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REGIOSPECIFIC TOTAL SYNTHESIS OF 6-DEOXYANTHRACYCLINES

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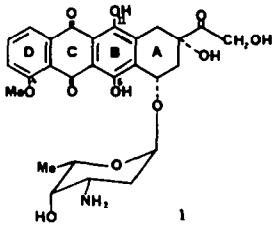
Abstract—Regiospecific approaches to 6-deoxyanthracyclinones, which have resulted in the synthesis of the novel anthracyclines 4-demethoxy-6-deoxydaunorubicin (**2**) and 6-deoxycarminomycin (**3**), are reported. The construction of the aglycone **4** is based on the coupling of 1,4-dimethoxy-2-lithionaphthalene (**10a**) to 1-formyl-2-carbomethoxy-4-acetylcyclohexane thioketal (**11**). A new improved regioselective route, which allows the preparation of 6-deoxyanthracyclinones bearing also substituents in ring D as illustrated by **5**, is based on the coupling of **10a** and of 1,4,5-trimethoxy-3-lithionaphthalene (**10b**) to lactone **28**.

The successful development of doxorubicin **1** (Adriamycin) as a major chemotherapic agent in the treatment of a range of human malignancies has aroused great interest in the total synthetic approaches to doxorubicin related anthracyclines. The anthraquinone system is an important structural feature of all anthracyclines. A wide range of oxygenated substitution patterns appears to be compatible with biological activity, although the existence of a direct contribution of the said substitution pattern on antitumor activity has not yet been established.[1] The intercalation complex of the antitumor anthracyclines with double stranded cell DNA is stabilized by π–π interaction of the base pairs with the drug planar chromophore moiety. The phenolic groups of the latter appear also to take part in the intercalation process as deduced by spectroscopic evidence.[2] Both X-rays diffraction and NMR studies indicate rings B and C to be in the interior of the shielding region of the DNA base pairs.[3] It has been suggested that hydroquinone-type ring B might take part in the redox reactions leading to radical species responsible of the toxicity of the antitumor anthracyclines.[4] Moreover the 11-deoxy analogs of daunorubicin, doxorubicin and carminomycin, isolated in our laboratories from *S. peucetius var. aureus*, have shown interesting antitumor properties.[5]



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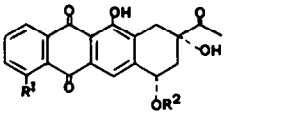
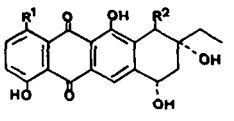


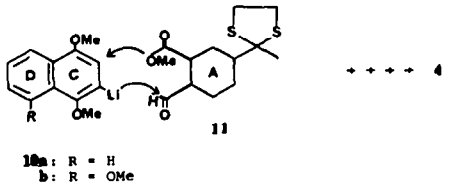
2 : R^1 = H; R^2 =
3 : R^1 = OH; R^2 =
4 : R^1 = R^2 = H
5 : R^1 = OH; R^2 = H



6 : R^1 = OH; R^2 = CO_2Me
7 : R^1 = R^2 = OH
8 : R^1 = H; R^2 = OH
9 : R^1 = R^2 = H

For these reasons there is current interest in the relationship between the phenolic substitution on ring B and antitumor activity or affinity for DNA in different series of daunorubicin or doxorubicin analogs.

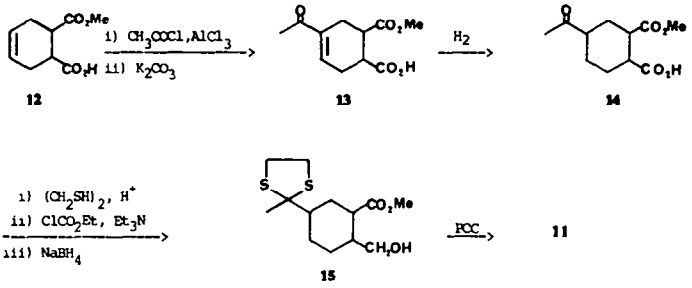
Our recent efforts in the area of the total synthesis of anthracyclines have been concentrated on the development of the 6-deoxy class and have led to the preparation of 4-demethoxy-6-deoxydaunorubicin (**2**) and 6-deoxy-carminomycin (**3**).[6] Recent advances in regiospecific synthesis of anthracyclinones have provided several new routes to daunomycinone,[1] or to its 11-deoxy analog;[7] little attention has been focused instead on the synthesis of 6-deoxyanthracyclinones represented hitherto by the rare naturally occurring pigments δ-rhodomycinone (**6**),[8] α_2-rhodomycinone (**7**), α-citromycinone (**8**) and γ-citromycinone (**9**).[9] Our synthetic approach to the construction of the aglycones **4** and **5** was based on the nucleophilic attack of the anionic species of a naphthalene derivative, which formally represents the D—C rings, on a function of a cyclohexanederivative, the A-ring precursor, determining the regiochemical step of the synthesis of the tetracycle. More particularly for the preparation of **4** (Scheme 1) the lithium derivative of 1,4-dimethoxynaphthalene (**10a**) was condensed to the key-intermediate (**11**). The substrate **12** was chosen as an



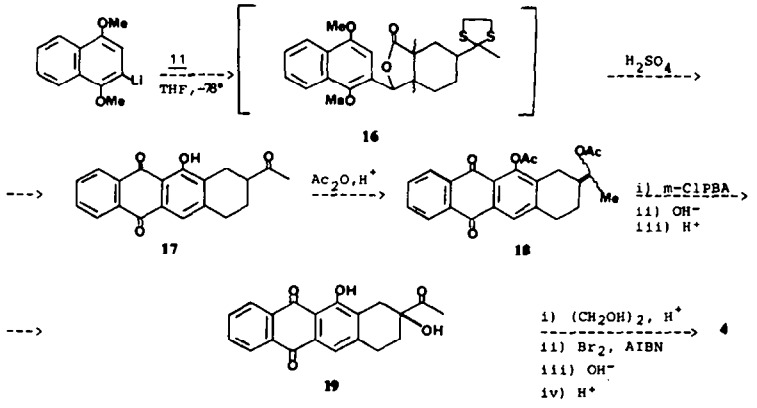
Scheme 1

inexpensive starting material for the preparation of (**11**) (Scheme 2). The reaction of **12** with acetyl chloride, followed by mild basic treatment, gave regioselectively the crystalline α,β-unsaturated ketone **13** in 57% overall yield. The regioselectivity of the acylation, affording only **13**, is probably due to the polarization induced on the double bond of **12** by an intermediate aluminum carboxylate. The structure of **13** was supported by spectroscopic and chemical evidence. Carbon atom α to carboxylic group is somewhat less deshielded than the carbon α to carbomethoxy group ($\Delta\delta$ = 1 ppm).[10] ^{13}C-NMR ($CDCl_3$) of **13** showed resonances *inter alia*, at 38.9 (C-1) and 39.3 ppm (C-2), while ^{13}C-NMR ($CDCl_3$) of the corresponding dimethyl ester showed resonances at 39.1 (C-2) and 39.4 ppm (C-1). The best agreement between the calculated and experimental values of **13**, considering the difference in shielding at C-1 and C-2 and the values shown by the dimethyl ester, was found for the structure with the carboxylic group at C-1. The conversion of **13** to methyl 3-acetylbenzoate *via* reduction of the carboxylic group to an hydroxyl group,[11] followed by easy aromatization, determined unequivocally the structure of **13**. The aldehyde **11** was obtained as an oil in 45% overall yield, upon catalytic reduction of the double bond, ketalization of the carbonyl group with 1,2-ethanedithiol, reduction with sodium borohydride of the mixed anhydride obtained with ethyl chloroformate to give alcohol **15** and finally oxidation of **15** with pyridinium chlorochromate (Scheme 2). The generation of the nucleophile **10a** by reaction of 1,4-dimethoxy-2-bromonaphthalene[12] with n-BuLi and the subsequent addition of **11** gave a crude reaction mixture, containing **16** as major component, which was treated directly with sulfuric acid to afford the tetracyclic anthraquinonic nucleus **17**, isolated in 10% overall yield (Scheme 3). The introduction of the tertiary hydroxyl group to give **19** was performed in 60% overall yield according to a known procedure,[13] based on the epoxidation of the enol acetate followed by hydrolysis. The final step in order to achieve **4** was the introduction of the hydroxyl group at C-7, *via* homolytic bromination with bromine followed by alkaline treatment with aqueous sodium hydroxyde. The ketal or ketone group of the side-chain, as already observed in other synthesis of anthracyclinones, could be responsible for the regioselectivity of the benzylic bromination at C-7 whereas the stereoselectivity of hydroxylation is probably due to the assistance of the C-9-OH.[14] The lack of introduction of C-7-OH in Kende's citromycinone synthesis[9c] is probably due to the presence of an ethyl group at C-9 allowing an easier attack of the C-10 methylene by the reagent.

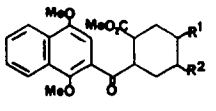
It is worth pointing out that the acylation of 1,4-dimethoxynaphthalene with **14** in the presence of $(CF_3CO)_2O/CF_3COOH$ afforded non regioselectively a mixture of **20a** and **b**, whose benzylic catalytic reduction and cyclization–oxidation in concentrated sulfuric acid gave isomers **17** and **21** separated by chromatography after introduction of the C-9-OH. The non regioselective course of the Friedel–Crafts



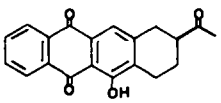
Scheme 2.



Scheme 3.



20a: R^1 = H; R^2 = COMe
b: R^1 = COMe; R^2 = H



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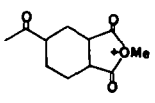

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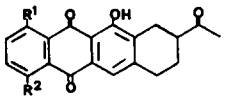
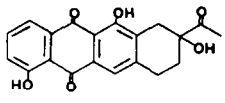
acylation should be attributed to the intermediate formation of oxonium species **22**.

The attempt to perform the synthesis of 6-deoxycarminomycinone (**5**) following the procedure



23 : R^1 = H; R^2 = OCH_3
24 : R^1 = OCH_3; R^2 = H

described for **4**, that is by coupling **10b**, obtained from 1,4,5-trimethoxy-3-bromonaphthalene,[15] with **11** showed lack of regioselectivity as it afforded 6-deoxydaunomycinone and 6-deoxyisodaunomycinone derivatives **23** and **24** respectively.[16] Therefore we developed a new improved regioselective route which allows one to obtain 6-deoxyanthracyclinones bearing also substituents in ring D as illustrated for **5**. The key-intermediate for the construction of the tetracycle is the lactone **28**, obtained from *trans* 1,2-dicarbomethoxy-4-cyclohexene (**25**),[17] as shown in Scheme 4. The α,β-unsaturated ketone **26**, obtained in 75% yield by addition of Ac_2O in presence of tin tetrachloride followed by an acid treatment, was converted to the exocyclic olefin **27** by reduction of the corresponding tosylhydrazone with catechol borane.[18] Permanganate oxidation in acetic acid of **27** and treatment of the resulting hydroxyketone with ethylene glycol and a catalytic amount of p-toluensulfonic acid gave the crystalline compound **28**. This AB synthon is particularly interesting because: (a) it has the functionalization at the future C-9 of **4** and **5**; (b) it condenses with **10a,b** in a completely regioselective fashion and might allow a control of the chirality at an early stage of the synthetic process through a classical optical resolution. The addition of **10a,b** to **28** at $-78°$ followed by treatment with MeOH · HCl afforded only esters **29a,b** in 60% yield after chromatographic purification. Reduction of **29a,b** with pyridine-borane complex[19] followed by alkaline hydrolysis and esterification with phenyldiazomethane afforded **30a,b** in 70% overall yield. Acetylation of both alcoholic groups was then carried out in order to avoid formation of the five-membered lactone under the Friedel–Crafts cyclization conditions. Hydrogenolysis of the benzyl ester followed by treatment with $(CF_3CO)_2O$/CF_3COOH and methanolysis of the resulting acetates afforded **31a,b** in 60% overall yield. Oxidation of the secondary alcohol, followed by oxidative dealkylation with $AlCl_3$ in the presence of air, gave **19** or **32**. The introduction of the C-7-OH in **32** to give **5**



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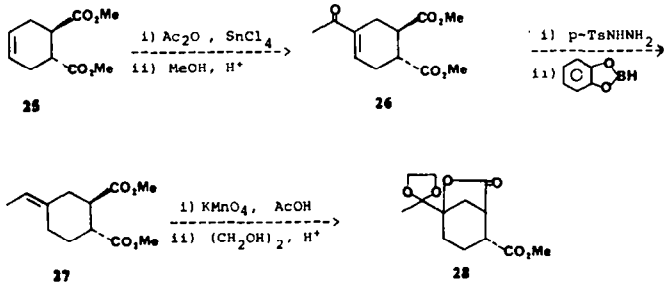
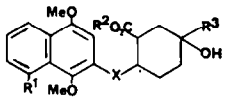
was performed, after ketalization at C-13, by bromination with bromine or with NBS and a radical initiator, followed by treatment with alkali or with silver acetate and methanolysis of the corresponding acetate.[20]

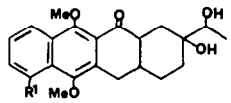
Glycosidation of **4** and **5** with 1-chloro-N,O-(trifluoroacetyl)daunosamine[21] was performed according to a stereoselective procedure[22] with



25 **26** **27** **28**

Scheme 4.

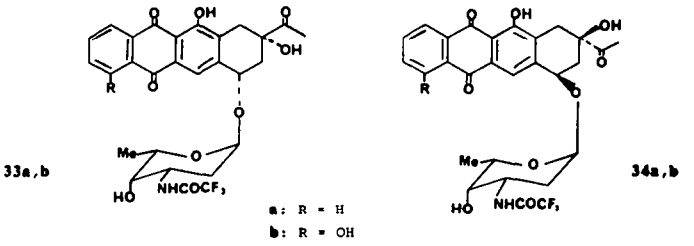




29a,b : X = CO; R^2 = Me; R^3 = COMe
30a,b : X = CH_2; R^2 = CH_2Ph; R^3 = CHOHMe

31a,b

a: R^1 = H
b: R^1 = OMe



$AgSO_3CF_3$ to yield the mixture of the two α-diastereoisomers **33a,b** and **34a,b**, which were separated by chromatography. The natural 7(*S*),9(*S*) configuration was assigned to **33a,b** on the basis of the similarity of their CD curves with that of daunorubicin.[23] Finally the free glycosides **2** and **3**, isolated as the hydrochlorides, were obtained from **33a,b** upon mild alkaline hydrolysis of the N-protecting group.

EXPERIMENTAL

M.ps, measured in capillaries, are uncorrected. ^{1}H-NMR spectra were obtained on VARIAN EM 360 and XL 200 spectrometers; values are in ppm downfield from TMS. IR and UV spectra were recorded on Perkin–Elmer 457 and Spectracomp 601 C. Erba spectrometers respectively. Optical rotations were measured with a Jasco DIP-140 polarimeter. Mass spectra were recorded on Varian Mat 311A spectrometer. CD curves were obtained on Auto-Dichrograph Mark V Jobin Yvon.†

cis - 1 - *Carboxy* - 2 - *methoxycarbonyl* - 4 - *acetyl* - 4 - *cyclohexene* (**13**). To a suspension of anhyd $AlCl_3$ (85 g, 0.64 mol) in anhyd CH_2Cl_2 (1.5 l), CH_3COCl (75 ml, 1 mol) was added dropwise at −5° under stirring and N_2, then a soln of **12** (40 g, 0.217 mol) in anhyd CH_2Cl_2 (750 ml) was added over 2 hr. The mixture was kept at −5° for 6 hr then at room temp overnight. After pouring into ice, the organic phase was separated off, washed with H_2O and evaporated to dryness. The residue dissolved in MeOH (500 ml) was treated with K_2CO_3 (50 g) under stirring at room temp for 5 hr. After filtration, elimination of solvent and dilution with water, the alkaline soln was washed with $CHCl_3$, then adjusted to pH 3 and extracted with $CHCl_3$. The residue, obtained by evaporation of solvent, was chromatographed on Kieselgel, affording, after crystallization from ether–petroleum ether, **13** (28 g, 57% overall yield). M.p. 94–96°. ^{1}H-NMR (60 MHz, $CDCl_3$) δ 2.33 (s, $COCH_3$), 2.55–2.95 (m, CH_2—C=C—CH_2), 3.00–3.30 (m, CH_3OCOCH, $HOCOCH$), 3.70 (s, $COOCH_3$), 6.91 (m, CH=C), 11.32 (s, COOH). IR(KBr): 1720, 1690, 1660 cm^{-1}. MS: *m/e* 226 (M^+). (Found: C, 58.34; H, 6.23; Calc for $C_{11}H_{14}O_5$: C, 58.4; H, 6.24%).

cis - 1 - *Carboxy* - 2 - *methoxycarbonyl* - 4 - *acetylcyclohexane* (**14**). A soln of **13** (4.68 g) in MeOH (120 ml) was hydrogenated at room temp and 1 atm. in the presence of 10% Pd/C (0.6 g). After removal of the catalyst by filtration, the solvent was removed *in vacuo* to give **14** in almost quantitative yield. The product was crystallized from ether–petroleum ether. M.p. 85°. (Found: C, 57.79; H, 7.15; Calc for $C_{11}H_{16}O_5$: C, 57.89; H, 7.06%).

cis - 1 - *Hydroxymethyl* - 2 - *methoxycarbonyl* - 4 - (1' - *ethylendithioethyl*) - *cyclohexane* (**15**). To a soln of **14** (3.2 g, 14.1 mmol) in CH_2Cl_2 (6.5 ml) 1,2-ethanedithiol (1.3 ml, 15.5 mmol) and $BF_3 \cdot Et_2O$ (0.64 ml) were added. After 3 hr the mixture was passed through a column of silica gel and eluted with a mixture of n-hexane/EtOAc affording the pure thioketal (3.1 g, 73% yield) which was dissolved in dry THF (62 ml), cooled at 0° and treated with $ClCOOC_2H_5$ (1.5 ml, 15.6 mmol) in the presence of Et_3N (2.1 ml, 15.3 mmol). The mixture was stirred for 1 hr then filtered off, cooled at −70° and treated with $NaBH_4$ (0.7 g, 14.6 mmol). After 1 hr the soln, adjusted to pH 7 with 0.1 N HCl, was evaporated to dryness *in vacuo*. The residue was chromatographed on Kieselgel to give **15** (2.4 g, 82% yield). HRMS calc $[C_{13}H_{22}S_2O_3^+]$: 290.1010 (Found: 290.1021). ^{1}H-NMR (60 MHz, CD_3COCD_3), *inter alia*: δ 1.27 (s, CH_3—C), 2.82 (s, S—CH_2—CH_2—S), 3.13 (s, $COOCH_3$).

cis - 1 - *Formyl* - 2 - *methoxycarbonyl* - 4 - (1' - *ethylendithioethyl*) - *cyclohexane* (**11**). To a soln of **15** (2.4 g, 8.3 mmol) in CH_2Cl_2 (12 ml) was added PCC (Pyridinium chlorochromate) (2.7 g, 12.5 mmol) suspended in CH_2Cl_2 (25 ml). After stirring for 3 hr at room temp the suspension was diluted with ether (70 ml), stirred for 30 min, then percolated through a Florisil column to give **11** (1.8 g, 74% yield). ^{1}H-NMR (60 MHz, $CDCl_3$) *inter alia*: δ 1.70 (s, CH_3—C), 3.27 (s, S—CH_2—CH_2—S), 3.67 (s, $COOCH_3$), 9.65 (s, CHO).

(±) - 4 - *Demethoxy* - 6,7,9 - *trideoxydaunomycinone* (**17**). A soln of 1,4-dimethoxy-2-bromonaphthalene (1.5 g, 5.8 mmol) in dry ether (15 ml) cooled at −78° was dropped, under N_2, into a solution of n-BuLi in hexane (6.2 mmol, 3.7 ml) diluted with ether (4 ml) and kept at −78°. To this soln stirred at −78° for 15 min, a precooled (−78°) soln of **11** (1.5 g, 5.8 mmol) in dry ether (8 ml) was added dropwise. After 30 min at −78° the mixture was allowed to warm to room temp. A 10% (w/v) NH_4Cl soln was added and the organic layer separated, washed with water, dried over Na_2SO_4 and evaporated *in vacuo* to give an oil that was directly treated at 0° with conc H_2SO_4 (5 ml). After 30 min the mixture was poured into ice and extracted with EtOAc. The organic layer was washed with water, sat $NaHCO_3$ aq brine, then dried over Na_2SO_4, filtered and evaporated to dryness. The residue was chromatographed on Kieselgel to give **17** (0.16 g, 10% yield) crystallized from ether–petroleum ether. M.p. 174–176°. ^{1}H-NMR (60 MHz, $CDCl_3 + CCl_4$), *inter alia*: δ 2.28 (s, $COCH_3$), 2.6–3.2 (m, 7-H, 10-H), 3.91 (m, 9-H), 7.5–8.4 (m, 5H), 12.88 (s, OH). IR(KBr): 2920, 1710, 1670, 1625 cm^{-1}. MS: *m/e* 320 (M^+). (Found: C, 74.76; H, 5.16. Calc for $C_{20}H_{16}O_4$: C, 74.99; H, 5.03%).

(±) - 4 - *Demethoxy* - 6,7 - *dideoxydaunomycinone* (**19**). A soln of **17** (0.32 g) in Ac_2O (38 ml) was refluxed for 18 hr in the presence of *p*-toluensulfonic acid (0.19 g). The residue was dissolved in CH_2Cl_2 (40 ml) and treated with *m*-chloroperbenzoic acid (0.258 g). After 2 hr at room temp, the mixture was washed with sat $NaHCO_3$ aq, water, dried over Na_2SO_4 filtered and the solvent removed *in vacuo*. The residue was dissolved in a mixture of MeOH/EtOH and treated with 30 ml of 1 N NaOH for 1 hr at room temp, then the soln was adjusted to pH 4 with 1 N HCl, diluted with water and extracted with CH_2Cl_2. The organic layer, washed with sat $NaHCO_3$ aq, water, dried over Na_2SO_4, was evaporated to dryness to give a crude material which was chromatographed on Kieselgel affording **19**, (0.18 g). M.p. 206–208°. ^{1}H-NMR (80 MHz, $CDCl_3$): δ 1.95 (m, 8-H), 2.38 (s, $COCH_3$), 3.01 (m, 7-H, 10-H), 3.83 (s, 9-OH), 7.6–8.3 (m, 5H), 13.03 (s, 11-OH). IR(KBr): 1705, 1665, 1625, 1590 cm^{-1}; UV(MeOH) λ max, 248, 256, 330, 408nm. (Found: C, 71.04; H, 4.79; Calc for $C_{20}H_{16}O_5$: C, 71.42; H, 4.80%).

(±) - 4 - *Demethoxy* - 6 - *deoxydaunomycinone* (**4**). A suspension of **19** (0.170 g, 0.5 mmol) in benzene (15 ml), ethylene glycol (0.4 ml) and *p*-toluensulfonic acid (0.015 g, 0.08 mmol) was refluxed for 4 hr using a Dean-Stark apparatus.

† The yields are unoptimized and the NMR spectra at 270 MHz were recorded on a Bruker spectrometer.

The mixture was cooled, washed with $NaHCO_3$ aq, water, and was evaporated to dryness to give the expected ketal (0.19 g, 0.5 mmol) crystallized from ether–petroleum ether. M.p. 214–215°. The ketal, dissolved in CCl_4 (125 ml) at 45°, was treated with Br_2 (1.5 ml of 0.6 M soln in CCl_4) in the presence of AIBN (0.23 g, 1.4 mmol). After 2 hr the mixture was cooled and extracted with 1 N NaOH. The alkaline aq. layer was washed with CH_2Cl_2 (2 × 50 ml) was acidified to pH 1 with 1 N HCl and extracted with CH_2Cl_2. The residue, obtained by evaporation of the solvent, was chromatographed on Kieselgel using as eluant the solvent mixture ethyl acetate/n-hexane to give **4** (0.056 g) as 13-ketal. This product was dissolved in CF_3COOH (2.5 ml) and H_2O (0.3 ml) at 0° and stirred at 0° for 45 min, then extracted with CH_2Cl_2. The organic layer was washed with sat. $NaHCO_3$ aq, water, dried over Na_2SO_4 and evaporated *in vacuo* to give **4** (0.045 g, 25% overall yield from **19**). M.p. 219–220°. ^{1}H-NMR (200 MHz, $CDCl_3$): δ 2.2–2.4 (m, 8-H), 2.41 (s, $COCH_3$), 2.94 (d, J = 18 Hz, 10-H ax), 3.07 (d, J = 18 Hz, 10-H eq), 4.08 (d, J = 10 Hz, 7-OH), 4.45 (s, 9-OH), 4.91 (bd, J = 10 Hz, 7-H eq; after D_2O addition W_H = 8 Hz), 7.82 (m, 2-H, 3-H), 8.00 (s, 6-H), 8.32 (m, 1-H, 4-H), 13.10 (s, 11-OH). (Found: C, 67.88; H, 4.57. Calc for $C_{20}H_{16}O_6$: C, 68.18; H, 4.58%).

Preparation of **20a** *and* **20b**. 1,4-Dimethoxynaphthalene (3.2 g, 0.017 mol) and **14** (4.08 g, 0.017 mol) were dissolved in a mixture of $(CF_3CO)_2O$ (50 ml), CF_3COOH (25 ml) and refluxed for 24 hr. The mixture was evaporated to dryness *in vacuo* and the residue, dissolved in CH_2Cl_2, was washed with sat. $NaHCO_3$ aq, water, dried over Na_2SO_4, and chromatographed on Kieselgel to give a mixture of **20a** and **20b** (3.5 g, 50% yield). ^{1}H-NMR (60 MHz, $CDCl_3$), *inter alia*: δ 2.18 (s, $COCH_3$), 3.65 (s, $COOCH_3$), 4.00–4.02 (2s, OCH_3), 7.01 (s, 1H), 7.5–8.5 (m, 4H). IR(film): 1720, 1710, 1660 cm^{-1}. MS: *m/e* 398 (M^+).

(±) - 4 - *Demethoxy* - 6,7,9 - *trideoxydaunomycinone* (**17**) *and* (±) - 4 - *demethoxy* - 7,9,11 - *trideoxydaunomycinone* (**21**). A soln of the isomeric mixture **20a** and **20b** (2.25 g, 5.5 mmol) in MeOH (200 ml) and conc HCl (1 ml) was hydrogenated at room temp and 1 atm for 4 days in the presence of 5% Pd/C (1.5 g). The crude material was treated with conc H_2SO_4 (30 ml) and heated at 80° for 1 hr then the mixture was poured into cold water and extracted with CH_2Cl_2. The organic phase, washed with sat. $NaHCO_3$ aq, water, was concentrated and chromatographed on Kieselgel to give a 1:1 mixture of isomeric **17** and **21** (0.5 g). ^{1}H-NMR (60 MHz, $CDCl_3$), *inter alia*: δ 2.30 (s, $COCH_3$), 2.6–3.1 (m, 7-H, 10-H), 3.63, 3.98 (m, 9-H), 7.4–8.4 (m, 5H), 12.71, 12.75 (s, phenolic OH). IR(KBr): 2940, 1710, 1670, 1625 cm^{-1}. MS: *m/e* 320 (M^+). (FoundC, 74.76; H, 5.16. Calc for $C_{20}H_{16}O_4$: C, 74.99; H, 5.03%). UV(MeOH): λ_{max} 330, 388, 408 nm.

The mixture **17**, **21** treated with Ac_2O followed by epoxidation of the resulting enolacetate and basic hydrolysis as described for the preparation of **19** allowed the separation by Kieselgel chromatography of (±)-**19** from (±) - 4 - demethoxy - 7,11 - dideoxydaunomycinone, identical to an authentic sample prepared following the procedure already described.[24]

Preparation of **23** *and* **24**. A soln of 1,4,5-trimethoxy-3-bromonaphthalene (1.2 g, 4 mmol) in dry THF (5 ml) cooled at −78° was dropped, under N_2, into a soln of n-BuLi in hexane (3.96 mmol, 2.4 ml) diluted in THF (5 ml) and kept at −78°. This soln was added dropwise to a precooled (−78°) soln of **11** (1.07 g, 3.71 mmol) in dry THF (5 ml). Following the same procedure used for **17** after chromatography on Kieselgel 6,7,9-trideoxydaunomycinone (**23**) and 6,7,9-trideoxyisodaunomycinone (**24**) (0.100 g; 8% yield) were obtained.[16]

23 MS *m/e* 350 (M^+); UV($CHCl_3$): λ_{max} 413 nm.

24 MS *m/e* 350 (M^+); UV ($CHCl_3$): λ_{max} 420 nm.

trans - 1,2 - *Dimethoxycarbonyl* - 4 - *acetyl* - 4 - *cyclohexene* (**26**). To a soln of **25** (44 g, 0.22 mol) in Ac_2O (160 ml) anhyd $SnCl_4$ (39.6 ml) was added dropwise at −10° and under vigorous stirring. After 6 hr the reaction was poured into ice/water, extracted with EtOAc and the organic layer washed with sat $NaHCO_3$ aq, H_2O and dried over Na_2SO_4. The residue was treated with 1 N HCl/MeOH (250 ml) and refluxed for 3 hr. The solvent was evaporated and the resulting material, dissolved in EtOAc, washed with sat $NaHCO_3$ aq, with H_2O, dried over Na_2SO_4, was purified by chromatography on Kieselgel affording **26** (35 g, 66% yield) obtained as an oil. ^{1}H-NMR (60 MHz, $CDCl_3$): δ 2.33 (s, $COCH_3$), 2.55–2.95 (m, $\underline{CH_2}$—C=CH$\underline{CH_2}$), 3.00–3.30 (m, 2$CH_3OOC\underline{CH}$), 3.70 (s, 2$COOCH_3$), 6.91 (m, CH=C). IR (film): 1720, 1660 cm^{-1}; MS: *m/e* 240 (M^+).

trans - 1,2 - *Dimethoxycarbonyl* - 4 - *ethylidenecyclohexane* (**27**). Compound **26** (34 g, 141 mmol) and tosylhydrazide (29.2 g) in anhyd EtOH (300 ml) were refluxed for 4 hr. The residue was crystallized from ether to give the corresponding tosylhydrazone (48 g, 85% yield) m.p. 166–168°. To this derivative, dissolved in $CHCl_3$ (1 l), catecholborane (28 ml) was added dropwise at 0°. After stirring for 2 hr at room temp, anhyd NaOAc (28 g) and H_2O (36 ml) were added and the mixture refluxed overnight with stirring. The mixture was washed with water, dried over Na_2SO_4 and chromatographed on Kieselgel to give **27** (24 g, 89% yield) as an oil. ^{1}H-NMR (60 MHz, $CDCl_3$), *inter alia*: δ 1.55 (d, J = 8 Hz, $\underline{CH_3}$—CH=), 3.67 (s, 6H, OCH_3), 5.23 (q, J = 8 Hz, H—C=). IR(film): 1740 cm^{-1}. HRMS Calc [$C_{12}H_{18}O_4^+$]: 226.1205. (Found: 226.1207).

Preparation of **28**. To a soln of **27** (23 g, 100 mmol) in acetone (690 ml), H_2O (70 ml) and AcOH (14 ml), a soln of $KMnO_4$ (23 g) in a mixture of water (115 ml) and acetone (575 ml) was added dropwise at room temp under vigorous stirring. After 1 hr the mixture was treated with a soln of $NaNO_2$ (11.5 g) in conc H_2SO_4 (23 ml) and H_2O (207 ml) and the brown ppt filtered off over celite. The colorless soln, diluted with sat NaCl aq (1 l) was extracted with EtOAc (2 × 1 l). The organic layer, washed with sat $NaHCO_3$ aq, dried over Na_2SO_4, was evaporated *in vacuo*. The obtained oil was dissolved in benzene (450 ml) and refluxed with *p*-toluenesulfonic acid (1.5 g) in a Dean-Stark apparatus. After 4 hr the soln was cooled, washed with sat $NaHCO_3$ aq, dried over Na_2SO_4 and chromatographed on Kieselgel to give the γ-lactone (9 g, 36% yield) m.p. 69–70°. ^{1}H-NMR (60 MHz, $CDCl_3$), *inter alia*: δ 2.30 (s, $COCH_3$), 3.73 (s, $COOCH_3$). IR(KBr): 1790, 1735, 1720 cm^{-1}. MS: *m/e* 226 (M^+). (Found: C, 58.50; H, 6.30. Calc for $C_{11}H_{14}O_5$: C, 58.4; H, 6.24%).

The γ-lactone (7.5 g), dissolved in benzene (300 ml), was refluxed with a Dean-Stark apparatus in the presence of *p*-toluenesulfonic acid (0.75 g) and ethylene glycol (6 ml). After 3 hr the soln was cooled, washed with sat $NaHCO_3$ aq, sat NaCl aq, and dried over Na_2SO_4. After chromatography on Kieselgel **28** (7.2 g, 80% yield) was obtained m.p. 71°. ^{1}H-NMR (60 MHz, $CDCl_3$), *inter alia*: δ 1.30 (s, CH_3—C), 3.73 (s, $COOCH_3$), 3.97 (s, OCH_2CH_2O). IR(KBr): 1780, 1730 cm^{-1}. MS: *m/e* 271 (MH^+). (Found: C, 57.58; H, 6.82. Calc for $C_{13}H_{18}O_6$: C, 57.77; H, 6.71%).

Preparation of **29a**. 1,4 - Dimethoxy - 2 - bromo - naphthalene (3.2 g, 12 mmol) dissolved in anhyd THF (30 ml) was added dropwise through a double ended needle and N_2 pressure to a soln of n-BuLi (12 mmol) in anhyd THF (30 ml) at −78°. After standing for 5 min, the formed Li-salt **10a** was transferred in the same manner to a soln of lactone **28** (2.7 g, 10 mmol) in anhyd THF (30 ml). After 1 hr at −78° the mixture was quenched with AcOH and the solvent removed *in vacuo*. The residue was dissolved in EtOAc, washed with sat NaCl aq and dried over Na_2SO_4. The solid material, obtained by removal of the solvent *in vacuo*, was dissolved in MeOH (250 ml) and conc HCl (20 ml) was added. After 3 hr at room temp the soln was neutralized with sat $NaHCO_3$ aq and MeOH removed *in vacuo*. After extraction with EtOAc, washing with sat NaCl aq, and drying over Na_2SO_4, the residue was chromatographed on Kieselgel to give **29a** (g 2.5, 60% yield). ^{1}H-NMR (60 MHz, $CDCl_3$), *inter alia*: δ 2.28 (s, CH_3CO), 3.68 (s, $COOCH_3$), 4.00 (s, 2 OCH_3), 6.7–8.4 (m, 5H). IR(film): 3450, 1730, 1710, 1670 cm^{-1}. MS: *m/e* 414 (M^+).

Preparation of **29b**. Following the procedure described for **29a**, starting from 1,4,5 - trimethoxy - 3 - bromo - naphthalene (3.5 g, 12 mmol) and **28** (2.7 g, 10mmol), **29b** (2.45 g, 56% yield)

was obtained. ^{1}H-NMR (60 MHz, $CDCl_3$), *inter alia*: δ 2.27 (s, CH_3CO), 3.70, 3.77, 4.00, 4.03 (s, 12H, OCH_3), 6.8–8.0 (m, 4H). IR(film): 3450, 1730, 1710, 1670 cm^{-1}. MS: *m/e* 444 ($M^{+\cdot}$).

Preparation of **30a**. To a soln of **29a** (2.3 g, 5.5 mmol) in CF_3COOH (30 ml) cooled at $-10°$, under stirring and N_2, Py/BH_3 complex (2.5 ml) was added dropwise. After standing for 1 hr at room temp the solvent was removed *in vacuo*; 10% NaOH (40 ml) was added and warmed at 90° to complete dissolution. After cooling, the aq solution was extracted at pH 4 with EtOAc. The volume was reduced to 50 ml by distillation *in vacuo* and an ethereal soln of phenyldiazomethane was added until disappearance of the parent acid. After destruction of the excess phenyldiazomethane, with AcOH, the soln was washed with sat $NaHCO_3$ aq, sat NaCl aq, dried over Na_2SO_4 and the solvent removed *in vacuo*. The residue was chromatographed over Kieselgel to give **30a** (1.85 g, 70% overall yield). ^{1}H-NMR (60 MHz, $CDCl_3$), *inter alia*: δ 1.23 (d, J = 4 Hz, $\underline{CH_3}$—CH), 3.80 (s, OCH_3), 3.87 (s, OCH_3), 5.07 (s, $\underline{CH_2}Ph$), 6.50 (s, 1H), 7.1–8.4 (m, 9H). IR(film): 3450, 1725 cm^{-1}. MS: *m/e* 478 ($M^{+\cdot}$).

Preparation of **30b**. From **29b** (2.44 g, 5.5 mmol) in the same fashion was obtained **30b** (1.95 g, 69% overall yield). ^{1}H-NMR (60 MHz, $CDCl_3$), *inter alia*: δ 1.30 (d, J = 4 Hz, $\underline{CH_3}$—CH), 3.70 (s, OCH_3), 3.83 (s, OCH_3), 3.97 (s, OCH_3), 5.17 (s, $\underline{CH_2}Ph$), 6.4–8.1 (m, 9H). IR (film): 3450, 1725 cm^{-1}. HRMS Calc $[C_{30}H_{36}O_7^+]$: 508.2461. (Found: 508.2453).

Preparation of **31a**. To a soln of **30a** (1.5 g, 3.13 mmol) in dry pyridine (10 ml) and Ac_2O (10 ml), 4-dimethylaminopyridine (0.2 g) was added and the soln kept overnight at room temp in the dark. The mixture was poured into ice/water and stirred for 30 min. After extraction with EtOAc the organic layer was washed with sat $NaHCO_3$ aq, brine and dried over Na_2SO_4. The residue was dissolved in MeOH (30 ml) and hydrogenolyzed in the presence of cyclohexene (10 ml) and 10% Pd/C (0.3 g) at reflux for 2 hr. The catalyst was filtered off and the residue was treated at 0° with $(CF_3CO)_2O$ (20 ml) and CF_3COOH (10 ml) for 1 hr, then the soln was diluted with EtOAc/water and neutralized with solid $NaHCO_3$. The organic phase was washed with brine, dried over Na_2SO_4 and the solvent removed *in vacuo*. The crude material was treated with MeOH (50 ml) in presence of NaOMe (1.5 g) at room temp for 16 hr, then neutralized with 1 N HCl, diluted with water and extracted with EtOAc. The organic layer was washed with saturated aq NaCl, dried over Na_2SO_4 and chromatographed on Kieselgel to give **31a** (0.86 g, 74% overall yield). ^{1}H-NMR (60 MHz, $CDCl_3$), *inter alia*: δ 1.23 (d, J = 4 Hz, CH—$\underline{CH_3}$), 3.87 (s, OCH_3), 3.95 (s, OCH_3), 7.1–8.4 (m, 4H). IR(KBr): 3350, 1675 cm^{-1}. HRMS Calc $[C_{22}H_{26}O_5^+]$: 370.1780. (Found: 370.1775).

Preparation of **31b**. From **30b** (1.6 g, 3.14 mmol) in the same fashion **31b** (0.87 g, 70% overall yield) was obtained. ^{1}H-NMR (60 MHz, $CDCl_3$) *inter alia*: δ 1.23 (d, J = 4 Hz, CH—$\underline{CH_3}$), 3.80 (s, OCH_3), 3.93 (s, OCH_3), 4.00 (s, OCH_3), 6.9–8.00 (m, 3H). IR (KBr): 3350, 1690 cm^{-1}. HRMS Calc. $[C_{23}H_{28}O_5^+]$: 400.1886. (Found: 400.1893).

(±)-4-*Demethoxy*-6,7-*dideoxydaunomycinone* (**19**). To a soln of **31a** (0.8 g, 2.1 mmol) in DMSO (8 ml) and TEA (3.2 ml) TEA/SO_3 complex (1.6 g) in DMSO (8 ml) was added at room temp under stirring. After 30 min the pH was adjusted to 3 with 1 N HCl and left 30 min longer. The mixture was poured into H_2O (100 ml) and extracted with EtOAc. The organic phase was washed with sat $NaHCO_3$ aq, sat NaCl aq and dried over Na_2SO_4. The residue was dissolved in nitrobenzene (15 ml) and $AlCl_3$ (2 g) was added. After standing overnight at 60° under stirring, the mixture was poured into a sat aq soln of oxalic acid, extracted with EtOAc, washed with sat $NaHCO_3$ aq, sat NaCl aq and dried over Na_2SO_4. The residue was chromatographed on Kieselgel to give **19** (0.48 g, 66% yield) m.p. 206–208°.

(±)-6,7-*Dideoxycarminomycinone* (**32**). **31b** (0.84 g, 2.1 mmol) was oxidized as described for **31a**. The residue was dissolved in nitrobenzene (10 ml) and anhyd $AlCl_3$ (1.7 g) was added. After 90 min at 70° under stirring more $AlCl_3$ (0.6 g) was added. After 1 hr the mixture was worked-up and purified in the described manner to give **32** (0.37 g, 50% yield) m.p. 214–216°. ^{1}H-NMR (200 MHz, $CDCl_3$): δ 1.89 (ddt, J = 13, 6, 2.2 Hz, 8-H eq), 2.07 (ddd, J = 13, 12.7, 5.6 Hz, 8-H ax), 2.38 (s, $COCH_3$), 2.91 (dd, J = 18, 1.3 Hz, 10-H ax), 2.99 (ddd, J = 17.6, 5.6, 2 Hz, 7-H eq), 3.07 (dd, J = 18, 2 Hz, 10-H eq), 3.25 (dddd, J = 17.6, 12.7, 6, 1.3 Hz, 7-H ax), 7.30 (dd, J = 8, 1.3 Hz, 3-H), 7.66 (s, 6-H), 7.67 (t, J = 8 Hz, 2-H), 7.83 (dd, J = 8, 1.3 Hz, 1-H), 12.70 (s, 4-OH), 13.10 (s, 11-OH). IR(KBr): 3500, 1705, 1625, 1600, 1575 cm^{-1}. UV(MeOH) λ_{max}: 230, 258, 290, 432 nm. (Found: C, 68.09; H, 4.60. Calc for $C_{20}H_{16}O_6$: C, 68.18; H, 4.58%).

(±)-6-*Deoxycarminomycinone* (**5**). Intermediate **32**, as C-13 ketal, (2.5 g, 6.3 mmol), NBS (1.2 g, 6.6 mmol), AIBN (0.5 g) suspended in CCl_4 (500 ml) were refluxed using a sun lamp with bubbling N_2. After 20 min the soln was cooled and the solvent removed *in vacuo*. The residue was dissolved in AcOH (250 ml) and AgOAc (3.2 g) was added in the dark. After stirring overnight at room temp, the solvent was evaporated and the residue dissolved in EtOAc. The Ag-salt was filtered off and the resulting soln, washed with sat $NaHCO_3$ aq, sat NaCl aq, dried over Na_2SO_4, was evaporated *in vacuo*. The residue was treated with 90% CF_3COOH (200 ml) at 0°. After 2 hr the solution was diluted with $EtOAc/H_2O$ and the acid neutralized with solid $NaHCO_3$. The organic phase was washed with sat NaCl aq and the solvent removed *in vacuo*. The mixture was dissolved in MeOH (300 ml) and treated with NaOMe (1.5 g). After standing for 2 hr at room temp under stirring, 1 N HCl was added to neutrality and the solvent evaporated. The residue was dissolved in EtOAc, washed with sat NaCl aq and dried over Na_2SO_4. The residue was chromatographed on Kieselgel affording **5** (0.77 g, 34% yield) m.p. 212–214°. ^{1}H-NMR (200 MHz, $CDCl_3$): δ 2.30 (m, 8-H), 2.40 (s, $COCH_3$), 2.99 (d, J = 18.4 Hz, 10-H ax), 3.12 (bd, J = 18.4, < 2 Hz, 10-H eq), 4.08 (d, J = 10 Hz, 7-OH), 4.46 (s, 9-OH), 4.92 (m, 7-H), 7.33 (d, J = 8 Hz, 3-H), 7.69 (t, J = 8 Hz, 2-H), 7.84 (d, J = 8 Hz, 1-H), 8.02 (s, 6-H), 12.70 (s, 4-OH), 13.14 (s, 11-OH). IR(KBr): 3500–3350, 1710, 1630, 1600, 1570 cm^{-1}. HRMS Calc $[C_{20}H_{16}O_7^+]$: 368.0896. (Found: 368.0894).

4-*Demethoxy*-6-*deoxy*-N-*trifluoroacetyldaunorubicin* (**33a**) *and* 7(R),9(R) *diastereoisomer* **34a**. To a soln of **4** (1.39 g, 3.95 mmol) in anhyd CH_2Cl_2 (850 ml) at 15°, solns **a** and **b** were added simultaneously under N_2 with stirring and in the dark [**a** containing 1-chloro-N,O-ditrifluoroacetyldaunosamine (3.36 g, 9.4 mmol) in anhyd CH_2Cl_2 (100 ml); **b** containing $AgSO_3CF_3$ (1.85 g, 7.2 mmol) in anhydrous ether (100 ml)]. After 10 min sym-collidine (0.92 ml, 7.3 mmol) was added and left to stand for additional 20 min, then sat $NaHCO_3$ aq (300 ml) was added and the stirring continued for 30 min. The organic phase was washed with sat NaCl aq and dried over Na_2SO_4. The residue was chromatographed on Kieselgel giving **33a** (0.6 g, 26% yield), **34a** (0.6 g, 26% yield) and recovered starting material **4** (0.45 g, 32%). **33a**: m.p. 238–239°; $[\alpha]_D^{25}$ +25° (*c* 0.12, MeOH); ^{1}H-NMR (270 MHz, $CDCl_3$) *inter alia*: δ 1.34 (d, J = 7 Hz, 5'-CH_3), 2.42 (s, $COCH_3$), 3.09 (d, J = 15 Hz, 10-H ax), 3.17 (d, J = 15 Hz, 10-H eq), 5.01 (m, W_H = 7 Hz, 7-H), 5.20 (m, W_H = 5.0 Hz, 1'-H), 6.76 (br, J = 8 Hz, NH), 7.82 (s, 6-H), 8.00 (m, 2-H, 3-H), 8.32 (m, 1-H, 4-H), 13.10 (s, 11-OH). IR(KBr): 1710, 1670, 1630, 1590 cm^{-1}. MS: *m/e* 577 ($M^{+\cdot}$); UV(MeOH): λ_{max} 204 nm (ε = 28,600), 246 (ε = 26,900), 262 (ε = 29,500), 328 (ε = 3030), 408 (ε = 6600). CD: $\Delta\varepsilon$ 229 nm = +7.23, $\Delta\varepsilon$ 284 nm = −1.27, $\Delta\varepsilon$ 338 nm = +1.07. **34a**: m.p. 140–145°; $[\alpha]_D^{25}$ −147° (*c* 0.08, MeOH). ^{1}H-NMR (270 MHz, $CDCl_3$), *inter alia*: δ 1.45 (d, J = 6.6 Hz, 5'-CH_3), 2.41 (s, $COCH_3$), 2.95 (d, J = 18.7 Hz, 10-H ax), 3.29 (dd, J = 18.7, 1.3 Hz, 10-H eq), 5.07 (dd, J = 3.9, 1.7 Hz, 7-H), 5.26 (m, 1'-H), 6.73 (bd, J = 8.0 Hz, NH), 7.75 (s, 6-H), 7.8–7.9 (m, 2-H, 3-H), 8.3–8.4 (m, 1-H, 4-H), 13.07 (s, 11-OH). CD: $\Delta\varepsilon$ 231 nm = −5.13, $\Delta\varepsilon$ 281 nm = +1.85, $\Delta\varepsilon$ 338 nm = −1.20.

6-*Deoxy*-N-*trifluoroacetylcarminomycin* (**33b**) *and* 7(R),9(R) *diastereoisomer* **34b**. **5** (1.45 g, 3.95 mmol) following the same procedure used for **33a**, gave **33b** (0.36 g, 15.4% yield), **34b** (0.37 g, 16% yield) and recovered starting material **5** (0.65 g, 44.8%). **33b**: m.p. 212–214°, $[\alpha]_D^{25}$ +26° (*c* 0.057, MeOH); ^{1}H-

NMR (200 MHz, $CDCl_3$): δ 1.36 (d, J = 6.6 Hz, 5'-CH_3), 1.8–1.9 (m, 2'-H), 1.96 (bd, J = 7 Hz, 4'-OH), 2.32 (m, 8-H), 2.42 (s, $COCH_3$), 3.05, 3.25 (2d, J = 19 Hz, 10-H), 3.69 (dd, J = 3, 7 Hz, 4'-H), 4.18 (dq, J = 1, 6.6 Hz, 5'-H), 4.22 (s, 9-OH), 4.39 (dt, J = 2, 9 Hz, 3'-H), 5.01 (m, 7-H), 5.20 (t, J = 2.7 Hz, 1'-H), 6.66 (bd, J = 9 Hz, NH), 7.32 (dd, J = 1.1, 8.4 Hz, 3-H), 7.70 (t, J = 8.4 Hz, 2-H), 7.80 (s, 6-H), 7.87 (dd, J = 1.1, 8.4 Hz, 1-H), 12.62 (s, 4-OH), 13.06 (s, 11-OH). MS: *m/e* 594 (MH^+); UV(MeOH): λ_{max} 208 nm (ε = 54,200), 230 (ε = 34,300), 258 (ε = 27,500), 290 (ε = 8600), 432 (ε = 11,700); IR(KBr): 3500–3400, 1710, 1625, 1600 cm^{-1} CD: $\Delta\varepsilon$ 232 nm = +16.70, $\Delta\varepsilon$ 295 nm = −1.34, $\Delta\varepsilon$ 341 nm = +1.85. **34b**: m.p. 175–178°; $[\alpha]_D^{25}$ −165° (*c* 0.062, MeOH); ^{1}H-NMR (200 MHz, $CDCl_3$): δ 1.44 (d, J = 6.5 Hz, 5'-CH_3), 1.9–2.0 (m, 2'-H), 2.18 (dd, J = 15, 3.3 Hz, 8-H ax), 2.28 (dd, J = 15, 3.3 Hz, 8-H eq), 2.41 (s, $COCH_3$), 2.96 (d, J = 19 Hz, 10-H ax), 3.30 (dd, J = 1, 19 Hz, 10-H eq), 3.61 (bm, 4'-H), 4.11 (dq, J = 6.5, 1 Hz, 5'-H), 4.25 (s, 9-OH), 4.26 (bm, 3'-H), 5.07 (t, J = 3.3 Hz, 7-H), 5.27 (t, J = 1.8 Hz, 1'-H), 6.64 (bd, J = 9 Hz, NH), 7.33 (dd, J = 1, 8 Hz, 3-H), 7.70 (t, J = 8 Hz, 2-H), 7.74 (s, 6-H), 7.86 (dd, J = 1, 8 Hz, 1-H), 12.66 (s, 4-OH), 13.10 (s, 11-OH). MS: *m/e* 594 (MH^+). CD: $\Delta\varepsilon$ 230 nm = −10.96, $\Delta\varepsilon$ 294 nm = +2.45, $\Delta\varepsilon$ 341 nm = −1.07.

4 - *Demethoxy* - 6 - *deoxydaunorubicin* (**2**). To a soln of **33a** (0.05 g, 0.087 mmol) in acetone (10 ml), under N_2 at 0°, 0.1 N NaOH (20 ml) was added. After stirring at 0° for 90 min, the pH was lowered to 4.5 with 0.1 N HCl at 0° and the neutral products were extracted with CH_2Cl_2. The acidic water layer was adjusted with 0.1 N NaOH to pH 8.5 at 0° and extracted with CH_2Cl_2. The organic layer was concentrated, cooled to 0° and 0.2 N MeOH—HCl was added to pH 3, and the solid, obtained by addition of Et_2O, was filtered and washed with Et_2O. After drying, **2** (0.04 g), as hydrochloride, was obtained. **2** (· HCl): m.p. 163–170°. IR(KBr): 1710, 1670, 1630, 1590 cm^{-1}; UV(MeOH/HCl): λ_{max} 208 nm (ε = 49,800), 248 (ε = 26,800), 262 (ε = 29,500), 328 (ε = 3000), 408 (ε = 6400). ^{1}H-NMR (200 MHz, D_2O): δ 1.30 (s, 5'-CH_3), 1.93 (dd, J = 8.0, 14.0 Hz, 8-H ax), 2.1–2.2 (m, 2'-H), 2.38 (dd, J = 5.0, 14.0 Hz, 8-H eq), 2.41 (s, $COCH_3$), 2.54, 2.79 (2d, J = 18 Hz, 10-H), 3.8–3.9 (m, 3'-H), 3.87 (bs, 4'-H), 4.19 (dq, J < 1, 6.6 Hz, 5'-H), 4.43 (dd, J = 5.0, 8.0 Hz, 7-H), 5.26 (m, 1'-H), 7.02 (s, 6-H), 7.7–7.8 (m, 1-H, 2-H, 3-H, 4-H). MS: *m/e* 482 (MH^+). (Found: C, 59.94; H, 5.70; N, 2.61; Cl, 6.48. Calc for $C_{26}H_{28}NO_8Cl$: C, 60.29; H, 5.45; N, 2.71; Cl 6.84%).

6-*Deoxycarminomycin* (**3**). **33b** (0.07 g, 0.118 mmol) was treated following the same procedure used for **2**, to give **3** (0.058 g, 95% yield), isolated as hydrochloride. **3** (· HCl): m.p. 171–175°. IR(KBr): 1710, 1625, 1605 cm^{-1}; UV(MeOH/HCl): λ_{max} 208 nm (ε = 17,300), 230 (ε = 30,300), 258 (ε = 23,700), 292 (ε = 7500), 434 (ε = 10,400). ^{1}H-NMR (200 MHz, D_2O, 45°): δ 1.37 (d, J = 6.2 Hz, 5'-CH_3), 1.9–2.2 (m, 8-H, 2'-H), 2.44 (s, $COCH_3$), 2.61, 2.94 (2d, J = 18.5 Hz, 10-H), 3.8–3.9 (m, 3'-H, 4'-H), 4.23 (dq, J < 1, 6.2 Hz, 5'-H), 4.53 (m, 7-H), 5.31 (bs, 1'-H), 7.0–7.2 (m, 1-H, 3-H, 6-H), 7.54 (t, J = 8.0 Hz, 2-H). MS: *m/e* 498 (MH^+).

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