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Synthesis of the monomeric counterpart of Marinomycin A and B†

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The synthesis of polyketide natural products has been a captivating pursuit in organic chemistry, with a particular focus on selectively introducing 1,3-polyol units. Among these natural products, Marinomycins A–D have garnered substantial interest due to their exceptional structural features and potent cytotoxicity. In this paper, we present a novel approach for synthesising the monomeric counterparts of Marinomycin A and B. Our method employs a previously established iterative cycle in conjunction with a standardised polyketide building block. Through this strategy, we showcase a promising pathway towards total and partial syntheses of these intriguing natural products.

Introduction

The Marinomycins, a family of four compounds referred to as Marinomycin A–D (**1–4**, Fig. 1), were initially discovered in 2006 by Fenical *et al.* from a marine actinomycete, *Marinospora*, on the coast of La Jolla, California.[1] These compounds have shown antibiotic properties against methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant *Enterococcus faecium* (VREF), with MIC values ranging from 0.1 to 0.6 μM, as well as potent anti-cancer activity against NCI's 60 cancer cell line panel, with LC_{50} values ranging from 0.2 to 2.7 μM, displaying especially high selectivity against six of the eight melanoma cell lines.[1] Marinomycin A, B, and C share a similar structure, differing only in the conformation of the double bond adjacent to the aromatic cores (Δ_{8-9}), while Marinomycin D possesses one extra carbon in its backbone. Notably, the macrocycles Marinomycin A (**1**) and B (**2**) feature a unique structural motif with a *C*2 symmetry. Fenical *et al.* demonstrated that under ambient light irradiation, a solution of pure Marinomycin A in methanol undergoes complete isomerisation at double bond Δ_{8-9}, forming a mixture of Marinomycins A–C in less than an hour. Harsh UV irradiation, as shown by Evans, Mackenzie, and Goss in 2019, vastly accelerates the isomerisation process of Marinomycins A–D to below 60 seconds, while encapsulation can extend its half-life.[2] The process of isomerisation as well as its complex macrocyclic polyketide structure make the synthesis of Marinomycin natural products a rather challenging task.[1]

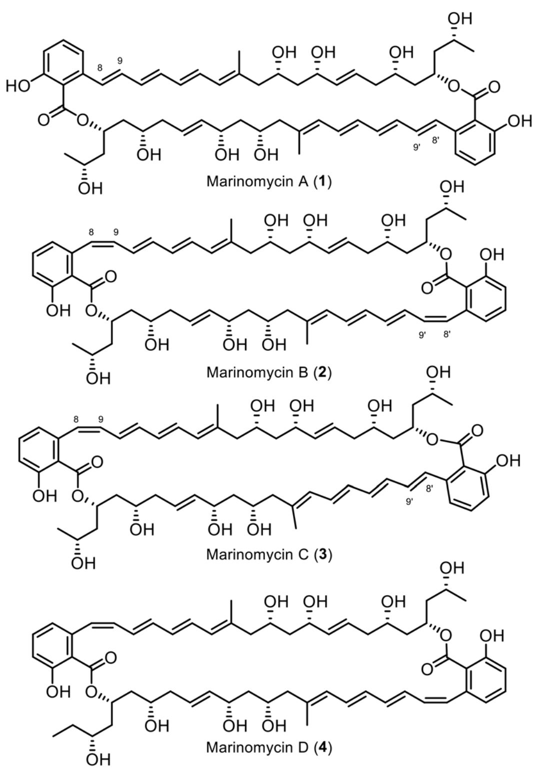

Fig. 1 Structures of Marinomycins A–D (**1–4**).

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To date, only three groups have successfully synthesised Marinomycin A, including Nicolaou *et al.* in 2006,[3,4] Evans *et al.* in 2012,[5] and Hatakeyama *et al.* in 2014.[6]

While Nicolaou *et al.* and Evans *et al.* employed consecutive construction strategies to synthesise the target molecule, Hatakeyama *et al.* chose a highly convergent direct dimerisation strategy of the monomeric compound. In addition to the completed total syntheses of Marinomycin A, Cossy *et al.* presented two synthetic approaches for the monomeric counterpart in 2007[7] and 2009.[8] Rajesh *et al.* further demonstrated a synthetic route for the C13–C28 fragment.[9]

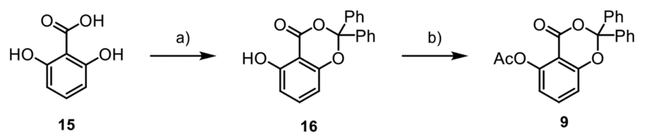
Results and discussion

Our approach to synthesise Marinomycin A and B revolves around utilising key monomer **5** that could be cyclised through a direct dimerisation *via* Sonogashira cross coupling (Scheme 1).[10,11] The triple bond in the resulting dimer (C-8–9 in **1** and **2**) would allow for selective *E*- or *Z*-reduction, thereby enabling access to both natural products.

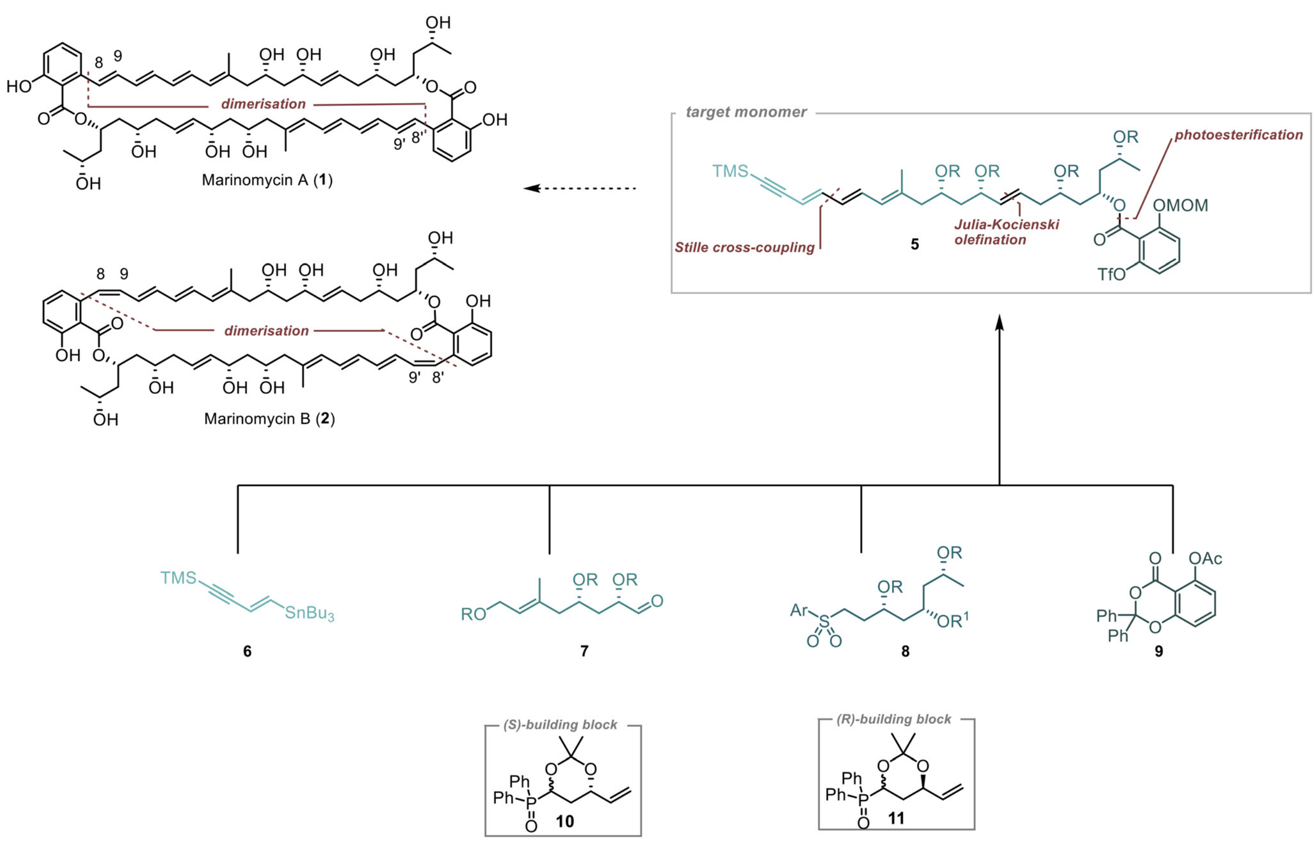
To form Monomer **5**, we utilised four building blocks: **6–9**. Fragment **6**, which contains the terminal alkyne and a double bond with a tributylstannyl moiety, allows for its connection to **7** *via* Stille cross-coupling.[12] The polyol fragments **7** and **8** should be linked together using Julia–Kocienski olefination.[13–15] The introduction of the densely substituted aromatic core was planned through a photochemical esterification method following the protocol established by de Brabander *et al.*[16–18]

1,3-Polyols were introduced on the basis of our previously described strategies.[19,20] we planned to employ the chiral building blocks **10** and **11** in an iterative fashion for the construction of the polyol-containing fragments **7** and **8**.[21,22] This strategic approach facilitates the controlled introduction of two stereogenic centres, resulting in an efficient and streamlined synthesis.

Our synthetic journey began with the assembly of aromatic core **9** from **15** (Scheme 2). Initially, we synthesised the benzodioxinone scaffold **16** through a reaction involving benzophenone, thionyl chloride, and DMAP. The obtained product was subsequently transformed into the final fragment **9** using



Scheme 2 Synthesis of **9**; (a) $Ph_2C{=}O$ (1.3 equiv.), $SOCl_2$ (1.3 equiv.), DMAP (5 mol%), 0 °C to rt, 18 h, (DME), 30%; (b) Ac_2O (1.8 equiv.), pyridine (5 equiv.), DMAP (10 mol%), 0 °C to rt, 2 h, (DCM), 89%.



Scheme 1 Planned approach for the synthesis of **1** and **2**, R = TBS, R^1 = PMB, Ar = phenyltetrazole.

acetic anhydride, DMAP, and pyridine, with an overall yield of 27%.

Fragment **6** was obtained through synthesis of vinylstannane **17** starting from propargyl alcohol **12**, which underwent a palladium-catalysed hydrostannylation (Scheme 3).[23,24] Through MnO_2-mediated oxidation Enal **18** was obtained in a high yield of 97%,[25,26] followed by conversion into the corresponding alkyne **19** *via* Colvin rearrangement.[27] Lastly, terminal alkyne **19** was TMS-protected, which gave the product **6** in 31% overall yield.

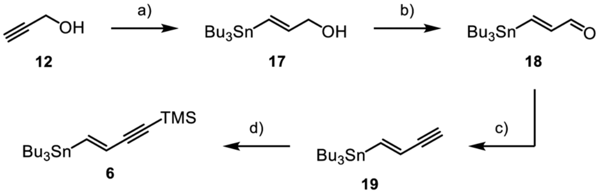
With the successful preparation of the first two fragments **6** and **9**, we were now poised to tackle the synthesis of the polyol fragments **7** and **8**.

The synthesis of fragment **7** started with the TBS-protection of (*Z*)-but-2-ene-1,4-diol (**13**) and subsequent ozonolysis of the double bond. Reaction with the commercially available Wittig reagent **21** then afforded aldehyde **22** in 94% yield with excellent selectivity of $E/Z > 20:1$ (Scheme 4).[28,29]

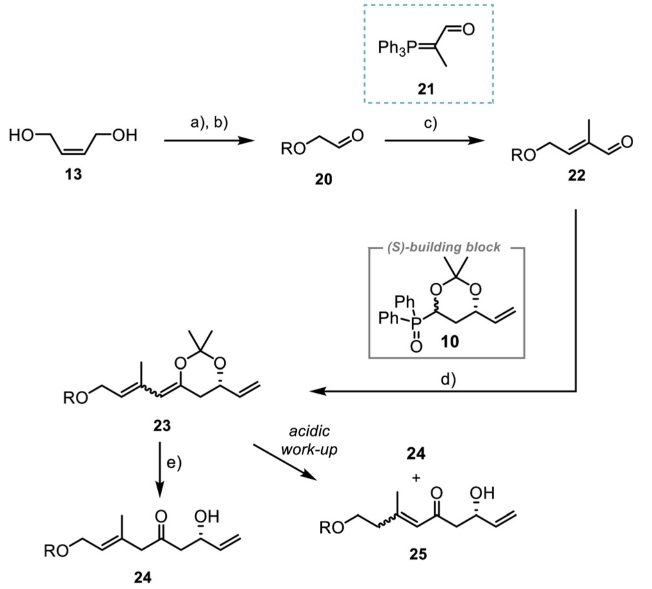
Next, the unsaturated aldehyde **22** was reacted with the polyketide building block **10**, using a Horner–Wittig reaction previously established by us.[21,22] The acetonide-protected alcohol **23** was obtained in 83% yield (dr 1 : 1). However, attempts to remove the acetonide during an acidic work-up gave a mixture of the desired compound **24** and the conjugated system **25**. Alternative tests utilising various Lewis acids or sterically demanding proton acids for the acetonide deprotection (ESI, Table 1 entries 1–3†)[30–32] led to the formation of complex mixtures. Best results were obtained with a variation of the methodology by Bai *et al.*[33] Further optimisation showed that the use of anhydrous $CeCl_3$ and addition of water improved the yield and **24** was obtained in 63% (ESI, Table 1, entry 7†).

Consequently, we performed a *syn*-selective Narasaka–Prasad reduction with β-hydroxyketone **24** to yield 1,3-diol **26** with excellent yield and diastereoselectivity (>20 : 1) (Scheme 5).[34–37] TBS-protection of the diol gave substrate **27** under standard conditions. However, all our attempts to convert terminal alkene **27** into aldehyde **7** were unsuccessful.

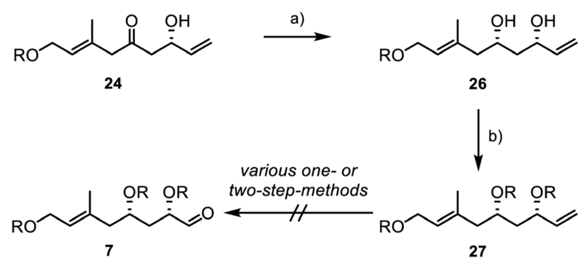
Despite testing a broad range of reaction conditions, the internal double bond was more reactive, and the direct conversion of the terminal double bond was never achieved. Also, several two-step sequences, involving the introduction of a 1,2-diol followed by its conversion into the aldehyde through glycol cleavage, did not yield the desired product. As a result, we decided to replace the TBS groups with an acetonide (Scheme 6).



Scheme 3 Synthesis of **6**; (a) $Pd_2(dba)_3$ (0.25 mol%), PCy_3 (2 mol%), Bu_3SnH (1.15 equiv.), 0 °C, 3 h, (DCM), 56%; (b) MnO_2 (20 equiv.), rt, 18 h, (acetone), 97%; (c) (i) *n*BuLi (1.35 equiv.), $TMSCHN_2$ (1.5 equiv.), −78 °C, 30 min, (ii) aldehyde **18** (1 equiv.), −78 °C to 0 °C, 90 min, (THF), 59%; (d) (i) *n*BuLi (1.2 equiv.), −78 °C, 1 h, (ii) TMSCl (1.2 equiv.), −78 °C, 1 h, (iii) −78 °C to rt, 16 h, (THF), 97%.

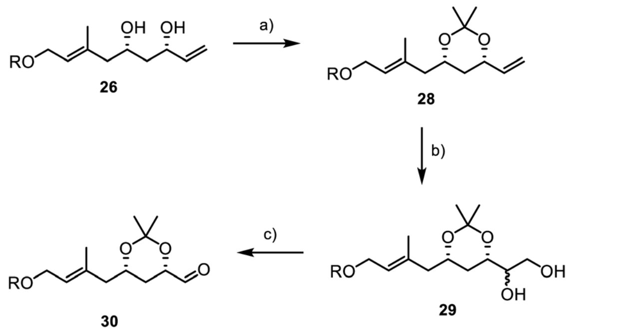


Scheme 4 Approach for the introduction of the first two stereogenic centres; R = TBS; (a) imidazole (4.8 equiv.), TBSCl (2.5 equiv.), rt, 16 h, (DCM), quant.; (b) (i) O_3, −78 °C, 20 min, (ii) PPh_3 (1.17 equiv.), rt, 1.5 h, (DCM), 81%; (c) **21** (1.2 equiv.), rt, 60 h, (benzene), 94%; (d) (i) DIPA (1.15 equiv.), *n*BuLi (1.15 equiv.), −78 °C, 15 min, (ii) **10** (1 equiv.), −78 °C, 60 min, (iii) aldehyde **22** (1.3 equiv.), −78 °C to rt, 90 min, (iv) KO*t*Bu (1.2 equiv.), rt, 60 min, (THF), 83%, (e) $CeCl_3$ (2 equiv.), oxalic acid (25 mol%), H_2O (2 equiv.), −78 °C, 16 h, (THF), 63%.

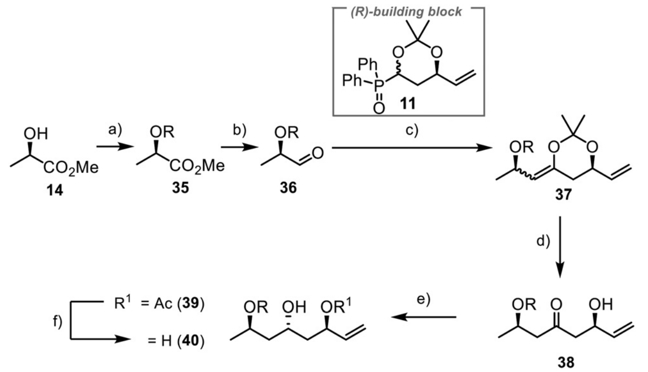


Scheme 5 Unsuccessful attempts to introduce the aldehyde function of fragment **7**; R = TBS; (a) Et_2BOMe (1.2 equiv.), $NaBH_4$ (1.1 equiv.), −78 °C, 2 h, (THF), 99%, dr > 20 : 1; (b) imidazole (4.8 equiv.), TBSCl (2.5 equiv.), 0 °C to rt, 2 h, (DMF), 90%.

We were delighted to find that under dihydroxylation conditions by Morken *et al.*, previously unsuccessful with TBS protected diol **27**, acetonide **28** was successfully and selectively converted to the 1,2-diol **29**.[38] Treating **28** with B_2pin_2 and catalytic amounts of caesium carbonate led to the formation of diol **29** with a diastereomeric ratio of 1 : 1. Subsequently, the diol was reacted with sodium periodate in a mixture of THF and water, affording the desired aldehyde **30** in 85% yield over two steps. However, it was later found that retaining the acetonide protecting group was not feasible, as subsequent results



Scheme 6 Introduction of the aldehyde moiety; R = TBS; (a) 2,2-dimethoxypropane (25 equiv.), PPTS (10 mol%), 330 mbar, 45 °C, 2 h, 98%; (b) (i) B_2pin_2 (2 equiv.), Cs_2CO_3 (30 mol%), 70 °C, 16 h, (ii) NaOH (6 equiv.), H_2O_2 (23.4 equiv.), 0 °C to rt, 4 h, (THF/MeOH, 3 : 1), dr 1 : 1; (c) $NaIO_4$ (2.2 equiv.), rt, 10 min, (THF/water, 1 : 1), 85% over two steps.

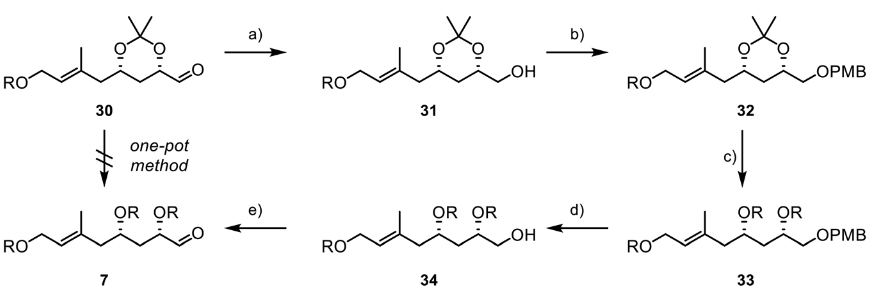


Scheme 8 Introduction of the three stereogenic centres of fragment **8**; R = TBS; (a) TBSCl (1.2 equiv.), imidazole (1.5 equiv.), rt, 30–60 min, (DMF), quant.; (b) DIBAL-H (1.2 equiv.), −78 °C, 1.5 h, (DCM), 87%; (c) (i) DIPA (2 equiv.), *n*BuLi (2 equiv.), −78 °C, 15 min, (ii) **11** (1 equiv.), −78 °C, 60 min, (iii) **35** (3 equiv.), −78 °C to rt, 90 min, (iv) KO*t*Bu (1.05 equiv.), rt, 60 min, (THF), 98%; (d) $CeCl_3$ (2 equiv.), oxalic acid (25 mol%), H_2O (2 equiv.), −78 °C, 16 h, (THF), 75%; (e) SmI_2 (0.75 equiv.), CH_3CHO (3.5 equiv.), −50 °C to −20 °C, 16 h, (THF), 96%, dr > 20 : 1; (f) K_2CO_3 (2 equiv.), 0 °C to rt, 60 min, (MeOH/H_2O, 3 : 1), 99%.

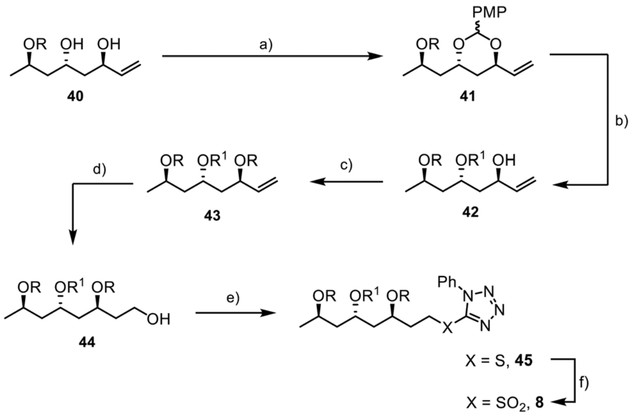
showed when subjecting **30** and **8** to a Julia–Kocienski olefination, where the acetonide function presented significant challenges in terms of selectivity and yield. Disappointingly, we were also unable to directly convert acetonide **30** into the desired TBS-protected substrate **7** due to the formation of various by-products resulting from the presence of the free hydroxyl groups and the aldehyde during deprotection.[39] In consequence, this necessitated a complex and multi-step deprotection–reprotection sequence involving the secondary alcohols to obtain **7**, as outlined in Scheme 7. First, the aldehyde function was reduced to primary alcohol **31**, followed by the installation of a PMB group to yield **32** (Scheme 7). Subsequently, reprotection with TBS chloride was carried out to form **33**. Finally, PMB deprotection and oxidation with IBX were performed, resulting in the successful acquisition of the desired aldehyde **7**.

The synthesis of fragment **8** commenced with (*R*)-methyl lactate **14** as a commercially available chiral starting material having the needed pre-existing stereogenic centre (Scheme 8). Installation of a TBS group at the free hydroxyl function and subsequent reduction of the ester to the aldehyde yielded the desired compound **36** in 87% yield over two steps.[40] The Horner–Wittig reaction between **36** and **11** proceeded smoothly, having 98% yield. However, direct deprotection with aqueous work-up was impractical due to elimination reactions. Previous efforts in our group indicated that such systems tended to undergo elimination when directly deprotected with hydrochloric acid, as typically done for acetonide deprotection. Fortunately, we successfully deprotected the acetonide moiety under the same conditions we used to produce **24**, yielding β-hydroxyketone **38** in 75% yield. This method demonstrated good selectivity and prevented the formation of unwanted elimination products. Selective *anti*-reduction was then accomplished using samarium(II) iodide and acetaldehyde under Evans–Tishchenko conditions.[41] The reaction provided excellent results with 96% yield and a dr of >20 : 1 for **39**. Deprotection lead to the formation of **40** in 99% yield. Alternative one-step methods, like the *anti*-reduction under Evans–Saksena conditions,[42,43] lead to the formation of **40** in good yields albeit with poor diastereoselectivities (see ESI†).

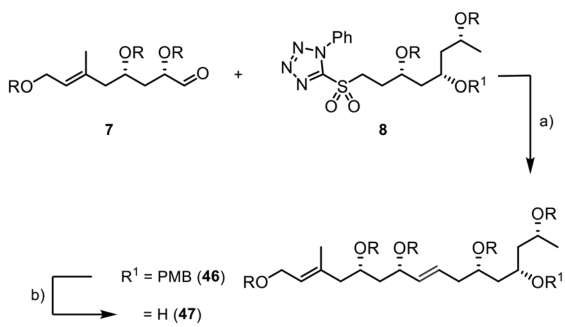
To introduce an orthogonal protecting group at C25 that allows for the late connection with the aryl unit through ester formation, we used 1-(dimethoxymethyl)-4-methoxybenzene to protect the 1,3-diol **40** (Scheme 9). Reductive opening of acetal **41** with DIBAL-H resulted in excellent selectivity, yielding the



Scheme 7 Final steps in the synthesis of fragment **7**; R = TBS; (a) DIBAL-H (1.3 equiv.), −78 °C, 1.5 h, (DCM), 92%; (b) NaH (1.2 equiv.), PMBCl (1.2 equiv.), TBAI (20 mol%), 0 °C to rt, 18 h, (DMF), 98%; (c) (i) PPTS (25 mol%), rt, 4 h, (MeOH),[44] (ii) TBSCl (6 equiv.), imidazole (10 equiv.), rt, 16 h, (DMF), 86% (2 steps); (d) DDQ (1.5 equiv.), 0 °C, 3 h, (DCM/pH7-buffer, 1 : 1), 64%; (e) IBX (1.5 equiv.), rt, 16 h, (DMSO), 79%.



Scheme 9 Final steps for the synthesis of fragment **8**; R = TBS; R^1 = PMB; PT = phenyltetrazole; PMP = *p*-methoxyphenyl; (a) 1-(dimethoxymethyl)-4-methoxybenzene (1.5 equiv.), PPTS (7 mol%), rt, 16 h, (DCM), 89%; (b) DIBAL-H (4.45 equiv.), 0 °C, 10 min, (DCM), 85%; (c) TBSCl (1.5 equiv.), imidazole (3 equiv.), rt, 16 h, (DMF), 95%; (d) 9-BBN (3 equiv.), rt, 15 min, then H_2O_2 (12 equiv.), NaOH (3 equiv.), rt, 4 h, (THF), 97%; (e) HS-PT (2 equiv.), DIAD (1.8 equiv.), PPh_3 (1.5 equiv.), 0 °C, 4 h, (THF), 94%; (f) $(NH_4)_6Mo_7O_{24}\cdot 4H_2O$ (20 mol%), H_2O_2 (10 equiv.), rt, 3 h, (EtOH), 90%.



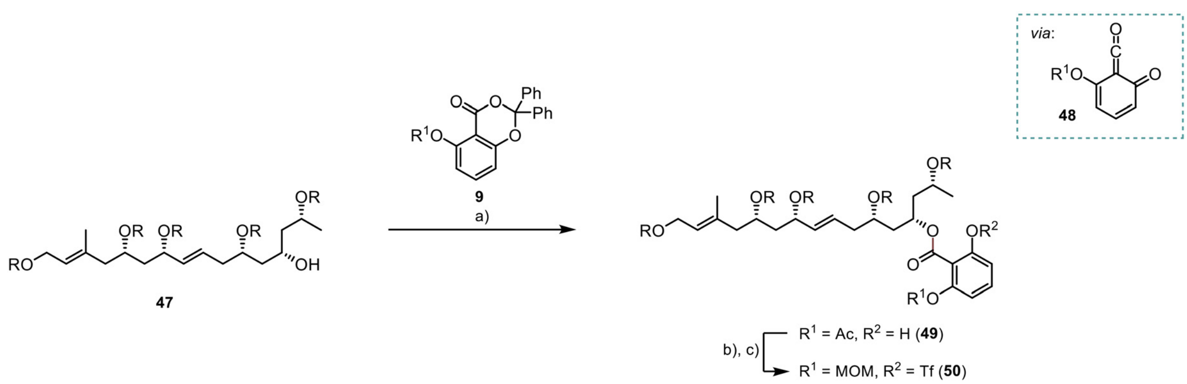
Scheme 10 Initial fragment assembly *via* Julia–Kocienski olefination; R = TBS; (a) (i) sulfone **8** (1.15 equiv.), KHMDS (1.2 equiv.), −78 °C, 30 min, (ii) aldehyde **7** (1 equiv.), −78 °C, 2.5 h, (DME), 85%, *E*/*Z* > 20 : 1; (b) DDQ (1.5 equiv.), 0 °C, 2 h, (DCM/pH7-buffer, 1 : 1), 90%.

desired product **42**.[45,46] Olefin **43** was obtained by TBS protection of the alcohol moiety, followed by the conversion of the double bond to the primary alcohol **44** in 97% yield using hydroboration and oxidative work-up.[47] The aryl sulfide was incorporated through a Mitsunobu reaction.[48] The final step involved the oxidation of the sulfide **45** to the sulfone **8**, which was achieved in high yield (90%), completing the synthesis of the final fragment.

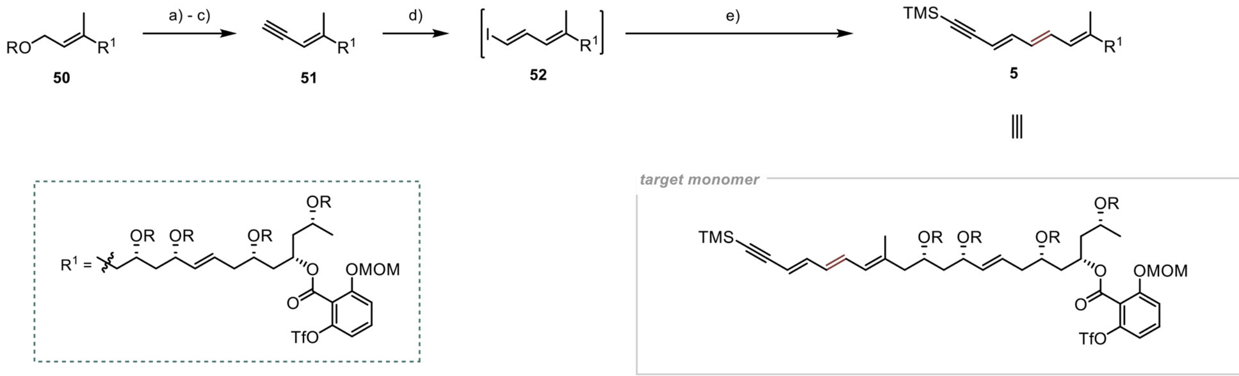
The assembly of the fragments started with a Julia–Kocienski reaction between **7** and **8**. The internal double bond of **46** was formed with an excellent *E*/*Z* selectivity of >20 : 1 and good yield of 85% (Scheme 10). The PMB group was then efficiently removed using DDQ in a buffered dichloromethane/water suspension, providing the desired product **47** in 90% yield (*E*/*Z* > 20 : 1).

The planned photoesterification represented a critical stage in the synthesis of the *ortho*-disubstituted benzoate **49** (Scheme 11). De Brabander *et al.* initially introduced this reaction, utilising light at a wavelength of 310 nm to generate the quinoketene **48** as the reactive intermediate.[16] Subsequently, the quinoketene was expected to be captured by the secondary alcohol **47** to yield the desired ester **49**. Following reaction optimisation, we achieved **49** with a moderate yield of 62%. Subsequently, we successfully protected the free phenol group as a triflate, in a high yield of 91%. However, unexpected instability issues arose with the preinstalled acetate group. Consequently, we opted for the deprotection and introduction of a MOM group, providing improved stability to the system **50** for subsequent reactions. This two-step transformation was achieved in a high yield of 95%.

Selective deprotection of the primary TBS group in the presence of the other secondary TBS groups proved to be a significant hurdle in the final steps of the synthesis of **51** (Scheme 12). However, after several unsuccessful attempts, we found suitable conditions for achieving the desired selectivity, adapting a protocol developed by Menche *et al.*,[49] where they overcame this obstacle by utilising an excess of sodium periodate in an aqueous THF solution. Adapting the protocol to sub-



Scheme 11 Photochemical introduction of the aromatic core; R = TBS; (a) **9** (2.5 equiv.), 310 nm, rt, 5 h, (DCM), 62%; (b) Tf_2O (2 equiv.), pyridine (5 equiv.), 0 °C to rt, 2.5 h, (DCM), 91%; (c) (i) K_2CO_3 (0.5 equiv.), rt, 1 h, (MeOH/THF, 1 : 1), (ii) MOMCl (2 equiv.), DIPEA (5 equiv.), 0 °C to rt, 16 h, (DCM), 95% (two steps).



Scheme 12 Final steps in the synthesis of the monomeric counterpart **5** of Marinomycin A and B; R = TBS; (a) $NaIO_4$ (6 equiv.), rt, 5 h, (THF/H_2O, 4 : 1), 41% (87% brsm); (b) MnO_2 (50 equiv.), rt, 16 h, (DCM), quant.; (c) (i) *n*BuLi (1.5 equiv.), $TMSCHN_2$ (1.8 equiv.), −78 °C, 1 h, (ii) aldehyde (1 equiv.), −78 °C to rt, 4.5 h, (THF), 67%; (d) (i) Cp_2ZrCl_2 (4 equiv.), $LiHBEt_3$ (4 equiv.), rt, 60 min, (ii) alkyne **51** (1 equiv.), rt, 60 min, (iii) NIS (5 equiv.), rt, 15 min, (THF), 47%; (e) **6** (1.1 equiv.), $Pd_2(dba)_3$ (10 mol%), Ph_3As (80 mol%), LiCl (15 equiv.), 40 °C, 2 h, (DMF), 36%.

strate **50** yielded the desired free hydroxyl group in 41% yield. Although the yield was modest, the remaining starting material was recoverable during chromatography, resulting in a yield of 87% (brsm). Subsequent oxidation with MnO_2 and Colvin rearrangement led to the formation of the terminal alkyne **51** in 67% yield over the two steps.[25,27] To generate the vinyl iodide **52**, a modified procedure from Lipshutz *et al.* was employed,[50] utilising an *in situ* generated Schwartz reagent and NIS as iodine source.[51] The desired iodide **52** was obtained in 47% yield. Due to the high light sensitivity and limited stability of this unsaturated compound, immediate utilisation was required for its subsequent Stille cross-coupling with stannane **6** under slightly modified conditions from Evans *et al.*[5] The synthesis of the monomeric counterpart **5** was accomplished under the specified conditions, resulting in a modest yield of 36% for the desired product. Nevertheless, we successfully attained our objective of synthesising this crucial intermediate for the preparation of Marinomycin A and B.

Conclusions

Our research outlines the synthesis of a novel monomeric precursor to Marinomycins A and B, accomplished *via* a convergent four-fragment approach. Our strategy integrated a polyketide building block previously established in literature, resulting in the final product attained through 24 steps for the longest linear sequence, with an overall yield of 0.6%. Looking ahead we will investigate the dimerisation of this monomer to synthesise Marinomycin A and B. Furthermore, we aim to enhance the synthesis by refining a more streamlined and efficient route for the fragments, while also improving the reliability of the final steps.

Conflicts of interest

The authors declare no conflict of interest.

Acknowledgements

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References

1 H. C. Kwon, C. A. Kauffman, P. R. Jensen and W. Fenical, *J. Am. Chem. Soc.*, 2006, **128**, 1622.
2 C. S. Bailey, J. S. Zarins-Tutt, M. Agbo, H. Gao, A. Diego-Taboada, M. Gan, R. B. Hamed, E. R. Abraham, G. Mackenzie, P. A. Evans and R. J. M. Goss, *Chem. Sci.*, 2019, **10**, 7549.
3 K. C. Nicolaou, A. L. Nold, R. R. Milburn and C. S. Schindler, *Angew. Chem., Int. Ed.*, 2006, **45**, 6527.
4 K. C. Nicolaou, A. L. Nold, R. R. Milburn, C. S. Schindler, K. P. Cole and J. Yamaguchi, *J. Am. Chem. Soc.*, 2007, **129**, 1760.
5 P. A. Evans, M.-H. Huang, M. J. Lawler and S. Maroto, *Nat. Chem.*, 2012, **4**, 680.
6 T. Nishimaru, M. Kondo, K. Takeshita, K. Takahashi, J. Ishihara and S. Hatakeyama, *Angew. Chem., Int. Ed.*, 2014, **53**, 8459.
7 D. Amans, V. Bellosta and J. Cossy, *Org. Lett.*, 2007, **9**, 1453.
8 D. Amans, L. Bareille, V. Bellosta and J. Cossy, *J. Org. Chem.*, 2009, **74**, 7665.
9 A. Rajesh, G. Sharma and K. Damera, *Synthesis*, 2015, **47**, 845.
10 K. Sonogashira, Y. Tohda and N. Hagihara, *Tetrahedron Lett.*, 1975, **16**, 4467.
11 D. Wang and S. Gao, *Org. Chem. Front.*, 2014, **1**, 556.
12 D. Milstein and J. K. Stille, *J. Am. Chem. Soc.*, 1978, **100**, 3636.
13 J. B. Baudin, G. Hareau, S. A. Julia and O. Ruel, *Tetrahedron Lett.*, 1991, **32**, 1175.
14 P. R. Blakemore, W. J. Cole, P. J. Kocieński and A. Morley, *Synlett*, 1998, 26.
15 F. Mittendorf, I.-E. Celik and S. F. Kirsch, *J. Org. Chem.*, 2022, **87**, 14899.

16 O. Soltani and J. K. de Brabander, *Angew. Chem., Int. Ed.*, 2005, **44**, 1696.
17 O. Soltani and J. K. de Brabander, *Org. Lett.*, 2005, **7**, 2791.
18 S. Bolshakov and J. L. Leighton, *Org. Lett.*, 2005, **7**, 3809.
19 H. Menz and S. F. Kirsch, *Org. Lett.*, 2009, **11**, 5634.
20 S. Kirsch, P. Klahn and H. Menz, *Synthesis*, 2011, 3592.
21 A. Bredenkamp, M. Wegener, S. Hummel, A. P. Häring and S. F. Kirsch, *Chem. Commun.*, 2016, **52**, 1875.
22 A. Bredenkamp, Z.-B. Zhu and S. F. Kirsch, *Eur. J. Org. Chem.*, 2016, 252.
23 L. Ferrié, J. Fenneteau and B. Figadère, *Org. Lett.*, 2018, **20**, 3192.
24 A. Darwish, A. Lang, T. Kim and J. M. Chong, *Org. Lett.*, 2008, **10**, 861.
25 C. T. Brain, A. Chen, A. Nelson, N. Tanikkul and E. J. Thomas, *Tetrahedron Lett.*, 2001, **42**, 1247.
26 C. T. Brain, A. Chen, A. Nelson, N. Tanikkul and E. J. Thomas, *Tetrahedron*, 2010, **66**, 6613.
27 E. W. Colvin and B. J. Hamill, *J. Chem. Soc., Chem. Commun.*, 1973, 151.
28 J. A. Lafontaine, D. P. Provencal, C. Gardelli and J. W. Leahy, *J. Org. Chem.*, 2003, **68**, 4215.
29 K.-V. Tran and D. Bickar, *J. Org. Chem.*, 2006, **71**, 6640.
30 J. Zhu and D. Ma, *Angew. Chem., Int. Ed.*, 2003, **42**, 5348.
31 T. J. Tewson and M. J. Welch, *J. Org. Chem.*, 1978, **43**, 1090.
32 K. S. Kim, Y. H. Song, B. H. Lee and C. S. Hahn, *J. Org. Chem.*, 1986, **51**, 404.
33 X. Xiao and D. Bai, *Synlett*, 2001, 535.
34 K.-M. Chen, K. G. Gunderson, G. E. Hardtmann, K. Prasad, O. Repic and M. J. Shapiro, *Chem. Lett.*, 1987, **16**, 1923.
35 K.-M. Chen, G. E. Hardtmann, K. Prasad, O. Repič and M. J. Shapiro, *Tetrahedron Lett.*, 1987, **28**, 155.
36 K. Narasaka and F.-C. Pai, *Tetrahedron*, 1984, **40**, 2233.
37 K. Narasaka and H. C. Pai, *Chem. Lett.*, 1980, **9**, 1415.
38 T. P. Blaisdell, T. C. Caya, L. Zhang, A. Sanz-Marco and J. P. Morken, *J. Am. Chem. Soc.*, 2014, **136**, 9264.
39 F. Ballaschk, Y. Özkaya and S. F. Kirsch, *Eur. J. Org. Chem.*, 2020, 6078.
40 S. M. Gibson, R. M. Lanigan, L. Benhamou, A. E. Aliev and T. D. Sheppard, *Org. Biomol. Chem.*, 2015, **13**, 9050.
41 D. A. Evans and A. H. Hoveyda, *J. Am. Chem. Soc.*, 1990, **112**, 6447.
42 D. A. Evans, K. T. Chapman and E. M. Carreira, *J. Am. Chem. Soc.*, 1988, **110**, 3560.
43 A. K. Saksena and P. Mangiaracina, *Tetrahedron Lett.*, 1983, **24**, 273.
44 R. van Rijsbergen, M. J. O. Anteunis and A. de Bruyn, *J. Carbohydr. Chem.*, 1983, **2**, 395.
45 J. Janssens, M. D. P. Risseeuw, J. van der Eycken and S. van Calenbergh, *Eur. J. Org. Chem.*, 2018, 6405.
46 H. Kumar, A. S. Reddy and B. S. Reddy, *Tetrahedron Lett.*, 2014, **55**, 1519.
47 H. C. Brown and J. Chen, *J. Org. Chem.*, 1981, **46**, 3978.
48 O. Mitsunobu and M. Yamada, *Bull. Chem. Soc. Jpn.*, 1967, **40**, 2380.
49 J. Li and D. Menche, *Synthesis*, 2009, 1904.
50 B. H. Lipshutz, R. Keil and E. L. EIlsworth, *Tetrahedron Lett.*, 1990, **31**, 7257.
51 P. C. Wailes and H. Weigold, *J. Organomet. Chem.*, 1970, **24**, 405.