Formal Asymmetric Synthesis of a 7-Methoxyaziridinomitosene

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Abstract: The conversion of (–)-2,3-*O*-isopropylidene-D-erythronolactone (**14**) and 2-benzyloxy-6-bromo-4-methoxy-3-methylaniline (**18**) into {(1*R*,2*R*)-(–)-1-azido-2,3,5,8-tetrahydro-7-methoxy-6-methyl-2-methanesulfonyloxy-5,8-dioxo-1*H*-pyrrolo[1,2-*a*]indol-9-yl}methyl phenyl carbonate (**39**) has been accomplished in 17 steps by way of the enaminone **26**. Key steps included the preparation of **26** by a Reformatsky reaction on a thiolactam precursor **25**, and intramolecular Heck reaction of **26** to form the indole ring. The preparation of **39** constitutes a formal synthesis of the fully functionalised 7-methoxyaziridinomitosene **12**, only the second such synthesis to have been accomplished.

Key words: antitumour agents, asymmetric synthesis, aziridines, enaminones, Heck reaction

The mitomycins,[1] e.g. mitomycin A (**1**) and mitomycin C (**2**), are quinone-containing antitumour antibiotics, the biological activity of which is attributable to DNA alkylation and cross-linking.[2] The unique mode of action of these antibiotics entails initial elimination of methanol followed by bioreduction of the quinone unit in the hypoxic environment of tumour cells to give a hydroquinone (a leucoaziridinomitosene), which is the active form of the drug. The sequence of reactions that spontaneously ensues eventually leads to the formation of covalent bonds between DNA and the electrophilic aziridine (C-1) and carbamate (C-10) sites. The mitomycins can be converted chemically into pyrrolo[1,2-*a*]indoles **3** (aziridinomitosenes),[3] several of which have shown substantial antitumour action without the need for prior bioreductive activation.[3a,4] Considerable effort has been devoted to the total synthesis of mitomycins and their analogues, including the aziridinomitosenes.[5] However, rarely have *de novo* syntheses of the latter succeeded in incorporating all of the reactive functionalities, namely 6,7-disubstituted quinone, carbamate and aziridine, into the same target structure. Thus, while aziridinomitosenes such as **4**,[6] **5**,[7] **6**,[8] **7**,[9] **8**[10] and **9**[11] (Figure 1), which bear a robust ester substituent at C-9 instead of the labile carbamate, have been synthesised; the only reported synthetic (as opposed to semisynthetic) aziridinomitosenes bearing all three reactive components appear to be the compounds **10**, **11**[4c] and **12**.[12] Of these, only compound **12**, prepared by Dong and Jimenez, also bears appropriate substituents in ring A. In this communication we report a new approach to the synthesis of **12**, which has resulted in only the second, albeit formal, synthesis of this fully functionalised 7-methoxyaziridinomitosene, which also has proven antitumour activity.[4b]

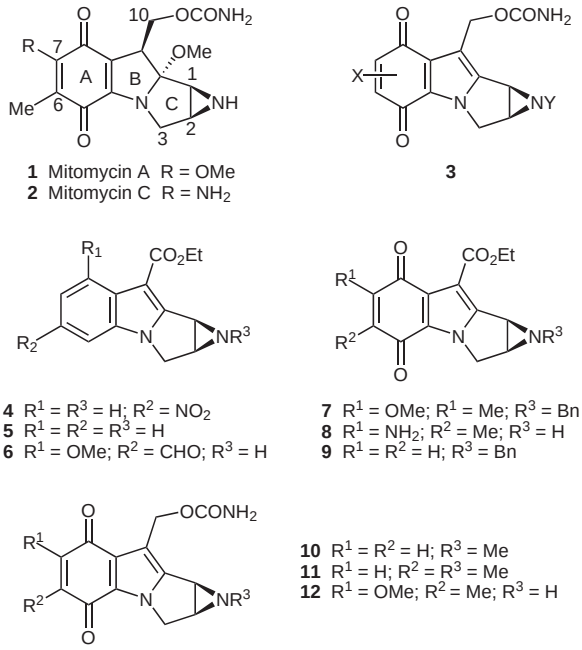

Figure 1

In an ongoing programme on the use of enaminones in the synthesis of alkaloids and related compounds,[13,14] we recently described an asymmetric synthesis of the *N*-phosphorylated aziridinomitosene analogue **13** from (–)-2,3-*O*-isopropylidene-D-erythronolactone (**14**) and 2-bromoaniline[15] (Scheme 1). The key steps of the route included a novel Reformatsky reaction of the thiolactam intermediate **15**, intramolecular Heck-type cyclisation of the resulting enaminone **16** to form the tetracyclic product **17**, and late-stage elaboration of the aziridine ring via a cyclic sulfite. We had previously demonstrated the versatility of the pivotal Heck-type cyclisation in a series of model cyclisations,[16] while a similar reaction featured in an earlier mitosene synthesis by Luly and Rapoport,[17] who cyclised an *N*-(2-bromobenzoquinone) enaminone to give a pyrrolo[1,2-*a*]indole-5,8-dione system directly. We expected that our route to **13** could easily be adapted for the preparation of **12** if we started with a suitably substituted 2-bromoaniline bearing functionality that would favour oxidation of the ring to the quinone level found in the target system.

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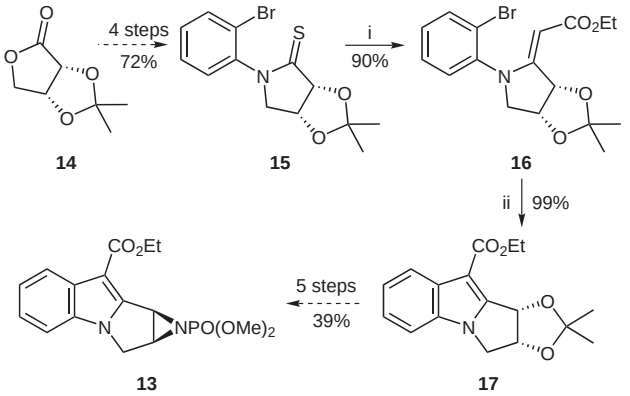
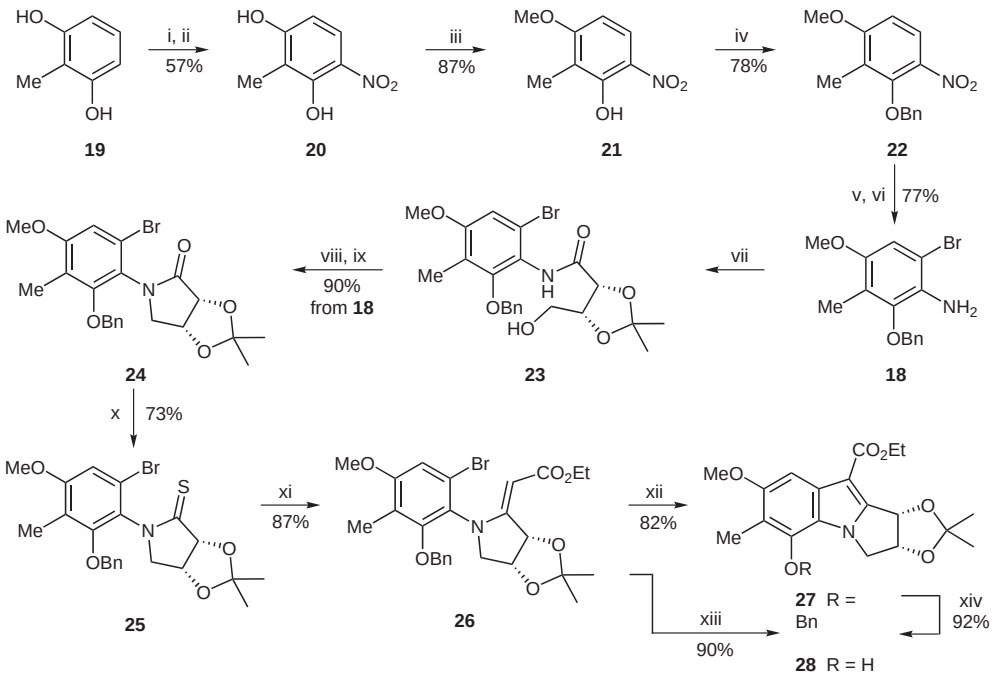


Scheme 1 *Reagents and conditions:* (i) Zn (5 equiv), $BrCH_2CO_2Et$ (3 equiv), I_2 (0.2 equiv), THF, ultrasound, then **15**, THF, reflux; (ii) $Pd(OAc)_2$ (0.1 equiv), PPh_3 (0.4 equiv), KOAc (7.5 equiv), Bu_4NBr (2.5 equiv), DMF–MeCN–H_2O (1:1:0.2), 100 °C, 5 h.

The precursor we settled on was 2-benzyloxy-6-bromo-4-methoxy-3-methylaniline (**18**), which we prepared in six steps from 2-methylresorcinol (**19**). Following a procedure introduced by Raphael and Ravenscroft,[18] **19** was treated with sodium nitrite in acidic medium, and the resulting nitroso intermediate was further oxidised to the nitro product **20** with 70% concentrated nitric acid (Scheme 2). Regioselective methylation of the less hindered hydroxy group with dimethyl sulfate at ambient temperature gave the crystalline product 3-methoxy-2-methyl-6-nitrophenol (**21**), the physical and spectroscopic properties of which agreed with those previously reported.[18] Benzylation of the second hydroxy group under more vigorous conditions yielded the doubly protected nitroresorcinol **22**, which was reduced to a rather sensitive aniline with hydrazine hydrate over Raney nickel in boiling methanol. The crude aniline was immediately brominated with molecular bromine in a mixture of dichloromethane and acetic acid to complete the synthesis of the desired bromoaniline **18** in 77% yield over the two steps. The entire reaction sequence from 2-methylresorcinol to **18** could also be performed on a scale of ca. 25 grams without purification of the intermediates in an overall yield of approximately 45%.

The absolute configuration of the aziridinomitosene target is derived from the second reaction partner, (–)-2,3-*O*-isopropylidene-D-erythronolactone (**14**), which was prepared in 77% yield by a published method that entails oxidative cleavage of D-isoascorbic acid with hydrogen peroxide followed by ketal exchange with 2,2-dimethoxypropane.[19] Since we had previously found that this lactone reacted poorly with 2-bromoaniline unless the latter was deprotonated first, we treated a solution of **18** in tetrahydrofuran with ethylmagnesium chloride at –50 °C before introducing **14** and allowing the mixture to warm to room temperature (Scheme 2). Although the alcohol intermediate **23** could be purified for characterisation purposes, we chose to convert it directly into the lactam **24**. The cyclisation was accomplished by mesylation followed by treatment with sodium hydride in a mixture of



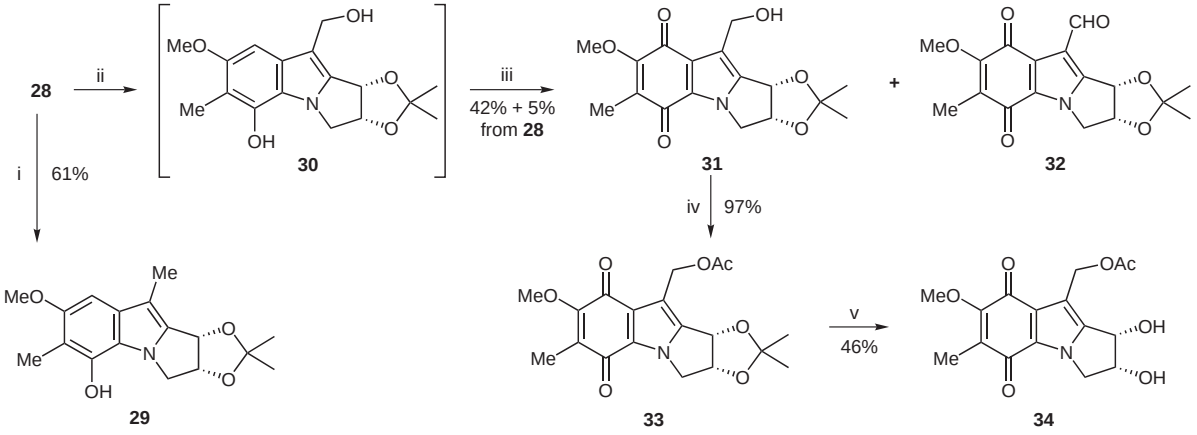
Scheme 2 *Reagents and conditions:* (i) $NaNO_2$, H_2SO_4, H_2O, r.t., 45 min; (ii) HNO_3 (70%), H_2O, r.t., 70 h; (iii) Me_2SO_4, K_2CO_3, acetone, r.t., 20 h; (iv) BnBr, K_2CO_3, acetone, reflux, 41 h; (v) $NH_2NH_2{\cdot}H_2O$, Raney nickel, MeOH, reflux, 1.5 h; (vi) Br_2, CH_2Cl_2–AcOH, r.t., 6 h; (vii) EtMgCl, THF, –50 °C, 50 min, then **14**, –50 °C to r.t., 22 h; (viii) MsCl, Et_3N, CH_2Cl_2, 0 °C to r.t., 7 d; (ix) NaH, THF–DMF, r.t., 20 h; (x) Lawesson's reagent, toluene, reflux, 2.5 h; (xi) $BrZnCH_2CO_2Et$ (from $BrCH_2CO_2Et$, Zn, I_2, THF, ultrasound), THF, reflux, 120 h; (xii) $Pd(OAc)_2$ (0.3 equiv), P(*o*-Tol)$_3$, Et_3N, DMF, MeCN, H_2O, reflux, 4 h; (xiii) $Pd(OAc)_2$ (1.6 equiv), P(*o*-Tol)$_3$, Et_3N, DMF, MeCN, H_2O, reflux, 4 h; (xiv) 10% Pd/C, H_2, EtOH, HCl (1 drop), r.t., 2 h.

tetrahydrofuran and *N*,*N*-dimethylformamide at room temperature. The conversion of the bromoaniline into lactam **24** could be performed on a 20-gram scale without purification of intermediates in an overall yield of 90%. The product was found to exist as a 1:1 mixture of two separable rotamers that could be individually characterised, although this was not necessary in view of the later convergence of these intermediates to a single product.

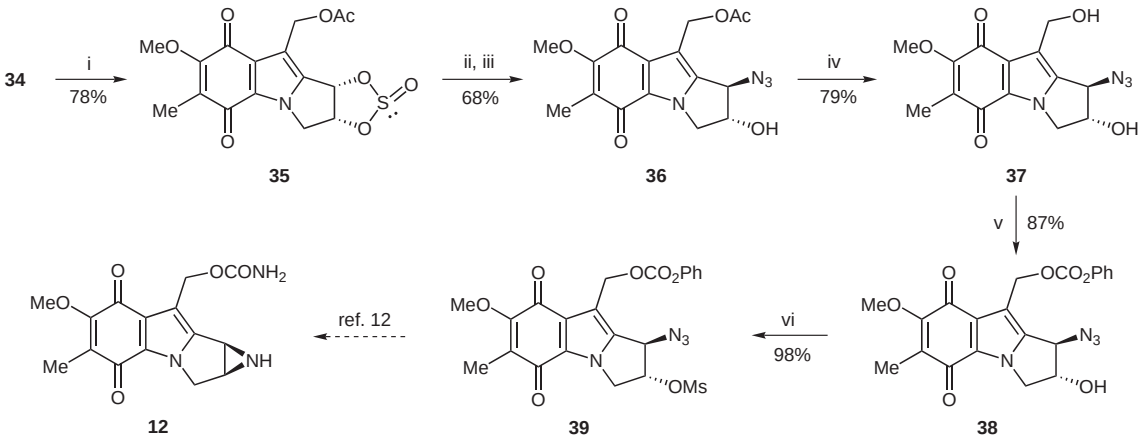
With both rings A and C in place, the next task was to complete the construction of the pyrrolo[1,2-*a*]indole skeleton by means of the tandem Reformatsky–Heck sequence that we had successfully used in preparing the model system **13**. To this end, the rotameric mixture of lactams was thionated with Lawesson's reagent in boiling toluene to yield the thiolactam **25**, also as a mixture of rotamers, in 73% yield. Not surprisingly, when the lactam rotamers were separated and individually subjected to thionation, both produced rotameric mixtures of the thiolactam. Conversion of **25** into the vinylogous urethane **26** was achieved by extended reaction in boiling tetrahydrofuran with an excess of the organozinc reagent formed by sonicating activated zinc powder with ethyl bromoacetate in the presence of iodine as catalyst.[20] The product, yet again a mixture of two rotamers, was obtained in reproducibly good yields of above 85% yield on scales as large as five grams. The crucial intramolecular Heck cyclisation reaction was then achieved by adapting conditions devised by Tietze and Petersen[21] in which a carefully balanced combination of solvent, base, ligand and additives was employed. In this case, the reactant was heated at reflux with palladium(II) acetate (0.3 equiv), tri-*o*-tolylphosphine and triethylamine in the mixed solvent system of *N*,*N*-dimethylformamide, acetonitrile and water (5:5:1) to give **27** in 82% yield.[22] In one case, when an excess of palladium acetate (1.6 equiv) was used, the benzyl protecting group was also lost, giving the free phenol **28** in 90% yield.

Three tasks remained in converting the advanced intermediate **27** into the desired aziridinomitosene target: oxidation of ring A to the quinone level; conversion of the ester in the newly formed ring B into the carbamoyloxymethyl substituent; and replacement of the ketal in ring C by an aziridine ring with inversion of configuration at both stereogenic sites. The timing of these interconversions proved to be tricky. In investigating several variants in which the order of the reactions was altered, we either ran into dead ends or discovered unwelcome competing processes. The most successful approach entailed initial removal of the benzyl protecting group from the pyrrolo[1,2-*a*]indole **27**, which was efficiently accomplished by hydrogenolysis over 10% palladium on carbon to give the phenol **28** in 92% yield. Thereafter, reduction of the ester to an alcohol with lithium aluminium hydride was immediately followed by oxidation of ring A to a quinone, which proved to be reasonably robust in further transformations (Scheme 3). The hydride reduction turned out to be particularly awkward; if the reaction were not carefully monitored by thin layer chromatography, over-reduction occurred, giving the 3-methylindole **29** in reasonable yield. With careful control of conditions, the desired diol **30** could be isolated in approximately 78% yield. However, since this compound decomposed quite rapidly, it was oxidised without further purification with molecular oxygen and a catalytic quantity of salcomine in *N*,*N*-dimethylformamide at room temperature to give the quinone **31** in a disappointing overall yield of 42%. This process also produced a small quantity (5%) of the aldehyde **32**.

At this point, problems with the sensitive hydroxymethyl substituent necessitated its protection. Acetylation of **31** under standard conditions afforded **33** in 97% yield. However, the subsequent hydrolysis of the acetonide proved to be surprisingly difficult to accomplish. We eventually succeeded by treating **33** with a mixture of acetic acid, tetrahydrofuran and water at 65 °C;[23] but diol **34** was obtained in only 46% yield. The formation of the aziridine ring by the double S_N2 displacement of the diol was then envisaged by the method we had previously used in making the aziridinomitosene model **13**.[15] Reaction of **34** with thionyl chloride and triethylamine in dichloromethane produced a 1:1 mixture of the two separable cyclic sulfite



Scheme 3 *Reagents and conditions:* (i) $LiAlH_4$ (3 equiv), THF, 0 °C to r.t., 50 h; (ii) $LiAlH_4$ (3 equiv), THF, 0 °C to r.t., 25 h; (iii) Salcomine, DMF, O_2, r.t., 3 h; (iv) Et_3N, Ac_2O, CH_2Cl_2, r.t., 18 h; (v) AcOH, THF, H_2O, 65 °C, 48 h.



Scheme 4 *Reagents and conditions*: (i) $SOCl_2$, Et_3N, THF, –15 °C to r.t., 1 h; (ii) NaN_3, DMF, 55 °C, 2 h; (iii) H_2SO_4, THF, H_2O, r.t., 2 h; (iv) K_2CO_3, MeOH, r.t., 1 h; (v) PhOCOCl, pyridine, CH_2Cl_2, 0 °C to r.t., 3 h; (vi) MsCl, Et_3N, CH_2Cl_2, r.t., 22 h.

diastereomers **35** in 78% yield (Scheme 4). As in our earlier studies, conversion of the sulfite into the more reactive sulfate was not necessary for further reaction with azide ion; simply treating the mixture of sulfite diastereomers with sodium azide in *N*,*N*-dimethylformamide at 55 °C followed by treatment with aqueous sulfuric acid gave the azido alcohol **36** as a single regioisomer in 68% yield. The most effective strategy from this point onwards involved hydrolysis of the acetate with potassium carbonate in methanol (79%), and selective acylation of the primary alcohol of product **37** with phenyl chloroformate (87%). Finally, treatment of the carbonate **38** with methanesulfonyl chloride and triethylamine in dichloromethane afforded the mesylate **39** in 98% yield. The spectroscopic data recorded on this compound[24] agreed with those reported by Dong and Jimenez,[12] who obtained the same intermediate by a quite different route. These authors completed the synthesis of **12** by treating **39** with gaseous ammonia to make the carbamate, followed by Staudinger reaction of the azide with triphenylphosphine and intramolecular displacement of the mesylate by the intermediate iminophosphorane.

Our preparation of **39** thus constitutes a formal synthesis of the target 7-methoxyaziridinomitosene **12**. Attempts are currently under way to improve the yields of the troublesome oxidation and ketal deprotection steps, and to apply the new methodology to the synthesis of additional analogues of **12** for biological evaluation.

Acknowledgment

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(20) **Synthesis of (–)-Ethyl (2*E*)-{(3a*R*,6a*S*)-5-[2-(Benzyloxy)-6-bromo-4-methoxy-3-methyphenyl]dihydro-2,2-dimethyl-3a*H*-[1,3]dioxolo[4,5-*c*]pyrrol-6 (5*H*)-ylidene}acetate (26)**: To a solution of ethyl bromoacetate (6.70 mL, 60.4 mmol, 5 equiv) in THF (250 mL) was added activated zinc powder (11.9 g, 181.9 mmol, 15 equiv) at r.t. After 5 min of stirring, iodine (2.15 g, 8.47 mmol, 0.7 equiv) was added in one portion, resulting in spontaneous reflux of the reaction mixture for a period of 5–10 min. The resulting greyish suspension was allowed to cool to r.t. over 1 h and then subjected to sonication for 1 h at 45 °C under an atmosphere of nitrogen. The mixture was allowed to cool to r.t. over 30 min, after which thiolactam **25** (rotameric mixture, 5.79 g, 12.1 mmol, 1 equiv) was added in one portion. The mixture was subsequently heated at reflux for 48 h, and then cooled to r.t. A further portion of organozinc reagent, prepared on the same scale as described above, was added, after which the mixture was heated again under reflux for 72 h. The reaction mixture was allowed to cool to r.t., and an ice–water mixture (200 mL) was added, which resulted in precipitation of inorganic solids. The organic material was extracted into Et_2O, which was dried ($MgSO_4$) and evaporated to yield a crude orange oil. Purification by column chromatography on silica gel using EtOAc–hexane (3:17, then 2:8) as eluent gave an inseparable mixture of vinylogous urethane rotamers **26** (5.62 g, 87%, 4:5 mixture of N-Ar rotamers by NMR spectroscopy; vide infra) as a viscous yellow oil–foam; R_f 0.41 (EtOAc–hexane 3:7); $[\alpha]_D^{23}$ –67.5 (*c* = 0.46, $CHCl_3$). IR ($CHCl_3$): 2981 (w), 1697 (s, C=O), 1476 (m), 1233 (w), 1134 (s), 735 (s) cm^{-1}. HRMS (EI): *m*/*z* [M^+] calcd for $C_{26}H_{30}NO_6{}^{79}Br$: 531.1257; found: 531.1266.
Minor Rotamer: ^1H NMR (300 MHz, $CDCl_3$): δ = 7.26–7.44 (m, 5 H, CH_2Ph), 6.92 (s, 1 H, 5-H), 5.65 (d, *J* = 6.3 Hz, 1 H, 3a-H), 4.86 (d, *J* = 11.4 Hz, 1 H, OCH_aH_bPh), 4.67 (d, *J* = 11.4 Hz, 1 H, OCH_aH_bPh), 4.56 (td, *J* ≈ 2.0, 6.2 Hz, 1 H, 6a-H), 4.38 (s, 1 H, $=CHCO_2Et$), 4.13 (q, *J* = 7.0 Hz, 2 H, OCH_2CH_3), 3.82 (s, 3 H, $ArOCH_3$), 3.77 (dd, *J* = 6.3, 10.8 Hz, 1 H, NCH_aH_b), 3.50 (dd, *J* = 1.8, 10.8 Hz, 1 H, NCH_aH_b), 2.12 (s, 3 H, $ArCH_3$), 1.41, 1.56 (2 × s, 6 H, 2 × CH_3), 1.22 (t, *J* = 7.0 Hz, 3 H, OCH_2CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 167.78 (C=O), 160.73 (C-4), 158.63, 156.40, 136.86, 128.57, 128.21, 127.97, 124.84, 121.45, 120.76 (arom C), 112.28 (O_2CMe_2), 111.12 (arom C), 84.46 ($=CHCO_2Et$), 80.29 (C-3a), 75.93 (OCH_2Ph), 75.01 (C-6a), 58.79 (OCH_2CH_3), 57.61 (C-6), 55.96 ($ArOCH_3$), 27.15, 25.33 (2 × CH_3), 14.42 (OCH_2CH_3), 9.59 ($ArCH_3$).
Major Rotamer: ^1H NMR (300 MHz, $CDCl_3$): δ = 7.26–7.44 (m, 5 H, CH_2Ph), 6.90 (s, 1 H, arom H), 5.93 (d, *J* = 6.6 Hz, 1 H, H-3a), 5.07 (d, *J* = 11.1 Hz, 1 H, OCH_aH_bPh), 4.94 (td, *J* = 2.4, 6.3 Hz, 1 H, H-6a), 4.71 (d, *J* = 11.1 Hz, 1 H, OCH_aH_bPh), 4.43 (s, 1 H, $=CHCO_2Et$), 4.13 (q, *J* = 7.0 Hz, 2 H, OCH_2CH_3), 3.83–3.89 (m, 2 H, NCH_2), 3.84 (s, 3 H, $ArOCH_3$), 1.99 (s, 3 H, $ArCH_3$), 1.36, 1.44 (2 × s, 6 H, 2 × CH_3), 1.22 (t, *J* = 7.0 Hz, 3 H, OCH_2CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 167.97 (C=O), 160.56 (C-4), 158.61, 156.21, 136.74, 128.31, 127.97, 127.48, 124.80, 121.47, 120.12 (arom C), 112.21 (O_2CMe_2), 111.12 (arom C), 85.04 ($=CHCO_2Et$), 80.03 (C-3a), 76.00 (OCH_2Ph), 75.19 (C-6a), 58.82 (OCH_2CH_3), 57.68 (C-6), 55.93 ($ArOCH_3$), 24.85, 26.75 (2 × CH_3), 14.40 (OCH_2CH_3), 9.45 ($ArCH_3$).

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(22) **Synthesis of (–)-Ethyl (3a*R*,10b*S*)-6-Benzyloxy-8-methoxy-2,2,7-trimethyl-3a,10b-dihydro-4*H*-[1,3]dioxolo-[4′,5′:3,4]pyrrolo[1,2-*a*]indole-10-carboxylate (27)**: A solution of the vinylogous urethane **26** (N-Ar rotameric mixture, 5.62 g, 10.6 mmol, 1.0 equiv) in a mixture of DMF (70 mL), MeCN (70 mL) and H_2O (15 mL) was thoroughly degassed with nitrogen for 10 min. Palladium(II) acetate (710 mg, 3.16 mmol, 0.3 equiv), P(*o*-tolyl)$_3$ (5.15 g, 16.9 mmol, 1.6 equiv) and Et_3N (14.7 mL, 105 mmol, 10 equiv) were added in succession and the resulting orange mixture was heated at reflux for 4 h. The dark brown reaction mixture was cooled to r.t., diluted with H_2O (200 mL) and stirred vigorously for 1 h. The mixture was extracted with CH_2Cl_2, which was then dried ($MgSO_4$) and evaporated to afford a dark brown oil. Purification by column chromatography on silica gel with EtOAc–hexane (1:9 then 2:8) as eluent gave the pyrrolo[1,2-*a*]indole **27** (3.92 g, 82%) as a pale yellow solid. Recrystallisation from EtOAc–hexane yielded a colourless crystalline solid; mp 90–91 °C; R_f 0.49 (EtOAc–hexane, 3:7); $[\alpha]_D^{23}$ –85.5 (*c* = 0.57, abs. EtOH). IR ($CHCl_3$): 2982 (w), 1697 (s, C=O), 1570 (m), 1454 (m), 1433 (m), 1275 (s), 1206 (m), 1129 (s), 747 (w) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.33–7.41 (m, 6 H, 9-H, CH_2Ph), 5.77 (s, *J* = 6.2 Hz, 1 H, 10b-H), 5.22 (br t, *J* ≈ 5.8 Hz, 1 H, 3a-H), 4.96 (d, *J* = 11.4 Hz, 1 H, OCH_aH_bPh), 4.90 (d, *J* = 11.4 Hz, 1 H, OCH_aH_bPh), 4.40 (q, *J* = 7.1 Hz, 2 H, OCH_2CH_3), 4.15–4.27 (m, 2 H, NCH_2), 3.91 (s, 3 H, $ArOCH_3$), 2.27 (s, 3 H, $ArCH_3$), 1.26, 1.44 (2 × s, 6 H, 2 × CH_3), 1.42 (t, *J* = 7.1 Hz, 3 H, OCH_2CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 164.82 (C=O), 155.28 (C-10), 146.45, 143.40, 136.70, 130.16, 128.65, 128.28, 127.74, 121.57, 115.68 (arom C), 112.61 (O_2CMe_2), 101.73 (C-10a), 98.09 (C-9), 81.60 (C-3a), 76.92 (OCH_2Ph), 76.41 (C-10b), 59.53 (OCH_2CH_3), 55.82 ($ArOCH_3$), 53.30 (C-4), 26.97, 25.59 (2 × CH_3), 14.48 (OCH_2CH_3), 9.61 ($ArCH_3$). HRMS (EI): *m*/*z* calcd for $C_{26}H_{29}NO_6$: 451.1995; found: 451.2006. Anal. Calcd for $C_{26}H_{29}NO_6{\cdot}0.5H_2O$: C, 67.81; H, 6.57; N, 3.04. Found: C, 67.99; H, 6.56; N, 3.19.

(23) Wiegerinck, P. H. G.; Flucks, L.; Hammink, J. B.; Mulders, S. J. E.; de Groot, F. M. H.; van Rozendaal, H. L. M.; Scheeren, H. W. *J. Org. Chem.* **1996**, *61*, 7092.

(24) **{(1*R*,2*R*)-(–)-1-Azido-2,3,5,8-tetrahydro-7-methoxy-6-methyl-2-methanesulfonyloxy-5,8-dioxo-1*H*-pyrrolo[1,2-*a*]indol-9-yl}methyl Phenyl Carbonate (39)**: R_f 0.13 (EtOAc–hexane, 3:7); $[\alpha]_D^{23}$ –121.6 (*c* = 1.02, $CHCl_3$). IR ($CHCl_3$): 3018 (m), 2939 (m), 2108 (s, N_3), 1761 (s, ester C=O), 1647 (s, quinone C=O), 1507 (m), 1365 (s), 1319 (s), 1246 (br s), 1210 (s), 1176 (s), 1106 (s), 960 (s) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.18–7.41 (m, 5 H, arom H), 5.56 (d, *J* = 13.4 Hz, 1 H, $CH_aH_bOCO_2Ph$), 5.50 (d, *J* = 13.4 Hz, 1 H, $CH_aH_bOCO_2Ph$), 5.47 (br dd, *J* ≈ 2.4, 4.2 Hz, 1 H, H-2), 5.28 (d, *J* = 1.2 Hz, 1 H, H-1), 4.50–4.64 (m, 2 H, NCH_2), 4.06 (s, 3 H, OCH_3), 3.07 (s, 3 H, OSO_2CH_3), 1.97 (s, 3 H, $ArCH_3$). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 178.79, 178.63 (2 × quinone C=O), 157.46 (C-10), 153.47 (carbonate C=O), 150.99 (arom C), 135.95 (C-7), 129.50, 128.15, 127.51, 126.19, 124.22, 120.97 (3 × arom C, C-4, C-6, C-9), 114.53 (C-10), 84.25 (C-2), 61.99, 61.78 (C-1, CH_2OCO_2Ph), 61.29 (quinone OCH_3), 51.71 (C-3), 38.71 (OSO_2CH_3), 8.49 (quinone CH_3). LRMS (FAB): *m*/*z* = 517 [MH^+].