture was extracted with ethyl acetate, and the extract was washed with water, dried (magnesium sulfate), and concentrated in vacuo. Purification of the residue by chromatography on silica, with 30% ethyl acetate in hexane as eluant, gave 79.3 mg (59%) of **63** as a yellow oil: $[\alpha]^{20}_D$ –11.4° ($c$ 3.11, $CHCl_3$); IR (neat) 2988, 2106, 1676, 1612 cm$^{-1}$; $^1$H NMR ($CDCl_3$) $\delta$ 3.88 (1H, d, $J$ = 9 Hz), 3.82 (1H, d, $J$ = 9 Hz), 3.78 (3H, s), 2.78 (1H, d, $J$ = 16 Hz), 2.63 (2H, d, $J$ = 16 Hz), 2.56 (1H, d, $J$ = 17 Hz), 1.41 (3H, s), 1.38 (3H, s); $^{13}$C NMR ($CDCl_3$) $\delta$ 189.9, 143.2, 142.2, 110.4, 78.7, 73.0, 61.0, 48.4, 38.6, 27.0, 26.7; MS $m/z$ 253 ($M^+$), 238, 225, 167, 140, 138, 125, 108, 102, 97, 80, 72, 70. Anal. Calcd for $C_{11}H_{15}N_3O_4$: C, 52.17; H, 5.97; N, 16.59. Found: C, 51.80; H, 5.66; N, 16.71.

**Iminophosphorane 64.** To a solution of **63** (110 mg, 0.43 mmol) in ether (5 mL) was added a solution of triphenylphosphine (228 mg, 0.87 mmol) in ether (5 mL), and the mixture was stirred for 4 h at room temperature. The mixture was concentrated in vacuo and the residue was purified by chromatography on silica, with ethyl acetate in hexane (2:1) as eluant, to give 198 mg (94%) of **64** as pale yellow plates: mp 63–66 °C; $[\alpha]^{23}_D$ +32.2° ($c$ 0.60, $CHCl_3$); IR (KBr) 3384, 1740, 1615, 1609, 1559, 1550, 1546, 1543, 1403, 1386, 1223, 1134 cm$^{-1}$; $^1$H NMR ($CDCl_3$) $\delta$ 7.68–7.62 (6H, m), 7.56–7.52 (3H, m), 7.49–7.45 (6H, m), 3.86 (1H, d, $J$ = 8 Hz), 3.81 (1H, d, $J$ = 8 Hz), 2.94 (1H, d, $J$ = 16 Hz), 2.81 (3H, s), 2.80 (1H, d, $J$ = 16 Hz), 2.75 (1H, dd, $J$ = 16, 2 Hz), 2.59 (1H, dd, $J$ = 16, 2 Hz), 1.38 (3H, s), 1.37 (3H, s); $^{13}$C NMR ($CDCl_3$) $\delta$ 188.3, 157.7, 157.6, 138.8, 138.6, 132.4, 132.3, 131.9, 131.8, 131.7 (×2), 131.1, 130.5, 129.8 (×2), 128.6, 128.4 (×2), 128.3, 109.1, 79.5, 79.4, 73.1, 57.7, 48.6, 46.9, 46.7, 27.2, 26.8; MS $m/z$ 487 ($M^+$), 262, 183, 153, 135, 126, 109, 108, 107; HRMS $m/z$ 487.1909, calcd for $C_{29}H_{30}NO_4P$ 487.1912. Anal. Calcd for $C_{29}H_{30}NO_4P$: C, 71.44; H, 6.20; N, 2.87. Found: C, 71.26; H, 6.08; N, 2.53.

**Mycosporin-gly Methyl Ester Acetonide (66).** A mixture of **64** (150 mg, 0.308 mmol) and freshly distilled methyl glyoxylate (555 mg, 6.30 mmol) in tetrahydrofuran (10 mL) was stirred for 6 h at room temperature. To the resulting orange solution was added a solution of sodium cyanoborohydride (447 mg, 7.0 mmol) in methanol (5 mL), and stirring was continued for 1.5 h. The mixture was concentrated, and the residue was chromatographed on silica, with ethyl acetate as eluant, to give 54 mg (59%) of **66** as colorless crystals: mp 168–171 °C; $[\alpha]^{23}_D$ –5.8° ($c$ 1.2, $CHCl_3$); IR (KBr) 3312, 1753, 1601, 1536, 1435, 1256, 1206, 1139 cm$^{-1}$; $^1$H NMR ($CDCl_3$) $\delta$ 5.70 (1H, br), 4.02 (2H, d, $J$ = 6 Hz), 3.90 (1H, d, $J$ = 9 Hz), 3.83 (1H, d, $J$ = 9 Hz), 3.80 (3H, s), 3.69 (3H, s), 2.77 (1H, d, $J$ = 16 Hz), 2.70 (1H, d, $J$ = 16 Hz), 2.59 (1H, d, $J$ = 16 Hz), 2.58 (1H, d, $J$ = 16 Hz), 1.42 (3H, s), 1.37 (3H, s); $^{13}$C NMR ($CDCl_3$) $\delta$ 186.2, 169.9, 150.5, 132.6, 109.9, 79.1, 77.2, 73.4, 59.5, 52.7, 47.5, 44.2, 27.5, 26.5; MS $m/z$ 299 ($M^+$), 214, 169, 148, 137, 136, 135, 109, 78, 73; HRMS $m/z$ 299.1368 ($M^+$), calcd for $C_{14}H_{21}NO_6$ 299.1369. Anal. Calcd for $C_{14}H_{21}NO_6$: C, 56.18; H, 7.07; N, 4.68. Found: C, 55.86; H, 6.90; N, 4.51.

**Mycosporin-gly Methyl Ester (67).** To a solution of **66** (11.0 mg, 0.04 mmol) in chloroform (1.0 mL) at 0 °C was added 50% aqueous trifluoroacetic acid (0.3 mL), and the solution was stirred for 20 min. The mixture was evaporated under reduced pressure, and the residue was subjected to preparative thin layer chromatography, with chloroform–methanol (3:1) as eluant, to give 5.1 mg (54%) of **67**: mp 109–113 °C; $[\alpha]^{23}_D$ –14.7° ($c$ 0.7, $H_2O$), –11.3° ($c$ 0.23, $H_2O$); IR (KBr) 3384, 1740, 1615, 1609, 1559, 1550, 1546, 1543, 1403, 1386, 1223, 1134 cm$^{-1}$; $^1$H NMR ($D_2O$) $\delta$ 4.26 (2H, s), 3.81 (3H, s), 3.61 (3H, s),

3.55 (2H, s), 2.83 (1H, d, $J$ = 17 Hz), 2.72 (1H, d, $J$ = 17 Hz), 2.66 (1H, d, $J$ = 17 Hz), 2.45 (1H, dd, $J$ = 17, 1 Hz), ; $^{13}$C NMR ($D_2O$) $\delta$ 189.0, 174.2, 160.1, 132.6, 74.0, 69.5, 61.2, 54.9, 45.8, 45.1, 34.5; MS $m/z$ 260 ($M^+$ + 1), 259 ($M^+$), 244, 241, 230, 228, 226, 212, 200, 198, 186, 182, 168, 167, 166, 154, 152, 140, 138; HRMS $m/z$ 259.1056, calcd for $C_{11}H_{17}NO_6$ 259.1056. The IR and $^1$H NMR data were identical to those recorded on **67** derived from a natural sample of mycosporin-gly (**13**).

**Mycosporin-gly Benzyl Ester Acetonide (68).** To a solution of **64** (118 mg, 0.242 mmol) in tetrahydrofuran (4 mL) was added a solution of benzyl glyoxylate (1.00 g, 6.10 mmol) in tetrahydrofuran (8 mL), and the mixture was stirred for 7 h at room temperature. To the resulting yellow solution was added dropwise a solution of sodium cyanoborohydride (25 mg, 0.40 mmol) in methanol (2 mL), and stirring was continued for 1 h. The mixture was concentrated under reduced pressure and the residue was chromatographed on silica, with ethyl acetate as eluant, to yield 52 mg (57%) of **68**: mp 141–143 °C; $[\alpha]^{23}_D$ −2.6° ($c$ 1.16, $CHCl_3$); IR (KBr) 3312, 1750, 1602, 1535, 1435, 1367, 1212, 1187, 1166, 1138 cm$^{-1}$; $^1$H NMR ($CDCl_3$) $\delta$ 7.36 (5H, s), 5.71 (1H, br), 5.20 (2H, s), 4.03 (2H, d, $J$ = 6 Hz), 3.84 (1H, d, $J$ = 9 Hz), 3.81 (1H, d, $J$ = 9 Hz), 3.65 (3H, s), 2.73 (1H, d, $J$ = 16 Hz), 2.66 (1H, d, $J$ = 16 Hz), 2.54 (2H, d, $J$ = 16 Hz), 1.38 (3H, s), 1.35 (3H, s); $^{13}$C NMR ($CDCl_3$) $\delta$ 186.1, 169.3, 150.5, 134.7, 132.5, 128.8, 128.7, 128.6, 109.8, 79.0, 72.3, 67.6, 59.4, 47.5, 44.4, 36.1, 27.4, 26.5; HRMS $m/z$ 375.1682 ($M^+$), calcd for $C_{20}H_{25}NO_6$ 375.1682. Anal. Calcd for $C_{20}H_{25}NO_6$: C, 63.99; H, 6.71; N, 3.73. Found: C, 63.98; H, 6.73; N, 3.52.

**Mycosporin-gly Benzyl Ester (69).** A mixture of **68** (28.0 mg, 0.075 mmol) and 50% aqueous trifluoroacetic acid in chloroform (1 mL) was stirred for 50 min at 0 °C. The mixture was concentrated under reduced pressure, and the residue was dissolved in methanol (1 mL). Triethylamine (50 mg) was added and after 5 min the mixture was evaporated in vacuo. The residue was chromatographed on silica, with 10% methanol in chloroform as eluant, to give 24.0 mg (96%) of **69** as a colorless foam: $[\alpha]^{23}_D$ +6.6° ($c$ 2.3, $CHCl_3$); IR (neat) 3381, 1743, 1625, 1570, 1553, 1538, 1404, 1195, 1138 cm$^{-1}$; $^1$H NMR ($CDCl_3$) $\delta$ 7.35 (5H, s), 6.07 (1H, m), 5.18 (2H, s), 4.07 (2H, d, $J$ = 6 Hz), 3.59 (3H, s), 3.47 (2H, s), 2.58 (2H, s), 2.48 (2H, s); $^{13}$C NMR ($CDCl_3$) $\delta$ 187.0, 169.8, 152.6, 134.9, 131.5, 128.7, 128.5, 77.2, 72.2, 68.6, 67.5, 59.3, 45.0, 44.4, 33.7; MS $m/z$ 335 ($M^+$), 317, 182, 167, 166, 91, 79, 77, 73; HRMS $m/z$ 335.1370, calcd for $C_{17}H_{21}NO_6$ 335.1369.

**Mycosporin-gly (13).** A mixture of **69** (8.7 mg, 0.027 mmol) and 10% palladium on carbon (7.7 mg) in methanol (3 mL) was stirred under hydrogen (1 atm) for 6 h. The mixture was filtered, and the filtrate was evaporated. The residue was purified by preparative thin layer chromatography to give 3.9 mg (58%) of **13** as a colorless foam: $[\alpha]^{23}_D$ + 5.1° ($c$ 0.39, MeOH); $^1$H NMR ($D_2O$) $\delta$ 4.16 (2H, s), 3.62 (3H, s), 3.56 (2H, s), 2.85 (1H, d, $J$ = 17 Hz), 2.73 (1H, d, $J$ = 17 Hz), 2.69 (1H, d, $J$ = 17 Hz), 2.45 (1H, d, $J$ = 17 Hz). Treatment of **13** with an ethereal solution of diazomethane gave **67**, identical in all respects with material prepared from **66**.

**Diester 70.** A mixture of **64** (44.0 mg, 0.090 mmol) and diethyl ketomalonate (79.0 mg, 0.451 mmol) in ether (5.0 mL) was refluxed for 2 h. After the mixture had cooled to room temperature, a solution of sodium cyanoborohydride (10 mg, 0.16 mmol) in methanol (1 mL) was added, and stirring was continued for 1.5 h. The mixture was concentrated, and the residue was purified by preparative layer chromatography, with ethyl acetate as eluant, to provide 25.4 mg (73%) of **70** as a pale yellow oil: $[\alpha]^{23}_D$ +0.6° ($c$ 2.3, $CHCl_3$); IR (neat) 3383, 2985, 1756, 1740, 1593 cm$^{-1}$; $^1$H NMR ($CDCl_3$) $\delta$ 5.95 (1H, br), 4.85 (1H, d, $J$ = 18 Hz), 4.32 (2H, q, $J$ = 7 Hz), 4.31 (2H, q, $J$ = 7 Hz), 3.90 (1H, d, $J$ = 9 Hz), 3.81 (1H, d, $J$ = 9 Hz), 3.69 (3H, s), 2.77 (1H, d, $J$ = 16 Hz), 2.72 (1H, d, $J$ = 16 Hz), 2.61 (1H, dd, $J$ = 16, 1 Hz), 2.56 (1H, dd, $J$ = 16, 1 Hz), 1.42 (3H, s), 1.37 (3H, s), 1.33 (3H, t, $J$ = 7 Hz), 1.32 (3H, t, $J$ = 7 Hz); $^{13}$C NMR ($CDCl_3$) $\delta$ 187.0, 166.2, 166.0, 148.0, 133.0, 109.8, 79.0, 73.1, 62.9 (×2), 59.5, 59.0, 47.6, 33.4, 27.3, 26.4, 13.9 (×2); MS $m/z$ 386 ($M^+$ + 1), 385 ($M^+$), 370, 312, 284, 254, 238, 226, 210, 180, 150, 138; HRMS $m/z$ 385.1736 ($M^+$), calcd for $C_{18}H_{27}NO_8$ 385.1737. Anal. Calcd for $C_{18}H_{27}NO_8$: C, 56.10; H, 7.06; N, 3.63. Found: C, 55.94; H, 6.99; N, 3.61.

**Mycosporin I (2).** To a solution of **70** (20.2 mg, 0.053 mmol) in methanol–water (5:1, 7 mL) at 0 °C was added sodium borohydride (11.9 mg, 0.314 mmol). The mixture was stirred for 3 h, 50% aqueous trifluoroacetic acid (1 mL) was added, and the mixture was stirred for a further 20 min at 0 °C. The solution was concentrated in vacuo and the residue was purified by preparative thin layer chromatography on silica, with 25% methanol in chloroform as eluant. A final purification was carried out by reverse-phase preparative TLC, with 20% methanol in water as eluant, to give 8.1 mg (59%) of **2**: IR (KBr) 1615, 1556, 1540 cm$^{-1}$; $^1$H NMR ($D_2O$) $\delta$ 3.88 (1H, m), 3.78 (2H, dd, $J$ = 12, 4 Hz), 3.68 (2H, ddd, $J$ = 12, 12, 7 Hz), 3.61 (3H, s), 3.57 (2H, s), 2.93 (1H, d, $J$ = 17 Hz), 2.83 (1H, d, $J$ = 17 Hz), 2.71 (1H, d, $J$ = 17 Hz), 2.43 (1H, d, $J$ = 17 Hz); $^{13}$C NMR ($D_2O$) $\delta$ 187.9, 160.6, 132.3, 74.1, 69.5, 63.2, 63.1, 61.0, 58.6, 44.9, 35.3; MS $m/z$ 262 ($M^+$ + 1), 250, 129, 125, 121; HRMS $m/z$ 261.1211, calcd for $C_{11}H_{19}NO_6$ 261.1212.

**Mycosporin I Bis(acetonide) (73). A. From Synthetic 2.** A mixture of **2** (12.0 mg, 0.040 mmol), 2,2-dimethoxypropane (0.5 mL), and pyridinium $p$-toluenesulfonate (1.9 mg, 0.01 mmol) in acetone (0.5 mL) was stirred for 3 d at room temperature. The mixture was diluted with water (25 mL) and extracted with ethyl acetate (2 × 30 mL), and the combined extracts were washed with brine, dried (magnesium sulfate), and concentrated in vacuo. The residue was chromatographed on silica and further purified by preparative layer chromatography, with ethyl acetate as eluant, to give 6.3 mg (40%) of **73** as an oil: $[\alpha]^{23}_D$ −2.4° ($c$ 0.63, $CHCl_3$); IR (neat) 3584, 1576, 1198, 1078 cm$^{-1}$; $^1$H NMR ($CDCl_3$) $\delta$ 5.99 (1H, br), 4.11 (2H, ddd, $J$ = 12, 9, 3 Hz), 3.85 (1H, dd, $J$ = 12, 9 Hz), 3.72 -3.60 (2H, m), 3.69 (3H, s), 3.45 (2H, m), 2.77 (1H, d, $J$ = 16 Hz), 2.71 (1H, d, $J$ = 16 Hz), 2.60 (1H, d, $J$ = 16 Hz), 2.56 (1H, d, $J$ = 16 Hz), 1.47 (3H, s), 1.44 (3H, s), 1.42 (3H, s), 1.36 (3H, s); $^{13}$C NMR ($CDCl_3$) $\delta$ 132.5, 109.9, 98.7, 88.5, 79.1, 77.4, 77.0, 73.4, 64.0, 63.9, 59.4, 47.4, 46.3, 28.5, 27.5, 26.4, 20.7. Anal. Calcd for $C_{17}H_{27}NO_6$: C, 59.81; H, 7.97; N, 4.10. Found: C, 59.69; H, 8.22; N, 4.29.

**B. From Natural 2.** A mixture of natural mycosporin I (7.1 mg, 0.027 mmol), 2,2-dimethoxypropane (0.5 mL), and pyridinium $p$-toluenesulfonate (2.0 mg, 0.01 mmol) in acetone (1.0 mL) was stirred for 3 d at room temperature. Workup and purification as described above yielded 4.1 mg (44%) of **73** as an oil: $[\alpha]^{23}_D$ −3.8° ($c$ 0.32, $CHCl_3$). Spectral properties were identical to those recorded on material prepared from synthetic **2**.

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