

Total Synthesis of the Boron-Containing Ion Carrier Antibiotic Macrodiolide Tartrolon B

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The first total synthesis of the boron-containing macrodiolide antibiotic tartrolon B is reported in full detail. Two convergent approaches to the target compound are described, the first of which eventually failed, due to sensitive functionality. In the second, successful route the key step was a stereoselective boron-mediated aldol addition of a bicyclic acetonide protected ketone to a diene-aldehyde. In this case the synthesis could be completed without major problems, using a Yamaguchi dimerization macrolactonization endgame.

Introduction

Over the past decade we have been interested in the total synthesis of structurally complex macrolides for different reasons.¹ One reason was that the molecular architecture of these compounds poses a challenge to the synthetic chemist; another reason was the enormous potential of many of these compounds as potential drugs, for instance as antibiotics or in tumor therapy. As an example, we gave a full account of the first total synthesis of tartrolon A and B,² which are ion carrier antibiotics of high activity.

The tartrolons were first isolated in 1994 by Höfle and Reichenbach from *Myxobacterium Sorangium cellulosum* strain So ce678.³ The fermentation furnishes tartrolon A (**2**) or B (**1**) (Figure 1) depending on the fermentation vessel. Glass vessels provide boron and hence allow the formation of **1**, whereas in steel fermenters the boron-free compounds **2** are formed as diastereomeric mixtures. Alternatively, the boron can be incorporated into **2** chemically. This leads to a fixation of the variable stereogenic center at C2 and forces **1** into a C_2 -symmetrical structure. The absolute and relative configuration of tartrolone B has been clarified by a single-crystal diffraction analysis⁴ of the potassium derivative (figure in the Supporting Information). In this structure the environment of both the boron and the potassium is remarkable, as both atoms are close together, in form of an inner ion pair. Boron forms a tetrahedral and potassium an octahedral complex with macrolide oxygens. The

C-2-OHs are shared by both coordination spheres. Another interesting feature is the planar conformation of the *E,Z*-diene section, which makes the surface of the molecule lipophilic. All oxygens are turned inside, to make the core region strongly hydrophilic. In this way the molecule appears optimized for carrying an ion through a lipophilic membrane. In fact both tartrolon A and B act as ion carriers and they are both active against Gram positive bacteria with MIC values of 1 $\mu\text{g/mL}$. This means that the presence of the boron is not required for the antibiotic activity.

Tartrolon is structurally related to the antibiotics boromycin,⁵ aplasmomycin,⁶ and borophycin⁷ which are all feature a very similar C-1-C-7-region, possibly the pharmacophore of the compounds (Figure 2). In contrast to tartrolon, these antibiotics all exist only with the boron core. Boromycin and aplasmomycin were both synthesized a while ago, whereas no attempt toward synthesizing borophycin has yet been made.

First-Generation Retrosynthesis

In view of the C_2 -symmetrical overall structure of the target compounds our first retrosynthetic plan aimed for a cyclodimerization of the monomeric seco acid **3** under Yamaguchi macrolactonization conditions (Scheme 1). For the synthesis of **3** an aldol-type addition of ketone **5** to aldehyde **4** was envisaged as the key step. This kind

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(1) Erythronolide B: Mulzer, J.; Kirstein, H. M.; Buschmann, J.; Lehmann, Ch.; Luger, P. *J. Am. Chem. Soc.* **1991**, *113*, 910. Epothilone B: Mulzer, J. *Chem. Mon.* **2000**, 205. Laulimalide: Mulzer, J.; Oehler, E. *Chem. Rev.* **2003**, *103*, 3753.

(2) Earlier reports: Mulzer, J.; Berger, M. *Tetrahedron Lett.* **1998**, *39*, 803–806. Mulzer, J.; Berger, M. *J. Am. Chem. Soc.* **1999**, *121*, 8393.

(3) (a) Schummer, D.; Irschik, H.; Reichenbach, H.; Höfle, G. *Liebigs Ann. Chem.* **1994**, 283. (b) Irschik, H.; Schummer, D.; Gerth, K.; Höfle, G.; Reichenbach, H. *J. Antibiot.* **1995**, *48*, 26.

(4) Schummer, D.; Schomburg, D.; Irschik, H.; Reichenbach, H.; Höfle, G. *Liebigs Ann. Chem.* **1996**, 965.

(5) (a) Hüter, R.; Keller-Schierlein, W.; Knüsel, F.; Prelog, V.; Rodgers, G. C.; Suter, P.; Vogel, G.; Zähler, H. *J. Antibiot.* **1967**, *20*, 1533. (b) Dunitz, J. D.; Hawley, D. M.; Miklos, D.; White, D. N. J.; Berlin, Y.; Marusic, R.; Prelog, V. *Helv. Chim. Acta* **1971**, *54*, 1709. Synthesis following that in: White, J. D.; Avery, M. A.; Choudhry, S. C.; Dhingra, O. P.; Gray, B. D.; Kang, M.-c.; Kuo, S.-c.; Whittle, A. J. *J. Am. Chem. Soc.* **1989**, *111*, 790.

(6) Okami, Y.; Okazaki, T.; Kitahara, T.; Umezawa, H. *J. Antibiot.* **1976**, *29*, 1019. Synthesis following that in: (a) Corey, E. J.; Pan, B.-C.; Hua, D. H.; Deardorff, D. R. *J. Am. Chem. Soc.* **1982**, *104*, 6816. (b) Corey, E. J.; Hua, D. H.; Pan, B.-C.; Seitz, S. P. *J. Am. Chem. Soc.* **1982**, *104*, 6818. (c) White, J. D.; Vedananda, T. R.; Kang, M.-c.; Choudhry, S. C. *J. Am. Chem. Soc.* **1986**, *108*, 8105.

(7) Hemscheidt, T.; Puglisi, M. P.; Larsen, L. K.; Patterson, G. M. L.; Moore, R. E.; Rios, J. L.; Clardy, J. *J. Org. Chem.* **1994**, *59*, 3467.

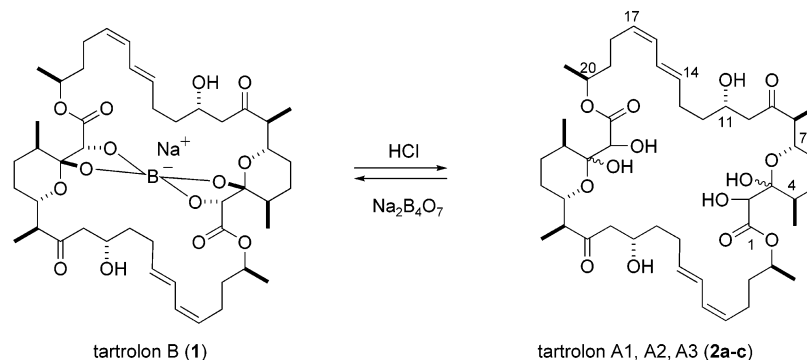


FIGURE 1. The interconversion of tartrolons A and B.

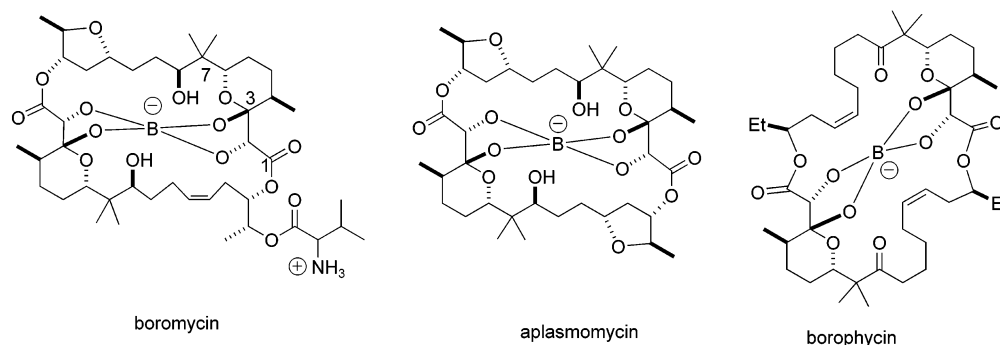
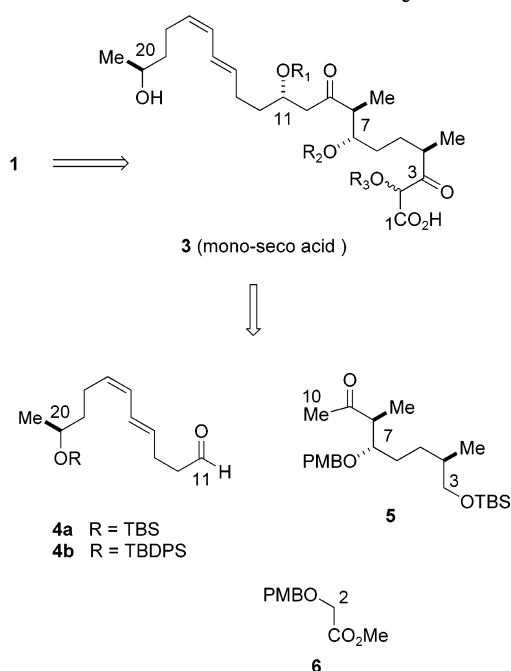


FIGURE 2. Related boron-containing macrolides.

SCHEME 1. First Generation Retrosynthesis



of aldol addition required a regioselective formation of the less substituted enolate and had to avoid the formation of the regioisomeric enolate, which would immediately lead to an elimination of the 7-alkoxy function. From literature precedence⁸ it was obvious that enolborinates were suited for this purpose; however, the stereocontrol over the newly created secondary alcohol

center had yet to be investigated. Following this aldol addition, a second one has to be used for attaching the glycol ester unit **6** to a C-3-aldehyde.

The synthesis of tartrolon **4a/b** is shown in Scheme 2a. The *E/Z*-diene moiety was to be generated stereoselectively from the corresponding *E*-ene-yne by a *Z*-selective Boland reduction.⁹ The sequence started with *O*-protected lactic ester **7**, which was reduced to the aldehyde and then subjected to a Wadsworth–Horner–Emmons olefination to generate the enoate. Hydrogenation of the double bond and reduction of the ester led to aldehyde **8**. Corey–Fuchs¹⁰ chain elongation generated alkyne **9**, which was deprotonated and after addition of lithium bromide¹¹ treated with acrolein to furnish enyne **10**. Johnson–Claisen rearrangement¹² occurred exclusively across the olefinic bond and generated the *E*-enyne-ester selectively. Cis hydrogenation⁹ of the alkyne followed by DIBAL-H reduction delivered aldehyde **4** in high overall yield (10 steps, ca. 25% overall yield).

In a second approach (Scheme 2b), aiming for the TBS derivative **4a**, aldehyde **8a** was subjected to a *Z*-selective Wittig reaction¹³ to furnish vinyl iodide **13**. Separately, 3-butyn-1-ol was *O*-tritylated and then converted to *E*-vinylstannane **14** by a free-radical-induced hydrostan-

(9) Boland, W.; Schroer, N.; Sieler, C. *Helv. Chim. Acta* **1987**, *70*, 1025.

(10) Corey, E. J.; Fuchs, P. L. *Tetrahedron Lett.* **1972**, 3769.

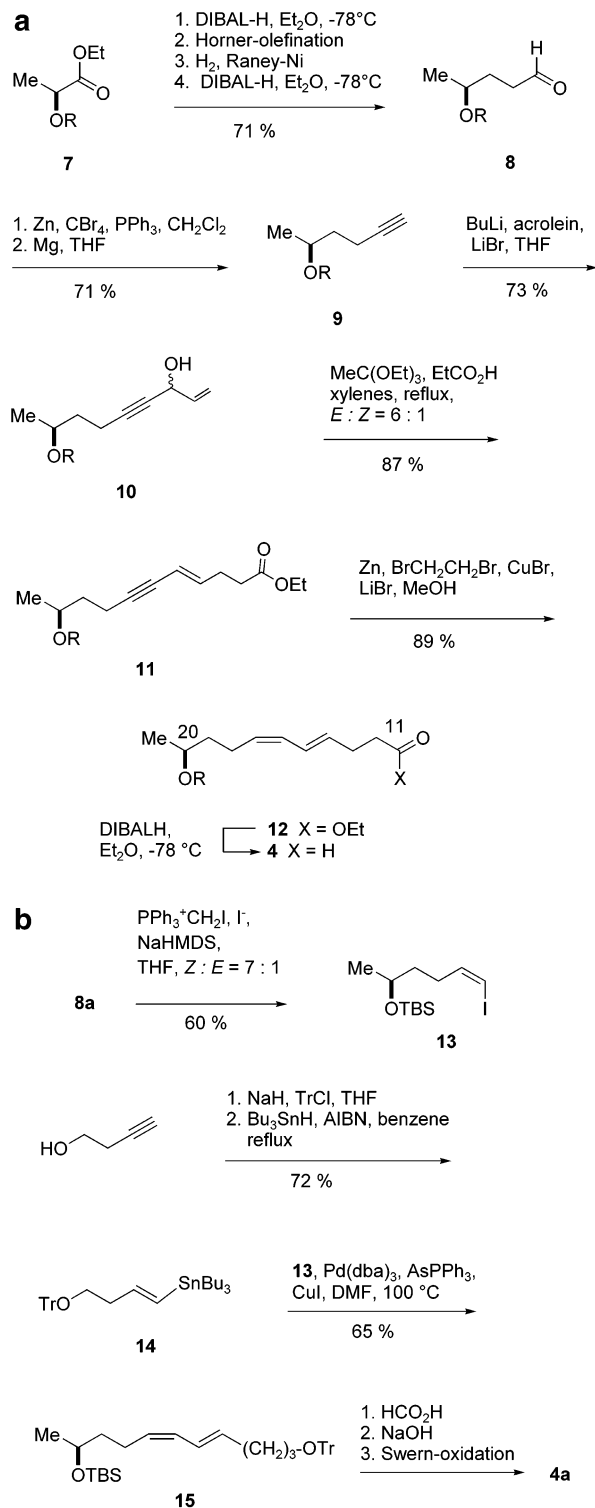
(11) (a) van Rijn, P. E.; Mommers, S.; Visser, R. G.; Verkruijse, H. D.; Brandsma, L. *Synthesis* **1981**, 459. (b) Carreira, E. M.; Du Bois, J. *J. Am. Chem. Soc.* **1994**, *116*, 10825. (c) Aerssens, M. H. P. J.; van der Heiden, R.; Heus, M.; Brandsma, L. *Synth. Commun.* **1990**, *20*, 3421.

(12) Johnson, W. S.; Werthmann, L.; Bartlett, W. R.; Brockson, T. J.; Li, T.; Faulkner, D. J.; Petersen, M. R. *J. Org. Chem.* **1970**, *35*, 741.

(13) (a) Stork, G.; Zhao, K. *Tetrahedron Lett.* **1989**, *30*, 2173. (b) Bestmann, H. J.; Rippel, H. C.; Dostalek, R. *Tetrahedron Lett.* **1989**, *30*, 5261.

(8) Cowden, C. J.; Paterson, I. *Org. React.* **1997**, *51*, 1.

SCHEME 2. (a) Synthesis of Aldehyde 4 (Series a, R = TBS; Series b, R = TBDPS) and (b) an Alternative Synthesis of Aldehyde 4a



nylation. Components **13** and **14** were connected via a Stille coupling¹⁴ with retention of the double bond configurations to form ene-yne **15**, which was then converted into aldehyde **4a**. Both routes exhibit similar Z-selectivity (6–7:1) and yield. From the practical view,

(14) Stille, J. K. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 508.

the second approach is more convergent and turned out more suitable.

Having secured appropriate quantities of aldehyde **4a/b** we turned to the synthesis of the ketone component **5**. Again, two alternative approaches were developed, which both rested on the concept that the stereogenic centers at C-4 and 8 in **5** be introduced in a configurationally unambiguous way by using commercially available methyl-2-methyl-3-hydroxypropionate (Roche's ester) in both the *R*- and the *S*-form to generate separate chiral fragments and join them to the carbon skeleton of **5**. In the first approach (Scheme 3a) *R*-ester **16** was transformed into the Weinreb amide¹⁵ **17**. On the other hand *S*-aldehyde **18** was elaborated into the lithium acetylide by a Corey–Fuchs protocol. The anion was immediately trapped with **17** to form alkynone **19** in good yield. Chiral reduction of the ketone with Alpine-borane¹⁶ gave the alcohol **20** with 80% de. After chromatographic separation the main diastereomer was hydrogenated to the 1,3-diol-derivative **21** with diimide and protected as the PMP acetal **22**.

Reduction with DIBAL-H shifted the PMB protecting group to the more hindered 7-position and liberated primary alcohol **23**, which was then converted to the methyl ketone **5** in three additional steps. Alternatively (Scheme 3b), the two *R*- and *S*-Roche-ester fragments were connected in the form of aldehyde **18** and phosphonate **25** via a Horner–Wadsworth–Emmons olefination¹⁷ to form enone **26**, which was reduced with the CBS¹⁸ reagent to the allylic alcohols **27** and **28** (ratio 9:1). Unfortunately ketone **29** (24%) was also formed by 1,4-reduction. Nevertheless, the products were easily separated and the overall yield of **27** was 65%. After hydrogenation of the olefinic bond intermediate **21** was formed and transformed into ketone **5** as before. Again both approaches were comparable with respect to selectivity and overall yield.

At this point we were able to prove the configuration at the newly created alcohol center (Scheme 4). Hence, the two diastereomers **27** and **28** were separated and converted into the cyclic acetals **22** and **30**, respectively. The ¹H NMR coupling constants and NOE experiments indicated chair conformations for both acetals. As the configuration at C-8 was known, the configuration at C-7 could be concluded from the vicinal ¹H–¹H-coupling constants. Thus, ³J_{H–7,8} was 9.9 Hz for acetal **22** and 2.2 Hz for **30**, which indicated a H–H diaxial arrangement for **22** and an axial–equatorial one for **30**.

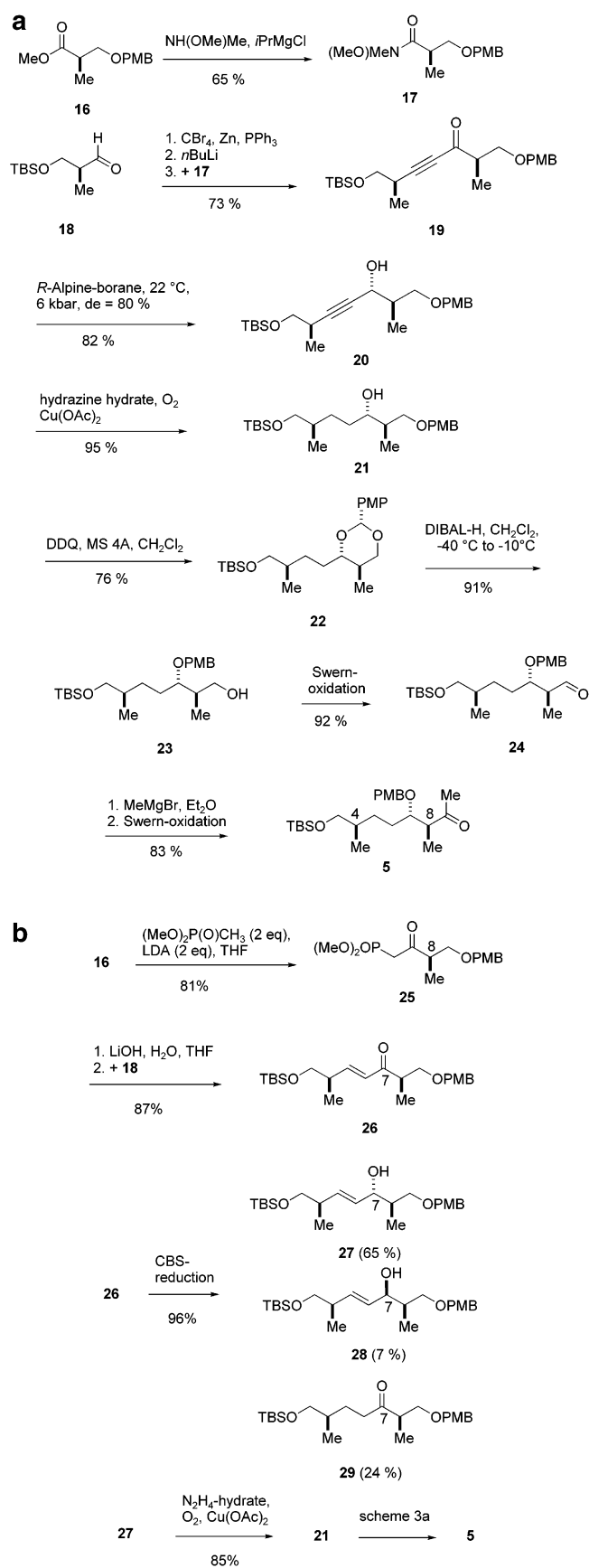
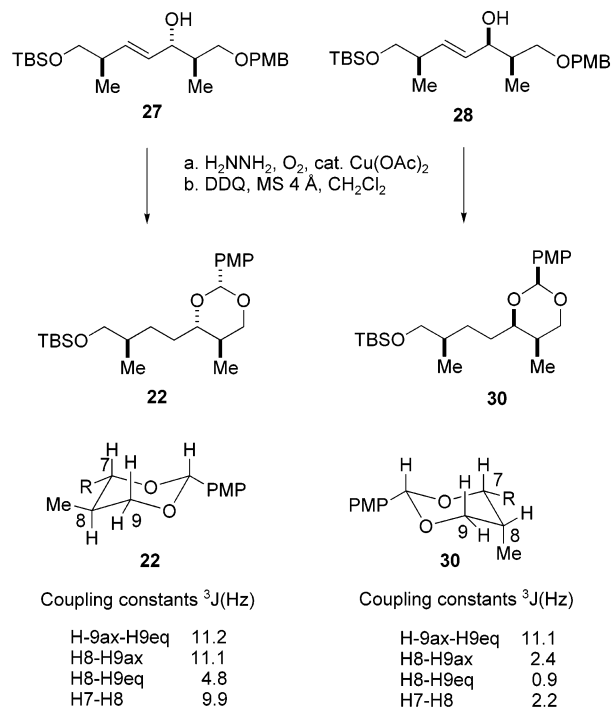
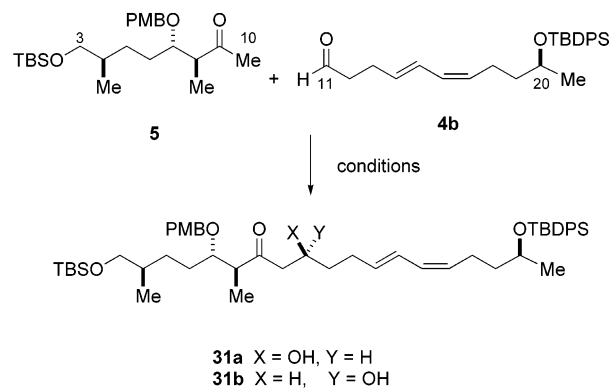
Reassured by these results we proceeded to the crucial aldol coupling between ketone **5** and aldehyde **4b** (Scheme 5). In the first experiment, ketone **5** was converted into the enolate with LDA and then treated at –78 °C for 2 min with aldehyde **4b**. The aldol addition proceeded in high yield and regioselectivity, however without any stereocontrol over the C-11-stereogenic center. We then turned to the boron-mediated enolization in the chiral

(15) Nahm, S.; Weinreb, S. M. *Tetrahedron Lett.* **1981**, *22*, 3815.

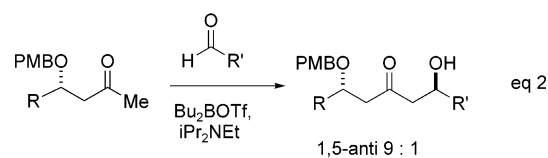
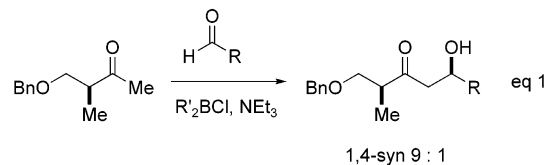
(16) (a) Midland, M. M.; McDowell, D. C.; Hatch, R. L.; Tramontano, A. *J. Am. Chem. Soc.* **1980**, *102*, 867. (b) Midland, M. M.; McLoughlin, J. I.; Gabriel, J. *J. Org. Chem.* **1989**, *54*, 153.

(17) Mulzer, J.; Martin, H. J.; List, B. *Tetrahedron Lett.* **1996**, *37*, 9177.

(18) (a) Corey, E. J.; Bakshi, R. K.; Shibata, S. *J. Am. Chem. Soc.* **1987**, *109*, 5551. (b) Review: Corey, E. J.; Helal, C. J. *Angew. Chem., Int. Ed.* **1998**, *37*, 1986.

SCHEME 3. (a) Synthesis of Ketone 5 and (b) Alternative Synthesis of Ketone 5

SCHEME 4. Structural Assignment of 27

SCHEME 5. Model Aldol Addition


Conditions	ratio 31a: 31b	yield
LDA	1 : 1	85 %
(+)-DIPCl, NEt_3	95 : 5	83 %
(-)-DIPCl, NEt_3	90 : 10	81 %

Comparison with literature data


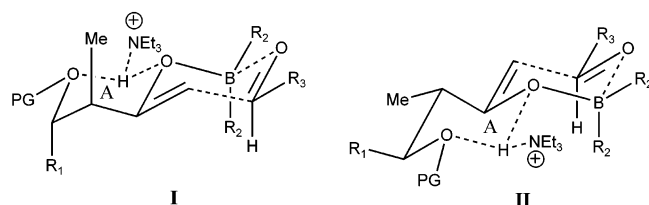


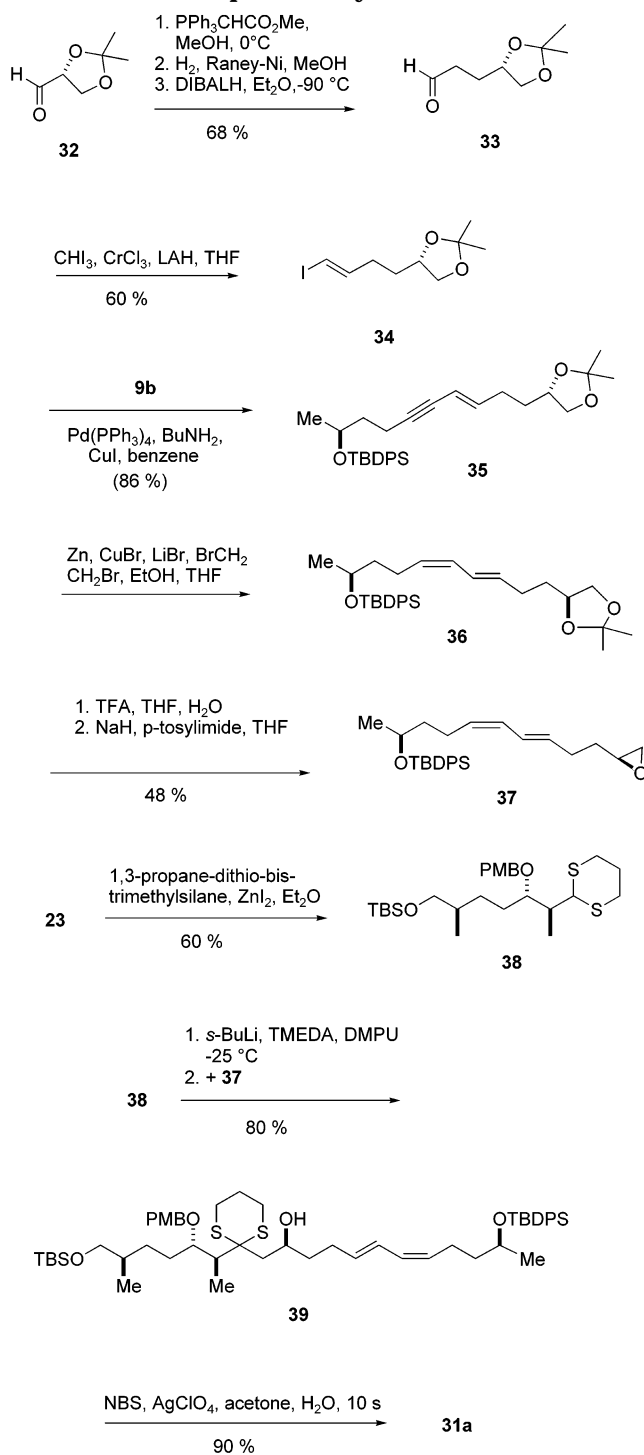
FIGURE 3. Presumable transition states of the aldol addition of ketone **5** to aldehyde **4b**.

version pioneered by Paterson¹⁹ and hoped for chiral induction from the auxiliary applied. To test the influence of the chiral additive, both enantiomers of diisopinocampheylboron chloride (DIPCL) were used. To our surprise, aldol adduct **31** was generated with high diastereomeric excess, however in about the same diastereomeric composition in both cases. This means that the reaction is not auxiliary but substrate (i.e. ketone-enolate) controlled and that the DIPCL acts via its bulk and not via its absolute configuration. Inspection of the literature revealed that in our case both the 7-*S*-alkoxide and the 8-*S*-methyl substituents in the ketone obviously cooperate to induce the 11-*S*-configuration in the adduct. For example, Evans' experiment²⁰ in eq 1 shows the influence of the methyl group, and Paterson's experiment¹⁹ in eq 2 the influence of the OPMB group. A rationalization of these findings is suggested in Figure 3.

For the aldol addition two transition state geometries **I** and **II** may be envisaged, of which **I** leads to the observed diastereomer. Both **I** and **II** represent *trans*-decalin-like geometries, with a Bronsted acid complex formed between the enolate and the protected side chain oxygens. Ring A is devoid of the normal 1,3-diaxial interactions of a cyclohexane ring; thus its stability is rather determined by the number of syn interactions, which is one less in **I** than in **II**.

Although the configuration at C-11 could be deduced from the literature precedence^{19,20} we wanted to be on the safe side and decided to synthesize aldol adduct **31a** via an alternative stereochemically unambiguous route, other than the aldol addition (Scheme 6).²¹ Hence, glyceraldehyde **32** was converted to aldehyde **33**, and then into *E*-vinyl iodide **34** via a Takai olefination.²² Castro–Sonogashira coupling²³ of **34** with acetylide **9b** led to ene-yne **35**, which was hydrogenated *Z*-selectively as before⁹ to form diene **36**. Next, the terminal acetonide was deprotected and transformed into epoxide **37** under retention of configuration. Separately, aldehyde **24** was converted into dithiane **38**, which was lithiated and treated with epoxide **37**.

SCHEME 6. Independent Synthesis of **31a**



(19) Paterson, I.; Yeung, K.-S.; Ward, R. A.; Smith, J. D.; Cumming, J. G.; Lambole, S. *Tetrahedron* **1995**, *51*, 9467. Paterson, I.; Gibson, K. R.; Oballa, R. M. *Tetrahedron Lett.* **1996**, *37*, 8585. Paterson, I.; Di Francesco, M. E.; Kuehn, T. *Org. Lett.* **2003**, *5*, 599.

(20) Evans, D. A.; Coleman, P. J.; Côté, B. *J. Org. Chem.* **1997**, *62*, 788.

(21) For a related strategy see: Smith, A. B., III; Doughty, V. A.; Lin, Q.; Zhuang, L.; McBriar, M. D.; Boldi, A. M.; Moser, W. M.; Murase, N.; Nakayama, K.; Sobukawa, M. *Angew. Chem., Int. Ed.* **2001**, *40*, 197.

(22) Takai, K.; Nitta, K.; Utimoto, K. *J. Am. Chem. Soc.* **1986**, *108*, 7408.

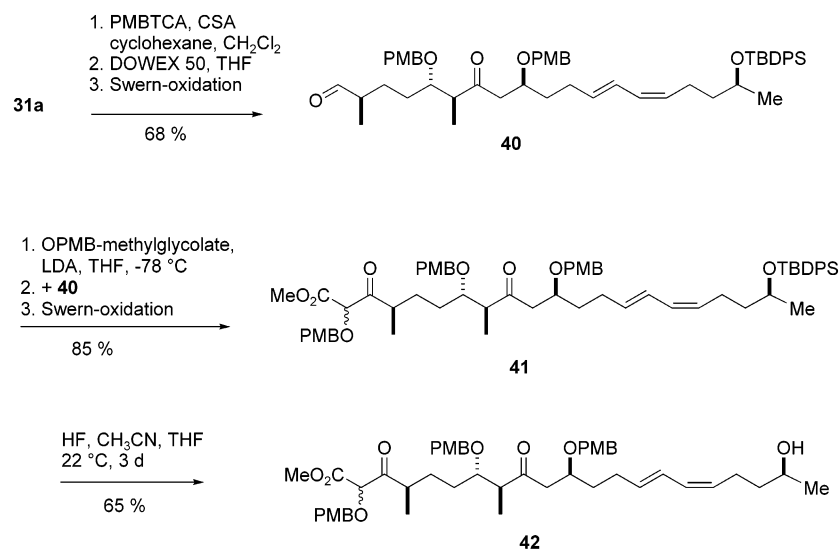
(23) (a) Sonogashira, K.; Tohda, Y.; Hagihara, N. *Tetrahedron Lett.* **1975**, *16*, 4467. (b) Stephens, R. D.; Castro, C. E. *J. Org. Chem.* **1963**, *28*, 3313.

Ring opening occurred selectively at the terminal position to form adduct **39**, which was converted into ketone **31a**. The material obtained was identical in every respect (NMR, HPLC) with compound **31a**, synthesized earlier.

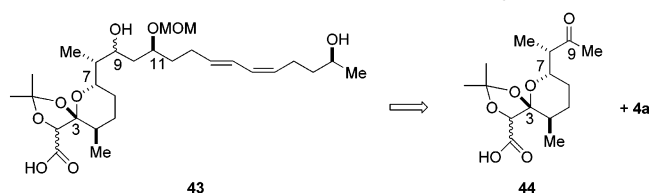
After this laborious but necessary interlude, the route to the monoseco acid **3** could be continued with confidence (Scheme 7).

Thus, intermediate **31a** was converted to aldehyde **40** and then subjected to an ester enolate aldol addition with

SCHEME 7. Synthesis of the Monoseco Acid Ester 42



SCHEME 8. Second Generation Retrosynthesis



glycolate **6**. After Swern oxidation²⁴ diketone **41** was obtained in 79% overall yield. To arrive at the desired hydroxy acid **3**, the 20-OTBDPS group had to be removed, and the methyl ester had to be hydrolyzed. The first operation was successful and provided us with hydroxy ester **42**, whose saponification, however, failed under a variety of conditions, all of which resulted in extensive decomposition of the material. In the end, we realized that this route was not viable, and we decided to reconsider our overall approach.

Second-Generation Synthesis

Obviously, the seco acid in its original form suffered from the lability of its β -keto-ester moiety, which made it prone to decarboxylation. On looking at the final functionalization in the tartrolons we realized that a more appropriate precursor would be a bicyclic acetal structure²⁵ such as **43**, which was very similar to the corresponding section in the natural products (Scheme 8). To tame the molecule even more we also replaced the 9-carbonyl by a hydroxyl group that could be oxidized in a later step. So, our new candidate for the seco acid derivative was **43** in place of the previous intermediate **3**. Still, we trusted our aldol strategy for preparing **43**, which meant that we could use aldehyde **4a** unchanged, whereas the ketone component now had to be synthesized in the form of the diketal derivative **44** (Scheme 9). Instead of returning to the procedure developed for the synthesis of **5**, we decided to test some new and hopefully

more concise methodology. Hence, “Roche’s ester” was homologated to known²⁶ ester **45** and reduced to aldehyde **46**. A Duthaler–Hafner crotylation²⁷ was used to form olefin **47** with >95% relative and absolute stereocontrol. Protecting group manipulation led to **48**, which was oxidized to aldehyde **49** and then treated with the enolate of 2-OTHP-methyl-glycolate. Aldol adduct **50** was formed as a mixture of diastereomeric alcohols. Swern oxidation led to ketone ester **51**, which was converted via Wacker oxidation²⁸ to diketone **52** in high yield. Now the stage was set for the acetalization, which was efficiently performed in two steps. First the THP groups were removed, and then acetone was added under strongly acidic conditions to generate the desired ketone ester acetal **44** in acceptable yield. Encouraged by these findings we performed the aldol addition of ketone **44** to aldehyde **4a** as before and obtained adduct **53** with a 4:1 diastereoselectivity (Scheme 10). This selectivity, which was significantly lower than the one for the model system, might be interpreted in terms of the new complexes **I'** and **II'** (Figure 4), of which again **I'** leads to the observed adduct. However, compared to the previous structure **I**, the annulation of an additional *cis*-decalin ring destabilizes **I'** and reduces the energy difference between **I'** and **II'**.

At this point we decided to rely on our earlier precedence for stereochemical assignment and to proceed without any stringent proof of the configuration at C-11 (Scheme 11). Hence, **53** was protected as the MOM-ether **54**, and the problematic 9-ketone was reduced to the alcohol **55**, from which monoseco acid **57** was prepared by successive desilylation and ester hydrolysis, now without any problems. The attempt to obtain the diolide **62** from the monomer **57** by a dimerization–cyclization sequence under Yamaguchi conditions²⁹ in one pot failed.

(26) Andrus, M. B.; Schreiber, S. L. *J. Am. Chem. Soc.* **1993**, *115*, 10420.

(27) Hafner, A.; Duthaler, R. O.; Marti, R.; Rihs, G.; Rothe-Streit, P.; Schwarzenbach, F. *J. Am. Chem. Soc.* **1992**, *114*, 2321.

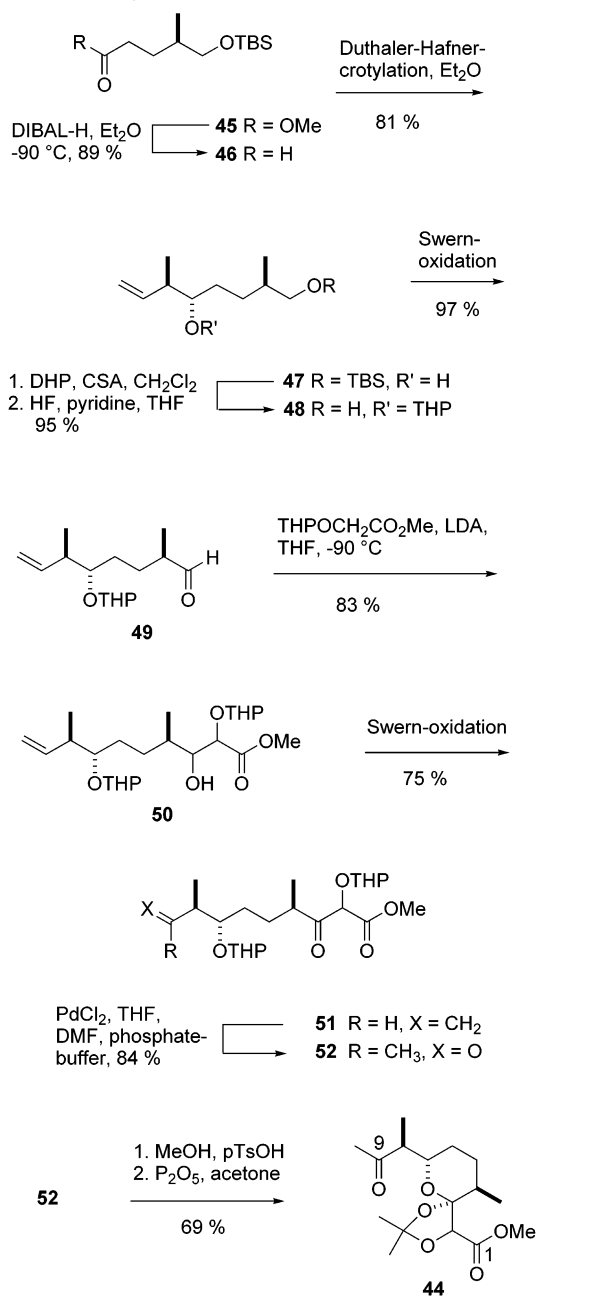
(28) Tsuji, J. *Synthesis* **1984**, 369.

(29) Inanaga, I.; Hirata, K.; Saeki, H.; Katsuki, T.; Yamaguchi, M. *Bull. Chem. Soc. Jpn.* **1979**, *52*, 1989.

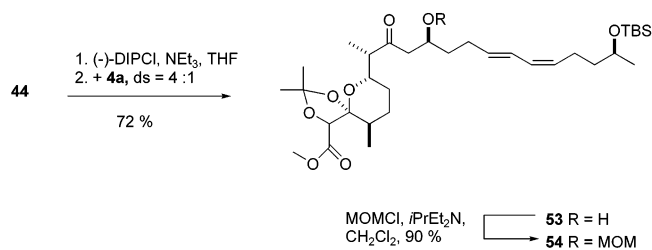
(24) Mancuso, A. J.; Swern, D. *Synthesis* **1981**, 165.

(25) Cf.: (a) Adams, M. A.; Duggan, A. J.; Smolanoff, J.; Meinwald, J. *J. Am. Chem. Soc.* **1979**, *101*, 5364. (b) Ireland, R. E.; Highsmith, T. K.; Gegnas, L. D.; Gleason, J. L. *J. Org. Chem.* **1992**, *57*, 5071.

SCHEME 9. Synthesis of Ketone 44



SCHEME 10. Aldol Addition of Aldehyde 4a and Ketone 44



Instead the monomacrolactone **58** was obtained in high yield, along with small amounts of the diolide **62**.

Nevertheless, this experiment gave us the information that the 9-OH was not involved in the macrolactonization, and hence did not need to be protected. Therefore

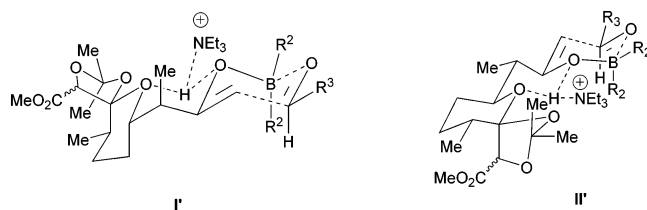
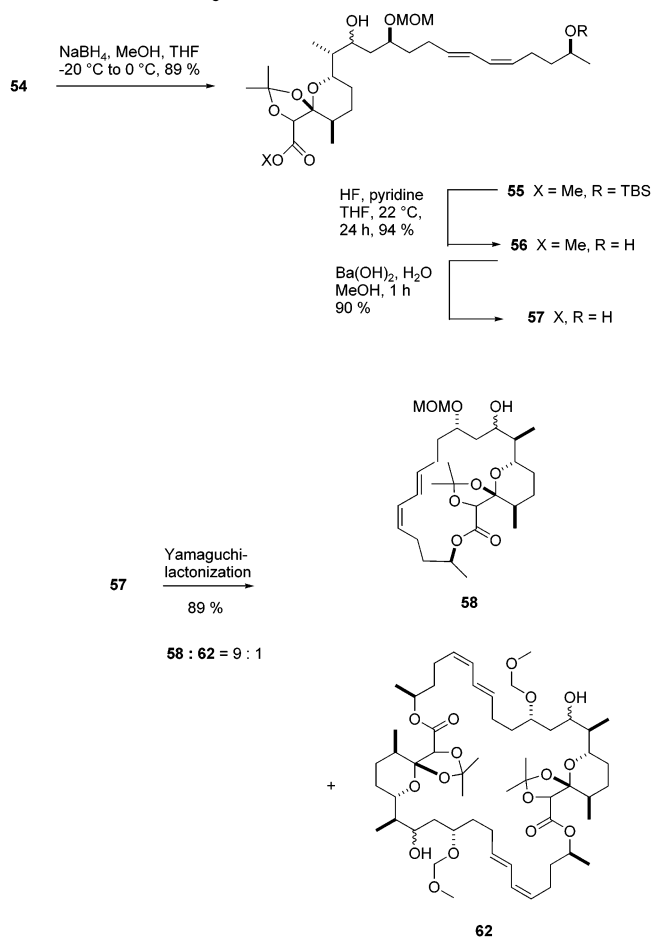


FIGURE 4. Presumable transition states of the aldol addition of ketone **44** to aldehyde **4a**.

SCHEME 11. Attempted Dimerization–Cyclization of Monoseco Acid 57



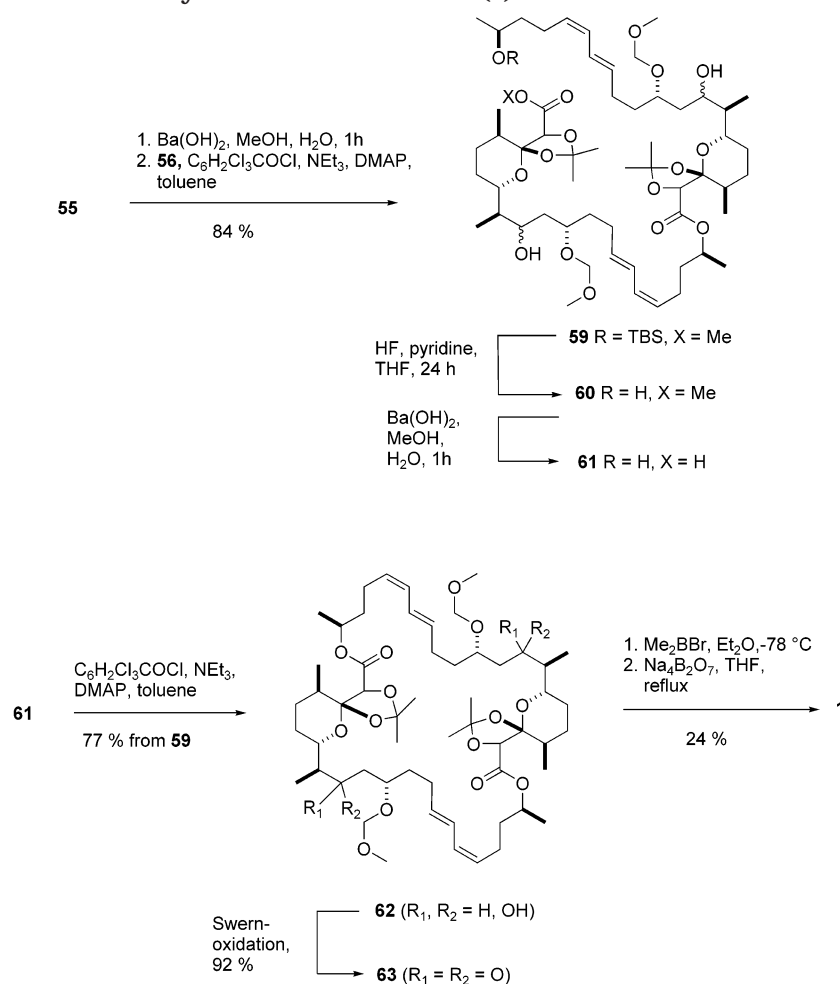
(Scheme 12), ester **55** was saponified to the acid, which was esterified with hydroxyester **56** to obtain dimer **59**. The macrolactonization of **59** to **62** had now to be performed without touching the ester function already present. First, the TBS group was removed, and then the methyl ester was hydrolyzed with barium hydroxide in methanol³⁰ to generate seco acid **61**, which was macrolactonized under Yamaguchi conditions to furnish **62**.

Reoxidation of the free 9-OH groups to the ketones and removal of the acetonide and MOM protective groups with dimethylboron bromide³¹ gave a mixture of the tartrolon A diastereomers, which were converted in tartrolon B with Borax under the conditions described

(30) Paterson, I.; Yeung, K.-S.; Ward, J. D.; Cumming, J. G.; Smith, J. D. *J. Am. Chem. Soc.* **1994**, *116*, 9391.

(31) Guindon, Y.; Yoakim, C.; Morton, H. E. *J. Org. Chem.* **1984**, *49*, 3912.

SCHEME 12. Completion of the Synthesis of Tartrolon B (1)



by Höfle et al.³ To our delight the material obtained proved to be identical with the authentic compound with respect to the ¹H and ¹³C NMR spectra (Supporting Information) as reported by Höfle.³²

Conclusion

In the end, we achieved the first total synthesis of tartrolon B in about 20 steps along the longest linear route, based on the known ester **45**. A key step had been the aldol addition between ketone **44** and the aldehyde **4a**, which proceeded in good yield and reasonable diastereoselectivity. Another interesting point was the ready formation of the 21-membered macrolide monomer **58** under Yamaguchi lactonization conditions. Apart from this we were struck by the fact that the first approach failed so completely. On the other hand, seemingly little modification was necessary for the second route. Success

(32) We thank Prof. G. Höfle for kindly providing us authentic samples of tartrolon B.

and failure were closely tied in this synthesis, and we learned a lesson about the importance of tactics in total synthesis, once the basic strategy has been fixed.

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Supporting Information Available: Experimental procedures and characterization data for all new compounds, ¹H and ¹³C NMR spectra and crystal structure of compound **1**, and ¹H NMR spectra of compounds **41** and **54**. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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