REVIEW ARTICLE

A C G publications

Org. Commun. 11:1 (2018) 1-11

organic communications

A review of the total synthesis of the most important marine natural products in the Red Sea

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(Received June 29, 2017; Revised August 23, 2017; Accepted August 24, 2017)

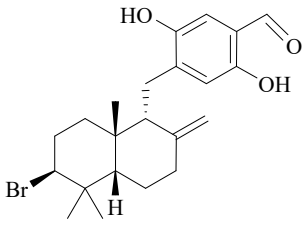
Abstract: This review aims to comprehensively highlight the chemical syntheses of marine natural products isolated from organisms in the Red Sea. The synthetic approaches in the construction of complex molecules and their potent applications in drug design are summarised.

Keywords: Red Sea; total synthesis; marine natural products; sterols.

1. Introduction

The growing need for the discovery of new drugs faces great challenge in their design, synthesis and bioactivity studies. In recent years, as one of the most active areas in marine natural products, the Red Sea has yielded a considerable number of drug candidates with various types of biological activities.[1,2] Thus, the marine natural compounds in the Red Sea have been subjected to a number of total synthetic studies for drug discovery. The total synthesis of marine natural products isolated in the Red Sea[3] can be divided into three categories: terpenes, alkaloids and sterols. This review covers the most important total syntheses accomplished to date through sophisticated synthetic strategies for achieving selectivity and efficiency in the formation of marine natural products.

2. Peyssonol A



Peyssonol A

Figure 1. Chemical structure of Peyssonol A

Peyssonol A (Figure 1), isolated from the Red Sea algae *Peyssonelia* sp,[1] is classified as a sesquiterpene and possesses three isoprene units. It has been shown to be a potent inhibitor in the RNA-directed DNA synthesis of the reverse transcriptase (RT) of the human immunodeficiency virus HIV.[2,3]

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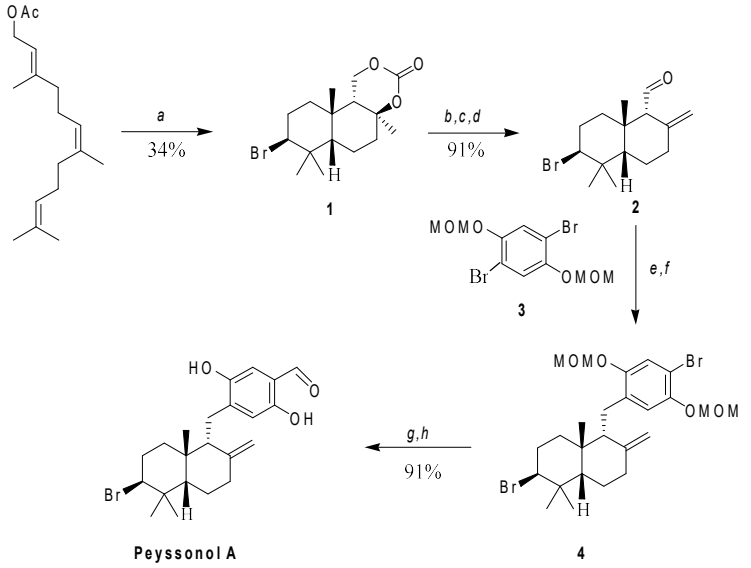
The article was published by ACG Publications
www.acgpubs.org/OC/ index.htm © January-March 2018 EISSN:1307-6175
DOI: http://doi.org/10.25135/acg.oc.37.18.01.064

The development of stereoselective halogenative polyene cyclisations has been reported in the literature.[3] The group attempted to prepare a stable halogenating reagent, capable of initiating cation-π-cyclisations by bromonium ions. The bromo diethylsulfonium bromopentachloroantimonate ion (BDSE) is used as an electrophilic bromine source. Geranyl acetate triene shows the ability to proceed with BDSE for bromonium cyclisation.[3] The axial C-9 orientation of geranyl acetate influences the regiochemistry of the product, bicyclic bromide **1**, through the reaction with BDSE. Swern oxidation was expected to transform **1** into **2** with a 91% yield. Methoxymethyl ether-substituted aromatic compound **3** was lithiated with BuLi to generate aryllithium, which attacked aldehyde **2** to afford **4**. Cleavage of methoxymethyl ether using *p*-TsOH in warm *t*-BuOH afforded peyssonol A in a 91% yield (Scheme 1).



Scheme 1. Total synthesis of peyssonol A.

Reagents and conditions: (a) BDSB, $MeNO_2$, 0 °C, 30 s; (b) K_2CO_3 MeOH, 40 °C, 30 min; (c) $(COCl)_2$, DMSO, CH_2Cl_2, -78 °C; (d) $SOCl_2$ Et_3Nm CH_2Cl_2, -97 °C, 1 h, over three steps; (e) **3,** *n*-BuLi (1.4 M in hexanes, 1.1 equiv.), THF, -78 °C, 20 min, then **4,** -78 °C, 20 min; (f) TFA, Et_3SiH, CH_2Cl_2, 0 °C, 30–90 min, 64%; (g) *n*-BuLi (1.4 M in hexanes, 1.2 equiv.), THF, -78 °C, 20 min, then DMF, -78 °C, 20 min; (h) *p*-TsOH·H_2O (0.2 M in *t*-BuOH), 65 °C, 2 h.

3. Norcembrenolide

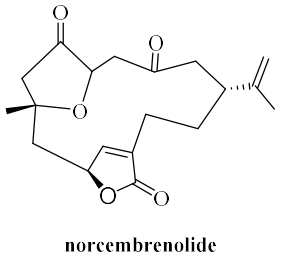
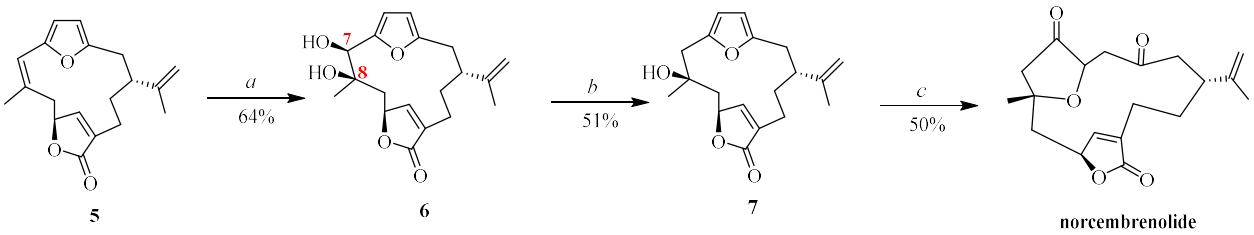


Figure 2. Chemical structure of Norcembrenolide

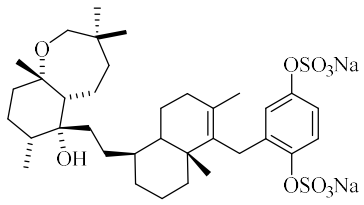
Norcembrenolide (Figure 2) was first isolated by Fenical *et al*.[4] Although its biological activities have not been explored to date, its construction was achieved in a convergent synthesis starting from Norrubifolide **5**.[4] The first step was the conversion of the C7-C8 double bond to a cis vicinal diol **6** as a single isomer in a 64% yield using osmium tetroxide and *N*-methyl morpholine-*N* oxide, which is known as the Upjohn dihydroxylation reaction. The stereogenic center at C7 was terminated with the aid of a deoxgenation reaction, providing **7** in a 51% yield. Jones reagent was used to oxidise the furan ring, leading to the formation of the *β*-ketotetrahydrofuranone, norcembrenolide, in a 50% yield (Scheme 2).



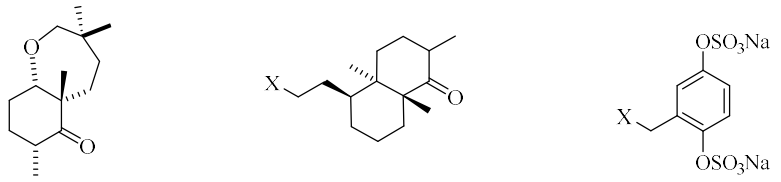
Scheme 2. Total synthesis of norcembrenolide.

Reagents and conditions: (a) OsO_4, NMO, THF, H_2O, 0 °C; (b) Et_3SiH, $BF_3.Et_2O$, -40 °C, 30 min; (c) Jones (O) acetone, -20 °C, 50%.

4. Shaagrockol C



Shaagrockol C

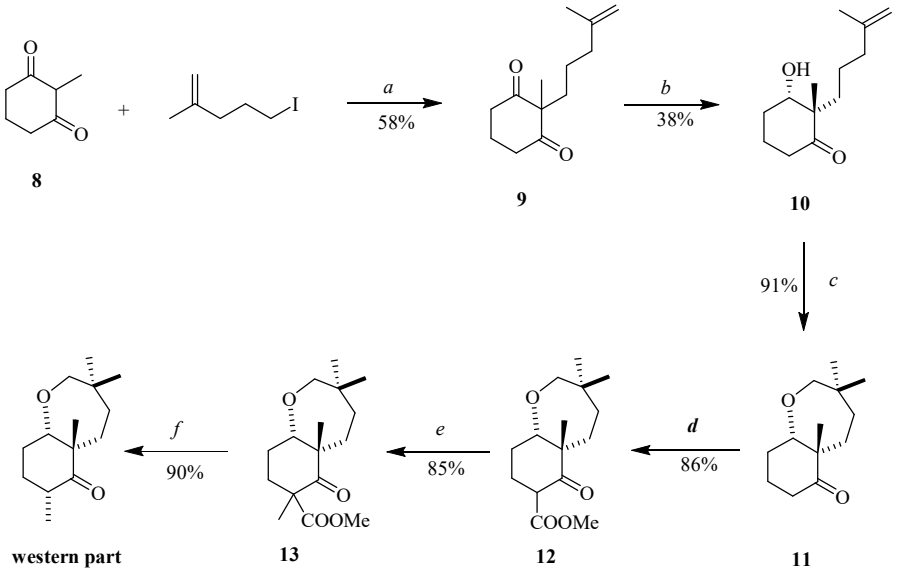


western Part Central part Eastern part

Figure 3. Chemical structure of Shaagrockol C and its parts

Shaagrockol C (Figure 3) and sesquiterpene derivatives from the Red Sea sponge *Toxiclona toxius* were first isolated by Kashman and Isaacs, who established its structure in 1992.[5,6] It shows antifungal activity against Candida albicans, and influences the inhibition of HIV RT. Shaagrockol C contains a hydroquinone disulfate ring, which is named as the eastern part, along with two different

bicyclic sesquiterpene systems (Western and central parts) linked together via an ethylene bridge.[8] The enantioselective total synthesis of Shaagrockol C has not been reported in the literature. Nevertheless, the first attempts at the enantioselective synthesis of the western part of Shaagrockol C were successful according to a synthetic study published in 2013. The first step is an insertion reaction of alkyl group at the alpha carbon by the exchange of a hydrogen atom, applying an alkylation method, using potassium *tert*-butoxide as a base together with a catalytic amount of a quaternary ammonium salt (Aliquat 336). The resulting diketone **9** was obtained in a 58% yield. The yeast reduction reaction represents the process of asymmetric reduction of carbonyl-containing compound **9**, where **9** with prochiral ketone was exposed to a hydrogen transfer to the *re* to yield *S* configuration at C-3 of **10** in a 38% yield.[7] In a strong acid, such as trifluoroacetic acid (TFA), an intramolecular cyclisation of **10** took place through the electrophilic activation of alkene to form oxepane **11** in a 91% yield, which undergone a carboxylation reaction at *β*-carbon to give **12** in a yield of 86%. Methyl iodide was used to introduce a methyl group at C-9, affording **13** in a yield of 85%. The decarboxylation reaction of *β*-keto ester in a dipolar protic solvent with lithium chloride afforded the western part of Shaagrockol C, where the methyl group is anti to the methyl group at C-7 (Scheme 3).



Scheme 3. Total synthesis of western part of Shaagrockol C.

Reagents and conditions: (a) *t*-BuOK (1.2 equiv.), Aliquat 336, DMSO, 80 °C; (b) baker yeast; (c) TFA (50 equiv.), CH_2Cl_2, r.t, 16 h; (d) NaH (1.0 equiv.), Me_2CO_3, THF, r.t, 10 h; (e) NaH (1.0 equiv.), CH_3I, THF, 0 °C, 16 h; (f) LiCl, HMPA, 95°C, 16 h.

5. Miraziridine A

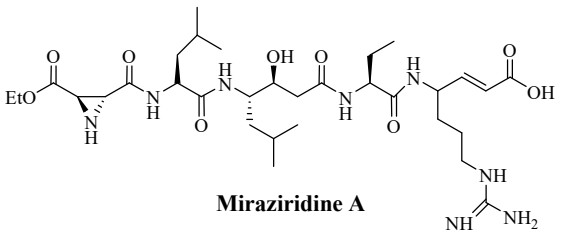
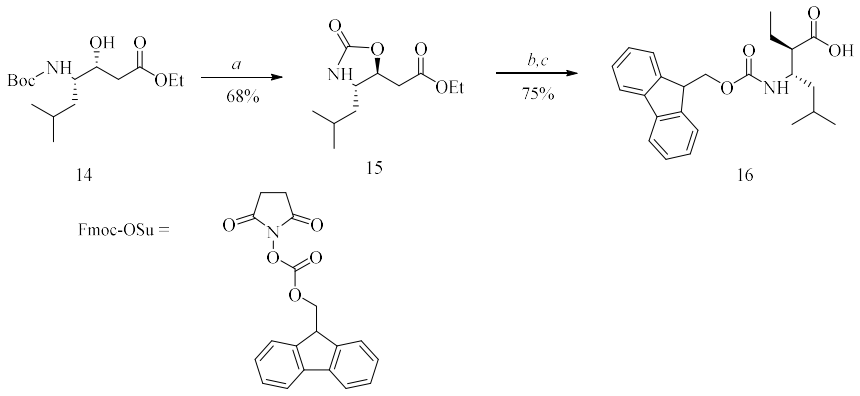


Figure 4. Chemical structure of Miraziridine A

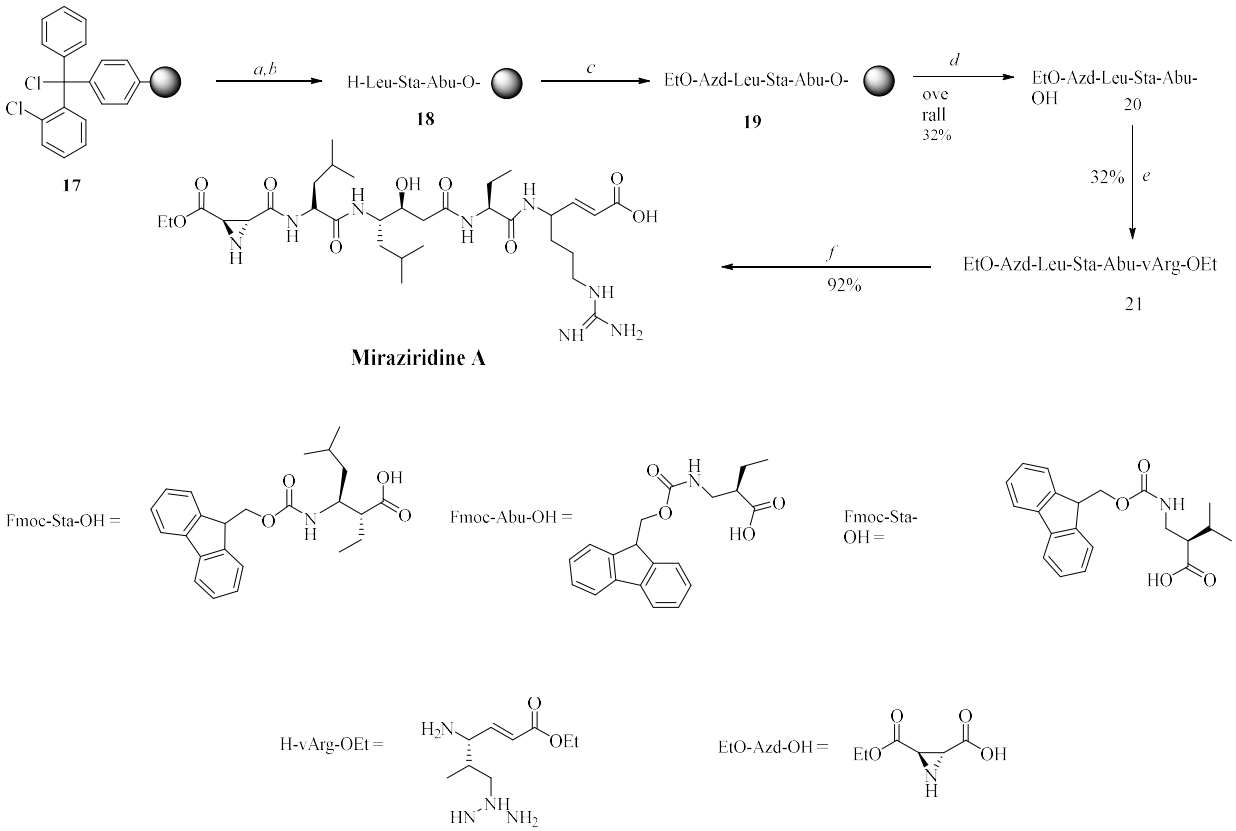
Miraziridine A (Figure 4) was isolated by Fusetani in 2000 from Red Sea *Theonella aff. Mirabilis*,[1] the structure of which was determined to have seven stereogenic centers by applying Marfey's methods and 2D NMR techniques.[8] Miraziridine A was found to inhibit the cysteine protease cathepsin B. Thus, the aziridine ring plays a key role in biological activities.[9] Their method to accomplish the synthesis of miraziridine A involved a peptide chain in a precursor step, while it was attached at one end to a solid support to complete the synthetic route of miraziridine A by enzymatic hydrolysis.[10] The first step was the inversion of the *β*-hydroxy group of (*3R,4S*)-Boc-statine-OEt **14**. Methanesulfonyl chloride was used for the process to affect the stereochemistry at C-3 and coexist in the formation of *β*- keto ester **15** in a 68% yield. Hydrolysis of the alkoxy group and FMOC protection occurred at the C-3 position to afford Fmoc-statine **16** in a 75% yield (Scheme 4). [11]



Scheme 4. Synthesis of (*3S,4S*)-Fmoc-statine **16**.

Reagents and conditions: (a) MsCl, Et_3N, CH_2Cl_2, -20 °C, 3 h; (b) LiOH, EtOH/H_2O, r.t; (c) Fmoc-OSu, Et_3N, MeCN/H_2O, 15 min, r.t.

A peptide chain was assembled as an attachment to a solid support. Fmoc-Abu-OH was initially reacted with 2-chlorotrityl chloride resin in DMF/CH_2Cl_2 in the presence of $^{i}Pr_2Net$, and the Fmoc protecting group was removed with a 20% piperidine/DMF mixture. The condensation reaction of Fmoc-Sta-OH with DIPC/ HOBt in the presence of $^{i}Pr_2Net$ was performed for the formation of the first part of product **18**.[10] A repeated condensation with Fmoc-Sta-OH and then deprotection yielded tripeptide resin **18**. Diphenylphosphoryl azide was used as a novel reagent for solid-phase peptide synthesis, applying the procedure developed by Vigneaud. In this approach, EtO-Azd-OH was condensed with **18** to allow the formation of tetrapeptide resin **19**. Removal of tetrapeptide derivative from the resin proceeded in the cleavage of hexafluoroisopropanol (HFIP) in CH_2Cl_2. EtO-Azd-Leu-Sta-Abu-OH **20** was recovered in a 32% yield, showing a single major peak by HPLC. HATU played a major role in the efficient coupling of tetrapeptide **20** with H-vArg-OEt to give **21** in a 32% yield. Porcine liver esterase was used in the ester cleavage, with the hydrolysis of a broad range of carboxyl esters proceeding in high to excellent enantioselectivity. A final deprotection was performed in the presence of porcine liver esterase in a Tris/HCl buffer (pH 6.5), affording miraziridine A in a 92% yield (Scheme 5).



Scheme 5. Total synthesis of miraziridine A.

Reagents and conditions: (a) Fmoc-Abu-OH, $^{i}Pr_2NEt$, DMF, CH_2Cl_2, piperidine, DMF, Fmoc-Sta-OH,DIPC, HOBt, $^{i}Pr_2NEt$, DMF; (b) Piperidine, DMF, Fmoc-Leu-OH, DIPC, HOBt, $^{i}Pr_2NEt$, DMF, piperidine, DMF; (c) EtO-Azd-OH, DPPA, Et_3N, DMF; (d) HFIP CH_2Cl_2; (e) H-vArg-OEt ,HATU, HOAt, $^{i}Pr_2NEt$, DMF; (f) Porcine liver esterase, Tris-HCl buffer (pH 6.5) .

6. Sterols

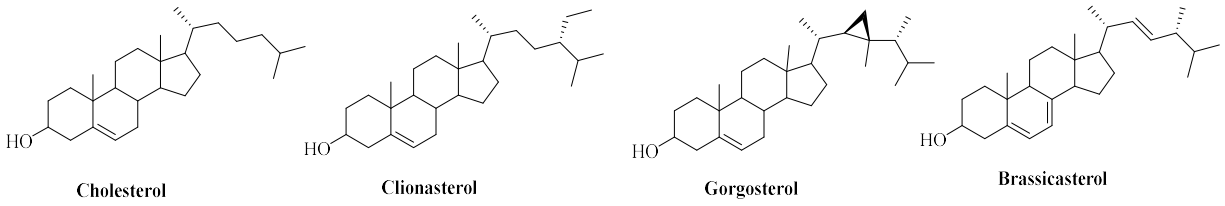
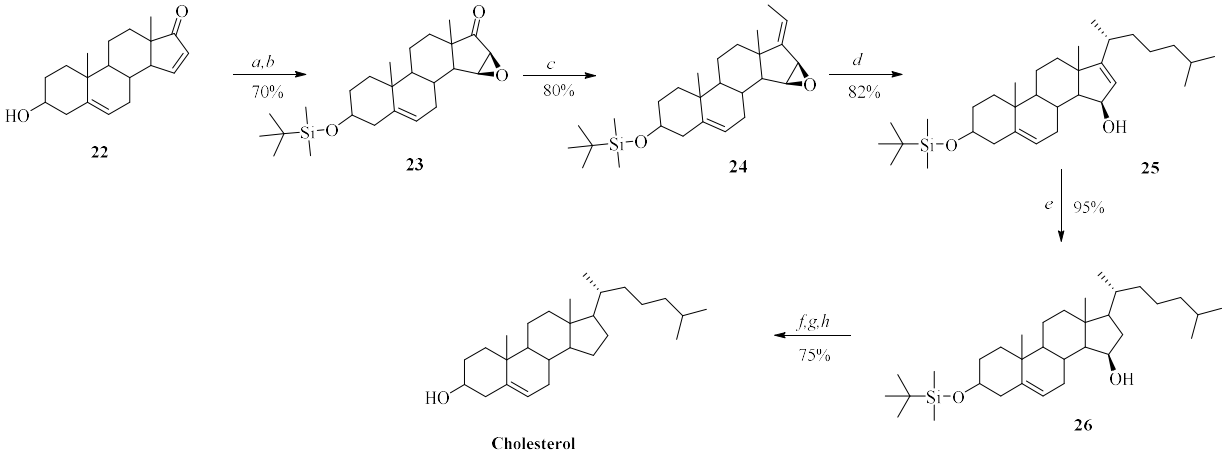


Figure 5. Chemical structure of reported sterols

Sterols (Figure 5) form one of the most important classes of natural substances and occur in a vast range of plants in the Red Sea.[1] They play a significant role in the human diet[11] and have fundamental biological processes, such as signal transduction, cellular sorting, cytoskeleton reorganisation, asymmetric growth, antitubercular parguesterols and infectious diseases.[12,13] Among these compounds are cholesterol, clionasterol, brassicasterol and gorgosterol, which are found in sponges in the Red Sea. They are secondary alcohols with a basic tetracyclic structure consisting of three six-membered rings and one five-membered ring with a short aliphatic chain.[14]

6.1. Cholesterol

Cholesterol was isolated from the Red Sea sponge *Negombata corticata*,[1] the total synthesis of which was reported by Marino and others.[15,16] They applied a stereospecific epoxidation of *α, β* - unsaturated ketone **22** using meta-chloroperoxybenzoic acid, with attack of a peroxy acid at the Re side rather than the Se side of the molecule because of steric hindrance of the methyl group. This was followed by protection of the OH group in the equatorial position with tert-butyldimethylsilyl. The keto epoxide **23** was obtained in an overall yield of 70%. The keto epoxide was subjected to a Wittig reaction. The reaction involved ethyltriphenylphosphonium bromide with keto steroid **23** to give only the *E*- diastereomer **24**. Application of an epoxide ring opening reaction by the addition of lithium isohexylcyanocuprate in ether at -78 °C led to control of two stereocenters. The 1,4-adduct **25** was produced in a 82% yield. Stereospecific hydrogenation of the allylic alcohol **25** over PtO_2 was conducted and the resulting hydroxycholesterol **26** was subjected to dehydroxylation and then deprotection to a yield of 70% cholesterol (Scheme 6).



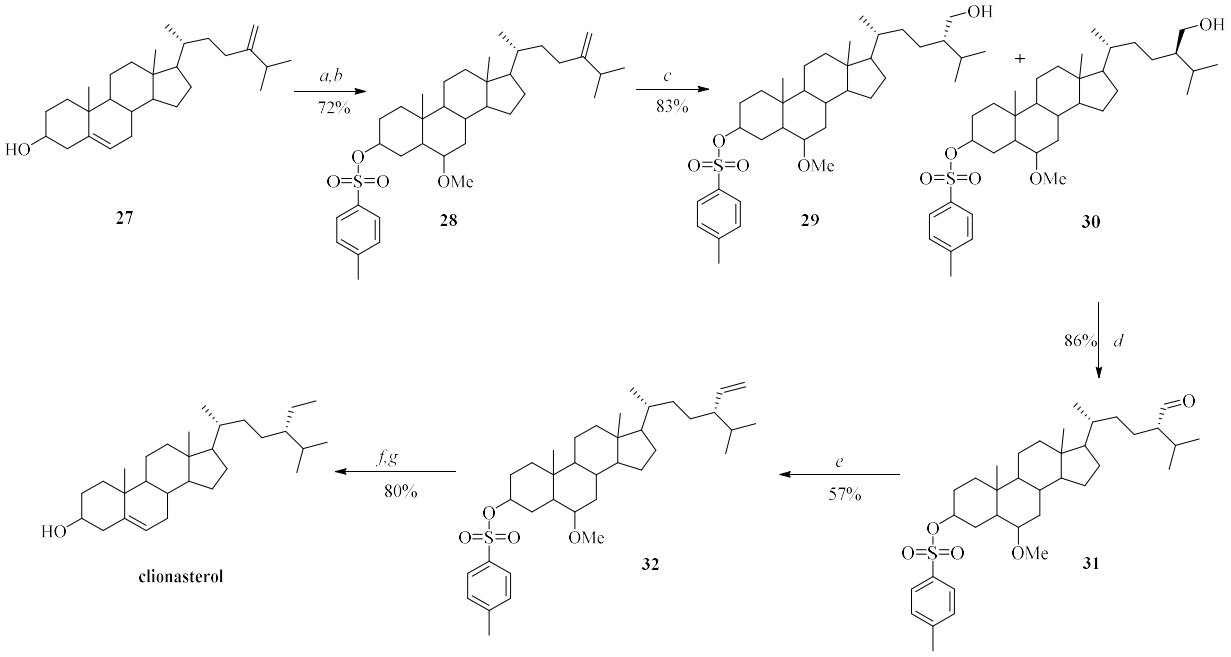
Scheme 6. Total synthesis of cholesterol.

Reagents and conditions: (a) mCPBA, chloroform, RT; (b) TBDMSCl, CH_2Cl_2, 25 °C; (c) $CH_3P(C_6H_5)_3Br$, LDA, THF, -78 °C; (d) lithium isohexylcyanocuprate, ether, -78 °C; (e) PtO_2, EtOAc; (f) $(CH_3)_2CH]_2N]_2PCl$**:** (g) Li, $C_2H_5NH_2$, -78 °C; (h) deprotection reaction**.**

6.2. Clionasterol

Clionasterol was isolated from the Red Sea sponge *Dragmacidon coccinea*. Much of the interest in clionasterol is as a consequence of its biological properties.[1] It exhibits an anti-inflammatory effect in human aortic endothelial cells and increases the antioxidant defence system.[17] Clionasterol can be constructed in a convergent synthesis starting from 24-methylenecholesterol **27**. Simultaneous protections of the hydroxyl group and double bond of 24-methylenecholesterol **27** with p-toluenesulfonyl chloride and potassium acetate occurred in one reaction to afford **28** in a 72% yield. Hydroboration of the double bond with a borane tetrahydrofuran complex and sodium hydroxide then provided the required hydroxyl compounds in a mixture of 83 % of **29** and **30**. They were separated by RF-HPLC. Alcohol **29** was oxidised to aldehyde **31** using Jones oxidation, followed by a Wittig reaction to afford **32**. Catalytic hydrogenation of the double bond was conducted with platinum in

ethyl acetate, and the methoxy group was then hydrolysed to remove the protecting group to form clinosterol[17] (Scheme 7).

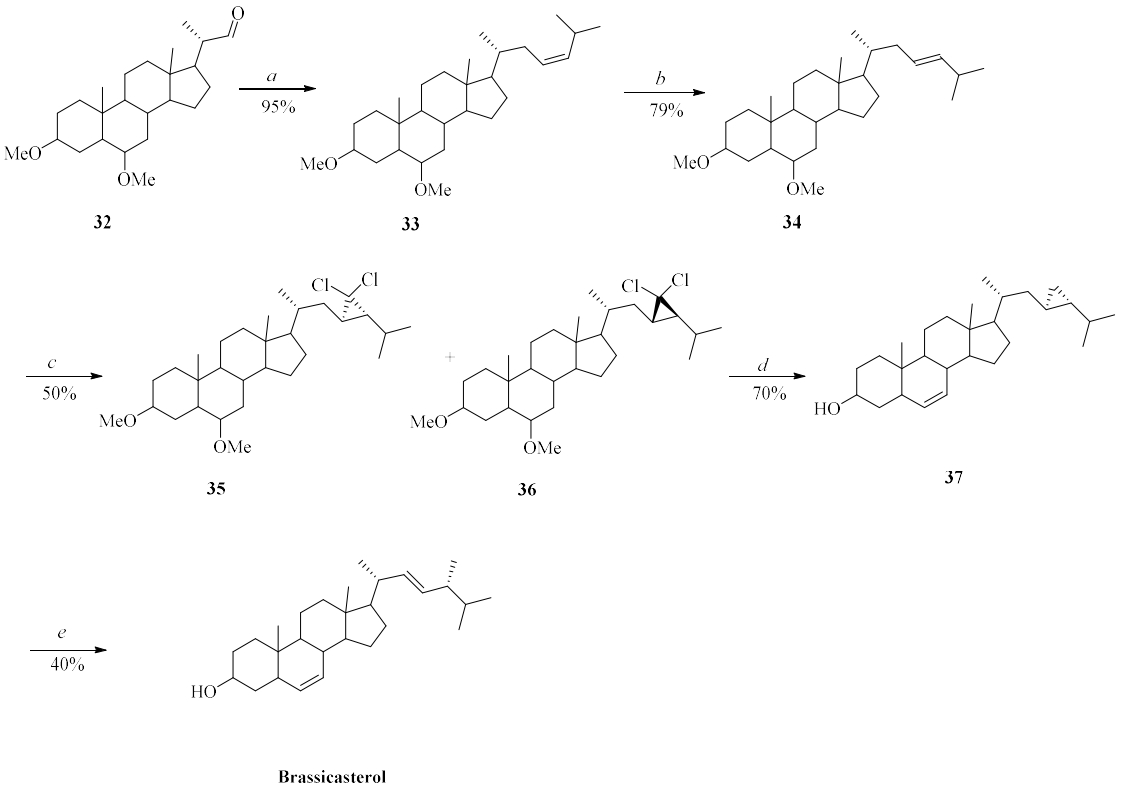


Scheme 7. Total synthesis of clionasterol.

Reagents and conditions: (a) pyridine, p-toluenesulfonyl chloride, 0 °C; (b) KOAc, MeOH, reflux; (c) BH_3, THF, 0 °C; (d) pyridine CrO_3, CH_2Cl_2; (e) $CH_3P(C_6H_5)_3I$, BuLi, ether, -78 °C; (f) PtO_2, EtOAc; (g) deprotection reaction**.**

6.3. Brassicasterol

Extraction of the Red Sea sponge *Dragmacidon coccinea* led to the isolation of brassicasterol.[1] It shows anti-aging and neuroprotective activity.[18] The synthesis of brassicasterol began with the preparation of alkene **33** from aldehyde **32** by the Wittig reaction. The product was preferentially formed with the *cis*-alkene (Z product) over the *trans*-alkene (E product). Z product **33** was then isomerised in a 79% yield to Z product **34** by the Vedejs and Fuchs method.[19] The reaction of *trans*-alkene **34** with *m*-chloroperbenzoic acid in methylene chloride and then with lithium diphenylphosphide and methyl iodide in tetrahydrofuran gave the two dichlorocyclopropanes **35** and **36**, which were separated by reverse phase HPLC.[19] Thus, **35** was isolated in a 50% yield. Reduction of dichlorocyclopropane **35** led to the formation of **37** by elimination of chloride ions from dichlorocyclopropane in liquid ammonia, followed by hydrolysis of the methoxy groups with aqueous dioxane in the presence of *p*-toluenesulfonic acid, yielding **37** at 70%. Acid-catalysed cyclopropane ring opening was activated by a standard acid-catalysed method to afford brassicasterol in a 40% yield (Scheme 8).

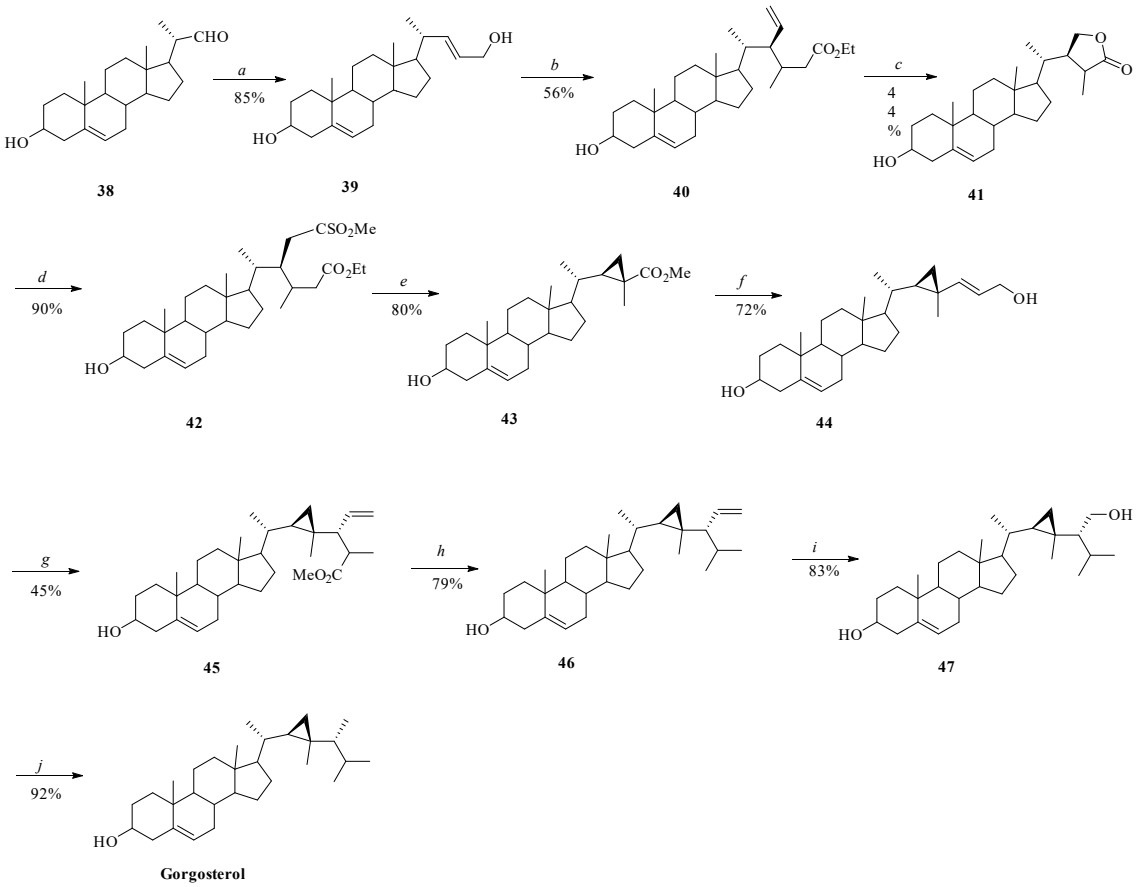


Scheme 8. Total synthesis of brassicasterol.

Reagents and conditions: (a) $Ph_3P{=}CHCOCH_3$, toluene; (b) $(C_6H_5)_2PLi$, MeI, THF; (c) m-CPBA, CH_2Cl_2, then Ph_2PLi, THF; (d) Li/NH_3, then p-TosOH, dioxane/water; (e) acid-catalysed cyclopropane ring opening

6.4. Gorgosterol

Gorgosterol is a secondary metabolite of the Red Sea soft coral Heteroxenia fuscescens. The structure of gorgosterol exists as a sterol with a cyclopropane ring in the side chain. It shows anti-inflammatory, antipyretic, analgesic and antioxidant activities.[1] In 1938, Terasawa succeeded in the enantioselective total synthesis of gorgosterol. The aldehyde **38** was subjected to a Wittig reaction,[20] stable ylides of which usually occur in higher than 90% E-selectivity. However, the use of triphenylphosphorane led to the formation of 85% alcohol **39**. In the Claisen–Johnson rearrangement, a combination of triethyl orthopropionate and propionic acid as a catalyst was used successfully. The more polar ester **40** was observed in a 56% yield. Ozonolysis and then reduction of the product gave optically pure lacton **41**, hydrolysis of which was achieved with aqueous potassium hydroxide. This was followed by methylation *in situ* to afford **42** in a 90% yield. Cyclisation of **42** in the presence of *t*-BuOK in THF gave cyclopropane **43** in a highly diastereoselective fashion. A synthetic methodology to convert cyclopropane **43** into allylic alcohol **44** was accomplished by efficient series of reactions: reduction, oxidation and a Wittig reaction.[20] Allylic alcohol **44** then underwent a Claisen-type rearrangement. Condensation of triethyl orthopropionate with allylic alcohol **44** afforded the rearranged ester **45** as a 9:1 mixture of diastereomers. Ester **45** was reduced with $LiAlH_4$. The resulting olefin **45** was subjected to ozonolysis that allowed the cleavage of alkene double bonds, which was followed by deoxygenation reaction, affording the compound **47**. Finally, gorgosterol was obtained upon recrystallisation (Scheme 9).



Scheme 9. Total synthesis of gorgosterol.

Reagents and conditions: (a) Ph_3PCHCO_2Et, (*i*-$Bu_2AlH)_2$, 0 °C; (b) $CH_3CH_2C(OC_2H_5)_3$, C_2H_5COOH, xylene, reflux; (c) $NaBH_4$, ether, 0 °C; (d) CH_2N_2, CH_3SO_3Na, (buffered with KH_2PO_4), -20 °C; (e) *t*-BuOK, THF, -0 °C; (f) $LiAlH_4$ (reduction), $C_5H_6NClCrO_3$ (oxidation), Ph_3PCHCO_2Et (Wittig reaction), (*i*-$Bu_2AlH)_2$ (DIBAH reduction) over four steps; (g) $CH_3CH_2C(OC_2H_5)_3$, C_2H_5COOH, xylene, reflux; (h) $LiAlH_4$, $C_5H_4ClNO_2S$; (i) $NaBH_4$; (j) $C_5H_{12}O_3S$.

7. Conclusions

This review presents the synthesis and main antioxidant features of bioactive natural compounds found in Red Sea marine organisms. We hope that the scheme outlined here for synthetic routes to marine natural products and the biological and pharmacological properties associated with them will be useful for future investigations of the conversion of natural to medicinal products and will encourage innovative research into these natural products.

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Conflicts of Interest

The author declares no conflicts of interest.

References

[1] Abou El-Ezz, R.; Ibrahim, A.; Habib, E.; Wahba, A.; Kamel, H.; Afifi, M.; Hassanean, H.; Ahmed, S. Review of natural products from marine organisms in the red sea. *IJPSR* **2017**, *8*, 940-974.

[2] a) Gerwick, W.; Moore, S. Lessons from the past and charting the future of marine natural products drug discovery and chemical biology. *Chem. Biol*. **2012**, *19*, 85-98. b) Loya, S.; Bakhaashvili, M.; Kashman, Y.; Hizi, A. Peyssonols A and B, Two novel inhibitors of the reverse transcriptases of human immunodeficiency virus types 1 and 2. *Arch. Biochem. Biophys*. **1995**, *316*, 789-801. c) Rahman, A. *Studies in Natural Products Chemistry,* Elsevier, 2005.

[3] Snyder, A.; Treitler, S.; Brucks, A. Simple reagents for direct halonium-induced polyene cyclizations. *J. Am. Chem. Soc*. **2010**, *132*, 14303-14314.

[4] Saitman, A.; Rulliere, P.; Sullivan, S.; Theodorakis, E. Total synthesis of norcembrenolide B and scabrolide D. *Org Lett*. **2011**, *13*, 5854-5857.

[5] Isaacs, S.; Kashman, Y. Shaagrockol B and C; two hexaprenylhydroquinone disulfates from the red sea sponge *Toxiclona toxius*. *Tetrahedron Lett*. **1992**, *33*, 2227-2230.

[6] Isaacs, S.; Hizi, A.; Kashman, Y. Toxicols A-C and toxiusol - new bioactive hexaprenoid hydroquinones from *Toxiclona toxius*. *Tetrahedron*. **1993**, *20*, 4275-4282.

[7] Menhour, B.; Aclinou, P.; Pete, J. Synthesis of bicyclic oxepanes: an enantioselective approach to the western part of shaagrockol C. *Mediterr. J. Chem*. **2013**, *2*, 522-540.

[8] Schaschke, N.; Miraziridine, A. Natures blueprint towards protease class-spanning inhibitors. *Bioorg. Med. Chem. Lett*. **2004**, *14*, 855-857.

[9] Nakao, Y.; Fujita, M.; Warabi, K.; Matsunaga, S.; Fusetani, N. Miraziridine A, a novel cysteine protease inhibitor from the marine sponge *Theonella aff. mirabilis*. *J. Am. Chem. Soc.* **2000**, *122*, 10462-10463.

[10] Konno, H.; Kubo, K.; Makabe, H.; Toshiro, E.; Hinoda, N.; Nosaka, K.; Akajia, K. Total synthesis of miraziridine A and identification of its major reaction site for cathepsin B. *Tetrahedron*. **2007**, *63*, 9502-9513.

[11] Piironen, V.; Lindsay, D.; Miettinen, T.; Toivo1, J.; Lampi, A. Plant sterols: biosynthesis, biological function and their importance to human nutrition. *J. Sci. Food. Agric*. **2000**, *80*, 939-966.

[12] Dufourc, E. Sterols and membrane dynamics. *J. Chem. Biol*. **2008**, *1*, 63-77.

[13] Kovganko, N.; Ananich, S. Steroidal triterpenes of cholesterol synthesis. *Molecules* **1999**, *18*, 4002-4017.

[14] Marino, J.; Abe, H. New stereospecific approach to steroid side chains: conversion of dehydroepiandrosterone to cholesterol, isocholesterol, and their 15.beta.-hydroxy derivatives. *J. Am. Chem. Soc*. **1981**, *103*, 2907-2909.

[15] Yoshinori, F.; Kimura, M.; Khalifa, F.; Ikekawa, N. Side chain structural requirement for utilization of sterols by the silkworm for growth and development. Non-stereoselective utilization of the 24-stereoisomeric pairs of 24-alkylsterols *Chem. Pharm. Bull*. **1984**, *32*, 4372-4381.

[16] Djerassi, C.; Mutzenbecher, G.; Fajoks, J.; Williams, D.; Budzikiewicz, H. Mass spectrometry in structural and stereochemical problems. LXV. 1 Synthesis and fragmentation behavior of 15-keto steroids. The importance of interatomic distance in the McLafferty rearrangement[2]. *J . Am. Chem.* Soc. **1962**, *87*, 817-826.

[17] Catalan, C.; Kokke, W.; Duque, C.; Djerassi, C. Synthesis of (24R)- and (24S)-5,28-stigmastadien-3.beta.-ol and determination of the stereochemistry of their 24-hydroxy analogs, the saringosterols. *J. Org. Chem.* **1983***, 48*, 5207-5214.

[18] Yujuan, S.; Lin, Y.; Cao, X.; Xiang, L.; Jianhua, Q. Sterols from mytilidae show anti-aging and neuroprotective effects via anti-oxidative activity. *Int. J. Mol. Sci*., **2014**, *15* 21673.

[19] Proudfoot, J. R.; Djerassi, C. Minor and trace sterols in marine invertebrates 48. The isolation, structure elucidation and synthesis of 23(R),24(R)-methylenecholesterol. *Tetrahedron Lett.* **1984***, 48,* 5493-5496.

[20] Terasawa, T.; Hirano, Y.; Fujimoto, Y.; Ikekawa, N. Stereocontrolled synthesis of gorgosterol. *J. Chem. Soc., Chem. Commun.* **1983***, 20*, 1180-1182.