Organic & Biomolecular Chemistry

Dynamic Article Links

Cite this: *Org. Biomol. Chem.*, 2011, **9**, 7877

www.rsc.org/obc

PAPER

A radical cyclization approach to the formal total syntheses of platencin†

Kalanidhi Palanichamy, Ayyagari V. Subrahmanyam and Krishna P. Kaliappan*

Received 12th July 2011, Accepted 18th August 2011
DOI: 10.1039/c1ob06155k

Two different strategies leading to formal total syntheses of platencin are described. The first strategy involving Claisen rearrangement and radical cyclization provides a rapid access to the core structure of platencin, and also use minimum protective-group operations. The second strategy, a protecting group-free route, utilizes a 6-*exo*-*trig* radical cyclization and aldol condensation as key steps leading to the formal synthesis of platencin.

Introduction

The "superbugs," a set of bacterial strains, have been posing a serious threat to human lives by developing resistance to most of the existing antibiotics, and hence there is a danger of the survival of these superbugs. This is primarily due to the fact that most of the currently available antibiotics are either old discoveries or synthetic modifications thereof. Consequently, there is an urgent need for the discovery of new classes of antibiotics that work with novel modes of action and also act on new targets. As many of the existing antibiotics work by inhibiting cell wall synthesis, protein synthesis, or nucleic acid synthesis of bacteria,[1] discovery of new antibiotics that work by unique modes of action is in demand. Thus, bacterial fatty acid biosynthesis, which is essential for bacterial survival is considered as an attractive target as there are many interesting enzymes which could be targeted.[2] To this end, several inhibitors of these enzymes have appeared in the literature, but none of them are suitable drug candidates due to their poor penetration and lack of target selectivity. Nevertheless, continued efforts on the discovery of new class of antibiotics eventually rewarded the Merck research group to isolate two novel potent antibiotics, platensimycin (**1**)[3] and platencin (**2**)[4] (Fig. 1) from the strain of *Streptomyces platensis* through a systematic screening of about 250 000 natural product extracts as part of their advanced target-based whole-cell screening strategy using antisense differential sensitivity assay.

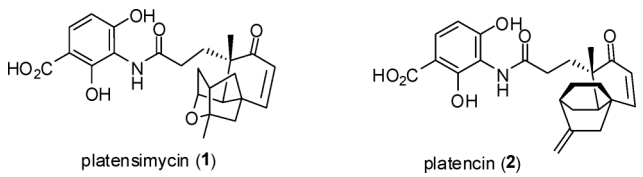


Fig. 1 Platensimycin and platencin.

Being an unprecedented class of antibiotics, platensimycin and platencin differ slightly in their mode of action though they both are structurally related. While platensimycin is a selective inhibitor of elongation condensing enzyme FabF, platencin is a balanced dual inhibitor of FabF and initiation condensing enzyme FabH.[5] Later, the Merck research group also reported the discovery of several congeners of platensimycin and platencin from the same cultural broth (Fig. 2, congeners of platencin).[6]

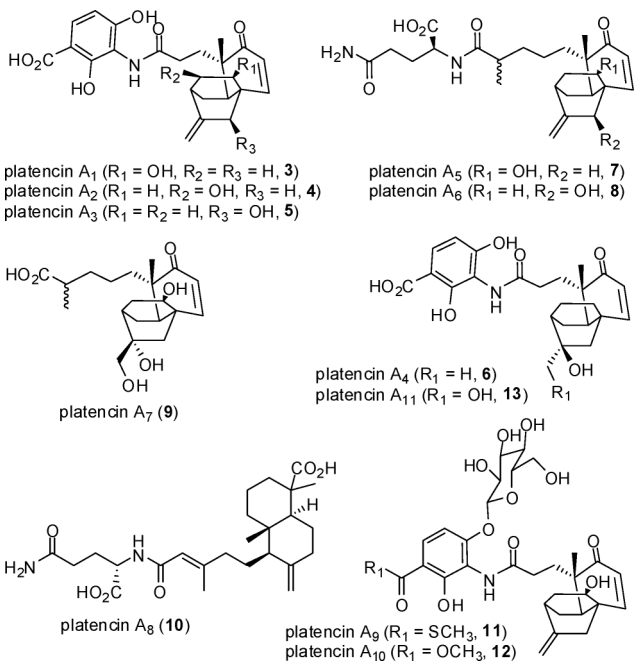


Fig. 2 Natural congeners of platencin.

However, none of them were found to exhibit superior activity than the parent molecules. Thus, the fascinating molecular architecture and the intriguing biological profile of platensimycin and platencin inspired the synthetic community immediately after

Department of Chemistry, Indian Institute of Technology Bombay, Powai, Mumbai, 400 076, India. E-mail: kpk@chem.iitb.ac.in; Fax: (+91) 22-2572-3480; Tel: (+91) 22-2576-7177

† Electronic supplementary information (ESI) available. See DOI: 10.1039/c1ob06155k

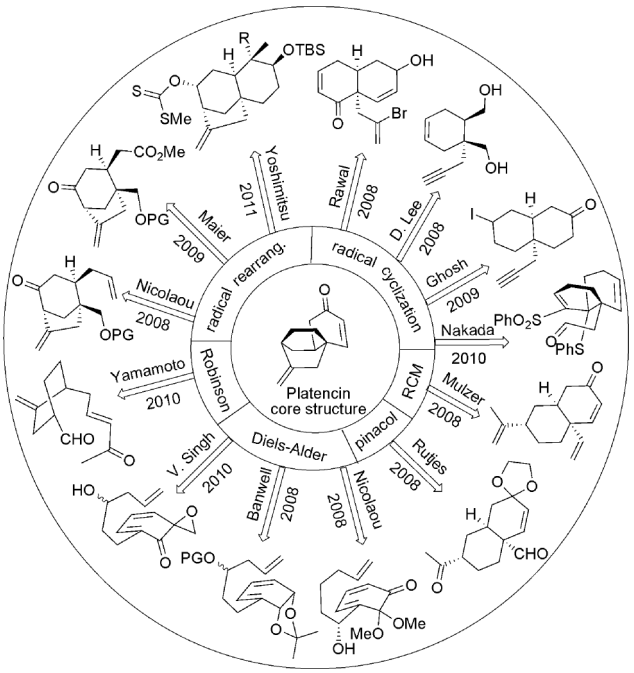


Fig. 3 Earlier synthetic approaches to platencin.

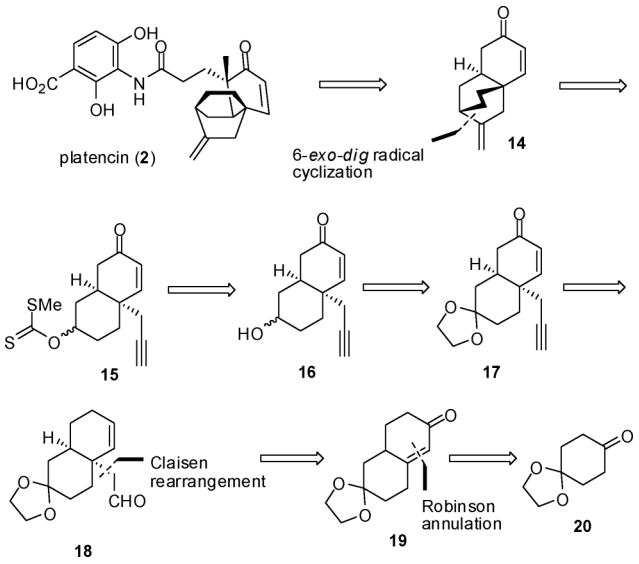
their isolation, and it has culminated in a few total (two for **1**, and four for **2**) and several formal syntheses for both molecules (Fig. 3 for platencin).[7–9] In continuation of our earlier report on a platensimycin analogue,[8d] and also in continuation of our interest in the synthesis of biologically active natural and unnatural products,[10] herein we present our initial endeavours on synthesis of platencin using two conceptually different approaches.

Results and discussion

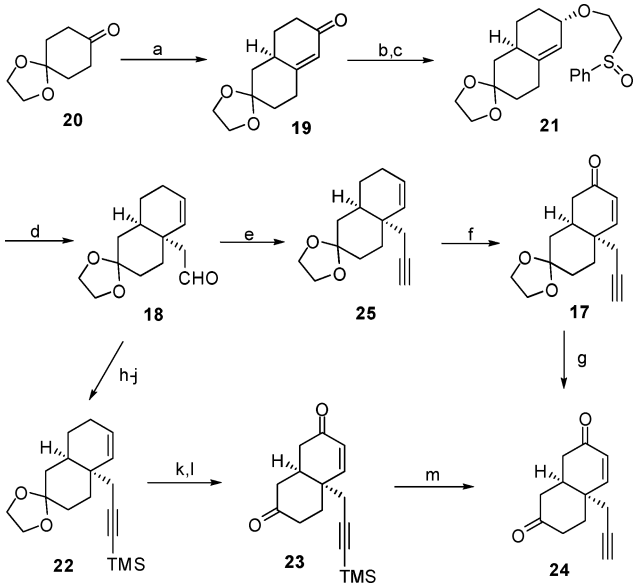
First strategy

In the first approach, we planned to extend the radical cyclization strategy utilized for the synthesis of the core structure of platensimycin, to achieve the formal synthesis of platencin. As per our retrosynthetic analysis delineated in Scheme 1, we envisaged that the tricyclic core **14**,[9a,b] an advanced intermediate in the earlier synthesis of platencin, could be constructed through a 6-*exo*-*dig* radical cyclization from xanthate **15**, which, in turn, could be derived from alcohol **16**. This alcohol **16** could be obtained from γ,δ-unsaturated aldehyde **18** in a few steps, and aldehyde **18** was envisioned from the corresponding allylic alcohol through Claisen rearrangement.[11] The enone **19**[12] that would afford the desired allylic alcohol could be derived from cyclohexanedione monoethylene ketal **20** through a Robinson-type annulation. Thus, as depicted in Scheme 2, the synthesis of enone **24** commenced with the construction of bicyclic enone **19**. To this end, cyclohexanedione monoethylene ketal **20** was treated with KOH and methyl vinyl ketone to afford enone **19** in moderate yield based on recovered starting material. A stereoselective DIBAL-H reduction[8d,13] of enone **19** furnished the corresponding allylic alcohol as the precursor for Claisen rearrangement.

After extensive experimentation, the modified Claisen rearrangement developed by Mandai[14] was identified as the best reaction conditions to afford the desired γ,δ-unsaturated aldehyde



Scheme 1 Retrosynthetic analysis.

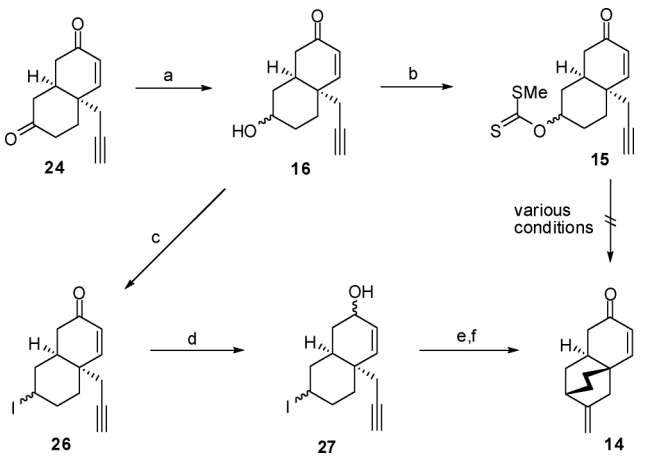


Scheme 2 *Reagents and conditions*: (a) KOH, methyl vinyl ketone, Et_2O, 0 °C, 3 h, 60% (brsm); (b) DIBAL-H, CH_2Cl_2, −78 °C, 1 h, 99%; (c) NaH, KH (cat.), phenylvinyl sulfoxide, THF, 0 °C to rt, 12 h, 98%; (d) $NaHCO_3$, decalin, 180 °C, 18 h, 69%; (e) diethyl 1-diazo-2-oxopropylphosphonate, K_2CO_3, MeOH, 0 °C to rt, overnight, 73%; (f) PDC, *t*BuOOH, Celite, benzene, 10 °C to rt, overnight, 44% (72% brsm); (g) *p*-TSA, MeOH/H_2O, rt, overnight, 85%; (h) CBr_4, PPh_3, Zn, CH_2Cl_2, 0 °C to rt, 12 h; (i) ethylene glycol, *p*-TSA, benzene, reflux, 12 h, 88% (two steps); (j) *n*BuLi, THF, −78 °C, 2 h, then TMSCl, −78 °C, 30 min, 73%; (k) PDC, *t*BuOOH, Celite, benzene, 10 °C to rt, overnight, 62% brsm; (l) 5% aq. acetone, *p*-TSA, 60 °C, 10 h, 85%; (m) TBAF, THF, 0 °C to rt, 1 h, 82%.

18. Thus, the allylic alcohol was treated with NaH and phenyl vinyl sulfoxide in the presence of catalytic amount of KH to provide the sulfoxide **21**, which upon heating with $NaHCO_3$ in decalin underwent elimination followed by Claisen rearrangement to furnish the desired aldehyde **18**. One-carbon homologation of this aldehyde to afford alkyne **22** was carried out through a three-step sequence, involving Corey–Fuchs olefination,[15] treatment

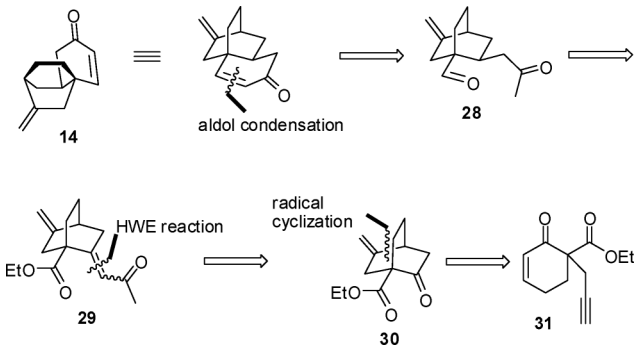
with *n*BuLi and TMSCl, and ketal formation. It was observed that the Corey–Fuchs reaction was accompanied by deprotection of the ketal group, presumably due to $ZnBr_2$ formed during the reaction conditions. Allylic oxidation of **22** with PDC and *t*BuOOH,[16] followed by ketal cleavage under acidic conditions provided ketone **23**, which upon cleavage of TMS group with TBAF led to the formation of ketone **24**. The lengthy nature of this route to transform aldehyde **18** into ketone **24** forced us to improve the efficiency of the strategy. Thus, treatment of aldehyde **18** with Bestmann–Ohira reagent[17] followed by allylic oxidation with PDC and *t*BuOOH, and subsequent ketal deprotection furnished ketone **24** in three steps from **18**.

A chemoselective reduction of ketone **24** with $NaBH_4$ at –20 °C afforded alcohol **16** as an inseparable mixture of diastereomers (Scheme 3). To carry forward this inseparable mixture might not encounter any difficulty as in principle they both would result in a single radical intermediate. With this alcohol synthesized, the final challenge was to successfully accomplish the core structure of platencin by a 6-*exo-dig* radical cyclization. Towards this end, alcohol **16** was treated with NaH and CS_2, and subsequent quenching with MeI, to afford xanthate **15**. Unfortunately, all our attempts to execute the key radical cyclisation of xanthate **15** were unsuccessful[18] under various reaction conditions with nBu_3SnH and AIBN, and revealing that xanthate **15** might be a poor radical precursor.



Scheme 3 *Reagents and conditions*: (a) $NaBH_4$, EtOH, –20 °C, 3 h, 77%; (b) NaH, THF, 0 °C, 20 min, then CS_2, rt, 30 min, then MeI, rt, 15 min, 91%; (c) PPh_3, I_2, Im, THF, 0 °C to RT, 1 h, 70%; (d) DIBAL-H, CH_2Cl_2, –78 °C, 1 h, 63%; (e) nBu_3SnH, AIBN, benzene, reflux, 2 h; (f) MnO_2, CH_2Cl_2, rt, overnight, 43% (over two steps).

This unexpected disappointment in accomplishing the radical cyclization forced us to bring this strategy to a halt at this stage, search for alternative conditions, and focus on the second strategy (Scheme 4, *vide infra*). When we were working on the second strategy, a report on the synthesis of platencin by the Ghosh's group[9k] appeared in the literature, wherein a similar such problem had been encountered and circumvented by using the corresponding iodide as the more reactive radical precursor. This observation invited us to revisit our strategy, and thus, iodide **26** was envisioned to be a better reactive substrate that could be conveniently obtained in good yield from alcohol **16** by treating with PPh_3, I_2 and imidazole. However, once again to our dismay,



Scheme 4 Retrosynthetic analysis.

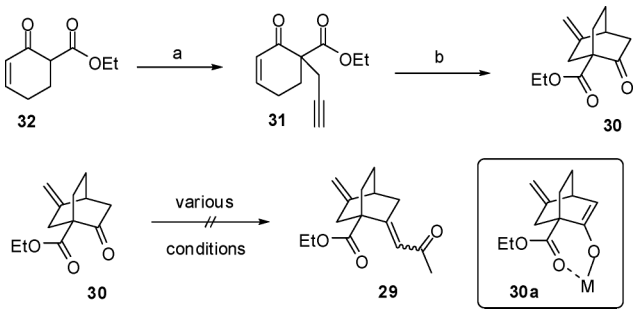
as in the case of xanthate **15**, all our efforts to execute the radical cyclisation of iodide **26** failed to give the desired tricyclic framework under various reaction conditions with nBu_3SnH and AIBN, resulting in only unidentified decomposition products. Although fully consumed, the fate of the substrate under the reaction conditions could not be determined.

The cumulative disappointment in realizing the radical cyclisation under various conditions called for an investigation on our substrate. Thus, as observed by the Rawal's group in their synthesis of platencin,[9b] we eventually found that the rigid nature of iodide **26** due to the enone moiety might not permit the substrate to adopt a suitable conformation in order to facilitate the radical cyclisation. To answer this rigidity issue, enone **26** was reduced with DIBAL-H to afford allylic alcohol **27** as an inseparable mixure of diastereomers. Pleasingly, a slow addition of a solution of nBu_3SnH and AIBN in benzene to a refluxing solution of iodide **27** in benzene by a syringe pump over 2 h resulted in the formation of the desired cyclised product, which was immediately treated with MnO_2 in CH_2Cl_2 to afford the tricyclic core **14** in 43% yield over two steps, thus completing a formal synthesis of platencin.[9a,b]

Second strategy

In parallel, our constant efforts to develop a short and efficient strategy that neglects protective-group operations led us to design another route, as exemplified in Scheme 4, for the construction of the tricyclic core structure of platencin. Accordingly, the intermediate **14** was envisioned to be derived from ketoaldehyde **28** through an intramolecular aldol condensation,[9a,d,h] and compound **28**, in turn, could be derived from **29** through a sequence of reductions and oxidation. Horner–Wadsworth–Emmons reaction[19] was envisioned as a means to derive enone **29** from ketoester **30**, which, in turn, could be constructed from compound **31** through a 6-*exo-trig* radical cyclisation. Finally, compound **31** could be traced back to the known ketoester **32**.[20]

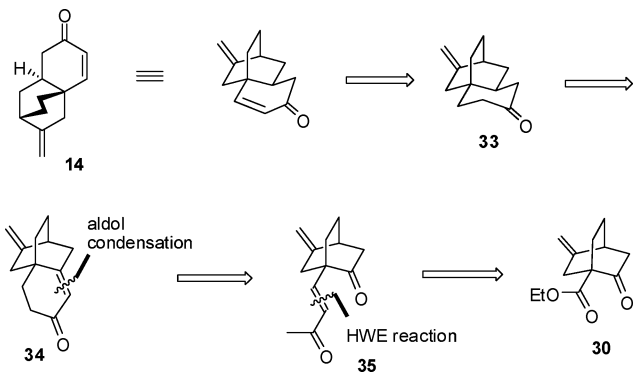
The synthesis of enone **14** commenced with the construction of ketoester **30**,[21] which is a known compound from cyclohexanone in seven steps. However, we intended to access this intermediate through an alternative short route as shown in Scheme 5. To this end, ketoester **32** which is readily accessible from cyclohex-2-enone was subjected to propargylation with propargyl bromide and K_2CO_3 to afford compound **31** in 72% yield. As anticipated, the planned 6-*exo-trig* radical cyclisation underwent smoothly by refluxing a solution of **31**, nBu_3SnH and AIBN in *t*BuOH for 5 h, followed by destannation with PPTS, to afford the



Scheme 5 *Reagents and conditions*: (a) propargyl bromide, K_2CO_3, acetone, reflux, 3.5 h, 72%; (b) nBu$_3$SnH, AIBN, tBuOH, reflux, 5 h, then PPTS, CH_2Cl_2, rt, overnight, 52% for two steps.

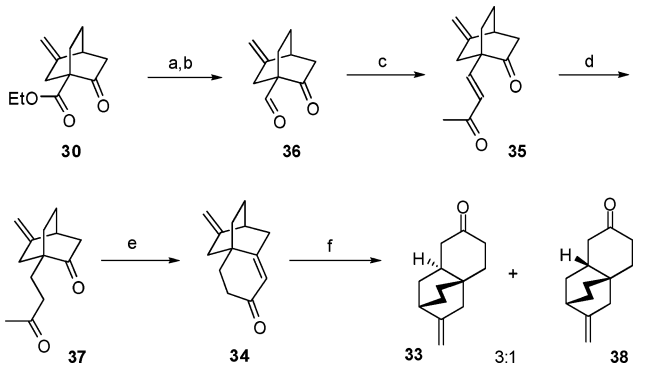
bicyclic ketoester **30** in 52% yield. With enough supply of bicyclic compound **30** in hand, our next task was to perform a three-carbon homologation to obtain enone **29**. Surprisingly, our various attempts to execute the Horner–Wadsworth–Emmons olefination under different conditions (NaH, KOH, nBuLi, DIPEA and LiCl, and Wittig reaction with corresponding stabilized phosphorane) at varying temperatures were unrewarding to deliver the desired product, presumably due to the formation of chelated enolate **30a**.

Due to the failure encountered in executing the Horner–Wadsworth–Emmons reaction, we slightly modified the strategy as shown in Scheme 6. Thus, enone **14** was envisaged to be derived from β-disubstituted enone **34** through transposition of the enone double bond. Further, an aldol condensation was envisioned as a means to construct the tricyclic enone **34** from the corresponding diketone, which, in turn, could be derived from enone **35**. A chemoselective Horner–Wadsworth–Emmons reaction of corresponding ketoaldehyde that could be derived from **30** would give access to the formation of enone **35**.



Scheme 6 Revised retrosynthetic analysis.

Accordingly, the synthetic strategy began with the reduction of ketoester **30** with LAH to afford corresponding diol, which upon oxidation under Swern conditions[22] furnished ketoaldehyde **36** in quantitative yield (Scheme 7). The ketoaldehyde **36** was then converted into enone **35** through Horner–Wadsworth–Emmons reaction in 89% yield as a single diastereomer. It is worth mentioning that in this case also the keto group was highly unreactive under the reaction conditions even in the presence of excess base and phophonate reagent. With the enone **35** synthesized, our next task was to selectively reduce the enone double bond in the presence of an exocyclic double bond. Eventually, treatment of **35** with



Scheme 7 *Reagents and conditions*: (a) LAH, Et_2O, 0 °C, 52%; (b) $(COCl)_2$, DMSO, Et_3N, CH_2Cl_2, −78 °C, 5 h, quant.; (c) diethyl 2-oxopropylphosphonate, NaH, THF, 0 °C, 30 min, 89%; (d) Ra-Ni, THF/H_2O, rt, 6.5 h, quant.; (e) NaOH, EtOH, rt, 12 h, 70%; (f) Ra-Ni, THF/H_2O, rt, 12 h, 85% (**33**:**38** = 3 : 1).

Raney Ni® (Ra-Ni) in THF allowed chemoselective reduction of enone double bond to furnish dione **37** in quantitative yield.[23] The closing of the ring was efficiently carried out through an intramolecular aldol condensation to result in the formation of tricyclic framework **34**. The final challenge left over to complete the synthesis was to accomplish a chemo- and stereoselective reduction of the sterically challenged β-disubstituted enone double bond of **34** in the presence of its exocyclic double bond. In our search for various conditions to effect this transformation, we eventually found that treatment of enone **34** with Ra-Ni in THF caused the reduction to afford an inseparable mixture of the desired tricyclic framework **33** and the other isomer **38** albeit in 3 : 1 ratio in favour of the desired one. Other attempted conditions such as, hydosilylation,[24,8m] Stryker's reduction,[25] and Crabtree's reduction[26] were unproductive, and left only the starting material to be recovered. Nevertheless, construction of tricyclic ketone **33** thus constitutes a formal synthesis as this skeleton has previously been elaborated into platencin.[9g,k,n]

Conclusions

In summary, we have successfully developed two different strategies for the formal synthesis of platencin, by exploiting the radical chemistry. While the first strategy utilizes Claisen rearrangement and radical cyclisation for the construction of the tricyclic core with the use of minimal protecting groups, the second one that employs an aldol condensation along with the radical cyclisation, entirely avoids protective-group operations throughout the strategy.

Experimental section

General methods

Unless and otherwise noted, all starting materials and reagents were obtained from commercial suppliers and used after further purification. Tetrahydrofuran was distilled from sodium benzophenone ketyl and toluene from sodium. Dichloromethane, *N*,*N*-dimethylformamide, hexanes and pyridine were freshly distilled from calcium hydride. All solvents for routine isolation of products and chromatography were of reagent grade and

glass distilled. Reaction flasks were dried in oven at 100 °C for 12 h. Air- and moisture-sensitive reactions were performed under an argon/UHP nitrogen atmosphere. Chromatography was performed using silica gel (100–200 mesh, Aceme, for gravity column chromatography; 230–400 mesh, Aceme, for Biotage flash column chromatography) with indicated solvents. All reactions were monitored by thin-layer chromatography carried out on 0.25 mm E. Merck silica plates (60F-254) using UV light as visualizing agent, and charring solution (prepared by dropwise addition of conc. H_2SO_4 (5 mL) to a solution of phosphomolybdic acid (1 g) and ceric sulphate (2 g) in water (95 mL)), alkaline $KMnO_4$ solution (prepared by dissolving $KMnO_4$ (2 g) and $NaHCO_3$ (4 g) in water (100 mL)), and heat as developing agents. Optical rotation was recorded on Autopol IV automatic polarimeter. IR spectra were recorded on Thermo Nicolet Avater 320 FT-IR and Nicolete Impact 400 machine. Mass spectra were obtained from Waters Micromass-Q-Tof micro™ (YA105) spectrometer. ^{1}H and ^{13}C NMR spectra were recorded either on Varian AS 400, Varian ASM 300 or Bruker 400. NMR data is in the order of chemical shifts, multiplicity (*s*, singlet; *br s*, broad singlet; *d*, doublet; *t*, triplet; *q*, quartet; *qnt*, quintet; *m*, multiplet), number of protons and coupling constant in hertz (Hz). The processing of NMR spectra was done using MestReNova NMR processing software.

3′,4′,8′,8a′-Tetrahydro-1′*H*-spiro[[1,3]dioxolane-2,2′-naphthalen]-6′(7′*H*)-one (19)[12]. To a solution of ketone **20** (0.1 g, 0.64 mmol) in Et_2O (1 mL) was added a solution of KOH (14.3 mg, 0.256 mmol) in ethanol (0.5 mL) at 0 °C, and the reaction mixture was stirred for 30 min at the same temperature. A solution of methyl vinyl ketone (0.061 mL, 0.742 mmol) in Et_2O (1 mL) was added to the reaction mixture at 0 °C over a period of 1 h. After the addition was completed, the reaction mixture was stirred for another 1 h. The reaction mixture was treated with water and the aqueous layer was washed with ethyl acetate (2 × 20 mL) and the organic layer was washed with water (20 mL), brine, dried over Na_2SO_4 and purified by silica gel column chromatography (20% ethyl acetate in hexanes) to afford the enone **19** (0.08 g, 60%, based on recovered starting material, brsm) as a white solid. R_f 0.52 (1 : 1 ethyl acetate–hexanes); mp 73–75 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 5.87 (s, 1H), 4.01 (dd, 4H, J = 3.2, 4.8 Hz), 2.86–1.57 (m, 9H), 1.48 (t, 2H, J = 17.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 199.6, 164.3, 124.9, 107.8, 64.5, 64.5, 41.5, 36.4, 35.1, 34.1, 32.2, 29.1; IR (neat) cm^{-1}: 2950, 2886, 1671, 1622, 1452, 1334, 1127, 1065, 917, 733; HRMS (EI) calc. for $C_{12}H_{17}O_3$ m/z 209.1178, found m/z 209.1177.

3′,4′,6′,7′,8′,8a′-Hexahydro-1′*H*-spiro[[1,3]dioxolane-2,2′-naphthalen]-6′-ol (19a). To a solution of enone **19** (0.1 g, 0.48 mmol) in CH_2Cl_2 (5 mL) was added DIBAL-H (0.96 mL, 0.96 mmol, 1 M in toluene) at −78 °C. The solution was stirred at the same temperature for 1 h. The reaction mixture was treated with a saturated solution of sodium potassium tartarate, and the mixture was stirred at rt until the solution became clear. The organic layer was separated from the reaction mixture and the aqueous layer was extracted with ethyl acetate (2 × 20 mL). The combined organic extracts were washed with water, brine and dried over Na_2SO_4. Concentration of the solution followed by silica gel column purification (20% ethyl acetate in hexanes) afforded the alcohol **19a** (0.096 g, 99%) as a white solid. R_f 0.52 (1 : 1 ethyl acetate–hexanes); mp 89–91 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 5.47 (s, 1H), 4.24–4.0 (m, 1H), 3.96 (d, 4H, J = 2.0 Hz), 2.32–1.15 (m, 12H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 141.2, 124.4, 108.7, 67.0, 64.3, 64.2, 42.4, 35.3, 34.1, 31.7, 31.4, 27.4; IR (neat) cm^{-1}: 3435, 2937, 2879, 1664, 1450, 1351, 1284, 1216, 1124, 1031, 947, 844, 758; HRMS (EI): calc. for $C_{12}H_{18}O_3Na$ m/z 233.1154, found m/z 233.1156.

6′-(2-(Phenylsulfinyl)ethoxy)-3′,4′,6′,7′,8′,8a′-hexahydro-1′*H*-spiro[[1,3]dioxolane-2,2′-naphthalene] (21). A solution of allylic alcohol **19a** (0.3 g, 1.42 mmol) in THF (6 mL) was added dropwise to a suspension of NaH (0.102 g, 2.14 mmol) in THF (2 mL) at 0 °C and stirred for 20 min. Then, the reaction mixture was warmed to room temperature and stirred for another 30 min. The reaction mixture was again cooled to 0 °C and treated with a solution of phenyl vinyl sulfoxide (0.65 g, 4.28 mmol) in THF (2 mL) followed by the addition of a catalytic amount of (1 mg) of KH. After being stirred at the same temperature for 10 min, the reaction mixture was slowly warmed to room temperature and stirred for 12 h. The mixture was treated with cold water and extracted with ethyl acetate (3 × 150 mL). The combined organic layers were washed with water, brine and dried (Na_2SO_4). After concentration, the resultant residue was purified by silica gel column chromatography (25% ethyl acetate in hexanes) to afford the sulfoxide **21** (0.51 g) in 98% yield as a yellow oil. R_f 0.26 (1 : 1 ethyl acetate–hexanes); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.67–7.64 (m, 2H), 7.54–7.47 (m, 3H), 5.53–5.44 (m, 1H), 3.99–3.66 (m, 6H), 3.56–3.51 (m, 1H), 3.01–2.98 (m, 2H), 2.32–2.18 (m, 3H), 1.99–1.76 (m, 4H), 1.60–1.14 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.4, 142.1, 130.8, 129.1, 123.9, 121.6, 121.3, 108.7, 75.2, 74.9, 64.3, 64.2, 60.7, 60.6, 58.7, 58.5, 42.4, 42.3, 35.4, 35.3, 34.2, 34.2, 31.8, 31.7, 27.3, 27.3, 27.2, 27.1; IR (neat) cm^{-1} 3054, 2935, 2859, 1714, 1664, 1477, 1444, 1354, 1283, 1174, 1068, 1035, 947, 751; HRMS (EI) calc. for $C_{20}H_{26}O_4SNa$ m/z 385.1450, found m/z 385.1464.

2-(3′,4′,4a′,7′,8′,8a′-Hexahydro-1′*H*-spiro[[1,3]dioxolane-2,2′-naphthalene]-4a′-yl)acetaldehyde (18). A solution of sulfoxide **21** (2.85 g, 7.86 mmol) in decalin (35 mL) was treated with solid $NaHCO_3$ (25 g, 38.6 mmol) in one portion and heated at 180 °C for 18 h. After being cooled to room temperature, the reaction mixture was treated with ethyl acetate (150 mL) and water (50 mL). The organic layer was separated and washed with water and brine. After drying (Na_2SO_4), the solvent was removed and the resultant yellow oil was loaded on a silica pad. The pad was washed with hexanes to remove the decalin and then washed with ethyl acetate which was concentrated and purified by a silica gel column chromatography (10% ethyl acetate in hexanes) to yield the aldehyde **18** (1.24 g, 69%) as a low melting solid. R_f 0.66 (1 : 2 ethyl acetate–hexanes); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 9.82 (t, 1H, J = 2.8 Hz), 5.79–5.70 (m, 1H), 5.51 (dd, 1H, J = 1.2, 9.6 Hz), 3.96 (s, 4H), 2.63 (dd, 1H, J = 2.8, 14.8 Hz), 2.33 (dd, 1H, J = 3.6, 14.8 Hz), 2.12–1.49 (m, 11H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 203.0, 131.7, 128.5, 108.7, 64.1, 64.1, 55.6, 36.7, 36.1, 35.4, 34.4, 31.0, 23.1, 21.2; IR (neat) cm^{-1} 3010, 2924, 2725, 1718, 1459, 1366, 1291, 1154, 1102, 1072, 1030, 947, 896, 771; HRMS (EI) calc. for $C_{14}H_{21}O_3$ m/z 237.1491, found m/z 237.1481.

(3-(3′,4′,4a′,7′,8′,8a′-Hexahydro-1′*H*-spiro[[1,3]dioxolane-2,2′-naphthalene]-4a′-yl)prop-1-ynyl)trimethylsilane (22). To a solution of aldehyde **18** (0.24 g, 1.04 mmol) in CH_2Cl_2 (15 mL) were

added CBr_4 (1.03 g, 3.126 mmol), PPh_3 (0.82 g, 3.126 mmol) and zinc powder (0.204 g, 3.126 mmol) at 0 °C. Then, the reaction mixture was warmed to room temperature and stirred for 12 h. The mixture was treated with cold water and extracted with ethyl acetate (3 × 10 mL). The combined organic layers were washed with water, brine and dried (Na_2SO_4). After concentration, the resultant residue **18a** was directly used for the next reaction without further purification.

To a flask containing a Dean–Stark apparatus was placed a solution of ethylene glycol (1 mL), benzene (20 mL) and *p*-TSA (30 mg). The trace amount of water present initially was removed from the reaction mixture *via* azeotropic distillation. Then the compound **18a** was added and the water generated from the reaction mixture was removed during 12 h. After slowly warming to room temperature, the mixture was treated with a saturated solution of $NaHCO_3$, and the organic layer was separated and the aqueous layer was extracted with ethyl acetate (3 × 150 mL). The combined organic layers were washed with water, brine and dried (Na_2SO_4). After concentration, the resultant residue was purified by silica gel column chromatography (5% ethyl acetate in hexanes) to afford the vinyl dibromide **18b** (0.35 g) in 88% (two steps). R_f 0.56 (1 : 9 ethyl acetate–hexanes); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.42 (t, 1H, J = 8.0 Hz), 5.72 (dt, 1H, J = 3.6, 6.8 Hz), 5.35 (dd, 1H, J = 1.2, 10.0 Hz), 3.94–3.90 (m, 4H), 2.35 (dd, 1H, J = 6.8, 15.2 Hz), 2.14 (dd, 1H, J = 7.6, 15.2 Hz), 2.02–1.25 (m, 11H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 135.6, 132.7, 128.1, 109.0, 89.3, 64.1, 64.1, 45.1, 37.3, 35.7, 33.7, 31.0, 23.3, 21.4; IR (neat) cm^{-1} 3011, 2925, 2879, 1613, 1439, 1367, 1290, 1215, 1186, 1152, 1092, 910, 757; HRMS (EI) calc. for $C_{15}H_{21}O_2Br_2$ m/z 390.9908, found m/z 390.9926.

To a solution of dibromo compound **18b** (1.75 g, 4.46 mmol) in THF (75 mL) was added *n*BuLi (8.36 mL, 1.6 M in hexane, 13.38 mmol) at −78 °C. After stirring at the same temperature for 2 h, TMSCl (1.92 mL, 15.17 mmol) was added to the reaction mixture and it was further stirred for 30 min. The mixture was then treated with cold water and extracted with ethyl acetate (3 × 50 mL). The combined organic layers were washed with water, brine and dried (Na_2SO_4). After concentration, the resultant residue was purified by silica gel column chromatography (5% ethyl acetate in hexanes) to afford the alkyne **22** (0.98 g) in 73% yield as a yellow oil. R_f 0.62 (1 : 9 ethyl acetate–hexanes); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 5.72 (dt, 1H, J = 3.2, 6.4 Hz), 5.44 (dd, 1H, J = 1.6, 10.0 Hz), 3.94–3.92 (m, 4H), 2.32 (d, 2H, J = 16.8 Hz), 2.22 (d, 1H, J = 16.8 Hz), 1.98–1.41 (m, 10H), 0.15 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 132.7, 127.7, 109.1, 104.6, 86.8, 64.0, 36.7, 35.6, 34.8, 33.4, 32.9, 31.1, 23.2, 21.3, 0.1; IR (neat) cm^{-1} 3010, 2930, 2170, 1640, 1259, 1217, 1152, 1100, 1028, 844, 763; HRMS (EI) calc. for $C_{18}H_{29}O_2Si$ m/z 305.1937, found m/z 305.1932.

4a-(3-(Trimethylsilyl)prop-2-ynyl)-4,4a,8,8a-tetrahydronaphthalene-2,7(1*H*,3*H*)-dione (23). To a solution of alkene **22** (0.1 g, 0.328 mmol) in benzene (3 mL) were added PDC (0.423 g, 1.31 mmol), *tert*-butyl hydroperoxide (0.118 g, 1.31 mmol) and Celite (0.4 g) at 10 °C. After being stirred at the same temperature for 10 min, the reaction mixture was slowly warmed to rt and stirred for 4 h. The mixture was treated with diethyl ether, filtered through a pad of Celite and the residue was washed with 40 mL of ethyl acetate. After concentration, the resultant compound was purified by silica gel column chromatography (8% ethyl acetate in hexanes) to afford the enone **22a** (0.18 g) in 62% (brsm) yield as a yellow oil. R_f 0.58 (1 : 4 ethyl acetate–hexanes); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.67 (dd, 1H, J = 1.6, 10.4 Hz), 6.02 (d, 1H, J = 10.4 Hz), 3.95–3.88 (m, 4H), 2.74 (dd, 1H, J = 4.8, 17.2 Hz), 2.54 (dd, 2H, J = 17.2, 3.6 Hz), 2.39–2.28 (m, 2H), 1.97–1.82 (m, 2H), 1.72–1.42 (m, 4H), 0.14 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 198.3, 154.7, 129.7, 107.8, 102.3, 88.6, 64.2, 64.1, 40.3, 38.8, 37.0, 36.8, 32.7, 31.4, 30.5, −0.09; IR (neat) cm^{-1} 3016, 2917, 2123, 1670, 1410, 1259, 1217, 1094, 1017, 770; HRMS (EI) calc. for $C_{18}H_{27}O_3Si$ m/z 319.1729, found m/z 319.1724.

To a solution of enone **22a** (0.045 g, 0.141 mmol) in 5% aqueous acetone (5 mL) was added *p*-TSA (6 mg) and the reaction mixture was heated at 60 °C for 10 h. After cooling to room temperature, ethyl acetate (10 mL) was added and the organic layer was separated. The aqueous layer was extracted with ethyl acetate (2 × 10 mL) and the combined organic layers were washed with water, brine and dried (Na_2SO_4). After concentration, the resultant compound was purified by silica gel column chromatography (10% ethyl acetate in hexanes) to afford the ketone **23** (35 mg) in 85% yield as a yellow oil. R_f 0.36 (1 : 4 ethyl acetate–hexanes); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.85 (dd, 1H, J = 0.8, 10.2 Hz), 6.10 (d, 1H, J = 10.2 Hz), 2.73–2.62 (m, 4H), 2.58–2.26 (m, 5H), 2.17–2.04 (m, 2H), 0.14 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 208.7, 196.8, 153.9, 129.8, 101.0, 89.5, 43.2, 40.2, 39.6, 38.7, 37.6, 33.6, 29.5, 29.5, −0.09; IR (neat) cm^{-1} 3016, 2959, 2175, 1716, 1681, 1415, 1388, 1251, 1217, 1042, 1023, 911, 846, 759; HRMS (EI) calc. for $C_{16}H_{23}O_2Si$ m/z 275.1467, found m/z 275.1468.

4a-(Prop-2-ynyl)-4,4a,8,8a-tetrahydronaphthalene-2,7(1*H*,3*H*)-dione (24). To a solution of ketone **23** (0.03 g, 0.109 mmol) in THF (1 mL) was added a solution of TBAF (1 M in THF, 0.16 mL, 0.163 mmol) at 0 °C. The mixture was warmed to room temperature and stirred for 1 h. The reaction mixture was treated with water and extracted with ethyl acetate (10 mL), the organic layer was separated and the aqueous layer was extracted with ethyl acetate (2 × 5 mL). The combined organic extracts were washed successively with water, brine and dried (Na_2SO_4). After concentration, the resultant product was purified by silica gel column chromatography (10% ethyl acetate in hexanes) to afford the alkyne **24** (12 mg) in 82% yield as a colorless oil. R_f 0.62 (1 : 2 ethyl acetate–hexanes); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.87 (dd, 1H, J = 0.8, 10.0 Hz), 6.11 (d, 1H, J = 10.2 Hz), 2.69–2.61 (m, 3H), 2.51–2.08 (m, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 208.5, 196.7, 153.7, 130.0, 78.8, 72.6, 43.1, 40.2, 39.5, 38.6, 37.6, 33.5, 28.1; IR (neat) cm^{-1} 3269, 3016, 2923, 2340, 1717, 1674, 1412, 1218, 1034, 777, 669; HRMS (EI) calc. for $C_{13}H_{15}O_2$ m/z 203.1072, found m/z 203.1072.

4a′-(Prop-2-ynyl)-3′,4′,4a′,7′,8′,8a′-hexahydro-1′*H*-spiro[[1,3]-dioxolane-2,2′-naphthalene] (25). To a solution of aldehyde **18** (0.21 g, 0.91 mmol) in MeOH (4 mL) was added a solution of diethyl 1-diazo-2-oxopropylphosphonate (0.30 g, 1.36 mmol) in MeOH (5 mL) followed by the addition of K_2CO_3 at 0 °C. After addition, it was brought to rt and stirred overnight. The reaction was quenched with sat. aq. NH_4Cl solution (10 mL) and extracted with ether (3 × 20 mL). The combined organic layers were washed with sat. aq. $NaHCO_3$ solution (10 mL), water (10 mL) and brine (10 mL) sequentially, dried and concentrated to afford the crude product which was purified by silica gel flash column chromatography (10–15% ethyl acetate in hexanes) to furnish

alkyne **25** (0.15 g) in 73% yield as a pale yellow oil. R_f 0.72 (1 : 3 ethyl acetate–hexanes); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 5.72 (dt, 1H, J = 3.2, 6.4 Hz), 5.44 (dd, 1H, J = 1.6, 6.4 Hz), 3.96–3.92 (m, 4H), 2.32 (d, 2H, J = 16.8 Hz), 2.22 (d, 1H, J = 16.8 Hz), 1.99–1.42 (m, 11H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 132.7, 127.7, 109.1, 104.6, 86.8, 64.0, 36.7, 35.6, 34.8, 33.4, 32.9, 31.1, 23.2, 21.3; IR ($CHCl_3$) cm^{-1} 3307, 3019, 2928, 2854, 2706, 2400, 2115, 1459, 1365, 1216, 1090, 757, 669; HRMS (EI) calc. for $C_{15}H_{21}O_2$ m/z 233.1542, found m/z 233.1546.

4a′-(Prop-2-ynyl)-4′,4a′,8′,8a′-tetrahydro-1′*H*-spiro[[1,3]dioxolane-2,2′-naphthalen]-7′(3′*H*)-one (17). To a solution of alkene **25** (0.15 g, 0.66 mmol) and Celite (0.79 g) in benzene (8 mL) were added PDC (0.998 g, 2.65 mmol), 70% *tert*-butyl hydroperoxide (0.365 mL, 2.65 mmol) at 10 °C. After being stirred at the same temperature for 10 min, the reaction mixture was slowly warmed to rt and stirred overnight. The mixture was treated with diethyl ether, filtered through a pad of Celite and the residue was washed with 40 mL of ethyl acetate. After concentration, the resultant compound was purified by silica gel flash column chromatography (15–20% ethyl acetate in hexanes) to afford enone **17** (0.07 g) in 44% (72% brsm) yield as a yellow oil. R_f 0.54 (1 : 3 ethyl acetate–hexanes); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.66 (dd, 1H, J = 1.5, 10.0 Hz), 6.02 (d, 1H, J = 10.0 Hz), 3.88 (s, 4H), 2.68–2.58 (m, 1H), 2.49–2.28 (m, 5H), 2.08 (t, 1H, J = 2.7 Hz), 1.94–1.81 (m, 1H), 1.70–1.44 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 198.3, 155.0, 130.7, 107.8, 102.3, 88.6, 64.2, 64.1, 40.3, 38.8, 37.0, 36.8, 32.7, 31.4, 30.5; IR ($CHCl_3$) cm^{-1} 3307, 3019, 2927, 1676, 1216, 1092, 758, 669; HRMS (EI) calc. for $C_{15}H_{19}O_3$ m/z 247.1334, found m/z 247.1344.

4a-(Prop-2-ynyl)-4,4a,8,8a-tetrahydronaphthalene-2,7(1*H*,3*H*)-dione (24). To a solution of ketal **17** (0.08 g, 0.325 mmol) in MeOH (6.5 mL) and water (6.5 mL) was added *p*-TSA (0.031 g, 0.163 mmol) at rt, followed by stirring overnight at the same temperature. The reaction mixture was quenched with sat. aq. $NaHCO_3$ solution, and extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were dried, concentrated, and purified by silica gel column chromatography as above obtained from **23**, to afford ketone **24** (0.053 g, 85%) as a colorless oil.

7-Hydroxy-4a-(prop-2-ynyl)-4a,5,6,7,8,8a-hexahydronaphthalen-2(1*H*)-one (16). To a solution of ketone **24** (4.5 mg, 0.022 mmol) in ethanol (0.5 mL) was added $NaBH_4$ (0.21 mg, 0.005 mmol) in ethanol (0.5 mL) over a period of 2 h at –20 °C. After the addition was completed, the reaction mixture was stirred for another 1 h at the same temperature. The mixture was treated with glacial acetic acid (0.01 mL) and stirred for 5 min at the same temperature. After solvent evaporation, the residue was partitioned between ethyl acetate (2 × 10 mL) and saturated NaCl (2 × 10 mL). The organic layer was dried over Na_2SO_4 and evaporated and the resultant compound was purified by silica gel column chromatography (15% ethyl acetate in hexanes) to afford **16** (3.5 mg, 77%) in 1 : 5 ratio as a yellow oil. R_f 0.36 (1 : 2 ethyl acetate–hexanes); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.63 (dd, 1H, J = 2.0, 10.2 Hz), 6.04 (d, 1H, J = 10.2 H), 3.72–3.64 (m, 1H), 2.81 (dd, 1H, J = 5.2, 17.6 Hz), 2.51 (t, 1H, J = 2.8 Hz), 2.47 (dd, 1H, J = 2.4, 13.6 Hz), 2.39–2.23 (m, 2H), 2.10 (t, 1H, J = 2.8 Hz), 1.96–1.24 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 197.9, 195.7, 155.4, 154.9, 129.9, 129.3, 110.0, 79.7, 76.6, 71.9, 69.4, 65.5, 40.5, 40.2, 38.8, 37.6, 37.1, 35.4, 34.0, 31.8, 29.5, 28.9; IR (neat) cm^{-1} 3425, 2928, 2346, 1701, 1669, 1415, 1053, 768; HRMS (EI) calc. for $C_{13}H_{17}O_2$ m/z 205.1229, found m/z 205.1227.

***S*-Methyl *O*-7-oxo-4a-(prop-2-ynyl)-1,2,3,4,4a,7,8,8a-octahydronaphthalen-2-yl carbonodithioate (15).** To a stirred suspension of NaH (4.9 mg, 0.204 mmol) in THF (2 mL) was added alcohol **16** (13 mg, 0.063 mmol) in THF (2 mL) at 0 °C. After stirring for 20 min at the same temperature, CS_2 (0.011 mL) was added and again stirred for another 30 min at room temperature. MeI (0.006 mL, 0.101 mmol) was added and was allowed to stirr for 15 min. The reaction mixture was then treated with 1–2 drops of AcOH. The reaction mixture was filtered and washed with ethyl acetate (2 × 20 mL). The organic layer was washed with water, brine and dried (Na_2SO_4). After evaporation of the solvent the resultant residue was purified by silica gel column chromatography (5% ethyl acetate in hexanes) to afford compound **15** (17 mg, 91%) as a yellow oil. R_f 0.72 (1 : 4 ethyl acetate–hexanes); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.66 (dd, 1H, J = 2.0, 13.8 Hz), 6.05 (d, 1H, J = 10.0 Hz), 5.58–5.51 (m, 1H), 2.80 (dd, 1H, J = 5.2, 17.6 Hz), 2.61–1.52 (m, 14H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 215.2, 197.6, 154.4, 131.8, 129.9, 80.6, 79.4, 78.2, 72.3, 72.0, 40.4, 39.9, 38.8, 36.8, 33.1, 32.7, 31.7, 29.3, 27.4, 26.0, 18.8, 17.9; HRMS (EI) calc. for $C_{15}H_{19}O_2S_2$ m/z 295.0826, found m/z 295.0834.

7-Iodo-4a-(prop-2-ynyl)-4a,5,6,7,8,8a-hexahydronaphthalen-2-(1*H*)-one (26). To a solution of alcohol **16** (0.022 g, 0.107 mmol) in THF (2.2 mL) was added sequentially imidazole (0.0218 g, 0.321 mmol), PPh_3 (0.0564 g, 0.215 mmol) and I_2 (0.0547 g, 0.215 mmol) at 0 °C. After addition, the reaction was stirred at rt for 1 h followed by the addition of 5% Na_2SO_3 solution (5 mL). The reaction mixture was extracted with Et_2O, and the organic layer was dried and concentrated to afford the crude product, which was purified by silica gel flash column chromatography (10–15% ethyl acetate in hexanes) to afford iodide **26** (0.023 g, 70%) as an inseparable diastereomers, and as a pale yellow oil. R_f 0.75 (1 : 3 ethyl acetate–hexanes); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.66 (d, 1H, J = 9.8 Hz), 6.00 (d, 1H, J = 10.1 Hz), 4.62 (br s, 1H), 2.69–2.29 (m, 5H), 2.14–2.05 (m, 4H), 1.83–1.63 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 198.2, 155.7, 129.3, 79.3, 72.2, 72.1, 39.5, 38.9, 36.6, 33.1, 32.5, 29.6, 29.0; IR ($CHCl_3$) cm^{-1} 3307, 3019, 2930, 2856, 1675, 1215, 758, 669; HRMS (EI) calc. for $C_{13}H_{16}OI$ m/z 315.0246, found m/z 315.0238.

7-Iodo-4a-(prop-2-ynyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-2-ol (27). To a solution of enone **26** (110 mg, 0.35 mmol) in CH_2Cl_2 (3 mL) was added DIBAL-H (0.385 mL, 0.385 mmol, 1 M in toluene) dropwise at –78 °C followed by stirring at the same temperature for 1 h. Then the reaction mixture was quenched with saturated aqueous sodium potassium tartrate solution (10 mL) at –78 °C and brought to room temperature. The reaction mixture was extracted with CH_2Cl_2 (3 × 10 mL), and the combined organic layers were dried and concentrated. The crude product was purified by flash column chromatography (10–25% ethyl acetate in hexanes) to afford allylic alcohol **27** (70 mg, 63%) as an inseparable mixture of diastereomers, and as a colorless oil. R_f 0.45 (1 : 3 ethyl acetate–hexanes); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 5.81–5.47 (m, 2H), 4.44–4.02 (m, 2H), 2.52–2.20 (m, 3H), 2.20–1.80 (m, 5H), 1.80–1.45 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.2, 138.2,

136.5, 135.1, 131.4, 130.2, 81.0, 80.9, 80.8, 71.5, 71.4, 71.3, 64.9, 64.3, 41.6, 41.5, 40.7, 40.3, 38.4, 37.4, 37.0, 37.0, 36.9, 35.4, 34.6, 34.4, 33.9, 33.7, 33.4, 32.8, 32.1, 27.9, 27.6; IR ($CHCl_3$) cm^{-1} 3684, 3306, 3019, 2931, 2400, 1522, 1426, 1215, 1021, 929, 758; HRMS (EI) calc. for $C_{13}H_{17}ONaI$ m/z 339.0222, found m/z 339.0215.

Core structure of platencin (14). To a solution of iodide **27** (70 mg, 0.22 mmol) in degassed dry benzene (50 mL) was added a solution of nBu$_3$SnH (154 mg, 0.53 mmol) and AIBN (8.7 mg, 0.052 mmol) in degassed dry benzene (5 mL) at reflux conditions over a period of 2 h by a syringe pump. After addition, the reaction mixture was cooled to room temperature, and the volatiles were removed in a rotovapor to afford the crude cyclised product. To a solution of the above crude allylic alcohol in CH_2Cl_2 (5 mL) was added MnO_2 (200 mg, 2.3 mmol) at room temperature. After stirring overnight at the same temperature, the reaction mixture was filtered through a pad of Celite and silica gel, washed with CH_2Cl_2. The combined filtrates were concentrated and purified by flash column chromatography (1–20% ethyl acetate in hexanes) to afford the core structure of platencin **14** (18 mg, 43% for two steps) as a colorless oil. R_f 0.65 (12% ethyl acetate in hexanes); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.56 (d, 1H, J = 10.0 Hz), 5.87 (dd, 1H, J = 10.0, 0.9 Hz), 4.83 (dt, 1H, J = 3.0, 1.6 Hz), 4.69 (dd, 1H, J = 4.0, 1.8 Hz), 2.48–2.39 (m, 2H), 2.36–2.28 (m, 2H), 2.19–2.07 (m, 2H), 2.04–1.97 (m, 1H), 1.80–1.65 (m, 3H), 1.54–1.48 (m, 1H), 1.20 (ddd, 1H, J = 12.6, 7.9, 1.5 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 200.3, 156.9, 149.1, 127.9, 107.1, 41.8, 41.1, 36.2, 35.8, 35.7, 35.1, 26.6, 24.7; IR ($CHCl_3$) cm^{-1} 3020, 2928, 2857, 1682, 1464, 1216, 1084, 1026, 759; HRMS (EI) calc. for $C_{13}H_{17}O$ m/z 189.1279, found m/z 189.1282. These data are in good agreement with the literature reports.[9b]

Ethyl 2-oxocyclohex-3-enecarboxylate (32)[20]. To a solution of cyclohexenone (1 g, 10.4 mmol) in THF (33 mL) was added a solution of LDA (16.66 mL, 12.5 mmol, 0.75 M solution in THF) dropwise at −78 °C over 10 min. After stirring for 45 min, ethylcyanoformate (1.13 g, 11.44 mmol) was added dropwise followed by stirring at −78 °C for 4 h. The reaction mixture was quenched with saturated aqueous NH_4Cl solution and extracted with EtOAc. The combined organic layers were washed with brine, dried and concentrated. The crude product was purified by flash column chromatography (15–25% ethyl acetate in hexanes) to afford ketoester **32** (1.15 g, 66%) as a yellow oil. R_f 0.55 (12% ethyl acetate in hexanes); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.03–6.99 (m, 1H), 6.07 (dt, 1H, J = 9.9, 1.8 Hz), 4.26–4.17 (m, 2H), 3.40 (dd, 1H, J = 9.9, 4.8 Hz), 2.56–2.45 (m, 1H), 2.40–2.33 (m, 2H), 2.27–2.17 (m, 1H), 1.34–1.20 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 193.9, 169.9, 150.5, 129.0, 61.1, 53.3, 25.5, 24.2, 14.0; IR ($CHCl_3$) cm^{-1} 3021, 2984, 2939, 1735, 1684, 1446, 1426, 1389, 1373, 1308, 1219, 1170, 1125, 1096, 1080, 1072, 757.

Ethyl 2-oxo-1-(prop-2-ynyl)cyclohex-3-enecarboxylate (31). To a solution of ketoester **32** (1.15 g, 6.84 mmol) in dry acetone (41 mL) was added K_2CO_3 in one portion at rt. After stirring for a few minutes, propargyl bromide (1.6 mL, 14.37 mmol, 80 wt% in toluene) was introduced dropwise. After addition, the reaction mixture was refluxed for 3.5 h followed by filtration through Celite and concentration to afford the crude material, which was purified by flash column chromatography (10–20% ethyl acetate in hexanes) to provide enone ester **31** (1.0 g, 72%) as a pale yellow oil. R_f 0.75 (12% ethyl acetate in hexanes); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.00–6.95 (m, 1H), 6.06 (dt, 1H, J = 10.2, 1.8 Hz), 4.18 (q, 2H, J = 7.0 Hz), 2.84 (dd, 1H, J = 16.8, 2.5 Hz), 2.72 (dd, 1H, J = 16.8, 2.5 Hz), 2.66–2.51 (m, 2H), 2.45–2.34 (m, 1H), 2.28–2.20 (m, 1H), 2.03 (t, 1H, J = 2.5 Hz), 1.24 (t, 3H, J = 6.9 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 194.1, 170.0, 150.2, 128.6, 79.4, 71.1, 61.6, 55.9, 29.7, 23.9, 23.5, 13.9; IR ($CHCl_3$) cm^{-1} 3308, 3020, 2984, 2933, 2401, 2122, 1731, 1683, 1388, 1216, 1019, 758; HRMS (EI) calc. for $C_{12}H_{14}O_3Na$ m/z 229.0841, found m/z 229.0845.

Ethyl 5-methylene-2-oxobicyclo[2.2.2]octane-1-carboxylate (30)[21]. To a solution of enone **31** (100 mg, 0.485 mmol) in dry tBuOH (25 mL) were added AIBN (16 mg, 0.097 mmol) and then nBu$_3$SnH dropwise rt. After addition, the reaction flash was immersed into an oil bath preheated to 120 °C, and refluxed at that temperature for 5 h. After cooling to rt, the solvent was evaporated, redissolved in CH_2Cl_2 (10 mL), and the treated with PPTS (400 mg). After stirring overnight at rt, the reaction mixture was quenched with saturated aqueous $NaHCO_3$ solution, extracted with EtOAc. The combined organic layers were dried and concentrated to afford the crude product, which was purified by flash column chromatography (10–20% ethyl acetate in hexanes) to furnish ketoester **30** (53 mg, 52%) as a pale yellow oil. ^{1}H NMR (400 MHz) δ 4.92 (d, 1H, J = 0.9 Hz), 4.77 (q, 1H, J = 2.0 Hz), 4.18 (q, 2H, J = 7.2 Hz), 2.98 (dq, 1H, J = 17.8, 2.6 Hz), 2.70 (t, 1H, J = 2.8 Hz), 2.64 (dt, 1H, J = 17.8, 2.1 Hz), 2.37 (dq, 2H, J = 2.8, 0.9 Hz), 2.34–2.26 (m, 1H), 1.94–1.73 (m, 3H), 1.28 (t, 3 H, J = 7.1 Hz); ^{13}C NMR (100 MHz) δ 209.5, 170.9, 145.5, 108.2, 61.0, 55.9, 44.2, 38.2, 34.4, 25.5, 25.2, 14.0; IR ($CHCl_3$) cm^{-1} 3021,2938, 2873, 1746, 1450, 1249, 1216 cm^{-1}; HRMS (EI) calc. for $C_{12}H_{17}O_3$ m/z 209.1178, found m/z 209.1174.

1-(Hydroxymethyl)-5-methylenebicyclo[2.2.2]octan-2-ol (30b). To a solution of ketoester **30** (120 mg, 0.576 mmol) in dry Et_2O (5 mL) was added LAH portion wise at 0 °C. After addition, the reaction mixture was stirred for another 2 h at 0 °C, and then quenched with wet Na_2SO_4/Celite (1 : 1 mixture with a little water) at 0 °C. After stirring at rt for 2 h, the reaction mixture was filtered through Celite, washed with EtOAc, and concentrated. The crude material was purified by flash column chromatography (40–60% ethyl acetate in hexanes) to afford diol **30b** (50 mg, 52%) as a mixture of diastereomers, and as a colorless oil. ^{1}H NMR (400 MHz) δ 4.82–4.74 (m, 1H), 4.70–4.59 (m, 1H), 4.01–3.92 (m, 1H), 3.58–3.42 (m, 2H), 2.32–2.22 (m, 1H), 2.18–2.02 (m, 2H), 2.0–1.95 (m, 1H), 1.95–1.72 (m, 2H), 1.68–1.38 (m, 3H), 1.28–1.20 (m, 1H); ^{13}C NMR (100 MHz) δ 150.2, 149.6, 105.9, 105.7, 72.7, 72.7, 70.6, 70.5, 39.1, 38.9, 38.7, 38.2, 36.1, 36.1, 35.3, 30.6, 26.2, 25.9, 25.4, 21.1; IR ($CHCl_3$) cm^{-1} 3382, 2934, 1216, 1031, 909, 759; HRMS (EI) calc. for $C_{10}H_{16}O_2Na$ m/z 191.1048, found m/z 191.1051.

5-Methylene-2-oxobicyclo[2.2.2]octane-1-carbaldehyde (36). To a solution of oxalyl chloride (218 mg, 1.72 mmol) in CH_2Cl_2 (2.1 mL) was added DMSO (208 mg, 2.67 mmol) dropwise at −78 °C. After stirring for 30 min, a solution of diol **30b** (50 mg, 0.297 mmol) in CH_2Cl_2 (2.1 mL) was added dropwise followed by stirring for 3 h at the same temperature. Then, Et_3N (344 mg, 3.41 mmol) was added dropwise at −78 °C, followed by stirring for 2 h. The reaction mixture was quenched with aqueous NH_4Cl solution, extracted with EtOAc. The combined organic layers

were dried and concentrated to provide the crude product, which was purified by flash column chromatography (15–20% ethyl acetate in hexanes) to afford ketoaldehyde **36** (50 mg, quantitative) as a colorless oil. ^{1}H NMR (400 MHz) δ 9.89 (s, 1H), 5.01 (m, 1H), 4.86 (m, 1H), 2.76 (dq, 2H, J = 17.6, 2.6 Hz), 2.58 (dt, 1H, J = 17.6, 2.3 Hz), 2.43 (m, 2H), 2.22–2.08 (m, 1H), 2.02–1.75 (m, 3H); ^{13}C NMR (100 MHz) δ 212.7, 201.7, 144.8, 109.4, 57.6, 45.1, 38.3, 32.0, 25.1, 24.0; IR ($CHCl_3$) cm^{-1} 3019, 2944, 2874, 1718 (broad), 1430, 1400, 1216, 758; HRMS (EI) calc. for $C_{10}H_{12}O_2Na$ m/z 187.0735, found m/z 187.0736.

(*E*)-5-Methylene-1-(3-oxobut-1-enyl)bicyclo[2.2.2]octan-2-one (35). To a suspension of NaH (14.6 mg, 0.365 mmol) in THF (0.8 mL) was added diethyl 2-oxopropylphosphonate (75.7 mg, 0.39 mmol) dropwise at rt. After 10 min, this solution was syringed out and added to a solution of keto aldehyde **36** (50 mg, 0.30 mmol) in THF (2.3 mL) at 0 °C. After stirring for 30 min at the same temperature, the reaction mixture was diluted with brine solution, and extracted with ether. The combined organic layers were dried and concentrated to afford the crude product, which was purified by flash column (20–25% ethyl acetate in hexanes) to yield enone **35** (55 mg, 89%) as a pale yellow oil. ^{1}H NMR (400 MHz) δ 7.10 (d, 1H, J = 16.9 Hz), 6.01 (d, 1H, J = 16.9 Hz), 4.99 (d, 1H, J = 0.8 Hz), 4.81 (d, 1H, J = 1.1 Hz), 2.78 (t, 1H, J = 2.9 Hz), 2.60 (q, 2H, J = 2.6 Hz), 2.43 (d, 2H, J = 2.9 Hz), 2.31 (s, 3H), 1.98–1.76 (m, 4H); ^{13}C NMR (75 MHz) δ 212.4, 198.7, 147.0, 146.9, 145.6, 130.6, 108.5, 49.7, 44.6, 38.1, 36.4, 28.4, 26.6, 26.6, 25.7; IR ($CHCl_3$) cm^{-1} 3019, 2943, 2876, 2400, 1720, 1676, 1630, 1259, 1216, 1100, 1032, 979, 908, 759; HRMS (EI) calc. for $C_{13}H_{17}O_2$ m/z 205.1229, found m/z 205.1228.

5-Methylene-1-(3-oxobutyl)bicyclo[2.2.2]octan-2-one (37). To a solution of enone **35** (55 mg, 0.269 mmol) in THF (3 mL) was added Ra-Ni (3 × 0.5 g) three times after every 1 h at rt. After addition, the reaction mixture was stirred further for 3.5 h, then diluted with ether, filtered through a pad of silica gel and washed with ether. The combined filtrates were concentrated and purified by flash column chromatography (30–35% ethyl acetate in hexanes) to yield diketone **37** (55 mg, quantitative) as a colorless oil. ^{1}H NMR (400 MHz) δ 4.89 (d, 1H, J = 1.1 Hz), 4.71 (d, 1H, J = 1.5 Hz), 2.67 (qnt, 1H, J = 2.9 Hz), 2.51–2.43 (m, 2H), 2.38–2.34 (m, 2H), 2.32–2.27 (m, 2H), 2.13 (s, 3H), 1.78–1.58 (m, 6H); ^{13}C NMR (100 MHz) δ 215.9, 209.0, 147.2, 107.7, 46.9, 44.9, 38.8, 38.4, 36.9, 30.0, 28.8, 27.5, 26.0; IR ($CHCl_3$) cm^{-1} 3019, 2953, 1716, 1430, 1216, 909, 758, 669; HRMS (EI) calc. for $C_{13}H_{18}O_2Na$ m/z 229.1204, found m/z 229.1212.

Enone 34. To a solution of diketone **37** (55 mg, 0.266 mmol) in EtOH (11 mL) was added NaOH (70 mg, 1.735 mmol) in one portion at rt. After stirring for 12 h, the reaction mixture was diluted with water, and extracted with ether. The combined organic layers were dried and concentrated to yield the crude product, which was purified by flash column (10–25% ethyl acetate in hexanes) to afford enone **34** (35 mg, 70%) as a colorless oil. ^{1}H NMR (400 MHz) δ 5.82 (t, 1H, J = 1.9 Hz), 4.83 (q, 1H, J = 2.3 Hz), 4.66 (q, 1H, J = 1.9 Hz), 2.53–2.45 (m, 3H), 2.41–2.30 (m, 3H), 2.24 (dt, 1H, J = 16.6, 2.2 Hz), 1.85–1.71 (m, 4H), 1.71–1.60 (m, 1H), 1.55–1.43 (m, 1H); ^{13}C NMR (100 MHz) δ 198.8, 170.4, 148.7, 124.2, 106.9, 39.9, 36.8, 36.5, 36.5, 34.0, 32.2, 30.4, 26.4, 20.5; IR ($CHCl_3$) cm^{-1} 3019, 2929, 1660, 1216, 758, 669; HRMS (EI) calc. for $C_{13}H_{17}O$ m/z 189.1279, found m/z 189.1271.

Ketone 33[9g,k,n]**.** To a solution of enone **34** (20 mg, 0.106 mmol) in THF (3 mL) was added Ra-Ni (3 × 0.5 g) three times after every 1 h at rt. After addition, the reaction mixture was stirred further for 4 h, then diluted with ether, filtered through silica gel and washed with ether. The combined filtrates were concentrated and purified by flash column chromatography (30–35% ethyl acetate in hexanes) to yield a 3 : 1 inseparable mixture of diastereomers **33** and **38** (17 mg, 85%) in favor of the desired isomer **33**, as a colorless sticky liquid. ^{1}H NMR (400 MHz) δ 4.74 (q, 1H, J = 2.3 Hz), 4.71 (q, 1H, J = 2.2 Hz, minor isomer) 4.60 (q, 1H, J = 2.0 Hz), 4.56 (q, 1H, J = 2.0 Hz, minor isomer), 2.79 (dq, 2H, J = 17.2, 2.0 Hz, minor isomer), 2.42–2.08 (m, 7H), 1.98–1.88 (m, 2H), 1.88–1.72 (m, 1H), 1.68–1.58 (m, 3H), 1.53–1.40 (m, 1H), 1.28–1.14 (m, 1H), 1.12–1.02 (m, 1H); ^{13}C NMR (100 MHz) δ 211.9, 150.8, 105.7, 46.5, 43.3, 39.0, 38.6, 37.9, 37.7, 37.0, 35.6, 35.5, 34.3, 33.7, 32.5, 26.7, 26.5, 24.2; IR ($CHCl_3$) cm^{-1} 3068, 3015, 2928, 2862, 1714, 1651, 1451, 1356, 1237, 910, 878, 756, 667; HRMS (EI) calc. for $C_{13}H_{19}O$ m/z 191.1436, found m/z 191.1432. These data are in good agreement with the previous literature reports.[9g,k,n] Only clearly discernible peaks are reported for the minor isomer **38** in the ^{1}H NMR spectrum.

Acknowledgements

We thank DST, New Delhi and SAIF, IIT Bombay for financial support and the use of spectral facilities, respectively. K.P.K. thanks DST for the award of the Swarnajayanti fellowship. K.P. and A.V.S. thank CSIR, New Delhi for fellowships.

Notes and references

1 F. von Nussbaum, M. Brands, B. Hinzen, S. Weigand and D. Habich, *Angew. Chem., Int. Ed.*, 2006, **45**, 5072–5129.
2 (*a*) J. W. Campbell and J. E. Cronan, *Annu. Rev. Microbiol.*, 2001, **55**, 305–332; (*b*) R. J. Heath, S. W. White and C. O. Rock, *Appl. Microbiol. Biotechnol.*, 2002, **58**, 695–703; (*c*) Y.-M. Zhang, H. Marrakchi, S. W. White and C. O. Rock, *J. Lipid Res.*, 2002, **44**, 1–10; (*d*) S. Smith, A. Witkowski and A. K. Joshi, *Prog. Lipid Res.*, 2003, **42**, 289–317; (*e*) R. J. Heath and C. O. Rock, *Curr. Opin. Investig. Drugs*, 2004, **5**, 146–153; (*f*) S. W. White, J. Zheng, Y. M. Zhang and C. O. Rock, *Annu. Rev. Biochem.*, 2005, **74**, 791–831; (*g*) Y. M. Zhang, S. W. White and C. O. Rock, *J. Biol. Chem.*, 2006, **281**, 17541–17544; (*h*) H. T. Wright and K. A. Reynolds, *Curr. Opin. Microbiol.*, 2007, **10**, 447–453; (*i*) Y. M. Zhang and C. O. Rock, *Nat. Rev. Microbiol.*, 2008, **6**, 222–233; (*j*) D. Habich and F. von Nussbaum, *ChemMedChem*, 2006, **1**, 951–954.
3 (*a*) J. Wang, S. M. Soisson, K. Young, W. Shoop, S. Kodali, A. Galgoci, R. Painter, G. Parthasarathy, Y. S. Tang, R. Cummings, S. Ha, K. Dorso, M. Motyl, H. Jayasuriya, J. Ondeyka, K. Herath, C. Zhang, L. Hernandez, J. Allocco, A. Basilio, J. R. Tormo, O. Genilloud, F. Vicente, F. Pelaez, L. Colwell, S. H. Lee, B. Michael, T. Felcetto, C. Gill, L. L. Silver, J. D. Hermes, K. Bartizal, J. Barrett, D. Schmatz, J. W. Becker, D. Cully and S. B. Singh, *Nature*, 2006, **441**, 358–361; (*b*) S. B. Singh, H. Jayasuriya, J. G. Ondeyka, K. B. Herath, C. Zhang, D. L. Zink, N. N. Tsou, R. G. Ball, A. Basilio, O. Genilloud, M. T. Diez, F. Vicente, F. Pelaez, K. Young and J. Wang, *J. Am. Chem. Soc.*, 2006, **128**, 11916–11920.
4 (*a*) J. Wang, S. Kodali, S. H. Lee, A. Galgoci, R. Painter, K. Dorso, F. Racine, M. Motyl, L. Hernandez, E. Tinney, S. L. Colletti, K. Herath, R. Cummings, O. Salazar, I. Gonzalez, A. Basilio, F. Vicente, O. Genilloud, F. Pelaez, H. Jayasuriya, K. Young, D. Cully and S. B. Singh, *Proc. Natl. Acad. Sci. U. S. A.*, 2007, **104**, 7612–7616; (*b*) H. Jayasuriya, K. B. Herath, C. Zhang, D. L. Zink, A. Basilio, O. Genilloud, M. T.

Diez, F. Vicente, I. Gonzalez, O. Salazar, F. Pelaez, R. Cummings, S. Ha, J. Wang and S. B. Singh, *Angew. Chem., Int. Ed.*, 2007, **46**, 4684–4688.
5 (*a*) E. D. Brown, *Nature*, 2006, **441**, 293–294; (*b*) H. Pearson, *Nature*, 2006, **441**, 260–261.
6 (*a*) S. B. Singh, J. G. Ondeyka, K. B. Herath, C. Zhang, H. Jayasuriya, D. L. Zink, G. Parthasarathy, J. W. Becker, J. Wang and S. M. Soisson, *Bioorg. Med. Chem. Lett.*, 2009, **19**, 4756–4759; (*b*) C. Zhang, J. Ondeyka, L. Dietrich, F. P. Gailliot, M. Hesse, M. Lester, K. Dorso, M. Motyl, S. N. Ha and J. Wang, *Bioorg. Med. Chem.*, 2010, **18**, 2602–2610; (*c*) Z. Yu, M. J. Smanski, R. M. Peterson, K. Marchillo, D. Andes, S. R. Rajski and B. Shen, *Org. Lett.*, 2010, **12**, 1744–1747; (*d*) C. Zhang, J. Ondeyka, K. Herath, H. Jayasuriya, Z. Guan, D. L. Zink, L. Dietrich, B. Burgess, S. N. Ha and J. Wang, *J. Nat. Prod.*, 2011, **74**, 329–340.
7 For selected reviews, see: (*a*) K. Tiefenbacher and J. Mulzer, *Angew. Chem., Int. Ed.*, 2008, **47**, 2548–2555; (*b*) D. T. Manallack, I. T. Crosby, Y. Khakham and B. Capuano, *Curr. Med. Chem.*, 2008, **15**, 705–710; (*c*) P. Harsh and G. A. O'Doherty, *Chemtracts*, 2009, **22**, 31–40; (*d*) X. Lu and Q. You, *Curr. Med. Chem.*, 2010, **17**, 1139–1155; (*e*) K. Palanichamy and K. P. Kaliappan, *Chem.–Asian J.*, 2010, **5**, 668–703; Also see: (*f*) K. C. Nicolaou, J. S. Chen, D. J. Edmonds and A. A. Estrada, *Angew. Chem., Int. Ed.*, 2009, **48**, 660–719; (*g*) K. C. Nicolaou, J. S. Chen and S. M. Dalby, *Bioorg. Med. Chem.*, 2009, **17**, 2290–2303.
8 For synthetic studies on platensimycin and its analogues, see: (*a*) K. C. Nicolaou, A. Li and D. J. Edmonds, *Angew. Chem., Int. Ed.*, 2006, **45**, 7086–7090; (*b*) K. C. Nicolaou, D. J. Edmonds, A. Li and G. S. Tria, *Angew. Chem., Int. Ed.*, 2007, **46**, 3942–3945; (*c*) Y. Zou, C.-H. Chen, C. D. Taylor, B. M. Foxman and B. B. Snider, *Org. Lett.*, 2007, **9**, 1825–1828; (*d*) K. P. Kaliappan and V. Ravikumar, *Org. Lett.*, 2007, **9**, 2417–2419; (*e*) K. C. Nicolaou, Y. Tang and J. Wang, *Chem. Commun.*, 2007, 1922–1923; (*f*) P. Li, J. N. Payette and H. Yamamoto, *J. Am. Chem. Soc.*, 2007, **129**, 9534–9535; (*g*) A. K. Ghosh and X. Kai, *Org. Lett.*, 2007, **9**, 4013–4016; (*h*) K. Tiefenbacher and J. Mulzer, *Angew. Chem., Int. Ed.*, 2007, **46**, 8074–8075; (*i*) G. Lalic and E. J. Corey, *Org. Lett.*, 2007, **9**, 4921–4923; (*j*) K. C. Nicolaou, T. Lister, R. M. Denton, A. Montero and D. J. Edmonds, *Angew. Chem., Int. Ed.*, 2007, **46**, 4712–4714; (*k*) K. C. Nicolaou, Y. Tang, J. Wang, A. F. Stepan, A. Li and A. Montero, *J. Am. Chem. Soc.*, 2007, **129**, 14850–14851; (*l*) K. C. Nicolaou, D. Pappo, K. Y. Tsang, R. Gibe and D. Y.-K. Chen, *Angew. Chem., Int. Ed.*, 2008, **47**, 944–946; (*m*) C. H. Kim, K. P. Jang, S. Y. Choi, Y. K. Chung and E. Lee, *Angew. Chem., Int. Ed.*, 2008, **47**, 4009–4011; (*n*) J. Matsuo, K. Takeuchi and H. Ishibashi, *Org. Lett.*, 2008, **10**, 4049–4052; (*o*) Y.-Y. Yeung and E. J. Corey, *Org. Lett.*, 2008, **10**, 3877–3878; (*p*) K. C. Nicolaou, A. F. Stepan, T. Lister, A. Li, A. Montero, G. S. Tria, C. I. Turner, Y. Tang, J. Wang, R. M. Denton and D. J. Edmonds, *J. Am. Chem. Soc.*, 2008, **130**, 13110–13119; (*q*) S. Y. Yun, J.-C. Zheng and D. Lee, *J. Am. Chem. Soc.*, 2009, **131**, 8413–8415; (*r*) A. K. Ghosh and K. Xi, *J. Org. Chem.*, 2009, **74**, 1163–1170; (*s*) K. C. Nicolaou, A. Li, S. P. Ellery and D. J. Edmonds, *Angew. Chem., Int. Ed.*, 2009, **48**, 6293–6295; (*t*) N. A. McGrath, E. S. Bartlett, S. Sittihan and J. T. Njardarson, *Angew. Chem., Int. Ed.*, 2009, **48**, 8543–8546; (*u*) K. C. Nicolaou, A. Li, D. J. Edmonds, G. S. Tria and S. P. Ellery, *J. Am. Chem. Soc.*, 2009, **131**, 16905–16918; (*v*) H. C. Shen, F.-X. Ding, S. B. Singh, G. Parthasarathy, S. M. Soisson, S. N. Ha, X. Chen, S. Kodali, J. Wang, K. Dorso, J. R. Tata, M. L. Hammond, M. MacCoss and S. L. Colletti, *Bioorg. Med. Chem. Lett.*, 2009, **19**, 1623–1627; (*w*) J. Wang, V. Lee and H. O. Sintim, *Chem.–Eur. J.*, 2009, **15**, 2747–2750; (*x*) K. P. Jang, C. H. Kim, S. W. Na, H. Kim, H. Kang and E. Lee, *Bioorg. Med. Chem. Lett.*, 2009, **19**, 4601–4602; (*y*) K. Tiefenbacher, L. Trondlin, J. Mulzer and A. Pfaltz, *Tetrahedron*, 2010, **66**, 6508–6513; (*z*) S. T.-C. Eey and M. J. Lear, *Org. Lett.*, 2010, **12**, 5510–5513; (*aa*) P. Magnus, H. Rivera and V. Lynch, *Org. Lett.*, 2010, **12**, 5677–5679; (*ab*) E. Z. Oblak and D. L. Wright, *Org. Lett.*, 2011, **13**, 2263–2265; (*ac*) J. Wang and H. O. Sintim, *Chem.–Eur. J.*, 2011, **17**, 3352–3357. For synthesis of side chain, see: (*ad*) P. Heretsch and A. Giannis, *Synthesis*, 2007, 2614–2616; (*ae*) N. Maras, P. S. Anderluh, U. Urleb and M. Kocevar, *Synlett*, 2009, 437–440; (*af*) J. McNulty, J. J. Nair and A. Capretta, *Tetrahedron Lett.*, 2009, **50**, 4087–4091.
9 For synthesis of platencin and its analogues, see: (*a*) K. C. Nicolaou, G. S. Tria and D. J. Edmonds, *Angew. Chem., Int. Ed.*, 2008, **47**, 1780–1783; (*b*) J. Hayashida and V. H. Rawal, *Angew. Chem., Int. Ed.*, 2008, **47**, 4373–4376; (*c*) K. Tiefenbacher and J. Mulzer, *Angew. Chem., Int. Ed.*, 2008, **47**, 2548–2555; (*d*) S. Y. Yun, J.-C. Zheng and D. Lee, *Angew. Chem., Int. Ed.*, 2008, **47**, 6201–6203; (*e*) D. C. J. Waalboer, M. C. Schaapman, F. L. van Delft and F. P. J. T. Rutjes, *Angew. Chem., Int. Ed.*, 2008, **47**, 6576–6578; (*f*) K. C. Nicolaou, Q.-Y. Toh and D. Y.-K. Chen, *J. Am. Chem. Soc.*, 2008, **130**, 11292–11293; (*g*) K. A. B. Austin, M. G. Banwell and A. C. Willis, *Org. Lett.*, 2008, **10**, 4465–4468; (*h*) G. N. Varseev and M. E. Maier, *Angew. Chem., Int. Ed.*, 2009, **48**, 3685–3688; (*i*) K. Tiefenbacher and J. Mulzer, *J. Org. Chem.*, 2009, **74**, 2937–2941; (*j*) O. V. Barykina, K. L. Rossi, M. J. Rybak and B. B. Snider, *Org. Lett.*, 2009, **11**, 5334–5337; (*k*) A. K. Ghosh and K. Xi, *Angew. Chem., Int. Ed.*, 2009, **48**, 5372–5375; (*l*) K. C. Nicolaou, G. S. Tria, D. J. Edmonds and M. Kar, *J. Am. Chem. Soc.*, 2009, **131**, 15909–15917; (*m*) S. Hirai and M. Nakada, *Tetrahedron Lett.*, 2010, **51**, 5076–5079; (*n*) V. Singh, B. C. Sahu, V. Bansal and S. M. Mobin, *Org. Biomol. Chem.*, 2010, **8**, 4472–4481; (*o*) P. Li and H. Yamamoto, *Chem. Commun.*, 2010, **46**, 6294–6295; (*p*) D. C. J. Waalboer, S. H. A. M. Leenders, T. Schuelin-Casonato, F. L. van Delft and F. P. J. T. Rutjes, *Chem.–Eur. J.*, 2010, **16**, 11233–11236; (*q*) K. Tiefenbacher, A. Gollner and J. Mulzer, *Chem.–Eur. J.*, 2010, **16**, 9616–9622; (*r*) G. Y. C. Leung, H. Li, Q.-Y. Toh, A. M.-Y. Ng, R. J. Sum, J. E. Bandow and D. Y.-K. Chen, *Eur. J. Org. Chem.*, 2011, 183–196; (*s*) S. Hirai and M. Nakada, *Tetrahedron*, 2011, **67**, 518–530; (*t*) T. Yoshimitsu, S. Nojima, M. Hashimoto and T. Tanaka, *Org. Lett.*, 2011, **13**, 3698–3701.
10 (*a*) K. P. Kaliappan and R. S. Nandurdikar, *Chem. Commun.*, 2004, 2506–2507; (*b*) K. P. Kaliappan and V. Ravikumar, *Org. Biomol. Chem.*, 2005, **3**, 848–851; (*c*) K. P. Kaliappan and R. S. Nandurdikar, *Org. Biomol. Chem.*, 2005, **3**, 3613–3614; (*d*) K. P. Kaliappan and A. V. Subrahmanyam, *Org. Lett.*, 2007, **9**, 1121–1124; (*e*) K. P. Kaliappan and V. Ravikumar, *J. Org. Chem.*, 2007, **72**, 6116–6126; (*f*) K. P. Kaliappan and P. Das, *J. Org. Chem.*, 2009, **74**, 6266–6274; (*g*) R. S. Nandurdikar, A. V. Subrahmanyam and K. P. Kaliappan, *Eur. J. Org. Chem.*, 2010, 2788–2799; (*h*) P. Gowrisankar, S. A. Pujari and K. P. Kaliappan, *Chem.–Eur. J.*, 2010, **16**, 5858–5862; (*i*) A. V. Subrahmanyam, K. Palanichamy and K. P. Kaliappan, *Chem.–Eur. J.*, 2010, **16**, 8545–8556.
11 (*a*) S. J. Rhoads and N. R. Raulins, *Org. React.*, 1975, **22**, 1–252; (*b*) F. E. Ziegler, *Chem. Rev.*, 1988, **88**, 1423–1452; (*c*) P. Wipf, *Compr. Org. Synth.*, 1991, **5**, 827–873; (*d*) M. Hiersemann and U. Nubbemeyer, 2007, *The Claisen Rearrangement*, Wiley-VCH.
12 Y. Nagasima, S. Takehara, M. Negishi and H. Takatsu, *Jpn. Kokai Tokkyo koho*, 2000239214, 2000.
13 (*a*) J.-M. Weibel and D. Heissler, *Tetrahedron Lett.*, 1994, **35**, 473–476; (*b*) J. R. Hanson, P. B. Hitchcock, M. D. Liman and S. Nagaratnam, *J. Chem. Soc., Perkin Trans. 1*, 1995, 2183–2187; (*c*) H. Groh, R. Schon, M. Ritzau, H. Kasch, K. Undisz and G. Hobe, *Steroids*, 1997, **62**, 437–443; (*d*) F.-D. Boyer and P.-H. Ducrot, *Synthesis*, 2000, 1868–1877.
14 T. Mandai, M. Ueda, S.-I. Hasegawa, M. Kawada and J. Tsuji, *Tetrahedron Lett.*, 1990, **31**, 4041–4044.
15 E. J. Corey and P. L. Fuchs, *Tetrahedron Lett.*, 1972, **13**, 3769–3772.
16 N. Chidambaram and S. Chandrasekaran, *J. Org. Chem.*, 1987, **52**, 5048–5051.
17 (*a*) S. Ohira, *Synth. Commun.*, 1989, **19**, 561–564; (*b*) S. Muller, B. Liepold, G. Roth and H. J. Bestmann, *Synlett*, 1996, 521–522.
18 A. V. Subrahmanyam, PhD Thesis, Indian Institute of Technology Bombay, India, 2008.
19 (*a*) J. Boutagy and R. Thomas, *Chem. Rev.*, 1974, **74**, 87–99; (*b*) W. S. Jr. Wadsworth, *Org. React.*, 1977, **25**, 73–253; (*c*) B. E. Maryanoff and A. B. Reitz, *Chem. Rev.*, 1989, **89**, 863–927; (*d*) S. E. Kelly, *Compr. Org. Synth.*, 1991, **1**, 729–817.
20 J. D. Cuthbertson, A. A. Godfrey and R. J. K. Taylor, *Synlett*, 2010, 2805–2807.
21 W. F. Berkowitz and P. J. Wilson, *J. Org. Chem.*, 1991, **56**, 3097–3102.
22 (*a*) K. Omura and D. Swern, *Tetrahedron*, 1978, **34**, 1651–1660; (*b*) A. J. Mancuso and D. Swern, *Synthesis*, 1981, 165–185; (*c*) T. T. Tidwell, *Org. React.*, 1990, **39**, 297–572; (*d*) T. T. Tidwell, *Synthesis*, 1990, 857–870.
23 A. F. Barrero, E. J. Alvarez-Manzaneda, R. Chahboun and R. Meneses, *Synlett*, 1999, 1663–1666.
24 I. Ojima and T. Kogure, *Organometallics*, 1982, **1**, 1390–1399.
25 (*a*) W. S. Mahoney, D. M. Brestensky and J. M. Stryker, *J. Am. Chem. Soc.*, 1988, **110**, 291–293; (*b*) M. R. Churchill, S. A. Bezman, J. A. Osborn and J. Wormald, *J. Am. Chem. Soc.*, 1971, **93**, 2063–2065; (*c*) M. R. Churchill, S. A. Bezman, J. A. Osborn and J. Wormald, *Inorg. Chem.*, 1972, **11**, 1818–1825.
26 (*a*) R. H. Crabtree, H. Felkin, T. Fellebeen-Khan and G. E. Morris, *J. Organomet. Chem.*, 1979, **168**, 183–195; (*b*) R. H. Crabtree, *Acc. Chem. Res.*, 1979, **12**, 331–337; (*c*) G. Stork and D. E. Kahne, *J. Am. Chem. Soc.*, 1983, **105**, 1072–1073; (*d*) R. H. Crabtree and M. W. Davis, *Organometallics*, 1983, **2**, 681–682.

