Synthesis of a Deoxyristomycinic Acid Derivative using Organomanganese Chemistry

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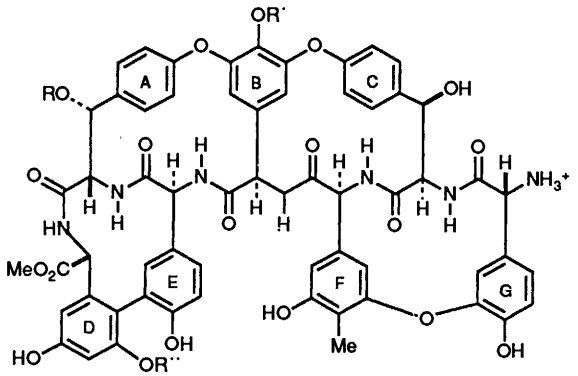
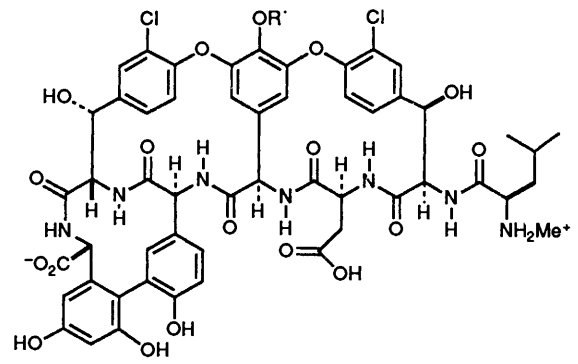
Coupling of (3-chloro-2-methylanisole)tricarbonylmanganese tetrafluoroborate with the phenoxide derived from methyl *N*-Boc-3-hydroxyphenylglycinate gave the diaryl ether manganese complex (**6**). This complex underwent regiospecific, stereoselective reaction with Schollkopf's chiral glycine enolate equivalent to give a mixture of dienyl-$Mn(CO)_3$ complexes that were converted in a two-step sequence into the protected deoxyristomycinic acid derivative (**12**).

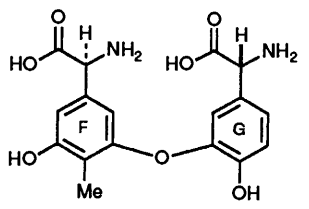
Ristocetin A (**1**) and vancomycin (**2**) are two members of a large group of glycopeptide antibiotics which have a number of structural features in common.[1] All the members of the group possess a heptapeptide backbone which is part of a polycyclic network composed of varying numbers of aryl ether linkages and a biphenyl unit. From the standpoint of total synthesis, a major challenge is the construction of suitably protected diaryl ethers in which one or more of the aromatic rings is a phenylglycine derivative. For ristocetin A, the F/G-ring diaryl ether is composed of two such units. Arylglycines are particularly susceptible to racemization, and so special methods are required to effect their coupling. The Ullmann method[2] employs the copper-catalysed reaction between a phenol and a halogenobenzene derivative in solvents such as pyridine at elevated temperature. These conditions are not suitable for the direct coupling of, *e.g.*, two arylalanines, although recent work has shown that one protected amino acid group can be tolerated.[3] The high temperatures employed in these reactions make them unsuitable for the preparation of compounds such as ristomycinic acid (**3**), a degradation product and structural component of ristocetin A.[4] This paper describes studies aimed at developing arene–manganese chemistry for the preparation of protected ristomycinic acid derivatives, which could be employed as building blocks for synthesis of ristocetin and related molecules. The present model study uses commercially available D-3-hydroxyphenylglycine as the *pro*-G-ring for deoxyristomycinic acid construction.



(**1**) Ristocetin A (R, R' and R'' = sugar units)



(**2**) Vancomycin (R' = sugar unit)



(**3**)

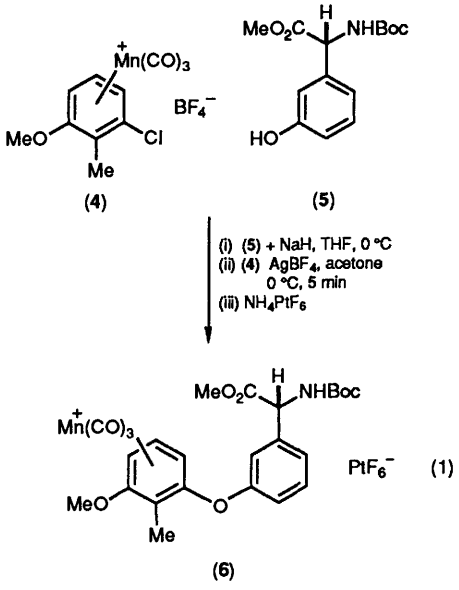
Results and Discussion

Our earlier preliminary studies[5] used *N*-acetyl-3-hydroxyphenylglycine methyl ester in a sequence leading to a deoxyristomycinic acid derivative. However, partial racemization of the G-ring arylglycine was observed during the sequence employed.†[6] This, together with the fact that a more easily removable *N*-protecting group is required if further elaboration is to be undertaken, prompted us to investigate the use of *N*-Boc-protected 3-hydroxyphenylglycine in an identical sequence of reactions.

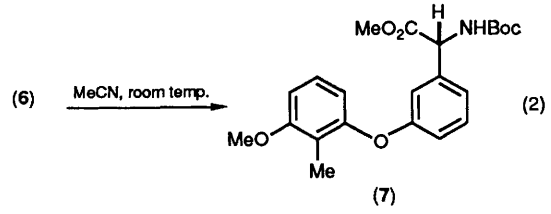
Preparation of the arene–manganese complex (**4**), which represents an F-ring precursor for ristomycinic acid, was accomplished in 94% yield on using a modification of the procedure described by Rybinskaya *et al.*[7] It may be noted that attempted conversion of 3-chloro-2-methylanisole into complex (**4**) by means of the more conventional procedure[8] [$Mn(CO)_5$-Br–AlC_3–heat], which works well for chlorobenzene and chlorotoluene, completely failed. The use of $Mn(CO)_5Br$–$AgBF_4$, which we have previously used to prepare tricarbonylmanganese complexes of veratrole,[9] gave only an 8% yield of

† In our earlier work (ref. 5), *N*-acetyl derivatives were used, even though it is well known that these are more prone to racemization, because we had previously obtained conditions for determining enantiomeric excess by NMR methods on a series of related compounds (see ref. 6). Not all *N*-Boc-protected compounds give satisfactory NMR splitting upon addition of $Eu(hfbc)_3$.

complex (**4**). The Boc-protected hydroxyphenylglycine (**5**) was prepared by standard methods without detectable racemization according to NMR/chiral-lanthanide-shift studies. Exposure of compound (**5**) to refluxing pyridine for 2 h resulted in complete racemization, thus precluding the use of Ullmann coupling reactions with this compound. Treatment of compound (**5**) with sodium hydride (1 mol equiv.) in tetrahydrofuran (THF) at room temperature (30 min) to generate the phenoxide, followed by reprotonation with ammonium tetrafluoroborate, caused *ca.* 14% racemization (according to specific rotation). On the other hand, exposure of compound (**5**) to sodium hydride in THF at 0 °C (20 min) followed by reprotonation gave recovered (**5**) which showed no racemization.



The reaction of complex (**4**) with the phenoxides derived from compounds related to (**5**) was unexpectedly problematic. In contrast to chlorobenzene–$Mn(CO)_3$, which undergoes rapid reaction with phenoxides in acetone at 0 °C,[8] only low yields of diaryl ether derivatives were obtained from complex (**4**). The problem appeared to be competing decomplexation of compound (**4**) and the product aryl ether–$Mn(CO)_3$ complex, caused by the acetone solvent.* This becomes the major reaction for chloroanisole–$Mn(CO)_3$ complexes since deactivation of the ring by the methoxy substituent retards the addition of aryloxide nucleophiles. The problem was solved by running the coupling reaction in the presence of silver tetrafluoroborate, and under these conditions complex (**4**) was converted into the desired diaryl ether complex (**6**) in 80–85% yield [equation (1)].



The function of the $AgBF_4$ does not appear to be acceleration of the coupling reaction. It is known[10] that decomplexation of arene–$Mn(CO)_3$ complexes by acetonitrile is accelerated by halide ions. On this basis, it appears that the $AgBF_4$ serves to remove chloride ion, thereby preventing the competing decomplexation. Removal of the $Mn(CO)_3$ moiety by overnight treatment of complex (**6**) with acetonitrile gave compound (**7**) [equation (2)], which was subjected to NMR spectroscopy in the presence of (+)-tris[(heptafluorobutyryl)camphorato]-europium(III) [Eu(hfbc)$_3$]. Comparison with a sample of compound (**7**) prepared from racemic (**5**) indicated that no detectable racemization of the arylglycine had occurred throughout this sequence.

The next step was the attachment of a glycine side-chain to the *pro*-F-ring (ristocetin lettering) by reaction of a chiral glycine enolate equivalent with the arene–$Mn(CO)_3$ system in complex (**6**). For this purpose, the Schöllkopf nucleophile (**8**) was chosen, since this is known to react with electrophiles stereoselectively *trans* to the isopropyl group.[11] Treatment of compound (**8**) with butyl-lithium, followed by reaction of the lithio derivative with complex (**6**) in THF at −78 °C, gave a mixture of diastereoisomeric dienyl–$Mn(CO)_3$ complexes (**9**). Since the dienyl-manganese moiety is itself chiral, analysis of the stereoselectivity of the reaction between substrates (**6**) and (**8**) was not attempted at this stage. Instead, the crude mixture of complexes was treated with *N*-bromosuccinimide (NBS) to effect their conversion into a pair of diastereoisomers (**10**) and (**11**), obtained in *ca.* 4:1 ratio which varied somewhat according to the conditions used for the coupling reaction. Separation of this mixture by flash chromatography allowed the isolation of pure product (**10**) in 35% overall yield from complex (**6**). This rather low yield is due to competing decomplexation of complex (**6**) to give compound (**7**), apparently by reaction with the lithio derivative of the piperazine (**8**). When the coupling reaction was attempted at −100 °C in THF, no dienyl complex (**9**) was formed and only compound (**7**) was isolated along with recovered substrate (**8**). Other conditions for this reaction have not been investigated.

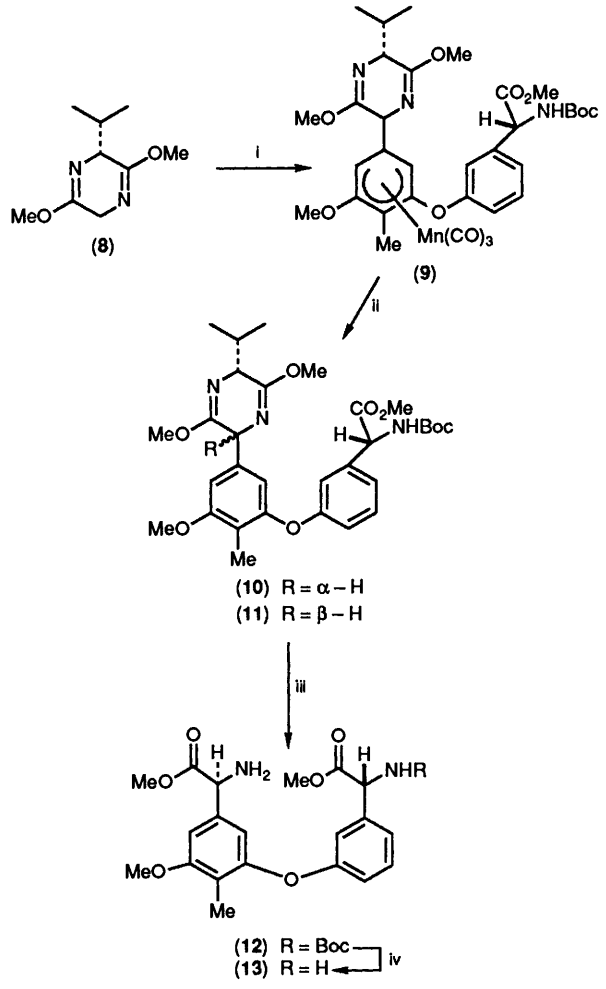
Treatment of compound (**10**) with 0.25M-hydrochloric acid effected its conversion into compound (**12**), in which the amino groups are differentiated (Scheme). The Boc protecting group on compound (**12**) could be removed by treatment with trifluoroacetic acid (TFA) in the presence of thioanisole. Compounds (**10**), (**12**), and (**13**) showed no racemization according to NMR analysis in the presence of Eu(hfbc)$_3$. Thus, the methodology described herein is appropriate for the construction of ristocetin F/G-ring sub-units in a state of high optical purity. Future work will be directed toward the synthesis of cyclic peptide derivatives based on this chemistry, and employing synthetic 3,4-dihydroxyphenylglycine derivatives as G-ring precursors.

Experimental

General Procedures.—IR spectra were recorded with a Perkin-Elmer 1420 instrument, and optical rotations with a Perkin-Elmer 241 digital polarimeter. NMR spectra were recorded on a Varian XL200 instrument, and mass spectra were obtained in-house on a Kratos MS25A instrument. M.p.s were determined on a Fisher-Johns apparatus and are uncorrected. All reactions and chromatographic separations were performed using deoxygenated solvents and under an inert atmosphere (dry, O_2-free nitrogen or argon) unless otherwise stated. Solvents were purified by distillation as follows: THF and benzene from Na–benzophenone ketyl; diethyl ether from $LiAlH_4$; dichloromethane and acetonitrile from CaH_2.

Preparation of 3-*Chloro*-2-*methylanisole.*—A stirred solution of 3-chloro-2-methylaniline (6.33 ml) in 48% aq. HBF_4 (50 ml) was cooled to 0 °C, and a solution of sodium nitrite (3.75 g) in water (25 ml) was added dropwise. After the addition was

* Acetonitrile has been used to effect decomplexation of arene–$Mn(CO)_3$ complexes (refs. 5, 6, and 8). We observed that acetone also caused similar decomplexation, but at a slower rate.



Scheme. *Reagents and conditions:* i, BuLi, THF, −78 °C; then (**6**), THF, −78 °C, 30 min; ii, NBS, Et_2O, room temp., 15 min; iii, 0.25M-HCl, THF, room temp., 16 h; iv, TFA, thioamide, CH_2Cl_2, 0 °C, 15 min.

complete, the bath was removed and the mixture was allowed to warm to room temperature. The insoluble diazonium salt was filtered off and washed successively with methanol and with diethyl ether. The dried solid was suspended in methanol and the suspension was heated to gentle reflux until the evolution of nitrogen ceased. The dark solution was reduced in volume on a rotary evaporator and the residue was partitioned between dichloromethane and water. The organic phase was dried ($MgSO_4$) and concentrated and the product was distilled to give 3-chloro-2-methylanisole as a liquid (2.80 g, 35%), b.p. 40–45 °C at 0.5 mmHg; $\nu_{max}(CHCl_3)$ 2 960, 1 583, 1 470, 1 440, 1 260, 1 050 cm^{-1}; $\delta_H(CDCl_3)$ 7.1 (1 H, d, *J* 8 Hz), 7.06 (1 H, t, *J* 8 Hz), 6.74 (1 H, d, *J* 8 Hz), 3.82 (3 H, s), and 2.30 (3 H, s) (Found: C, 61.6; H, 5.8. Calc. for C_8H_9ClO: C, 61.35; H, 5.79%).

Preparation of Tricarbonyl(3-chloro-2-methylanisole)manganese(I) *Tetrafluoroborate* (**4**).—Aqueous 48% HBF_4 (1 ml) was added to a cooled (ice-bath), stirred suspension of $[MnCl(CO)_4]_2$ (202 mg, 0.5 mmol) in trifluoroacetic anhydride (8 ml) containing 3-chloro-2-methylanisole (2 ml). The ice-bath was removed after the water had been consumed in an exothermic reaction, and the mixture was heated under reflux for 3 h (exclusion of air was not necessary). During this period white fumes were evolved from the reaction mixture, and this underwent several colour changes. After 3 h a yellow colour was observed, the solution was concentrated under reduced pressure, and the residue was dissolved in the minimum amount of acetone. This solution was added dropwise to stirred diethyl ether, and the resulting precipitate was filtered off and washed with diethyl ether to give pure *compound* (**4**) (180 mg, 94% based on $[MnCl(CO)_4]_2$: unchanged 3-chloro-2-methylanisole may be recovered from the filtrate); $\nu_{max}(MeCN)$ 2 080 and 2 025 cm^{-1}; $\delta_H(CD_3CN)$ 6.74 (1 H, t, *J* 7.5 Hz), 6.24 (1 H, d, *J* 7.5 Hz), 5.94 (1 H, d, *J* 7.5 Hz), 4.08 (3 H, s), and 2.44 (3 H, s) (Found: C, 34.20; H, 2.25. $C_{11}H_9BClF_4MnO_4$ requires C, 34.55; H, 2.37%).

Preparation of N-*Boc-3-hydroxyphenylglycine Methyl Ester* (**5**).—A mixture D-3-hydroxyphenylglycine (250 mg, 1.5 mmol) and toluene-*p*-sulphonic acid monohydrate (800 mg, 3.2 mmol) in methanol (10 ml) was heated under reflux for 8 h. The reaction mixture was cooled to room temperature and the solvent was removed under reduced pressure. The residue was dissolved in water, and sodium hydrogen carbonate (264 mg, 3.14 mmol) was added to liberate the free amine. The mixture was extracted with ethyl acetate, and the organic phase was dried (Na_2SO_4) and evaporated to give crude *3-hydroxyphenylglycine methyl ester* (168 mg, 62%). Recrystallization from ethanol gave pure material (84 mg, 31%) m.p. 175—177 °C, and concentration of the mother liquors followed by crystallization gave a second crop (52 mg, 19%); ν_{max}(Nujol) 3 320w, 3 260w, 3 180w, 1 739m, 1 585m cm^{-1}; $\delta_H[(CD_3)_2SO]$ 9.39 (1 H, s), 7.10 (1 H, t, *J* 8.0 Hz), 6.80–6.70 (2 H, m), 6.64 (1 H, ddd, *J* 8.1, 2.4, 1.0 Hz), 4.41 (1 H, s), 3.58 (3 H, s), and 2.28 (2 H, br s).

A solution of the methyl ester (72 mg, 0.4 mmol) in t-butyl alcohol (2 ml) was stirred at room temperature while a solution of di-t-butyl carbonate (88 mg, 0.4 mmol) in diethyl ether (4 ml) was added dropwise. After being stirred for 1 h, the mixture was diluted with diethyl ether (20 ml) and washed successively with water (3 × 5 ml) and brine, and dried (Na_2SO_4). The solvent was removed under reduced pressure and the residue was recrystallized from ethyl acetate–hexane to give the title, *protected ester* (**5**) (80 mg, 71%) as a white crystalline solid, m.p. 126–128 °C. A second crop was obtained by concentration of the liquors and crystallization (25 mg, 22%; total yield 93%), m.p. 121–125 °C; $[\alpha]_D$ −15.5° (*c* 0.1, $CHCl_3$). One batch of this material was refluxed in pyridine for 2 h and gave $[\alpha]_D$ −0.1° (*c* 0.07, $CHCl_3$); this was used as a comparison sample for NMR chiral-lanthanide-shift study [Eu(hfbc)$_3$] which showed that *compound* (**5**) was optically pure within the limits of detection; $\nu_{max}(CHCl_3)$ 3 590w, 3 425, 2 980, 1 740s, 1 710s, 1 600, 1 490, 1 450, 1 437, 1 390, 1 365, 1 160, 1 060, 1 030, 1 000, and 890 cm^{-1}: $\delta_H(CDCl_3)$ 7.20 (1 H, t, *J* 8.1 Hz), 6.95–6.85 (2 H, m), 6.79 (1 H, d, *J* 8.1 Hz), 6.36 (1 H, br s), 5.68 (1 H, d, *J* 7.0 Hz), 5.25 (1 H, d, *J* 7.0 Hz), 3.71 (3 H, s), and 1.43 (9 H, s) (Found: C, 59.5; H, 6.9; N, 4.8%; M^+, 281.1259. $C_{14}H_{19}NO_5$ requires C, 59.76; H, 6.81; N, 4.98%; *M*, 281.1263).

Coupling Reaction Between Complex (**4**) *and Protected* 3-*Hydroxyphenylglycine* (**5**).—To a stirred suspension of sodium hydride (40 mg of 60% dispersion in mineral oil, 1.0 mmol NaH) in THF (10 ml) cooled to 0 °C was added dropwise a solution of compound (**5**) (281 mg, 1.0 mmol) in THF (5 ml). After 20 min, the solvent was removed under reduced pressure at 0 °C and the residue was dissolved in acetone (10 ml) at 0 °C in a reaction flask wrapped in aluminium foil to exclude light. The solid arene–manganese complex (**4**) (382 mg, 1.0 mmol) was added, immediately followed by a solution of silver tetrafluoroborate (293 mg, 1.5 mmol) in acetone (6 ml). The reaction mixture was stirred at 0 °C for 5 min, quenched with dil. aq. NH_4BF_4 (50 ml), and extracted with dichloromethane (3 × 10 ml). The combined organic extracts were washed with water (3 × 5 ml), dried ($MgSO_4$), and concentrated to *ca.* 5 ml. Addition of this solution to diethyl ether gave an insoluble gum. Accordingly, the tetrafluoroborate salt obtained after decantation of the

diethyl ether was taken up in cold acetone, shaken with cold aq. ammonium hexafluorophosphate, and extracted with dichloromethane as above. Addition of the concentrated extracts to stirred diethyl ether gave the *complex* (**6**) (hexafluorophosphate) as a yellow solid, which was removed by filtration, washed with diethyl ether, and dried *in vacuo* (520 mg, 82% yield); $\delta_H(CD_3CN)$ 7.58 (1 H, t, *J* 7.9 Hz), 7.44 (1 H, d, *J* 7.9 Hz), 7.3–7.2 (2 H, overlapping s and d), 6.59 (1 H, t, *J* 7.2 Hz), 6.13 (1 H, br s), 5.76 (1 H, d, *J* 7.3 Hz), 5.48 (1 H, d, *J* 7.3 Hz), 5.34 (1 H, br d, *J* 7 Hz), 4.01 (3 H, s), 3.68 (3 H, s), 2.35 (3 H, s), and 1.39 (9 H, s) (Found: C, 44.0; H, 3.7; N, 2.1. $C_{25}H_{27}F_6MnNO_9P$ requires C, 43.79; H, 3.97; N, 2.04%).

Decomplexation of (**6**): *Preparation of Methyl* [N-*t*-*Butoxycarbonyl*-3-(3-*methoxy*-2-*methylphenoxy*)]*phenylglycinate* (**7**).—A solution of the arene–manganese complex (**6**) (68.5 mg, 0.1 mmol) in acetonitrile (1 ml) was stirred overnight at room temperature. The mixture was diluted with diethyl ether, washed successively with water and brine, dried (Na_2SO_4), and the solvent was removed. Purification by preparative TLC afforded *compound* (**7**) (30 mg, 75%) which was optically pure according to NMR analysis in the presence of Eu(hfbc)$_3$; $\nu_{max}(CHCl_3)$ 3 430, 3 000, 2 990, 1 740, 1 710, 1 600, 1 580, 1 480, 1 470, 1 435, 1 370, 1 340, 1 310, 1 240, 1 160, 1 100, and 1 060 cm^{-1}; $\delta_H(CDCl_3)$ 7.26 (1 H, t, *J* 7.9 Hz), 7.12 (1 H, t, *J* 8.2 Hz), 7.03 (1 H, d, *J* 7.6 Hz), 6.93 (1 H, t, *J* 1.9 Hz), 6.80 (1 H, dd, *J* 8.0, 1.8 Hz), 6.70 (1 H, d, *J* 8.2 Hz), 6.62 (1 H, d, *J* 8.2 Hz) 5.49 (1 H, br d, *J* 5.3 Hz), 5.28 (1 H, br d, *J* 7.4 Hz), 3.87 (3 H, s), 3.72 (3 H, s), 2.08 (3 H, s), and 1.43 (9 H, s) (Found: M^+, 401.1841. $C_{22}H_{27}NO_6$ requires *M*, 401.1838).

Reaction of Complex (**6**) *with Schollkopf's Nucleophile: Preparation of Diaryl Ether* (**10**).—To a stirred solution of the Schollkopf reagent (**8**) (736 mg, 4.0 mmol) in THF (40 ml) cooled to −78 °C was added BuLi (1.6 ml of a 2.5M solution in hexanes). After 20 min the solid arene–manganese complex (**6**) (1.256 g, 2.0 mmol) was added and the mixture was stirred at − 78 °C for 30 min, quenched rapidly with aq. ammonium chloride at −78 °C, and extracted with diethyl ether in the usual way. The product dienylmanganese complexes were not isolated. Instead, the ethereal solution was dried ($MgSO_4$), filtered, and stirred with NBS (356 mg, 2.0 mmol) for 15 min at room temperature. The reaction solution was washed successively with aq. sodium hydrogensulphite, water, and brine, and was dried ($MgSO_4$). Evaporation of solvent, followed by flash chromatography (EtOAc–hexanes, 1:2) allowed recovery of excess of reagent (**8**) (309 mg, 85% recovery of unchanged material) and separation of the diastereoisomeric products (**10**) (409 mg, 35%) and (**11**) (95 mg, 8%). Spectral data for (**10**): $[\alpha]_D$ −135° (*c* 0.23, $CHCl_3$); $\nu_{max}(CHCl_3)$ 3 440w, 2 980m, 1 740s, 1 695s, 1 610m, 1 580, 1 490, 1 460, 1 420, 1 370, 1 340, 1 310, 1 240, 1 160, 1 110, 1 060, and 870 cm^{-1}; $\delta_H(CDCl_3)$ 7.23 (1 H, t, *J* 7.9 Hz), 7.02 (1 H, d, *J* 7.7 Hz), 6.96 (1 H, t, *J* 2.0 Hz), 6.77 (1 H, ddd, *J* 8.0, 2.1, 0.9 Hz), 6.71 (1 H, d, *J* 1.0 Hz), 6.54 (1 H, s), 5.47 (1 H, br d), 5.27 (1 H, br d, *J* 7.8 Hz), 5.11 (1 H, d, *J* 4.9 Hz), 3.95 (1 H, t, *J* 4.7 Hz), 3.84 (3 H s), 3.73 (3 H, s), 3.71 (3 H, s), 3.64 (3 H, s), 2.14 (1 H, 14 lines, J_{hept} 6.8, J_d 4.5 Hz), 2.05 (3 H, s), 1.43 (9 H, s), 1.02 (3 H, d, *J* 6.9 Hz), and 0.70 (3 H, d, *J* 6.8 Hz) (Found: C, 63.45; H, 6.7; N, 7.4. $C_{31}H_{41}N_3O_8$ requires C, 63.78; H, 7.08; N, 7.20%).

NMR spectral data for compound (**11**): 7.23 (1 H, t, *J* 8.0 Hz), 7.01 (1 H, d, *J* 7.8 Hz), 6.94 (1 H, t, *J* 2.0 Hz), 6.77 (1 H, dd, *J* 7.8, 2.0 Hz), 6.61 (1 H, d, *J* 1.3 Hz), 6.47 (1 H, s), 5.5 (1 H, br d, *J* 7.2 Hz), 5.27 (1 H, d, *J* 7.4 Hz), 4.99 (1 H, d, *J* 3.6 Hz), 4.04 (1 H, t, *J* 3.4 Hz), 3.86 (3 H, s), 3.73 (3 H, s), 3.69 (3 H, s), 3.64 (3 H, s), 2.34 (1 H, J_{hept} 6.8, J_d 3.3 Hz), 2.03 (3 H, s), 1.43 (9 H, s), 1.08 (3 H, d, *J* 6.8 Hz), and 0.73 (3 H, d, *J* 6.8 Hz).

Preparation of Diaryl Ether (**12**).—To a stirred solution of the adduct (**10**) (435 mg, 0.75 mmol) in THF (10 ml) was added dropwise 0.25M-hydrochloric acid (20 ml). The reaction mixture was stirred overnight at room temperature, extracted with diethyl ether (3 × 10 ml), and the remaining aqueous solution was adjusted to pH 8 by the addition of conc. ammonia. Extraction with diethyl ether (3 × 10 ml) followed by washing of the combined extracts with brine, drying ($MgSO_4$), and removal of solvent gave the *diaryl ether* (**12**), which was purified by flash chromatography (EtOAc–hexanes 1:2) to give an oil (275 mg, 75%); $\nu_{max}(CHCl_3)$ 3 440w, 3 010w, 2 970m, 1 740s, 1 720s, 1 610m, 1 585s, and 1 490s cm^{-1}; $\delta_H(CDCl_3)$ 7.26 (1 H, t, *J* 7.9 Hz), 7.03 (1 H, d, *J* 7.8 Hz), 6.93 (1 H, s), 6.79 (1 H, d, *J* 8.4 Hz), 6.74 (1 H, s), 6.59 (1 H, s), 5.5 (1 H, br d, *J* 6.4 Hz), 5.27 (1 H, br d, *J* 7.3 Hz), 4.56 (1 H, br d), 3.88 (3 H, s), 3.73 (3 H, s), 3.70 (3 H, s), 2.06 (3 H, s), and 1.43 (9 H, s) (NH_2 resonance not located) (Found: C, 61.1; H, 6.4; N, 5.6. $C_{25}H_{32}N_2O_8$ requires C, 61.45; H, 6.61; N, 5.74%).

Deblocking of Compound (**12**) *to Give Deoxyristomycinic Acid Derivative* (**13**).—To a stirred solution of compound (**12**) (200 mg, 0.41 mmol) and thioanisole (1.4 ml, 12 mmol) in dichloromethane (20 ml) cooled to 0 °C was added dropwise TFA (10 ml). After the mixture had been stirred for a further 15 min at 0 °C, the ice-bath was removed and the stirred mixture was warmed to room temperature during 1.5 h then was evaporated under reduced pressure and the residue was taken up in diethyl ether. The solution was extracted with 0.25M-hydrochloric acid and the cooled extracts were basified with ice-cold conc. ammonia. Extraction with diethyl ether in the usual way gave the deprotected *deoxyristomycinic acid derivative* (**13**) (124 mg, 78%); $\delta_H(CDCl_3)$ 7.27 (1 H, t, *J* 7.9 Hz), 7.05 (1 H, d, *J* 7.8 Hz), 6.97 (1 H, s), 6.80 (1 H, d, *J* 7.8 Hz), 6.73 (1 H, s), 6.61 (1 H, s), 4.60 (1 H, br s), 4.56 (1 H, br s), 3.88 (3 H, s), 3.72 (3 H, s), 3.70 (3 H, s), 2.07 (3 H, s), 2.2–1.9 (4 H, br) (Found: M^+, 338.1631. $C_{20}H_{24}N_2O_6$ requires *M*, 388.1634).

Acknowledgements

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