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Total Synthesis of γ-Indomycinone and Kidamycinone by Means of Two Regioselective Diels–Alder Reactions

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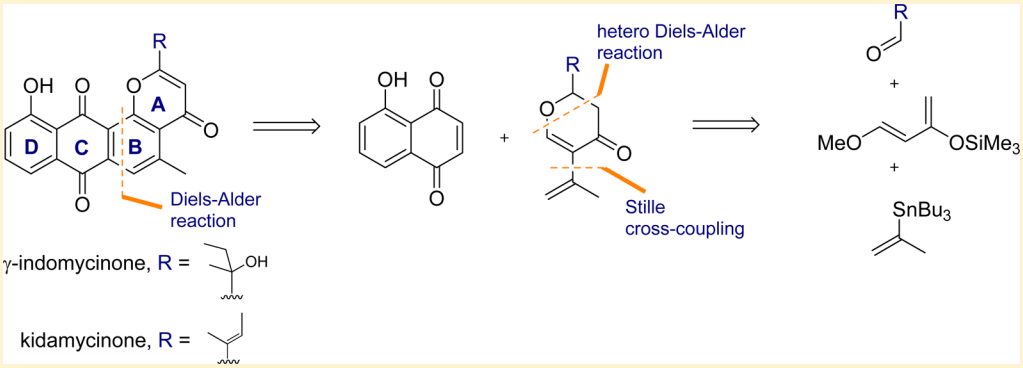
Supporting Information



ABSTRACT: An efficient access for the synthesis of pluramycinones is described. Total syntheses of racemic γ-indomycinone and kidamycinone were achieved by means of two Diels−Alder reactions. A first Diels−Alder condensation followed by a Stille cross-coupling is used for the elaboration of the desired substituted dienes which will be involved in the second pericyclic reaction with juglone to construct the tetracyclic core of pluramycinones.

INTRODUCTION

The pluramycin family represents a group of natural compounds first isolated from *Streptomyces pluricolorescens* by Maeda and co-workers.[1] This class of molecules exhibits antimicrobial activity against Gram-positive bacteria and anticancer activity (especially against Ehrlich ascites carcinoma, leukemia L1210, Sarcoma-180, and Fukuoka's sarcoma).[2] Quite recently, Beerman et al. analyzed thoroughly the mode of action of hedamycin at the cellular scale (see Figure 1). A slowdown in cell growth was observed at subnanomolar concentrations. This phenomena was explained by a direct inhibition of DNA replication through the activation of several DNA damage checkpoint proteins (p53, chk1, and chk2) leading to a blocking in cell cycle progression in G2 or G1 phase, depending on the concentration of hedamycin.[3] During the 1990s, Hurley and co-workers had widely investigated the molecular mode of action of pluramycins with NMR, X-ray, and molecular modeling studies.[4] As a result of this work, the antitumoral activity is now understood and explained through both reversible DNA intercalation and irreversible DNA alkylation. This singular dual-action is a result of the complex molecular structure of these compounds. As shown on Figure 1, the pluramycin skeleton is a 4*H*-anthra[1,2-*b*]pyran-4,7,12-trione, also called ABCD tetracycle, functionalized by two deoxy-aminosugars (referenced as rings E and F) by *C*-glycosidic linkages respectively at C-8 and C-10, and an unsaturated and/or oxygenated side-chain at C-2 (Figure 1).[5] These carbohydrates moieties are responsible for DNA recognition and sequence selectivity as they form a hydrogen-bridge-bound complex in both minor and major grooves of the DNA double helix. In some cases, while E ring (angolosamine) is linked to the tetracyclic core of pluramycine by a β-anomeric linkage, NMR and X-ray studies have shown the F ring (*N*,*N*-dimethylvancosamine) to be in its unfavorable α-anomeric form which tends to epimerize to its thermodynamically preferred β-form in slightly acidic or basic media.[6] On account of this poor stability, the introduction of the aminosugars

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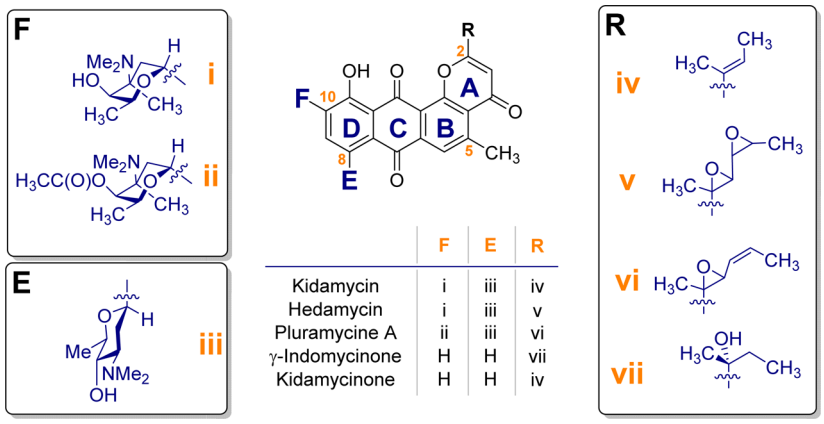
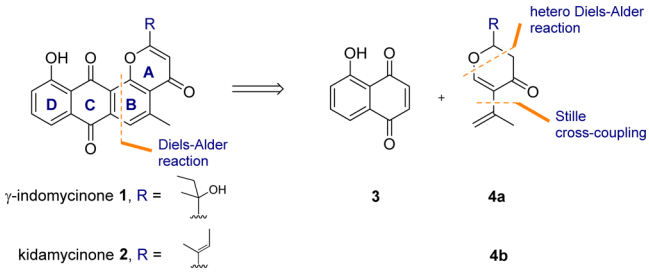


Figure 1. Structures of pluramycins and pluramycinones.

remains the last hurdle slowing down total syntheses of pluramycins. Indeed, whereas many methods have been described to build *C*-aryl glycosides,[7] all attempts to link both *β*-angolosamine and *α*-*N*,*N*-dimethylvancosamine moieties on a pluramycin skeleton failed. The construction of this elaborated structure remains thus a challenge for synthetic organic chemists. Added to the intricate structure of pluramycins, the synthetic challenge resides in avoiding the annoying degradation behavior in acidic, basic, and oxidative conditions[6] in addition to their light sensitivity in both aerobic and anaerobic solutions.[8]

From a biosynthetic point of view, while the formation of the tetracyclic scaffold is well-known as it proceeds via subsequent Claisen-like condensations, the origin of the side chain at C-2 as well as the formation of *C*-glycosidic connections are not fully understood.[9] As a proof of the synthetic interest of pluramycins, construction of the aglycon frame has been reported by many groups since the pioneering work of Hauser in 1979, describing the synthesis of the kidamycinone *O*-methyl ether.[10] Following a biomimetic strategy, Mc Donald published in 2005 an interesting synthesis giving access to both kidamycin and altromycin aglycones from a common tetracyclic intermediate.[11] The same biomimetic approach was applied in 2007 to build the backbone of *γ*-indomycinone[12] which was also synthesized by several groups through Diels−Alder reactions.[13−15] Construction of aglycones is therefore well-known but, to the best of our knowledge, despite many endeavors, interest and developments during the past decade,[16−21] there is still no reported methodology to prepare natural pluramycin containing both *β*-angolosamine (see Figure 1, ring E) and *α*-*N*,*N*-dimethylvancosamine (see Figure 1, ring F) moieties. Two major problems can be highlighted: (1) the introduction of the glycosidic subunits at the first stages of a linear synthesis increases possible unwanted side reactions, such as epimerization, (2) the introduction of the glycosidic subunits by direct glycosylation reactions in the last steps of the synthesis, on a properly functionalized and bulky tetracycle, may suffer from poor regio- and/or stereoselectivity in combination with poor yields. With the aim of developing a methodology which could overstep these barriers, we herein report a full account of the total syntheses of racemic *γ*-indomycinone and kidamycinone through a novel approach. The described strategy differs from the earlier described pathways by addition of the DC framework to the A ring while creating the B ring by means of a Diels−Alder reaction as depicted in retrosynthetic Scheme 1.

Scheme 1. Retrosynthetic Analysis of the Tetracyclic Core of *γ*-Indomycinone (1) and Kidamycinone (2)



Dienes **4a** and **4b** could be synthesized through a Stille cross-coupling from the iodinated corresponding dihydropyranone, which in turn should result from a hetero Diels−Alder reaction between Danishefsky's diene and the well-suited aldehyde. This convergent strategy takes on its full meaning as the R group on ring A, which is major responsible for the pluramycin diversity, can be easily changed at the beginning of the synthesis using the appropriate aldehyde in the first hetero Diels−Alder reaction. Thus, our flexible strategy could be applied to conveniently access a variety of pluramycins using glycosylated juglone at C-6 and C-8.

RESULTS AND DISCUSSION

Our attention initially focused on the synthesis of *γ*-indomycinone.[15] The racemic 2-benzyloxy-2-methylbutanal **5** was synthesized in two steps from commercially available 3-methylpenten-3-ol (Scheme 2). First, benzylation of the tertiary alcohol of the racemic 3-methylpenten-3-ol was achieved by treatment with NaH, benzyl bromide, and a substoichiometric amount of TBAI in DMF.[22] Then, the resulting protected allylic alcohol was submitted to ozonolysis in a mixture of dichloromethane and methanol at −78 °C followed by a reductive workup with dimethyl sulfide to provide aldehyde **5** in 89% yield over two steps. It should be mentioned that attempts to carry out the first step of this sequence, using benzyl 2,2,2-trichloroacetimidate[23] as the benzylating agent and triflic acid as the catalyst, led to aldehyde **5** with lower overall yield (80%).

With aldehyde **5** in hand, we next focused our efforts on the formation of the dihydropyranone skeleton. In this way, Lewis acid-activated hetero-Diels−Alder condensation[24] of aldehyde **5** onto Danishefsky's diene afforded 2,3-dihydro-4*H*-pyran-4-one **6** as a mixture of both diastereomers. Best results in terms of

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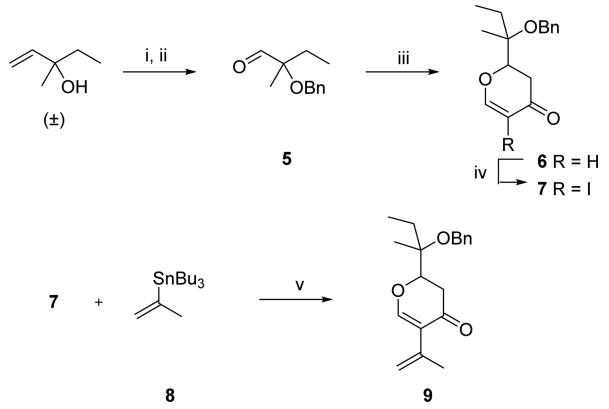
Scheme 2. Preparation of Diene 9[a]



[a]Reagents and conditions: (i) NaH, BnBr, TBAI, DMF, 0 °C to rt, 20 h; (ii) O_3, CH_2Cl_2, MeOH, −78 °C then Me_2S, 89% (2 steps); (iii) Danishefsky's diene, $ZnCl_2$, THF, 40 °C, 18 h, then TFA, CH_2Cl_2, rt, 15 min, 71%; (iv) I_2, CCl_4/Pyr. (1/1), rt, 2 h, 81%; (v) $Pd_2(dba)_3$, $AsPh_3$, CuTC, THF, DMSO, 40 °C, 16 h, 92%.

yield and diastereoselectivity were obtained using $ZnCl_2$ as catalyst (rd 87/13). Even though the newly created stereogenic center will be destroyed in the penultimate state of our strategy (see Scheme 4), in order to facilitate the purification procedures as well as NMR analysis of intermediates at each step, the major diastereomer **6** (unknown stereochemistry) has been isolated in pure form in 71% yield.

Prior to performing a palladium-catalyzed Stille cross-coupling reaction, dihydropyranone **6** was subjected to a direct Johnson-type α-iodination reaction, using iodine in a 1:1 pyridine/CCl_4 mixture,[25] to provide the corresponding α-iodoenone derivative **7** in 81% yield. Then, pivotal cross-coupling of 3-iodo-dihydropyran-4-one **7** with tributyl-(isoprenyl)stannane **8**[26] was investigated to install the α-isoprenyl group on enone **9**. Following conditions developed by Fuwa and Sasaki,[27] using a combination of $Pd_2(dba)_3$ as precatalyst, Ph_3As as soft ligand to accelerate the rate-limiting transmetalation step, and copper(I) 2-thiophenecarboxylate (CuTC) as catalyst to promote transmetalation of vinyl stannane **8** into more reactive copper species,[28] the desired diene **9** was obtained in an excellent yield of 92%.

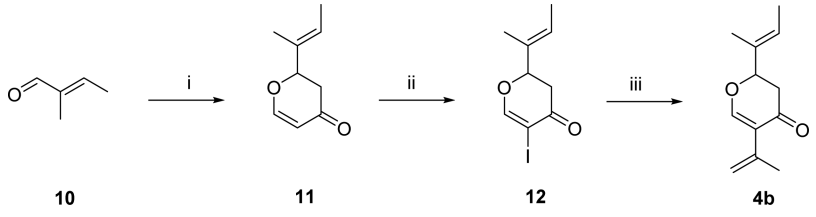
For the synthesis of kidamycinone **2**, the same strategy has been employed starting from the commercially available *trans*-2,3-dimethylacrolein **10** as depicted in Scheme 3. $BF_3{\cdot}Et_2O$ mediated hetero Diels−Alder reaction of *trans*-2,3-dimethylacrolein **10** with Danishefsky's diene was conducted at −78 °C as reported in the literature for α,β-unsaturated aldehydes[24] to afford the desired adduct **11** in 89% yield. Next, α-iodination of **11** was performed using close conditions compared to those used for compound **6** with iodine and pyridine in dry CH_2Cl_2 to give the desired 3-iodo-dihydropyranone **12** in 94% yield.[29] Finally, the latter intermediate **12** was subjected to previously described Stille cross-coupling reaction conditions to lead to the expected diene **4b** in 95% yield.

Dienes **9** and **4b** bearing a deactivating electron withdrawing group in C-2 position were found not to be reactive toward dienophile, such as juglone **3**.[30] Therefore, we decided to perform the reduction of the ketone function under Luche's conditions prior to the cycloaddition step (Scheme 4).[31] Starting from diene **9**, the resulting crude secondary alcohol **13** was directly engaged in a Diels−Alder condensation with juglone **3**. While regioselectivity of cycloaddition could be easily determined using 2D HMBC NMR experiments on compound **14**, *endo* or *exo* selectivity could not be determined on this substituted tetracycle, but will be later discussed on a kidamycinone intermediate (*vide infra*). To promote the aromatization of ring B, the unstable primary cycloadduct was then engaged without purification in a one-pot two-step sequence involving the epoxidation of the newly created C−C double bond with *m*-CPBA followed by treatment of the resulting crude epoxide with an excess of triethylamine in the presence of air to provide intermediate **14** in 64% global yield from diene **9**. No trace of the other regioisomer was found in the crude mixture confirming that regioselectivity in cycloaddition of juglone with polar dienes, such as **9**, is based on the presence of a strong internal hydrogen bond between phenolic proton and oxygen atom of the adjacent carbonyl group.[32]

The last steps to access to γ-indomycinone **1** consisted in the recovering of the ketone moiety followed by oxidation of the chromanone moiety and debenzylation of the tertiary alcohol. Oxidation of the secondary alcohol **14** was performed with PCC in 70% yield.[33] Dehydrogenation of the resulting ketone **15** was accomplished in 78% yield by Patonay's procedure[34] using substoichiometric amount of I_2 in DMSO at 95 °C. To avoid palladium catalyzed hydrogenolytic debenzylation conditions which are incompatible with the presence of a α,β-unsaturated ketone in ring A, cleavage of the hindered tertiary benzyl ether in intermediate **16** was performed using DDQ in refluxing chlorobenzene[35] to furnish racemic γ-indomycinone (±)-**1** in 78% yield.

Following the same multisteps strategy (*vide supra*), but starting from diene **4b**, reduction of the carbonyl group using Luche's conditions afforded diene **17** (84%) and cycloaddition with juglone **3** gave the unstable cycloadduct **18** (Scheme 5). At this stage, the aromatization of ring B of primary adduct **18** was investigated, taking into account that the presence of an extracyclic electron-rich double bond could greatly complicate the epoxidation step of this sequence compared to the precedent synthesis with intermediate **14**. First attempts were

Scheme 3. Preparation of Diene 4b[a]



[a]Reagents and conditions: (i) Danishefsky's diene, $BF_3.OEt_2$, Et_2O, −78 °C, 5 h, then TFA, CH_2Cl_2, rt, 1 h, 89%; (ii) I_2, pyridine, CH_2Cl_2, 0 °C, 30 min then rt, 2.5 h, 94%; (iii) **8**, $Pd_2(dba)_3$, $AsPh_3$, CuTC, THF, DMSO, 40 °C, 16 h, 95%.

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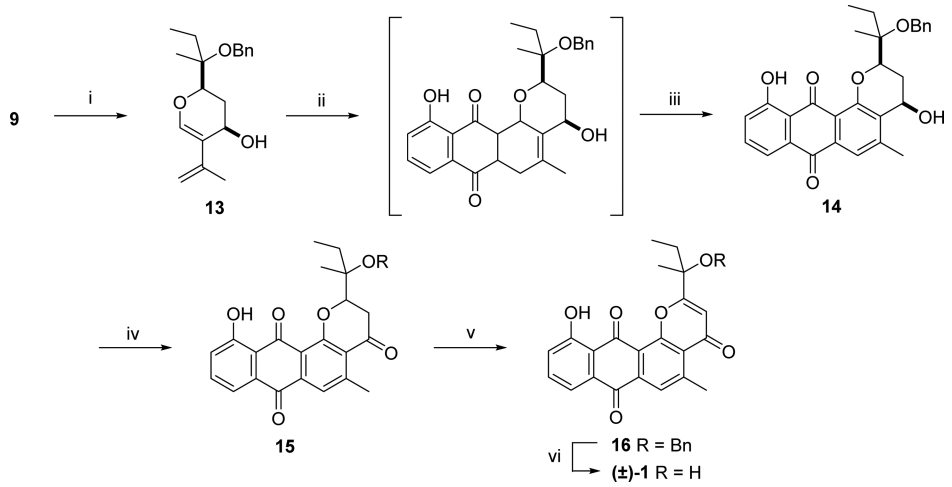
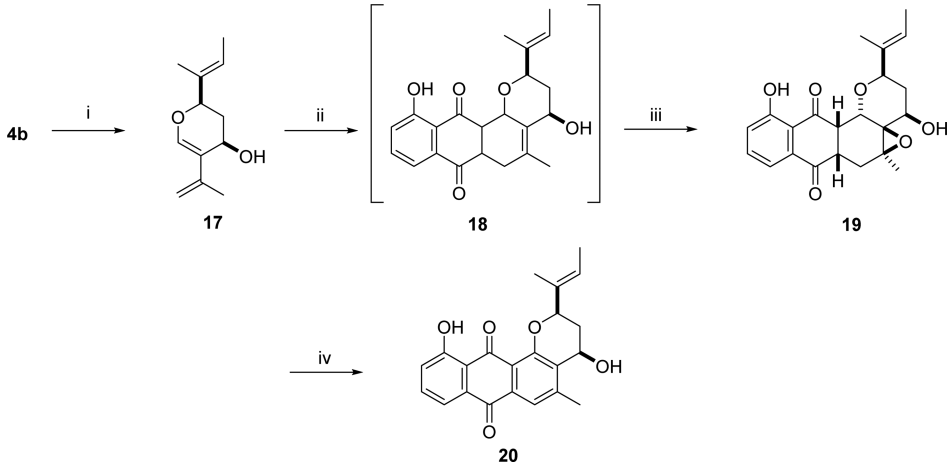
Scheme 4. Synthesis of Racemic γ-Indomycinone (1)[a]



[a]Reagents and conditions: (i) $CeCl_3.7\ H_2O$, $NaBH_4$, THF/MeOH, −78 °C, 15 min then −30 °C over 1 h; (ii) juglone **3**, CH_3CN, 40 °C, 16 h; (iii) *m*-CPBA, CH_2Cl_2, rt, 16 h then Et_3N, air, rt, 1 h, 64% (3 steps); (iv) PCC, CH_2Cl_2, 40 °C, 24 h, 70%; (v) I_2, DMSO, 95 °C, 24 h, 78%; (vi) DDQ, PhCl, 140 °C, 1 h, 78%.

Scheme 5. Synthesis of Kidamycinone Intermediate 20[a]



[a]Reagents and conditions: (i) $CeCl_3.7\ H_2O$, $NaBH_4$, THF/MeOH, −78 °C to −30 °C, 2 h, 84%; (ii) juglone **3**, CH_3CN, 40 °C, 14 h; (iii) $VO(acac)_2$, *t*BuOOH, CH_2Cl_2, rt, 2 h; (iv) Et_3N, air, CH_2Cl_2, rt, 14 h, 74% (3 steps).

performed using *m*-CPBA. Even if anchimeric assistance of the allylic hydroxyl moiety could exert a positive effect by directing the peracid to the desired double bond,[36] presence of the extracyclic 2-butenyl group unfortunately led to a mixture of epoxidized derivatives. In sharp contrast, vanadium-catalyzed epoxidation of **18** using vanadyl acetylacetonate and with *tert*-butyl hydroperoxide[37] as primary oxidant afforded epoxy alcohol **19** as a single diastereoisomer with excellent chemo- and stereoselectivity. Subsequent treatment with triethylamine under aerobic conditions furnished compound **20** in 74% yield over the three steps. As for the previous case, no trace of the other regioisomer has been found in the crude mixture (*vide supra*).

The structure of the epoxy alcohol **19** was established by NMR data. Further confirmation was achieved by single crystal X-ray analysis[38] (Figure 2), and the relative configuration of all stereocenters helped us to rationalize the stereochemical course of each single step of this carbonyl reduction−hetero Diels−Alder condensation−epoxidation sequence.

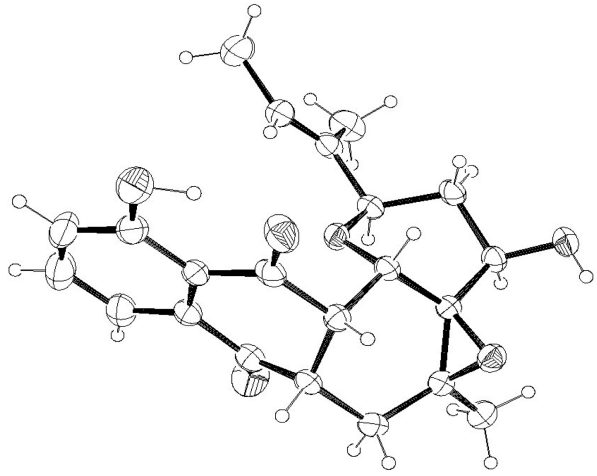


Figure 2. X-ray structure of intermediate **19**. The thermal ellipsoid contour probability levels is 30%.

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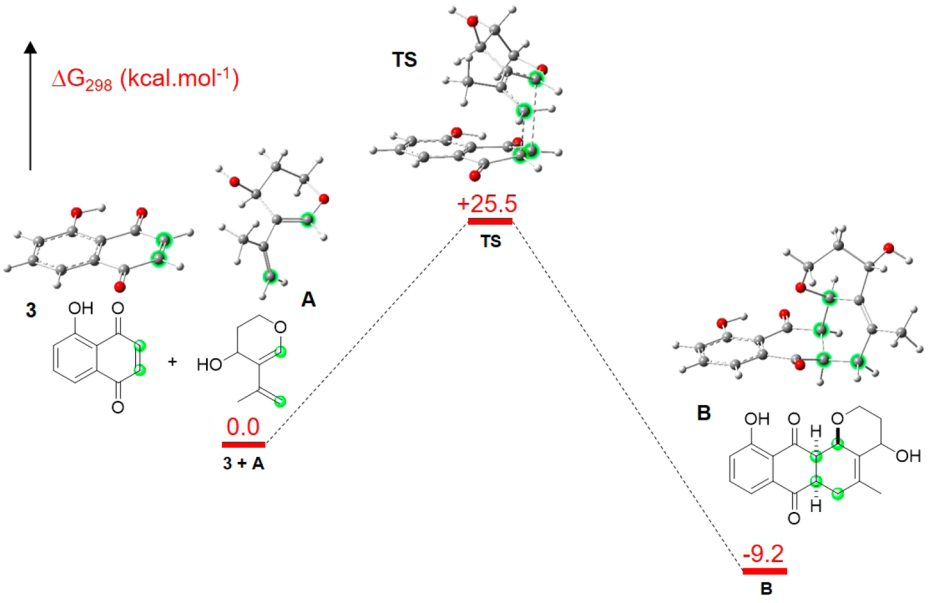


Figure 3. Computed reaction profile leading to intermediate **B** (model for cycloadduct **18**) via an *endo* transition state. DFT method: B3LYP/6-31G(d) PCM in acetonitrile at the same level theory. ΔG values are given in kcal·mol^{-1}. Carbon atoms involved in ring B formation have been highlighted in green.

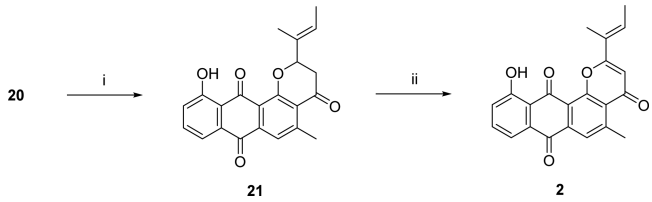
Relative *syn*-relation of 2-butenyl and hydroxyl groups confirmed that reduction of the carbonyl group under Luche's conditions occurred on the less hindered face of the dihydropyranone ring. The stereoselectivity of the vanadium-catalyzed olefin epoxidation was also confirmed by the relative *syn*-relation between the oxiran ring and the hydroxyl group with respect to the regiocontrol effect by this hydroxyl group. Regarding the relative configurations of the three other stereocenters, the complete stereoselectivity of the cycloaddition could be accounted by an *endo* transition state with minimization of steric interactions (Figure 3). These results in hand, we decided to study the expected transition state by computational methods. In order to adapt the conditions for both kidamycinone and γ-indomycinone, DFT computations were carried out on simplified diene **A** (Figure 3). Starting from juglone **3** and diene **A**, a reasonable reaction profile has been calculated.[39] The Diels–Alder sequence passes through an asynchronous concerted mechanism highlighted by a dissymmetric approach of diene toward dienophile. Despite this asynchronicity, only one transition state (TS) has been found in free activation energy of 25.5 kcal/mol leading to cycloadduct **B**.

The final stage of the synthesis of kidamycinone required oxidation of the secondary alcohol and dehydrogenation of the resulting ketone into the corresponding α,β-unsaturated carbonyl moiety to implant the flavone unit. It is worth noting that this sequence should be operated under mild reaction conditions to offer a high functional group tolerance as it could be required for the preparation of more complex members of this family, such as kidamycin with angolosamine and *N*,*N*-dimethylvancosamine moieties linked on ring D (see Figure 1).

Therefore, oxidation of alcohol **20** was evaluated under various conditions.

First attempts were performed using MnO_2 as oxidizing agent.[40] Unfortunately, a large amount of agent (more than 50 equiv) was necessary to reach satisfactory conversions. Use of tetrapropylammonium perruthenate (TPAP) with *N*-methylmorpholine oxide (NMO) as co-oxidant[41] also required more than 50 mol% of catalyst to give satisfactory result. In other hand, oxidation of alcohol **20** with a catalytic amount of 2,2,6,6-tetramethyl-1-piperidinyloxyl (TEMPO)[42] and [bis(acetoxy)-iodo]benzene (BAIB) as a stoichiometric oxidant gave a low conversion. Fortunately, the use of two equivalents of Dess-Martin periodinane[43] in a mixture of dimethyl sulfoxide and dichloromethane led to an excellent conversion and a satisfactory 88% yield of **21** (Scheme 6).

Scheme 6. Final Steps of the Kidamycinone Synthesis[a]



[a]Reagents and conditions: (i) DMP, CH_2Cl_2/DMSO (2:1), rt, 2 h, 88% ; (ii) I_2, DMSO, 95 °C, 14 h, 68%.

It was then expected to achieve the synthesis of the targeted molecule **2** by dehydrogenation of intermediate **21**. In contrast with reports from the literature,[44] initial attempts using IBX in DMSO failed. A mixture of chalcone derivative **22** (Figure 4) formed by dihydropyranone ring opening, and starting material **21** in 6:4 ratio was obtained in which the desired adduct **2** was detected as traces. In the other hand, all efforts to carry on this transformation employing the well-known $Pd(OAc)_2$ promoted Ito–Saegusa oxidation[45] of the corresponding TMS-, TES-, and TIPS-silyl enol ethers, respectively, **23**, **24**, and **25** (Figure 4), to afford enone **2** were unsuccessful leading to complex mixtures. Next, we turned our attention to DDQ oxidation[46] and various conditions were screened. At the best, treatment of flavone **21** with 5 equiv of DDQ in dioxane/DMSO (3:1) at 40 °C provided a mixture of the desired targeted compound **2**, chalcone **22**, and starting material **21** in 45:30:25 ratio. Fortunately, treatment of **21** in DMSO with substoichiometric

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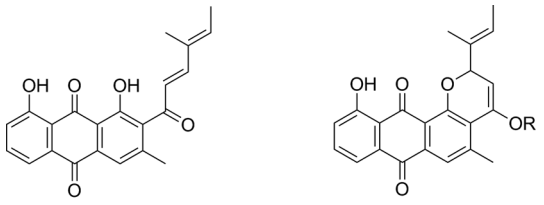

22 **23** (R=TMS) **24** (R=TES) **25** (R=TIPS)

Figure 4. Byproduct (**22**) and desired intermediates (**23**–**25**) in dehydrogenation attempts.

amount of iodine at 95 °C cleanly provided kidamycinone **2** which was isolated in 68% yield (Scheme 6).[34]

In summary, we have developed a general strategy for the synthesis of anthrapyranic skeletons which allowed us to synthesize racemic γ-indomycinone (**1**) in 11 steps and kidamycinone (**2**) in 9 steps with overall yields of 13 and 28%, respectively. Efforts are currently focused on the preparation of suitably substituted juglones in order to propose convergent synthesis of natural pluramycins.

EXPERIMENTAL SECTION

General Information. Anhydrous reactions were carried out under an atmosphere of argon using flame-dried glassware and standard syringe/septa techniques. Tetrahydrofuran was distilled over sodium and benzophenone, dichloromethane, toluene, and diethyl ether were dried using a solvent purification system. petroleum ether refers to the petroleum fraction bp 40–60 °C. Commercial reagents were used as supplied, unless otherwise indicated. Flash chromatography was performed with silica gel Kieselgel SI60 40–63 μm. Combi-Flash chromatography was performed using 40 μm silica prepacked cartridges. Mobile phases are reported in relative composition (e.g., 1:1 EtOAc/petroleum ether v/v). Melting points were determined using a melting point apparatus and are uncorrected/calibrated. ^{1}H NMR spectra were recorded on a 300 MHz spectrometer. ^{13}C NMR spectra were recorded on a 75 MHz spectrometer. ^{119}Sn NMR spectra were recorded on a 112 MHz spectrometer. Spectra were fully assigned using DEPT, COSY, HSQC, and HMBC. Chemical shifts are reported relative to $CDCl_3$ (δ 7.26 ppm), C_6D_6 (δ 7.16 ppm), or DMSO-d_6 (δ 2.50 ppm) for ^{1}H NMR and $CDCl_3$ (δ 77.16 ppm), C_6D_6 (δ 128.06 ppm), or DMSO-d_6 (δ 29.5 ppm) for ^{13}C NMR. High-resolution mass spectra (HRMS) were recorded on ESI or MALDI with Q-Tof analyzers within a tolerance of 5 ppm of the theoretically calculated value and measurements are given in Da.

2-Benzyloxy-2-methylbutanal (***5***). A 60% sodium hydride dispersion in mineral oil (3.20 g, 80.0 mmol) was washed twice with pentane under argon at 0 °C before being taken in DMF (200 mL) and 3-methylpenten-3-ol (4.80 mL, 40.0 mmol) was added. After 30 min stirring, benzyl bromide (7.20 mL, 60.0 mmol) was added followed by *tetra*-butyl ammonium iodide (1.74 g, 4.80 mmol). After 30 min stirring, the mixture was allowed to warm up to room temperature. After 20 h the mixture was cooled to 0 °C and quenched by addition of a saturated solution of NH_4Cl (150 mL) and was extracted with EtOAc (2 × 200 mL). The combined organic layers were washed with water (2 × 200 mL) and brine (2 × 200 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The crude product was directly used in the next step without any further purification. A solution of freshly formed alkene (7.61 g, 40.0 mmol) in CH_2Cl_2/MeOH (170 mL/12 mL) at −78 °C under argon was ozonized until a blue color persisted. The mixture was purged with argon until complete disappearance of the color. At this point, Me_2S (32 mL, 400 mmol) was added and the mixture was allowed to warm to room temperature overnight. A saturated solution of $NaHCO_3$ was added (60 mL) and the aqueous phase was extracted with CH_2Cl_2 (2 × 100 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (petroleum ether/Et_2O 95:5) to afford the title compound **5** (6.84 g, 35.6 mmol, 89%) as a colorless oil. R_f 0.80 (petroleum ether/Et_2O 80:20), ν_{max} (neat)/cm^{-1} 2977, 1718, 1497, 1167; δ_H (300 MHz; $CDCl_3$) 9.67 (s, 1H, CHO), 7.37–7.28 (m, 5H, $H_{aromatic}$), 4.49 and 4.44 (part of an AB system, J = 11.2 Hz, 2H, CH_2O), 1.88 and 1.65 (AB part of an ABX system, J = 14.6 Hz, J = 7.5 Hz, 2H, $CH_3C\underline{H}_2$), 1.32 (s, 3H, CH_3), 0.94 (t, J = 7,5 Hz, 3H, $C\underline{H}_3CH_2$); δ_C (75 MHz, $CDCl_3$) 205.2 (CHO), 138.4 ($C_{aromatic}$), 128.4 (2 × $CH_{aromatic}$), 127.7 ($CH_{aromatic}$), 127.4 (2 × $CH_{aromatic}$), 82.9 (C), 66.1 (CH_2O), 27.7 ($CH_3\underline{C}H_2$), 17.7 (CH_3), 7.3 ($\underline{C}H_3CH_2$); m/z (ESI+) $[M+H]^+$ 193.1223 calcd for $C_{12}H_{17}O_2$ 193.1226.

2-(2-(Benzyloxy)butan-2-yl)-2,3-dihydro-4H-pyran-4-one (***6***). To a solution of zinc chloride (freshly fused under vacuum) (4.04 g, 29.6 mmol) in THF (120 mL), was added aldehyde **5** (5.70 g, 29.6 mmol) dissolved in THF (50 mL). After 10 min stirring, Danishefsky's diene (11.5 mL, 59.2 mmol) was added. After 18 h at 40 °C, the solution was quenched by addition of a saturated solution of $NaHCO_3$ and extracted with Et_2O (3 × 100 mL). The combined organic layers were washed with brine (150 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The crude product was diluted in CH_2Cl_2 (40 mL) and trifluoroacetic acid (0.90 mL, 11.8 mmol) was added. The solution was stirred for 15 min at room temperature and then concentrated. The crude product was purified by silica gel column chromatography (petroleum ether/EtOAc 95:5 to 90:10) to afford the title compound **6** (5.47 g, 21.0 mmol, 71%) as a pale yellow oil. R_f 0.37 (petroleum ether/EtOAc 85:15); ν_{max} (neat)/cm^{-1} 2970, 1678, 1567, 1257; δ_H (300 MHz; $CDCl_3$) 7.38 (d, J = 5.9 Hz, 1H, CH═C$\underline{H}$O), 7.37–7.29 (m, 5H, $H_{aromatic}$), 5.42 (dd, J = 5.9 Hz, J = 1.2 Hz, 1H, C$\underline{H}$═CHO), 4.50 and 4.45 (AB system, J = 11.2 Hz, 2H, CH_2O), 4.42 (X part of an ABX system, J = 14.5 Hz, J = 3.8 Hz, 1H, −CHO), 2.74–2.41 (AB part of an ABX system, J = 16.9 Hz, J = 14.5 Hz, J = 3.8 Hz, J = 1.2 Hz, 2H, CH_2C═O), 1.81 and 1.71 (AB part of an ABX system, J = 14.8 Hz, J = 7.4 Hz, 2H, $CH_3C\underline{H}_2$), 1.33 (s, 3H, CH_3), 0.94 (t, J = 7.4 Hz, 3H, $C\underline{H}_3CH_2$); δ_C (75 MHz, $CDCl_3$) 193.4 (CO), 162.9 (CH═$\underline{C}$HO), 138.9 ($C_{aromatic}$), 128.3 (2 × $CH_{aromatic}$), 127.4 ($CH_{aromatic}$), 127.1 (2 × $CH_{aromatic}$), 107.3 (C$\underline{H}$═CHO), 81.5 (CHO), 77.2 ($\underline{C}$OBn), 63.8 (Ph$\underline{C}H_2O$), 36.5 ($\underline{C}H_2CO$), 27.5 ($CH_3\underline{C}H_2$), 18.5 (CH_3), 7.3 ($\underline{C}H_3CH_2$). m/z (MALDI) $[M+Na]^+$ 283.1294 calcd for $C_{16}H_{20}O_3Na$ 283.1305.

2-(2-(Benzyloxy)butan-2-yl)-5-iodo-2,3-dihydro-4H-pyran-4-one (***7***). Iodine (8.22 g, 32.4 mmol) dissolved in a CCl_4/pyridine mixture (1:1, 30 mL) was added dropwise at 0 °C to a solution of starting ketone **6** (4.22 g, 16.2 mmol) in CCl_4/pyridine (1:1, 30 mL). The mixture was stirred for 2 h at room temperature, then diluted with CH_2Cl_2 (100 mL) and washed with water (50 mL), HCl 1 M (2 × 50 mL), and 20% aqueous $Na_2S_2O_3$ (2 × 50 mL). The organic layer was dried over Na_2SO_4 and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (petroleum ether/Et_2O 80:20) to afford the title compound 7 (5.13 g, 13.3 mmol, 82%) as a pale yellow solid. R_f 0.31 (petroleum ether/Et_2O 90:10); Mp 72–73 °C; ν_{max} (neat)/cm^{-1} 2971, 1671, 1595, 1273, 512; δ_H (300 MHz; $CDCl_3$) 7.81 (d, J = 0.6 Hz, 1H, IC═CHO), 7.37–7.27 (m, 5H, $H_{aromatic}$), 4.47 (X part of an ABX system, J = 14.5 Hz, J = 3.8 Hz, 1H, CHO), 4.55 and 4.46 (AB system, J = 11.2 Hz, 2H, PhCH_2O), 2.97 and 2.83 (AB part of an ABX system, J = 16.9 Hz, J = 14.5 Hz, J = 3.8 Hz, J = 1.2 Hz, 2H, CH_2C═O), 1.72–1.64 (AB part of an ABX_3 system, J = 14.8 Hz, J = 7.4 Hz, 2H, $CH_3C\underline{H}_2$), 1.32 (s, 3H, CH_3), 0.96 (t, J = 7.4 Hz, 3H, $C\underline{H}_3CH_2$); δ_C (75 MHz, $CDCl_3$) 187.3 (CO), 165.7 (IC═$\underline{C}$HO), 138.7 ($C_{aromatic}$), 128.5 (2 × $CH_{aromatic}$), 127.5 ($CH_{aromatic}$), 127.2 (2 × $CH_{aromatic}$), 82.4 (CHO), 77.1 (C), 76.9 (I$\underline{C}$═CHO), 63.9 (CH_2O), 36.3 ($\underline{C}H_2CO$), 27.5 ($CH_3\underline{C}H_2$), 18.6 (CH_3), 7.4 ($\underline{C}H_3CH_2$); m/z (MALDI) $[M+Na]^+$ 409.0286 calcd for $C_{16}H_{19}IO_3Na$ 409.0271.

2-(2-(Benzyloxy)butan-2-yl)-5-(prop-1-en-2-yl)-2,3-dihydro-4H-pyran-4-one (***9***). To a solution of vinyl iodide 7 (2.00 g, 5.20 mmol) in a deoxygenated mixture of THF and DMSO (1:1, 250 mL) under argon atmosphere were added successively isopropenyltributyltin **8**[26] (3.44 g, 10.4 mmol), tris(dibenzylideneacetone)dipalladium (476 mg,

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0.52 mmol), triphenylarsine (1.27 g, 4.16 mmol), and copper(I)-thiophene-carboxylate (1.28 g, 6.76 mmol). The mixture was stirred at 40 °C overnight, then treated by addition of a saturated solution of NaF (150 mL). The resulting mixture was vigorously stirred for 1 h. The residue was filtered through a pad of Celite, extracted with Et_2O. The combined organic layers were dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The crude product was purified by silica gel column chromatography (petroleum ether/Et_2O 95:5) to afford the title compound **9** (1.44 g, 4.78 mmol, 92%) as a colorless oil. R_f 0.50 (petroleum ether/Et_2O 90:10); ν_{max} (neat)/cm^{-1} 2970, 1677, 1568, 1256; δ_H (400 MHz; $CDCl_3$) 7.43 (d, J = 0.6 Hz, 1H, C═CHO), 7.43−7.32 (m, 5H, $H_{aromatic}$), 5.23 (dd, J = 2.0 Hz, J = 0.6 Hz, 1H, C═CHH), 4.98 (dd, J = 2.0 Hz, J = 1.5 Hz, 1H, C═CHH), 4.51 and 4.46 (AB system, J = 11.3 Hz, 2H, CH_2O), 4.40 (X part of an ABX system, J = 15.2 Hz, J = 3.0 Hz, 1H, CHO), 2.74 and 2.60 (AB part of an ABX system, J = 16.6 Hz, J = 15.2 Hz, J = 3.0 Hz, 2H, CH_2C═O), 1.93 (s, 3H, CH_3 propenyl), 1.81 and 1.69 (AB part of an ABX_3 system, J = 15.0 Hz, J = 7.5 Hz, 2H, CH_3CH_2), 1.33 (s, 3H, CH_3), 0.94 (t, J = 7.5 Hz, 3 H, CH_3CH_2); δ_C (100 MHz, $CDCl_3$) 192.0 (CO), 159.8 (C═CHO), 139.0 ($C_{aromatic}$), 137.4 (CH_3C═CH_2), 128.4 (2 × $CH_{aromatic}$), 127.4 ($CH_{aromatic}$), 127.2 (2 × $CH_{aromatic}$), 121.0 (C═CHO), 115.2 (C═CH_2), 81.6 (CHO), 77.2 (OCMe(Et)), 63.9 (CH_2O), 37.1 (CH_2C═O), 27.7 (CH_3CH_2), 22.3 (CH_3C═CH_2), 18.6 (CH_3), 7.5 (CH_3CH_2); m/z (MALDI) $[M+H]^+$ 301.1789 calcd for $C_{19}H_{25}O_3$ 301.1798.

*2-(2-(Benzyloxy)butan-2-yl)-4,11-dihydroxy-5-methyl-3,4-dihydro-2H-anthra[1,2-b]pyran-7,12-dione (**14**).* To a solution of diene **9** (1.33 g, 4.43 mmol) in THF/MeOH (1:1, 80 mL) was added cerium chloride heptahydrate (1.65 g, 4.43 mmol). After dissolution of the cerium salts, the solution was cooled to −78 °C and sodium borohydride (335 mg, 8.86 mmol) was added in one portion. The mixture was stirred at −78 °C for 15 min, then the temperature was raised to −50 °C and left to warm up to −30 °C over an hour. The mixture was concentrated under reduced pressure and the product extracted from the salts with CH_2Cl_2 (3 × 100 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated. The resulting diene was dissolved in acetonitrile (30 mL) and juglone (926 mg, 5.32 mmol) was added. The resulting mixture was stirred at 40 °C overnight. Solvent was evaporated, the residue dissolved in CH_2Cl_2 (50 mL) and *m*-CPBA acid (2.95 g, 12.0 mmol) was added. The mixture was stirred at room temperature overnight and then triethylamine (6.18 mL, 44.3 mmol) was added, the mixture was stirred for an extra hour. The residue was concentrated under reduced pressure and purified by silica gel column chromatography (petroleum ether/EtOAc 70:30) to afford the title compound **14** (1.34 g, 2.84 mmol, 64%) as a yellow solid. R_f 0.60 (petroleum ether/EtOAc 60:40); mp 179−181 °C (dec.) ; ν_{max} (neat)/cm^{-1} 3392, 2966, 1667, 1633, 1582, 1261; δ_H (300 MHz; $CDCl_3$) 13.28 (s, 1H, Ar−OH), 7.76 (X part of an AMX system, J = 7.6 Hz, J = 1.1 Hz, 1H, $H_{aromatic}$), 7.70 (s, 1H, $H_{aromatic}$), 7.42 (M part of an AMX system, J = 8.3 Hz, J = 7.6 Hz, 1H, $H_{aromatic}$), 7.28 (A part of an AMX system, J = 8.3 Hz, J = 1.1 Hz, 1H, $H_{aromatic}$), 7.15−7.06 (m, 3H, $H_{aromatic}$), 6.82−6.75 (m, 2H, $H_{aromatic}$), 4.74 (M part of an ABMX system, J = 10.9 Hz, J = 5.9 Hz, J = 4.0 Hz, 1H, CH(OH)), 4.45−4.37 (X part of an ABX system, 1H, CH(O)), 4.41 and 4.33 (AB system, J = 10.5 Hz, 2H, CH_2O), 3.97 (d, J = 10.9 Hz, 1H, CH(OH)), 2.53 and 2.42 (AB part of an ABMX system, J = 15.0 Hz, J = 5.9 Hz, J = 5.8 Hz, J = 4.0 Hz, 2H, CH_2(CHOH)), 2.42 (s, 3H, CH_2═CCH_3), 2.05−1.79 (AB part of an ABX_3 system, J = 15.2 Hz, J = 7.5 Hz, 2H, CH_3CH_2), 1.67 (s, 3H, CH_3), 1.01 (t, J = 7.5 Hz, 3H, CH_3CH_2); δ_C (75 MHz, $CDCl_3$) 188.6 (CO), 183.0 (CO), 162.5 ($C(OH)_{aromatic}$), 157.2 ($C_{aromatic}$), 148.0 ($CCH_{3aromatic}$), 137.5 ($C_{aromatic}$), 135.6 ($C_{aromatic}$), 133.9 ($C_{aromatic}$), 132.9 ($C_{aromatic}$), 131.3 ($C_{aromatic}$), 128.4 (2 × $CH_{aromatic}$), 127.7 (3 × $CH_{aromatic}$), 124.7 ($CH_{aromatic}$), 121.9 ($CH_{aromatic}$), 118.6 ($CH_{aromatic}$), 117.9 ($C_{aromatic}$), 117.4 ($C_{aromatic}$), 80.8 (COBn), 78.0 (CH(O)), 65.4 ($PhCH_2O$), 60.5 (CH(OH)), 30.5 and 29.5 (CH_2CHOH and CH_3CH_2), 20.2 and 19.2 (Ar−CH_3 et CH_3), 8.4 (CH_3CH_2); m/z (MALDI) $[M+Na]^+$ 495.1763 calcd for $C_{29}H_{28}O_6Na$ 495.1778.

*2-(2-(Benzyloxy)butan-2-yl)-11-hydroxy-5-methyl-3,4-dihydro-2H-anthra[1,2-b]pyran-4,7,12-trione (**15**).* To a solution of alcohol **14** (300 mg, 0.63 mmol) in anhydrous CH_2Cl_2 (20 mL) under argon atmosphere, was added pyridinium chlorochromate (0.41g, 1.90 mmol). Resulting mixture was refluxed overnight then concentrated under reduced pressure. The crude product was purified on silica gel column chromatography (petroleum ether/EtOAc 80:20) to afford the title compound **15** (210 mg, 0.44 mmol, 70%) as a yellow solid. R_f 0.76 (petroleum ether/EtOAc 80:20); Mp 179−180 °C ; ν_{max} (neat)/cm^{-1} 3072, 2971, 1678, 1641, 1568, 1257; δ_H (300 MHz; $CDCl_3$) 13.11 (s, 1H, Ar−OH), 7.77 (dd, X part of an AMX system, J = 7.6 Hz, J = 1.1 Hz, 1H, $H_{aromatic}$), 7.75 (s, 1H, $H_{aromatic}$), 7.64 (dd, M part of an AMX system, J = 8.3 Hz, J = 7.6 Hz, 1H, $H_{aromatic}$), 7.34 (dd, A part of an AMX system, J = 8.3 Hz, J = 1.1 Hz, 1H, $H_{aromatic}$), 7.32−7.26 (m, 5H, $H_{aromatic}$), 4.69−4.62 (X part of ABX system, 1H, CHO), 4.58 and 4.54 (AB system, J = 10.5 Hz, 2H, CH_2O), 3.01 and 2.91 (AB part of an ABX system, J = 15.0 Hz, J = 5.8 Hz, 2H, CH_2(C═O)), 2.77 (s, 3H, Ar−CH_3), 2.14 and 1.82 (AB part of an ABX_3 system, J = 15.2 Hz, J = 7.5 Hz, 2H, CH_3CH_2), 1.62 (s, 3H, CH_3), 1.01 (t, J = 7.5 Hz, 3H, CH_3CH_2); δ_C (75 MHz, $CDCl_3$) 193.9 (CO), 187.6 (CO), 182.5 (CO), 163.4 (C(OH)), 162.6 ($C_{aromatic}$), 150.0 ($CCH_{3aromatic}$), 139.3 ($C_{aromatic}$), 137.2 ($C_{aromatic}$), 136.0 ($CH_{aromatic}$), 132,6 ($C_{aromatic}$), 128.5 (2 × $CH_{aromatic}$), 127.4 ($CH_{aromatic}$), 127.3 (2 × $CH_{aromatic}$), 125.2 ($CH_{aromatic}$), 124.5 ($C_{aromatic}$), 123.2 ($CH_{aromatic}$), 119.1 ($C_{aromatic}$), 119.0 ($CH_{aromatic}$), 117.2 ($C_{aromatic}$), 81.3 (COBn), 78.2 (CH(O)), 64.6 (CH_2O), 38.8 (CH_2(C═O)), 28.1 (CH_3CH_2), 24.0 (Ar−CH_3), 18.7 (CH_3), 7.7 (CH_3CH_2); m/z (ESI+) $[M+Na]^+$ 493.1635 calcd for $C_{29}H_{26}O_6Na$ 493.1622.

*2-(2-(Benzyloxy)butan-2-yl)-11-hydroxy-5-methyl-anthra[1,2-b]pyran-4,7,12-trione (**16**).* To a solution of ketone **15** (150 mg, 0.32 mmol) in DMSO (14 mL) was added iodine (30 mg, 0.13 mmol). The resulting mixture was stirred under argon atmosphere at 95 °C overnight. After cooling to room temperature, the reaction mixture was quenched by addition of brine (15 mL), extracted with CH_2Cl_2 (3 × 20 mL). Combined organic layers were washed with a solution of $Na_2S_2O_3$ (20%), dried over Na_2SO_4, and concentrated under reduced pressure. The crude product was purified on silica gel column chromatography (petroleum ether/EtOAc 95:5) to afford the title compound **16** (0.117g, 0.249 mmol, 78%) as a yellow solid. R_f 0.31 (petroleum ether/EtOAc 90:10); Mp 201−202 °C ; ν_{max} (neat)/cm^{-1} 3069, 2975, 1685, 1672, 1650, 1581, 1551, 1265; δ_H (300 MHz; $CDCl_3$) 12.91 (s, 1H, Ar−OH), 8.06 (d, J = 0.6 Hz, 1H, $H_{aromatic}$), 7.83−7.80 (X part of an AMX system, J = 7.6 Hz, J = 1.2 Hz, 1H, $H_{aromatic}$), 7.73−7.65 (M part of an AMX system, J = 8.3 Hz, J = 7.6 Hz, 1H, $H_{aromatic}$), 7.41−7.26 (m, 6H, $H_{aromatic}$), 6.64 (s, 1H, OC═CH), 4.59 and 4.53 (AB system, J = 10.5 Hz, 2H, CH_2O), 3.02 (d, J = 0.6 Hz, 3H, $ArCH_3$), 2.22 and 2.14 (AB part of an ABX_3 system, J = 15.2 Hz, J = 7.5 Hz, 2H, CH_3CH_2), 1.81 (s, 3H, CH_3), 0.94 (t, J = 7.5 Hz, 3H, CH_3CH_2); δ_C (75 MHz, $CDCl_3$) 187.2 (CO), 181.9 (CO), 179.3 (CO), 170.7 (OC═CH), 162.6 (C(OH)), 156.4 ($C_{aromatic}$), 149.8 ($CCH_{3aromatic}$), 138.3 ($C_{aromatic}$), 136.3 ($CH_{aromatic}$), 136.0 ($C_{aromatic}$), 132.2 ($C_{aromatic}$), 128.4 (2 × $CH_{aromatic}$), 127.5 ($CH_{aromatic}$), 127.1 (2 × $CH_{aromatic}$), 126.5 ($C_{aromatic}$), 125.6 ($CH_{aromatic}$), 125.3 ($CH_{aromatic}$), 119.9 ($C_{aromatic}$), 119.3 ($CH_{aromatic}$), 116.8 ($C_{aromatic}$), 111.3 (OC═CH), 79.1 (COBn), 64.8 (CH_2O), 31.7(CH_3CH_2), 24.6 (Ar−CH_3), 22.0 (CH_3), 8.0 (CH_3CH_2); m/z (ESI+) $[M+Na]^+$ 491.1476 calcd for $C_{29}H_{24}O_6Na$ 491.1465.

*2-(2-(Hydroxy)butan-2-yl)-11-hydroxy-5-methyl-anthra[1,2-b]pyran-4,7,12-trione (**1**).* To a solution of benzyl-protected alcohol **16** (84 mg, 0.18 mmol) in chlorobenzene (9 mL), under argon atmosphere, was added DDQ (163 mg, 0.72 mmol), and the resulting mixture heated up to 140 °C. After 1 h stirring, the reaction mixture was concentrated under reduced pressure and the crude product was purified on silica gel column chromatography (toluene/EtOAc 80:20) to afford γ-indomycinone **1** (53 mg, 0.14 mmol, 78%) as a yellow solid. All spectroscopic data for **1** are identical in all respects with those of the natural product described in literature.[12a,47] R_f 0.19 (toluene/EtOAc 80:20); Mp 289−290 °C ; ν_{max} (neat)/cm^{-1} 3359, 2959, 2925, 2873, 1674, 1639, 1582, 1446, 1262, 1184, 765, 750; δ_H (700 MHz; DMSO) 12.69 (s, 1H, Ar−OH), 7.94 (s, 1H, $H_{aromatic}$), 7.78 (br. t, X part of an AMX system, J = 7.6 Hz, J = 1.2 Hz, 1H, $H_{aromatic}$), 7.69 (dd, M part of an AMX system, J = 8.3 Hz, J = 7.6 Hz, 1H, $H_{aromatic}$), 7.39

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(dd, A part of an AMX system, J = 8.3 Hz, J = 1.1 Hz, 1H, $H_{aromatic}$), 6.48 (s, 1H, OC=CH), 5.55 (s, 1H, OH), 2.91 (s, 3H, Ar−CH_3), 2.07 and 1.84 (AB part of an ABX_3 system, J = 15.2 Hz, J = 7.5 Hz, 2H, $CH_3C\underline{H}_2$), 1.61 (s, 3H, CH_3), 0.84 (t, J = 7.5 Hz, 3H, $C\underline{H}_3CH_2$); δ_C (175 MHz, DMSO) 187.0 (CO), 181.4 (CO), 178.3 (CO), 173.9 (O$\underline{C}$=CH), 161.4 ($C(OH)_{aromatic}$), 155.6 ($C_{aromatic}$), 148.3 ($\underline{C}CH_{3aromatic}$), 136.7 ($C_{aromatic}$), 135.8 ($C_{aromatic}$), 132.1 ($C_{aromatic}$), 125.5 ($CH_{aromatic}$), 124.7 (2 × $CH_{aromatic}$), 119.8 ($CH_{aromatic}$), 118.7 ($C_{aromatic}$), 116.8 ($C_{aromatic}$), 109.0 (OC=$\underline{C}$H), 72.7 (C(OH)), 32.9 ($CH_3\underline{C}H_2$), 26.7 (Ar−CH_3), 23.4 (CH_3), 7.8 ($\underline{C}H_3CH_2$); m/z (ESI+) $[M+H]^+$ 379.1183 calcd for $C_{22}H_{19}O_6$ 379.1176.

*(E)-2-(But-2-en-2-yl)-2H-pyran-4(3H)-one (**11**).* To a solution of Danishefsky's diene (11.3 mL, 52.2 mmol) in diethyl ether at −78 °C was added *trans*-1,3-dimethylacrolein (14.0 mL, 145.1 mmol) under argon atmosphere. After 15 min stirring, trifluoride boron etherate (9.32 mL, 75.5 mmol) was added in one portion and the resulting mixture stirred for 5 h at −78 °C. The reaction was quenched by a dropwise addition of a saturated solution of $NaHCO_3$ (200 mL) after letting the reaction mixture to warm up for 30 min. The mixture was then extracted with diethyl ether (3 × 250 mL), organic layers were gathered, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was dissolved in dry CH_2Cl_2 (300 mL). Trifluoroacetic acid (4.00 mL, 75.5 mmol) was added dropwise and the mixture stirred for 1 h at room temperature under argon atmosphere before being quenched by addition of a saturated solution of $NaHCO_3$ (200 mL). The aqueous phase was extracted with diethyl ether (3 × 250 mL), and combined organic layers dried over $MgSO_4$, filtered and concentrated *in vacuo*. The crude product was purified by distillation under vacuum (81 °C, 0.39 mbar) using a Kugelrohr apparatus to afford the title compound **11** (7.03 g, 46.3 mmol, 89%) as a yellow oil. ν_{max} (neat)/cm^{-1} 2919, 1672, 1588, 1404, 1268, 1217, 1037, 985, 910, 825, 787; δ_H (300 MHz ; $CDCl_3$) 7.39 (d, J = 6.1 Hz, 1 H, OC$\underline{H}$CH), 5.63 (q quint, J = 6.8 Hz, J = 1.2 Hz, 1 H, $CH_3C\underline{H}$), 5.39 (dd, J = 6.1 Hz, J = 1.2 Hz, 1 H, CHC$\underline{H}$C(O)), 4.71 (X part of an ABXY system, J = 14.5 Hz, J = 3.4 Hz, 1 H, OCH), 2.76 (A part of an ABXY system, J = 16.6 Hz, J = 14.5 Hz, 1 H, (O)CC$\underline{H}$H′), 2.35 (B part of an ABXY system, J = 16.6 Hz, J = 3.4 Hz, J = 1.2 Hz, 1 H, (O)CCH$\underline{H}$′), 1.71 (quint, J = 1.2 Hz, 3 H, CH_3) 1.66 (br. d, J = 6.8 Hz, 3 H, CH_3); δ_C (75 MHz, $CDCl_3$) 193.0 (CO), 163.5 (CH$\underline{C}$HO), 132.4 (C), 124.9 ($\underline{C}HCH_3$), 106.9 ($\underline{C}$HCO), 84.7 ($CH_2\underline{C}$HO), 40.7 (CH_2), 13.4 (CH$\underline{C}H_3$), 11.8 ($C\underline{C}H_3$); m/z (ESI+) $[M+Na]^+$ 175.0729 calcd for $C_9H_{12}O_2Na$ 175.0730.

*(E)-2-(but-2-en-2-yl)-5-iodo-2H-pyran-4(3H)-one (**12**).* To a solution of iodine (15.00 g, 59.1 mmol) in anhydrous CH_2Cl_2 (100 mL) at 0 °C, under argon atmosphere, was added freshly dried pyridine (10.2 mL, 131.4 mmol). A solution of **11** (4.00 g, 26.2 mmol) in anhydrous CH_2Cl_2 (100 mL) was then added dropwise. The resultant reaction mixture was maintained under stirring for 30 min at 0 °C protected from light before being allowed to warm up to room temperature for 2.5 h. The reaction was then quenched with a saturated solution of $Na_2S_2O_3$ (200 mL), partitioned between a saturated solution of $NaHCO_3$ (300 mL) and CH_2Cl_2 (250 mL), and was then extracted with CH_2Cl_2 (3 × 250 mL). The combined organic layers were dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was then purified by combi-flash chromatography (petroleum ether/EtOAc 100:0 to 92:8) to afford the title compound **12** (6.87 g, 24.7 mmol, 94%) as a pale yellow solid. R_f 0.63 (petroleum ether/EtOAc 85:15); Mp 48−50 °C; ν_{max} (neat)/cm^{-1} 3028, 2914, 1661, 1552, 1370, 1352, 1264, 1112, 964, 931, 812, 490; δ_H (300 MHz ; $CDCl_3$) 7.80 (s, 1 H, OC$\underline{H}$CH), 5.65 (q quint, J = 6.5 Hz, J = 1.2 Hz, 1 H, $CH_3C\underline{H}$), 4.88 (X part of an ABX system, J = 14.2 Hz, J = 3.5 Hz, 1 H, OC$\underline{H}$), 2.91 (A part of an ABX system, J = 16.6 Hz, J = 14.2 Hz, 1 H, (O)CC$\underline{H}$H′), 2.72 (B part of an ABX system, J = 16.6 Hz, J = 3.5 Hz, 1 H, (O)CCH$\underline{H}$′), 1.69 (quint, J = 1.2 Hz, 3 H, CH_3), 1.67 (dquint, J = 6.5 Hz, J = 1.2 Hz, 3 H, CH_3); δ_C (75 MHz, $CDCl_3$) 186.7 (CO), 166.3 (IC$\underline{C}$HO), 131.5 (C), 125.9 ($\underline{C}HCH_3$), 85.5 (CI) 77.3 ($CH_2\underline{C}$HO), 40.1 (CH_2), 13.3 (CH$\underline{C}H_3$), 11.7 ($C\underline{C}H_3$); m/z (ESI+) $[M+Na]^+$ 300.9696 calcd for $C_9H_{11}O_2INa$ 300.9696.

*(E)-2-(But-2-en-2-yl)-5-(prop-1-en-2-yl)-2H-pyran-4(3H)-one (**4b**).* Iodide derivative **12** (4.00 g, 14.4 mmol), isopropenyltributyltin **8**[26] (9.52 g, 28.8 mmol), triphenylarsine (1.76 g, 5.75 mmol), tris(dibenzylideneacetone)dipalladium(0) (1.32 g, 1.44 mmol), and copper(I) thiophenecarboxylate (3.56 g, 18.7 mmol) were dissolved in a THF/DMSO (1:1, 200 mL) mixture and stirred at 40 °C under argon atmosphere for 16 h. The reaction mixture was then treated at room temperature by addition of a saturated solution of sodium fluoride (150 mL) and stirred for one extra hour with Celite. The residue was filtered through a pad of Celite, extracted with diethyl ether. The combined organic layers were dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The resulting crude product was purified on combi-flash chromatograhy (petroleum ether/EtOAc 100:0 to 98:2) to afford the title compound **4b** (2.64 g, 13.7 mmol, 95%) as a yellow oil. R_f 0.67 (petroleum ether/EtOAc 90:10); ν_{max} (neat)/cm^{-1} 2921, 1672, 1578, 1358, 1311, 1254, 1125, 1057, 894, 824; δ_H (300 MHz ; $CDCl_3$) 7.43 (d, J = 0.6 Hz, 1 H, OC$\underline{H}$), 6.64 (q quint, J = 6.6 Hz, J = 1.3 Hz, 1 H, $CH_3C\underline{H}$), 5.19 (dq, J = 2.3 Hz, J = 0.9 Hz, 1 H, C$\underline{H}$H′), 4.96 (dq, J = 2.3 Hz, J = 1.4 Hz, 1 H, CH$\underline{H}$′), 4.72 (X part of an ABX system, J = 14.4 Hz, J = 3.3 Hz, 1 H, OCH), 2.79 (A part of an ABX system, J = 16.4 Hz, J = 14.4 Hz, 1H, C$\underline{H}$H′C(O)), 2.40 (B part of an ABX system, J = 16.4 Hz, J = 3.3 Hz, 1H, CH$\underline{H}$′C(O)), 1.92 (dd, J = 1.4 Hz, J = 0.9 Hz, 3 H, CH_3), 1.70 (quint, J = 1.3 Hz, 3 H, CH_3), 1.66 (br. d, J = 6.6 Hz, 3 H, CH_3); δ_C (75 MHz, $CDCl_3$) 191.7 (CO), 160.4 (C$\underline{C}$HO), 137.5 ($CH_2\underline{C}CH_3$), 132.4 ($CH_3\underline{C}CH$), 124.9 ($CH_3\underline{C}H$), 120.6 ($\underline{C}H_2CCH_3$), 115.1 ($\underline{C}$CO), 85.5 (O$\underline{C}$HCH$_2$), 41.1 (CO$\underline{C}H_2$), 22.3 ($CH_2\underline{C}CH_3$), 13.4 (CH$\underline{C}H_3$), 11.8 (CHC$\underline{C}H_3$); m/z (ESI+) $[M+Na]^+$ 215.1043 calcd for $C_{12}H_{16}O_2Na$ 215.1043.

*(E)-2-(But-2-en-2-yl)-5-(prop-1-en-2-yl)-3,4-dihydro-2H-pyran-4-ol (**17**).* To a solution of diene **4b** (0.54 g, 2.81 mmol) in THF/MeOH (1:1, 50 mL) was added cerium chloride heptahydrate (1.15 g, 3.09 mmol). After complete dissolution of cerium salts, the solution was cooled down to −78 °C. Sodium borohydride (0.24 g, 6.32 mmol) was then added in one portion. The resulting mixture was stirred at the same temperature for 30 min before being warmed up to −50 °C and left to warm up to −30 °C over 45 min. Solvents were evaporated under reduced pressure and the residue was dissolved in the least amount of CH_2Cl_2 possible before being filtered through a pad of Celite, washed with CH_2Cl_2 (3 × 100 mL), and concentrated under reduced pressure. The crude product was then purified on Combi-Flash chromatography (petroleum ether/EtOAc 100:0 to 95:5) to afford the title compound **17** (0.44 g, 2.3 mmol, 81%) as a clear colorless oil. R_f 0.45 (petroleum ether/EtOAc 90:10); ν_{max} (neat)/cm^{-1} 3401, 2922, 1724, 1630, 439; δ_H (300 MHz ; $CDCl_3$) 6.68 (s, 1 H, OC$\underline{H}$), 5.58 (q quint, J = 6.8 Hz, J = 1.2 Hz, 1 H, $CH_3C\underline{H}$), 4.95 (m, 1 H, CH$\underline{H}$′C), 4.87 (quint, J = 1.3 Hz, 1 H, C$\underline{H}$HC), 4.66 (ddd, J = 7.2 Hz, J = 6.3 Hz, J = 5.8 Hz, 1 H, OC$\underline{H}$), 4.32 (br. dd, J = 8.9 Hz, J = 3.0 Hz, 1 H, C$\underline{H}$OH), 2.20 (ddd, J = 13.6 Hz, J = 6.3 Hz, J = 3.0 Hz, 1 H, C$\underline{H}$H′CHOH), 2.08 (ddd, J = 13.6 Hz, J = 8.9 Hz, J = 7.2 Hz, 1 H, CH$\underline{H}$′CHOH), 2.03 (dd, J = 5.8 Hz, 1 H, CHH′CHO$\underline{H}$), 1.87 (dd, J = 1.3 Hz, J = 0.6 Hz, 3 H, CH_3), 1.67 (quint, J = 1.2 Hz, 3 H, CH_3), 1.64 (dquint, J = 6.8 Hz, J = 1.2 Hz, 3 H, CH_3); δ_C (75 MHz, $CDCl_3$) 144 (OCH), 139.1 ($\underline{C}$COH), 134.2 ($CH_3\underline{C}$CH), 121.7 ($CH_3\underline{C}H$), 118.0 ($CH_2\underline{C}CH_3$), 109.6 ($\underline{C}H_2CCH_3$), 78.9 (CHOH), 62.3 (OCH), 35.3 ($\underline{C}H_2$CHOH), 20.6 ($\underline{C}H_3CCH_2$), 13.2 ($\underline{C}H_3$CH), 12.3 ($\underline{C}H_3$C); m/z (ESI+) $[M-H]^+$ 193.1222 calcd for $C_{12}H_{17}O_2$ 193.1223.

*((E)-But-2-en-2-yl)-4,11-dihydroxy-5-methyl-3,4,6,6a,12q,12b-hexahydroanthra[2,3-h]oxireno [1, 2-b]pyrene-7,12(2H,6H)-dione (**19**).* To a solution of diene **17** (650 mg, 3.35 mmol) in CH_3CN (40 mL) was added 5-hydroxynaphthalene-1,4-dione **3** (583 mg, 3.35 mmol), the resulting mixture was stirred at 40 °C overnight. Solvent was evaporated and the residue, identified as being **18**, was dissolved in CH_2Cl_2 (80 mL) under argon atmosphere, vanadyl acetylacetonate (134 mg, 0.53 mmol) was added in one portion and the resulting mixture stirred for 45 min. A solution of *tert*-butyl hydroperoxide (5.5 M in decane, 0.92 mL, 5.25 mmol) was added dropwise via a syringe pump system and the resulting mixture was stirred for 2 h at room temperature The reaction was quenched by addition of a saturated solution of $Na_2S_2O_3$ (30 mL), extracted with CH_2Cl_2 (3 × 50 mL), dried over $MgSO_4$, and concentrated under reduced pressure. The

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crude product was purified on combi-flash chromatography ($CHCl_3$/MeOH 99.8:0.2) to afford the title compound **19** (990 mg, 2.58 mmol 77%) as a yellow solid. R_f 0.18 ($CHCl_3$/MeOH 99.8:0.2); Mp 139−140 °C ; ν_{max} (neat)/cm^{-1} 3510, 2993, 2822, 1701, 1631, 1578, 1455, 1245, 1162, 1075, 754; δ_H (300 MHz; $CDCl_3$) 12.09 (s, 1H, Ar−OH), 7.56 (dd, J = 8.4 Hz, J = 7.6 Hz, 1H, $H_{aromatic}$), 7.40 (dd, J = 7.6 Hz, J = 1.2 Hz, 1H, $H_{aromatic}$), 7.16 (dd, J = 8.4 Hz, J = 1.2 Hz, 1H, $H_{aromatic}$), 5.23 (br. qquint, J = 1.5 Hz, J = 6.8 Hz, 1H, CH_3CHC), 4.62 (d, J = 3.4 Hz, 1 H, OCH), 3.96 (br. t, X part of an ABXY system, J = 6.4 Hz, 1H, CHOH), 3.83 (br. t, Y part of an ABXY system J = 6.4 Hz, 1H, OCH), 3.33 (dd, J = 3.4 Hz, J = 5.8 Hz, 1H, C(O)CHCH), 3.07 (ddd, J = 1.0 Hz, J = 8.0 Hz, J = 5.8 Hz, 1H, C(O)CHCH$_2$), 2.94 and 2.11−2.01 (m and AB part of an ABXY system, J = 16.0 Hz, J = 8.0 Hz, J = 1.0 Hz, 4H, $CHCH_2CO$ + CH_2CHOH), 1.53 (s, 3H, CCH_3), 1.45 (br. dquint, J = 1.3 Hz, J = 6.8 Hz, 3H, CH_3CH), 1.18 (s, 3H, CCH_3); δ_C (75 MHz, $CDCl_3$) 204.7 (CO), 195.4 (CO), 161.5 ($C_{aromatic}$), 137.5 (C), 136.6 ($C_{aromatic}$), 134.2 ($C_{aromatic}$), 122.6 ($CH_{aromatic}$), 120.7 (CH_3CH), 119.2 ($C_{aromatic}$), 117.0 ($CH_{aromatic}$), 74.9 (OCH), 66.5 (C epoxide), 64.9 (C epoxide), 64.7 (OCH), 63.6 (CHOH), 49.1 (C(O)CH), 41.9 (C(O)CH), 33.0 (CH_2CHOH), 26.3 (CH_2CCH_3), 21.1 (CH_3CO), 13.3 (CH_3CH), 12.5 (CH_3C) ; m/z (ESI+) $[M+Na]^+$ 407.1452 calcd for $C_{22}H_{24}O_6Na$ 407.1465.

*(E)-2-(But-2-en-2-yl)-4,11-dihydroxy-5-methyl-3,4-dihydro-2H-anthra[1,2-b]pyran-7,12-dione (**20**).* To a solution of epoxide **19** (990 mg, 2.58 mmol) was added Et_3N (3.40 mL, 25.8 mmol) at room temperature under air atmosphere. The resulting reaction mixture was stirred for 1 h, then concentrated under reduced pressure and purified by Combi-flash chromatography ($CHCl_3$/MeOH 99.8:0.2) to afford the title compound **20** (845 mg, 2.32 mmol, 90%) as a yellow solid. R_f 0.22 (petroleum ether/EtOAc 80:20); mp 159−161 °C (dec.) ; ν_{max} (neat)/cm^{-1} 3258, 2924, 1673, 1632, 1583, 1405, 1318, 1285, 1260, 1188, 1037, 875, 794, 751; δ_H (300 MHz; $CDCl_3$) 13.11 (s, 1H, Ar−OH), 7.77 (s, 1H, $H_{aromatic}$), 7.76 (dd, J = 7.4 Hz, J = 1.2 Hz, 1H, $H_{aromatic}$), 7.61 (dd, J = 7.4 Hz, J = 8.2 Hz, 1H, $H_{aromatic}$), 7.28 (dd, J = 8.2 Hz, J = 1.2 Hz, 1H, $H_{aromatic}$), 5.63 (qquint, J = 1.5 Hz, J = 6.7 Hz, 1H, CH_3CHC), 4.98−4.89 (m, 2 H, 2 OCH), 2.58 (s, 3H, CH_3), 2.5−2.35 (m, 2H, $OCHCH_2$), 1.75 (s, 3H, CH_3), 1.60 (d, J = 6.7 Hz, 3H, CH_3CH); δ_C (75 MHz, $CDCl_3$) 188.4 (CO), 182.9 (CO), 162.5 ($C_{aromatic}$), 156.6 ($C_{aromatic}$), 147.9 ($C_{aromatic}$), 135.7 ($CH_{aromatic}$), 134.7 ($C_{aromatic}$), 134.5 (C), 133.0 ($C_{aromatic}$), 130.6 ($C_{aromatic}$), 124.9 ($CH_{aromatic}$), 122.0 ($CH_{aromatic}$), 120.8 ($CHCH_3$), 119.0 ($CH_{aromatic}$), 118.4 ($C_{aromatic}$), 117.1 ($C_{aromatic}$), 77.9 (OCH), 62.3 (CH(OH)), 34.3 (CH_2CHOH), 20.6 (Ar−CH_3), 13.6 (CCH_3), 13.3 ($CHCH_3$); m/z (ESI+) $[M+Na]^+$ 387.1208 calcd for $C_{22}H_{20}O_5Na$ 387.1208.

*(E)-2-(But-2-en-2-yl)-11-hydroxy-5-methyl-3,4-dihydro-2H-anthra[1,2-b]pyran-4,7,12-trione (**21**).* To a solution of benzylic alcohol **20** (500 mg, 1.37 mmol) in a mixture CH_2Cl_2/DMSO (4:2, 6 mL) was added Dess-Martin periodinane (1.16 g, 2.74 mmol) at room temperature. The resulting mixture was stirred for 2 h, then quenched by addition of a saturated solution of $Na_2S_2O_3$ (10 mL) and a saturated solution of $NaHCO_3$ (10 mL) and extracted with CH_2Cl_2 until the organic phase became colorless. The combined organic layers were concentrated under reduced pressure, dissolved in EtOAc and washed with cold brine. After having been dried over $MgSO_4$, the crude mixture was concentrated and purified on Combi-flash chromatography ($CHCl_3$/MeOH 99.8:0.2) to afford the title compound **21** (447 mg, 1.23 mmol, 88%) as a yellow solid. R_f 0.18 (petroleum ether/EtOAc 90:10); Mp 204−205 °C ; ν_{max} (neat)/cm^{-1} 3367, 2919, 1676, 1631, 1579, 1550, 1476; δ_H (300 MHz; $CDCl_3$) 13.01 (s, 1H, Ar−OH), 7.79 (dd, J = 7.4 Hz, J = 1.2 Hz, 1H, $H_{aromatic}$), 7.67 (s, 1H, $H_{aromatic}$), 7.55 (dd, J = 7.4 Hz, J = 8.4 Hz, 1H, $H_{aromatic}$), 7.23 (dd, J = 8.4 Hz, J = 1.2 Hz, 1H, $H_{aromatic}$), 5.76 (qquint, J = 1.0 Hz, J = 6.7 Hz, 1H, CH_3CH), 4.91 (br. d, X part of an ABX system, J = 12.5 Hz, J = 3.0 Hz, 1H, 2 $OCHCH_2$), 2.96 and 2.80 (AB part of an ABX system, J = 12.5 Hz, J = 3.0 Hz, 1H, 2 $OCHCH_2$), 2.73 (s, 3H, Ar−CH_3), 1.81 (br. quint, J = 1.0 Hz, 3H, CH_3CH), 1.67 (dquint, J = 6.7 Hz, J = 1.0 Hz, 3H, CCH_3); δ_C (75 MHz, $CDCl_3$) 193.3 (CO), 187.7 (CO), 182.5 (CO), 163.6 ($C_{aromatic}$), 162.6 ($C_{aromatic}$), 150.0 ($C_{aromatic}$), 137.4 ($C_{aromatic}$), 136.0 ($CH_{aromatic}$), 132.6 ($C_{aromatic}$), 132.4 (C), 125.3 ($CH_{aromatic}$), 124.3 ($C_{aromatic}$), 124.0 ($CHCH_3$), 123.1 ($CH_{aromatic}$), 119.7 ($C_{aromatic}$), 119.1 ($CH_{aromatic}$), 82.3 (OCH), 42.6 (CH_2), 24.1 (Ar−CH_3), 13.6 ($CHCH_3$), 12.7 (CCH_3); m/z (ESI+) $[M-H]^+$ 361.1078 calcd for $C_{22}H_{17}O_5$ 361.1076.

*(E)-2-(But-2-en-2-yl)-11-hydroxy-5-methyl-4H-anthra[1,2-b]pyran-4,7,12-trione (**2**).* To a solution of saturated ketone **21** (40 mg, 0.11 mmol) in DMSO (5 mL) under argon atmosphere, iodine (12 mg, 50 μmol) was added in one portion and the mixture was stirred overnight at 95 °C. Then, the reaction was quenched by addition of brine (30 mL), extracted with CH_2Cl_2 (3 × 30 mL) and the combined organic layers were washed with a saturated solution of $Na_2S_2O_3$ (40 mL) and brine (40 mL) before being dried over $MgSO_4$, and concentrated under reduced pressure. The crude product was purified by Combi-Flash chromatography (petroleum ether/EtOAc from 90:10 to 80:20) to afford kidamycinone **2** (27 mg, 80 μmol, 68%) as a yellow solid. All spectroscopic data for **2** are identical in all respects with those described in literature.[11] R_f 0.14 (petroleum ether/EtOAc 85:15); mp 255−256 °C ν_{max} (neat)/cm^{-1} 3070, 2961, 2851, 1670, 1628, 1457, 1316, 1259, 1078, 1014, 839, 790; δ_H (300 MHz; $CDCl_3$) 12.89 (s, 1H, Ar−OH), 7.99 (d, J = 0.7 Hz, 1H, $H_{aromatic}$), 7.79 (dd, J = 7.5 Hz, J = 1.3 Hz, 1H, $H_{aromatic}$), 7.66 (dd, J = 7.5 Hz, J = 8.2 Hz, 1H, $H_{aromatic}$), 7.46 (qq, J = 1.0 Hz, J = 7.1 Hz, 1H, $CHCH_3$), 7.33 (dd, J = 8.2 Hz, J = 1.3 Hz, 1H, $H_{aromatic}$), 6.35 (s, 1H, (O)CH), 2.99 (d, J = 0.7 Hz, 3H, Ar−CH_3), 2.02 (qd, J = 7.1 Hz, 3H, $CHCH_3$), 1.99−1.91 (m, 3H, CCH_3); δ_C (75 MHz, $CDCl_3$) 187.5 (CO), 182.0 (CO), 179.8 (CO), 164.2 ($C_{aromatic}$), 162.7 ($C_{aromatic}$), 156.3 ($C_{aromatic}$), 150.0 (C), 136.5 ($C_{aromatic}$), 136.1 ($CH_{aromatic}$), 134.6 ($CHCH_3$), 132.4 ($C_{aromatic}$), 127.4 (CCH_3), 126.5 ($C_{aromatic}$), 125.6 ($CH_{aromatic}$), 125.4 ($CH_{aromatic}$), 119.7 ($C_{aromatic}$), 119.5 ($CH_{aromatic}$), 116.9 ($C_{aromatic}$), 108.9 ($OCCH$), 24.3 (Ar−CH_3), 15.2 ($CHCH_3$), 12.3 (CCH_3); m/z (ESI+) $[M+H]^+$ 361.1068 calcd for $C_{22}H_{17}O_5$ 361.1076.

*1,8-Dihydroxy-3-methyl-2-((2E,4E)-4-methylhexa-2,4-dienoyl)-anthracen-9,10-dione (**22**).* To a solution of ketone **21** (100 mg, 0.27 mmol) in a mixture 1,4-dioxane/DMSO/phosphate buffer pH = 7 (3:1:1, 5 mL) was added DDQ (313 mg, 1.38 mmol) under argon atmosphere. The resulting mixture was heated up to 40 °C and stirred for 18 h. Then, the reaction mixture was concentrated under reduced pressure and the residue was purified by silica gel chromatography ($CHCl_3$/MeOH 99.8:0.2) to afford the title compound **22** (58 mg, 0.16 mmol, 60%) as an orange powder. R_f 0.21 ($CHCl_3$/MeOH 99.9:0.1); Mp 160−162 °C (dec.); ν_{max} (neat)/cm^{-1} 3045, 2923, 1723, 1670, 1620, 1577, 1449, 1262, 753, 730; δ_H (300 MHz; $CDCl_3$) 12.23 (s, 1H, Ar−OH), 12.01 (s, 1H, Ar−OH), 7.84 (dd, J = 7.5 Hz, J = 1.1 Hz, 1H, $H_{aromatic}$), 7.71 (s, 1H, $H_{aromatic}$), 7.70 (dd, J = 7.5 Hz, J = 8.4 Hz, 1H, $H_{aromatic}$), 7.31 (dd, J = 8.4 Hz, J = 1.1 Hz, 1H, $H_{aromatic}$), 6.97 (d, J = 15.9 Hz, 1H, $CHCHC(O)$), 6.40 (d, J = 15.9 Hz, 1H, $CHCHC(O)$), 6.00 (qd, J = 7.1 Hz, J = 1.0 Hz, 1H, CH_3CH), 2.35 (s, 3H, Ar−CH_3), 1.85 (br. quint, J = 1.0 Hz, 3H, CH_3C), 1.82 (br. d, J = 7.1 Hz, 3H, CH_3CH); δ_C (75 MHz, $CDCl_3$) 195.6 (CO), 192.7 (CO), 181.7(CO), 162.8 ($C_{aromatic}$), 159.6 ($C_{aromatic}$), 152.3 ($CHCHC$), 146.4 ($C_{aromatic}CH_3$), 139.8 ($CHCH_3$), 137.4 ($CH_{aromatic}$), 135.6 ($C_{aromatic}$), 134.6 (CCH_3), 133.7 ($C_{aromatic}$), 133.2 ($C_{aromatic}$), 125.3 (C(O)CHCH), 125.0 ($CH_{aromatic}$), 122.1 ($CH_{aromatic}$), 120.3 ($CH_{aromatic}$), 116.0 ($C_{aromatic}$), 114.2 ($C_{aromatic}$), 20.3 (Ar−CH_3), 15.0 ($CHCH_3$), 12.0 (CCH_3); m/z (ESI+) $[M+H]^+$ 363.1230 calcd for $C_{22}H_{19}O_5$ 363.1232.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.7b00544.

^1H and ^{13}C NMR spectra for products **1**, **2**, **4b**, **5**−**7**, **9**, **11**, **12**, **14**−**17**, and **19**−**22** (PDF)

X-ray crystallographic data for product **19** (CIF)

IRC animation (MPG)

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Notes

The authors declare no competing financial interest.

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