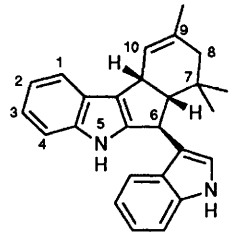
Polyphosphate Ester-catalysed Cyclodehydration of Monoesters of *N*-Substituted 3-(Indol-3'-yl)-5-methylcyclohex-4-ene-1,2-dicarboxylic Acids; Stereoselective Synthesis of Methyl 9-Methyl-6-oxo-5-tosyl-5,6,6aβ,7β,8,10aβ-hexahydroindeno[2,1-*b*]indole-7α-carboxylate. *X*-Ray Molecular Structure of Methyl 5-Methoxy-9-methyl-6-oxo-5,6,6aβ,7β,8,10aβ-hexahydroindeno[2,1-*b*]-indole-7-carboxylate

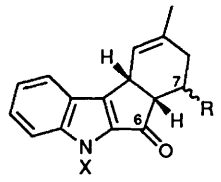
Kin-Fai Cheng,* Tze-Tat Wong, Wing-Tak Wong, and Ting-Fong Lai
Department of Chemistry, University of Hong Kong, Pokfulam Road, Hong Kong

The effect of the *N*-substituents on the polyphosphate ester-(PPE)-catalysed cyclodehydration of a monoester of *N*-substituted 5-methyl-3-(indol-3'-yl)cyclohex-4-ene-1,2-dicarboxylic acids (**41**) is presented. Stereoselective synthesis of methyl 9-methyl-6-oxo-5-tosyl-5,6,6aβ,7β,8,10aβ-hexahydroindeno[2,1-*b*]indole-7α-carboxylate (**2**), the key synthetic intermediate for C(7)-functionalized antifertility agent yuehchukene (YCK) (**1**) analogues, is described.

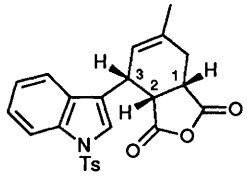
In connection with our current studies[1,2] directed towards the synthesis of analogues of yuehchukene (**1**),[3] a potential antifertility agent,[4] employing an intermolecular Diels–Alder reaction, we planned to synthesize compound (**2**) as the key intermediate compound. The keto ester (**2**) possesses the basic structural unit of yuehchukene, the 9-methyl-5,6,6aβ,7,8,10aβ-hexahydroindeno[2,1-*b*]indole tetracycle (**4**), and has suitably positioned functionalities at C-6 and C-7 for elaboration into different substituents at these positions. In this paper we report a stereoselective method to obtain compound (**2**) from the anhydride (**5**).



(**1**)

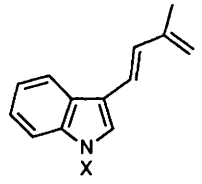


(**2**) X = Ts, R = CO_2Me
(**3**) X = Ts, R = H
(**4**) X = H, R = H

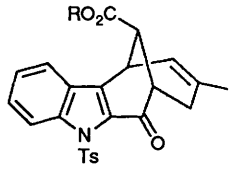


(**5**)

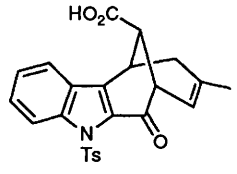
Our proposed method to secure compound (**2**) was to subject the anhydride (**5**), readily obtainable from intermolecular Diels–Alder reaction between the diene (**6**) and maleic anhydride, to $AlCl_3$-catalysed intramolecular acylation conditions. Unfortunately, when the anhydride (**5**) was treated with $AlCl_3$, the expected product (**2**) was not formed; instead bridged cyclic compounds (**9**) and (**12**) were isolated. In view of the results obtained from this study,[2] we envisaged that an alternative approach to compound (**2**) might be effected *via* a route which involved cyclodehydration of the dicarboxylic acid (**13**) with polyphosphate ester (PPE).[5] If this cyclodehydration were to proceed in the desired manner, the C(1)-carboxylic acid group should be selectively transformed into another functionality such as an alcohol (**18**) or ester (**14**) so that it would not compete with the C(2)-carboxylic acid in the cyclodehydration.



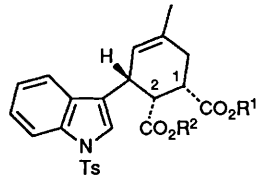
(**6**) X = Ts
(**7**) X = OMe
(**8**) X = H



(**9**) R = H
(**10**) R = Me
(**11**) R = Et

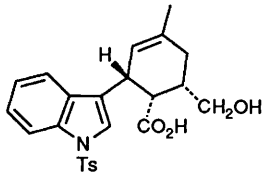


(**12**)

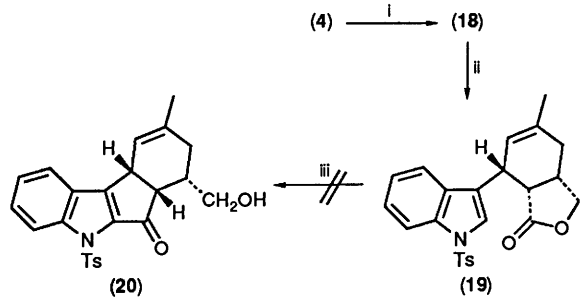


(**13**) $R^1 = R^2 = H$
(**14**) R^1 = Me, R^2 = H
(**15**) R^1 = Et, R^2 = H
(**16**) $R^1 = R^2$ = Me
(**17**) R^1 = H, R^2 = Me

The stereochemical environments of the two carboxy groups in the anhydride (**5**) were quite different. The C(2)-carboxy group was sterically hindered by the adjacent indolyl substituent. Thus, as expected, sodium borohydride reduction of compound (**5**) selectively reduced the C(1)-carboxy group and afforded the hydroxy acid (**18**). However, treatment of com-



(**18**)



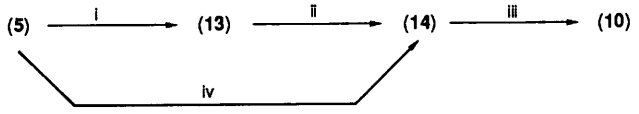
Scheme 1. *Reagents and conditions:* i, $NaBH_4$; ii, PPE, $CHCl_3$, reflux; iii, $AlCl_3$, $CHCl_3$, reflux.

Table 1. ^1H Chemical shift of the methyl group of mono- and di-esters of dicarboxylic acids (**13**), (**23**), and (**26**).

	δ_H	
Compound	C^1-CO_2Me	C^2-CO_2Me
(**14**)	3.66	
(**16**)	3.69	2.85
(**22**)	3.67	
(**27**)	3.69	
(**28**)	3.66	3.05
(**30**)		3.09

pound (**18**) with PPE in refluxing chloroform did not give the desired hydroxy ketone (**20**) but instead yielded the lactone (**19**). Although the lactone (**19**) was not the target compound, we yet hoped it could be transformed to the tetracycle (**20**) by intramolecular acylation. Disappointingly, when the lactone (**19**) was treated with $AlCl_3$ in refluxing $CHCl_3$ it resisted intramolecular acylation and the starting lactone was recovered without any ketone (**20**) being detected (Scheme 1).

The anhydride (**5**) was then converted selectively into its monomethyl ester (**14**) (Scheme 2) by, first, hydrolysis of the anhydride (**5**) to the dicarboxylic acid (**13**), followed by esterification selectively at the C(1)-carboxy group of the diacid (**13**)



Scheme 2. *Reagents and conditions:* i, aq. H_2SO_4, THF–acetone; ii, BF_3·MeOH, THF; iii, PPE, $CHCl_3$, reflux; iv, Na/Hg, DME, MeOH, Na_2HPO_4, room temp., 1.5 h.

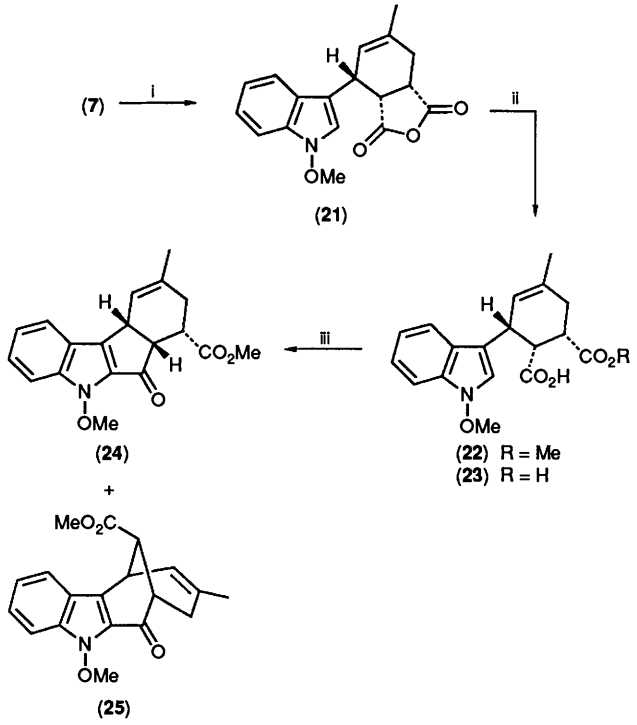
with BF_3–methanol in tetrahydrofuran (THF). The structural assignment of the monoester thus formed, which showed a sharp singlet for the methoxy methyl at δ 3.69 in its ^1H NMR spectrum, as compound (**14**), and not its isomer (**17**), was based on the consideration that the C(1)-carboxy group was more easily accessible than the C(2)-carboxy group, and so should be esterified preferentially. Further support was drawn from the value of the ^1H chemical shift of the methoxy methyl group. From a number of mono- and di-esters of the dicarboxylic acid (**41**) prepared during the course of the present study, it was seen that the methyl signal of the C(1)-methyl ester appears at δ 3.6–3.7, whereas that of the C(2)-methyl ester resonated at δ 2.8–3.1 (see Table 1). The same ester (**14**) could also be obtained more directly by treatment of the anhydride (**5**) with sodium amalgam in the presence of disodium hydrogen phosphate buffer.[6]

When the monoester carboxylic acid (**14**) was subjected to cyclodehydration with PPE in refluxing chloroform, a single keto ester product was isolated. However, the IR spectrum of this product exhibited a ketone carbonyl absorption at 1 678 cm^{-1}, considerably lower than the expected value of 1 702 cm^{-1} as shown by the tetracycle (**3**),[1] indicating a 5-membered cyclic ketone had not been formed. On the other hand, the product exhibited spectral data very similar to those of compound (**9**) which we had prepared earlier.[1] Indeed, when the keto acid (**9**) was esterified with diazomethane, the ester so obtained was identical with this cyclodehydration product. Thus, the cyclodehydration product of compound (**14**) was the bridged cyclic compound (**10**).

A similar result was obtained from the PPE cyclodehydration of the monoethyl ester (**15**), obtained from ethanolysis of the anhydride (**5**), which gave rise to the bridged cyclic compound (**11**).

These observations suggested that an intramolecular transesterification must have taken place prior to the cyclodehydration. We decided to study this reaction further.

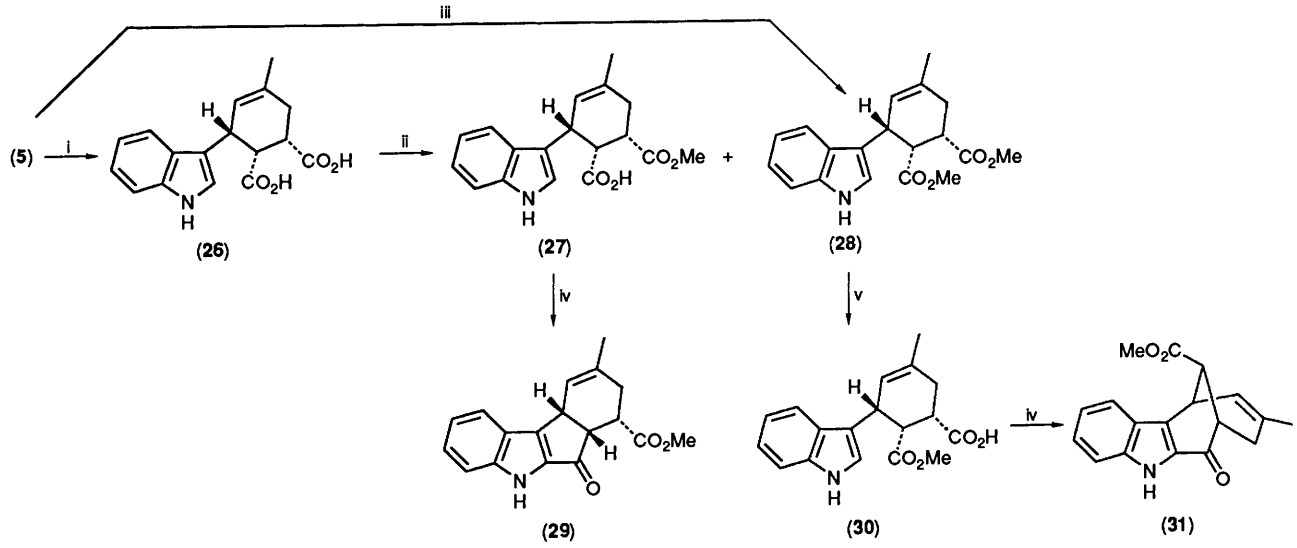
At the time of investigation, we had in our hands a quantity of the *N*-methoxy diene (**7**).[7] Sequential treatment of the diene (**7**) with maleic anhydride, and methanolysis of the Diels–Alder adduct (**21**), afforded the desired monoester (**22**) of the diacid together with a small amount of the diacid (**23**) (Scheme 3). The



Scheme 3. *Reagents and conditions:* i, Maleic anhydride, benzene, 80 °C; ii, MeOH, THF; iii, PPE, $CHCl_3$, reflux.

purity of the isolated ester (**22**) was evidenced by a single peak on HPLC analysis, and the appearance of a sharp singlet in ^1H NMR spectrum at δ 3.67 (see Table 1). Treatment of the monoester acid (**22**) with PPE in refluxing chloroform afforded a mixture of two compounds in a ratio of 4:1, separable by flash column chromatography on silica gel.[8] The major product was shown to be the desired tetracyclic keto ester (**24**) by single-crystal X-ray analysis (Figure). The minor product which exhibited spectral data very similar to those of ester (**10**) was the bridged cyclic compound (**24**).

It became obvious that the substituent on the indole nitrogen in the monoester carboxylic acid could alter the reaction pathway, generating different cyclodehydration products. We therefore prepared three more monoester carboxylic acids—the *N*-unsubstituted (**27**), *N*-benzyl (**35**), and *N*-methyl (**36**) monoester acids—for further study.



Scheme 4. *Reagents and conditions:* i, 3M-MeOH–KOH; ii, BF_3·MeOH, reflux; iii, Na/Hg, Na_2HPO_4, MeOH–DME; iv, PPE, $CHCl_3$, reflux; v, 3M-aq. KOH, THF, TBAHS, reflux.

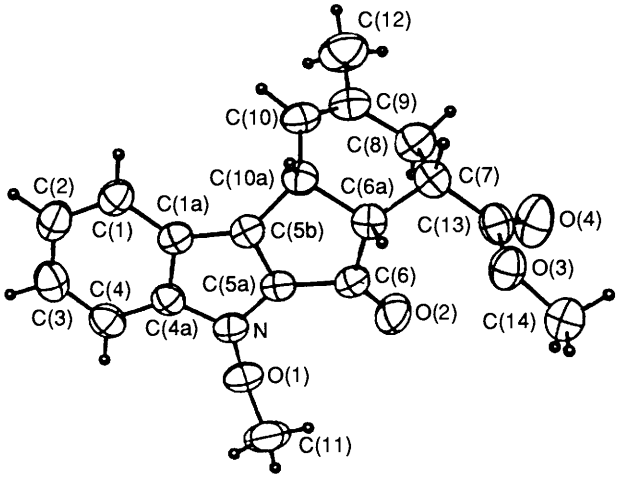


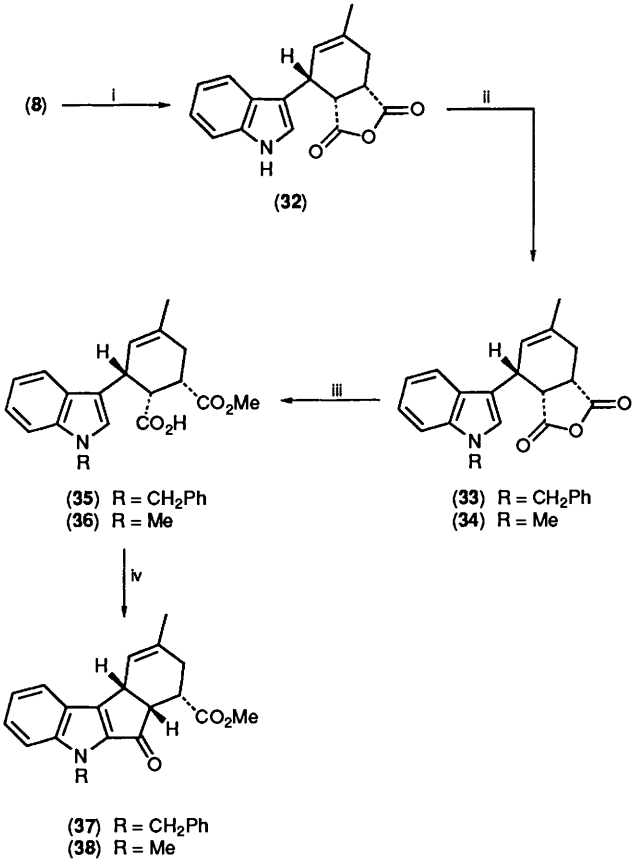
Figure. ORTEP drawing for compound (**24**) with atomic numbering scheme.

Table 2. Product of PPE cyclodehydration of compound (**41**) with different *N*-substituents.

Entry	*N*-Substituent	Tetracyclic product : Bridged cyclic product	Yield (%)
1	Ts	0 : 100	62
	(**14**)	(**10**)	
2	OMe	80 : 20	61
	(**22**)	(**24**) (**25**)	
3	H	100 : 0	66
	(**27**)	(**29**)	
4	CH_2Ph	100 : 0	55
	(**35**)	(**37**)	
5	Me	100 : 0	74
	(**36**)	(**38**)	

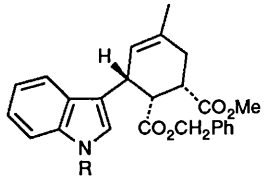
Compound (**27**) was prepared by treatment of the anhydride (**5**) with 3M-methanolic KOH in THF whereby both the *N*-tosyl group and the anhydride were hydrolysed giving rise to the dicarboxylic acid (**26**). Esterification of (**26**) with BF_3–methanol afforded mainly the desired monoester (**27**) (73%) and a small amount of the diester (**28**) (16%) (Scheme 4).

N-Benzyl monoester (**35**) was obtained by sequential Diels–Alder reaction of the diene (**8**)[9] with maleic anhydride, *N*-alkylation, and methanolysis of the adduct (**32**) (Scheme 5). In a similar manner, the *N*-methyl monoester (**36**) was obtained from the anhydride (**32**).



Scheme 5. *Reagents and conditions:* i, Maleic anhydride, benzene, 60 °C; ii, $PhCH_2Br$, TBAHS, NaOH, benzene [(**32**) ⟶ (**33**)]; MeI, TBHAS, NaOH, benzene [(**32**) ⟶ (**34**)]; iii, BF_3·MeOH, reflux, 2 h [(**33**) ⟶ (**35**)]; HCl, MeOH, reflux, 2 h [(**34**) ⟶ (**36**)]; iv, PPE, $CHCl_3$, reflux.

It is pertinent to point out that attempts to prepare the *N*-benzyl ester (**35**) by direct alkylation of compound (**27**) with aqueous sodium hydroxide and benzyl bromide in the presence of a phase-transfer catalyst [tetrabutylammonium hydrogen sulphate (TBAHS)][10] resulted in the formation of mixed diesters (**39**) and (**40**), and compound (**35**) was not produced.



(**39**) R = H
(**40**) R = CH_2Ph

When the *N*-unsubstituted monoester acid (**27**), its *N*-benzyl derivative (**35**), and *N*-methyl derivative (**36**) were separately treated with PPE in refluxing chloroform, the corresponding desired tetracyclic keto esters (**29**), (**37**), and (**38**) were obtained as the sole products in reasonable yield (55–74%) and no trace of the bridged cyclic compounds could be detected.

The present study showed that the cyclodehydration reaction was significantly influenced by the *N*-substituent of the indole (see Table 2). While *N*-tosyl derivative (**14**) gave exclusively the bridged cyclic compound, the unsubstituted (**27**), the *N*-benzyl (**35**), and the *N*-methyl (**36**) derivatives afforded exclusively the tetracyclic products. On the other hand, the *N*-methoxy derivative (**22**) yielded a mixture of tetracyclic and bridged cyclic products in the ratio 4:1 (see Table 2).

These results could be rationalized by assuming a mechanism as depicted in Scheme 6 and by considering the effect of *N*-substituents on the relative rates of cyclodehydration and transesterification.

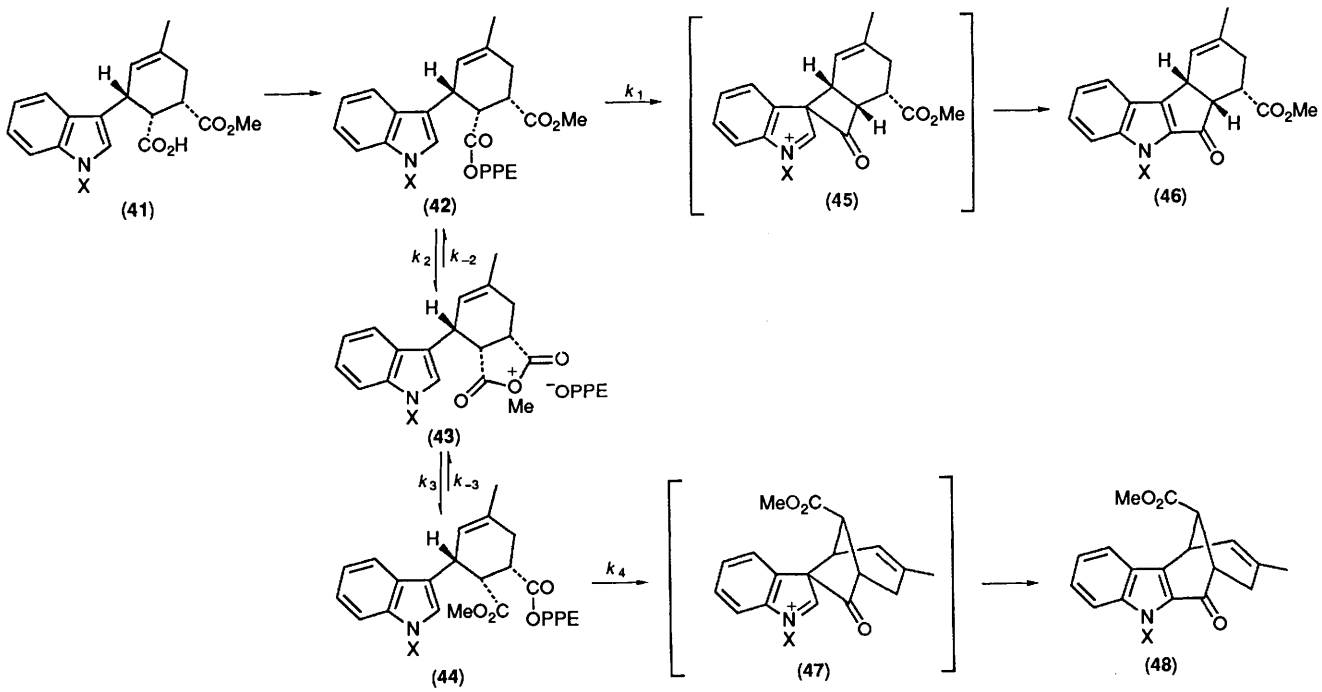
Polyphosphate ester (PPE) has been used widely as an agent for cyclodehydration[11] and esterification.[12] Although little is known about the structure of PPE,[13,14] it has been suggested that PPE activates the carboxylic acid by forming a good leaving group.[15] Thus we believe that, initially, PPE reacts with the carboxylic acid (**41**) giving rise to an activated carboxylic derivative (**42**) (Scheme 6). When the indole nitrogen was unsubstituted (entry 3, Table 2) or attached to electron-donating alkyl groups (entries 4 and 5), cyclodehydration (**42**) ⟶ (**46**) proceeded very much faster than the transesterification (**42**) ⟶ (**44**), *i.e.* $k_1 \gg k_2$. Thus only tetracyclic product was observed. On the other hand, when the indole nitrogen was attached to a powerful electron-withdrawing group (entry 1), cyclodehydration (**42**) ⟶ (**46**) became unfavourable because of non-availability of the nitrogen lone-pair necessary for the reaction. Therefore equilibration of the activated isomeric carboxylic derivatives (**42**) and (**44**) *via* (**43**) could be set up, *i.e.* $k_1 \ll k_2$. Eventual cyclodehydration of (**44**) to (**48**) took place in preference to that of (**42**) to (**46**), since formation of the latter involved an energetically unfavourable four-membered cyclic intermediate (**45**). Thus only the bridged cyclic product was observed. When the *N*-atom was attached to a weakly electron-withdrawing group (entry 2), cyclodehydration (**42**) ⟶ (**46**) competed favourably over transesterification (**42**) ⟶ (**44**); and once compared (**44**) was formed it would undergo cyclodehydration to give (**48**), *i.e.* $k_3 > k_1 \approx k_2$. Thus a mixture of both tetracyclic ester (**46**) and bridged cyclic ester (**48**) was observed.

Our rationale was substantiated by the fact that when the isomeric monoester carboxylic acid (**30**), obtained by partial hydrolysis of the diester (**28**), was treated with PPE in refluxing chloroform, only the bridged cyclic product (**31**) was isolated (Scheme 4).

The keto ester (**29**) was readily transformed to the title compound (**2**) by re-introduction of the *N*-protection tosyl group. Thus, it is now possible to secure the tetracyclic keto ester (**2**), the key intermediate in the synthesis of C(7)-functionalized YCK analogues, from the anhydrides (**5**). Transformation of compound (**2**) into a variety of yuehchukene analogues is in progress.

Experimental

M.p.s. were measured on a Reichert Kofler-block apparatus and



Scheme 6.

are uncorrected. IR spectra were recorded on a Perkin-Elmer 577 spectrophotometer and calibrated with polystyrene. NMR spectra were recorded on a JEOL FX-90Q and a Bruker WM-400 spectrometer for solutions in deuteriochloroform unless otherwise stated, with tetramethylsilane as internal standard. Mass spectra were recorded on a Hitachi RMS-4 and a VG 70-70F high-resolution mass spectrometers. UV spectra were recorded on a Shimadzu UV 240 spectrophotometer. TLC was performed using Merck pre-coated silica gel F-254 plates (thickness 0.25 mm). Flash chromatography was carried out with Kieselgel 60 (Merck) as the stationary phase.[8] Analytical HPLC was performed on a Beckmann Model 331 HPLC System with Model 163 variable-wavelength UV–visible detector. Organic extracts were dried over anhydrous sodium sulphate and evaporated at aspirator pressure using a rotary evaporator. Light petroleum refers to the fraction boiling in the range 40–60 °C and was redistilled before use. All reactions requiring anhydrous conditions were conducted in apparatus dried in an oven at 120 °C and under a static atmosphere of dry nitrogen. New compounds whose elemental compositions were established through accurate mass determination were shown to be homogeneous by spectroscopic and chromatographic methods. All compounds described are racemic.

(1RS,2SR,3SR)-5-*Methyl*-3-(1′-*tosylindol*-3′-*yl*)*cyclohex*-4-*ene*-1,2-*dicarboxylic Acid* (**13**).—A solution of the anhydride (**5**) (2 g, 4.6 mmol) and dilute H_2SO_4 (15 ml) in a mixture of THF (75 ml) and acetone (15 ml) was heated under reflux for 4 h. The resulting solution was cooled, poured into water, and extracted with diethyl ether. The extract was washed successively with water and brine, dried, and evaporated to yield the diacid (**13**) as a pale yellow solid (1.66 g, 80%), m.p. 187–189 °C; λ_{max}(EtOH) 227 (log ε 4.48) and 257 nm (4.05); ν_{max}(Nujol) 3 600–2 400vbr, 1 700br, 1 600, 1 370, 1 175, 760, 750, and 680 cm^{-1}; δ_H(90 MHz; [$^2H_6$]acetone) 1.82 (3 H, br s, 5-Me), 2.31 (3 H, s, Ar*Me*), 2.32–2.97 (2 H, m, 6-H_2), 3.20 (1 H, ddd, $J_{1,2}$ 3.5, $J_{1,6}$ 6.12 and 11.16 Hz, 1-H), 3.62 (1 H, dd, $J_{1,2}$ 3.5, $J_{2,3}$ 6.12 Hz, 2-H), 4.23 (1 H, br m, 3-H), 4.47 (2 H, vbr, exchangeable with D_2O, 2 × OH), 5.56 (1 H, br s, 4-H), 7.10–7.47 (5 H, m, ArH), and 7.66–7.96 (4 H, m, ArH); δ_C[22.5 MHz; $(CD_3)_2SO$ and $(CD_3)_2CO$] 21.37 (Ar*Me*), 23.59 (5-Me), 30.09 (C-6), 35.97 (C-3), 42.42 and 44.75 (C-1 and -2), 114.03 (C-7′), 120.81 and 121.40 (C-4 and -4′), 123.73 (C-5′), 124.82 (C-2′), 125.11 (C-6′ and -3′), 127.47 (2 × C-2″), 130.80 (2 × C-3″), 131.56 (C-3′a), 135.57 (C-7′a), 135.68 (C-1″ and -5), 145.81 (C-4″), 173.16 (2-CO), and 175.30 (1-CO); *m*/*z* 453 (M^+, 12%), 436 (20), 435 (M − H_2O, 60), 337 (18), and 181 (100).

(1RS,2RS,6SR)-6-*Hydroxymethyl*-4-*methyl*-2-(1′-*tosylindol*-3′-*yl*)*cyclohex*-3-*enecarboxylic Acid* (**18**).—To a suspension of sodium borohydride (0.1 g, 2.76 mmol) in THF (7 ml) at 0 °C was added dropwise a solution of the anhydride (**5**) (1 g, 2.3 mmol) in THF (10 ml). The resulting solution was stirred at room temperature for 12 h and poured into water. The aqueous layer was neutralized by dil. HCl and was extracted with dichloromethane. Work-up and purification of the crude product by flash chromatography on silica gel eluted with diethyl ether afforded the hydroxy acid (**18**) (0.79 g, 58%) as a white solid, m.p. 107–109 °C; ν_{max}(Nujol) 3 360, 3 500–2 700vbr, 1 700br, 1 600, 1 380, 1 195, 1 180, 1 130, 1 100, 1 025, 980, and 760 cm^{-1}; δ_H(90 MHz) 1.79 (3 H, br s, 4-Me), 2.04 (2 H, m, 5-H_2), 2.27 (3 H, s, Ar*Me*), 2.42 (1 H, m, 6-H), 3.36–3.56 (3 H, m, 1-H and 6-CH_2), 3.95 (1 H, m, 2-H), 4.50 (2 H, br s, exchangeable with D_2O, CO_2H and OH), 5.43 (1 H, br s, 3-H), and 7.11–7.96 (9 H, m, ArH); *m*/*z* 439 (M^+, 35%), 421 (M − H_2O, 92), 337 (M − $C_4H_6O_3$, 16), 266 (67), 265 (55), 182 (100), and 167 (59).

(3aRS,7SR,7aSR)-5-*Methyl*-7-(1′-*tosylindol*-3′-*yl*)-3a,4,7,7a-*tetrahydrophthalide* (**19**).—A solution of the hydroxy acid (**18**) (85 mg, 1.9 mmol) in anhydrous $CHCl_3$ (1 ml) and PPE (167 mg, 3.88 mmol) was refluxed for 0.5 h. The resulting dark green solution was cooled, poured into water, and extracted with diethyl ether. Purification of the crude product by chromatography on silica gel yielded the lactone (**19**) as a white solid (65 mg, 80%), ν_{max}(Nujol) 3 050, 1 770, 1 600, 1 390, 1 190, 1 140, 1 100, 760, and 690 cm^{-1}; δ_H(90 MHz) 1.82 (3 H, br s, 5-Me), 2.78 (3 H, s, Ar*Me*), 2.05–2.63 (2 H, m, 4-H_2), 3.04 (2 H, m, 3a- and 7a-H), 3.86 (1 H, dd, *J* 3.1 Hz, 8.5 Hz, 3-H), 3.98 (1 H, br m, 7-H), 4.22 (1 H, dd, *J* 5.7 Hz, 9.0 Hz, 3-H), 5.76 (1 H, br s, 6-H), and 7.13–7.95 (9 H, m, ArH); *m*/*z* 421 (M^+, 100%), 266 (M − $C_7H_7SO_2$, 64), 265 (64), 182 (95), and 67 (45).

(1RS,2SR,3SR)-1-*Methyl Hydrogen* 5-*Methyl*-3-(1′-*tosylindol*-3′-*yl*)*cyclohex*-4-*ene*-1,2-*dicarboxylate* (**14**).—*Method A*. The diacid (**13**) (0.52 g, 1.41 mmol) in anydrous methanol and BF_3·MeOH (20%; 60 ml) was heated under reflux for 1 h. The resulting solution was cooled, poured into water, and extracted with diethyl ether. The combined extracts were washed successively with water and brine, dried, and evaporated to dryness. Flash chromatography of the residue on silica gel eluted with diethyl ether–light petroleum (7:3) yielded the *monoester acid* (**14**) (0.378 g, 70.4%) as a pale yellow solid, m.p. 189–190 °C (from Et_2O–CH_2Cl_2) (Found: C, 64.4; H, 5.5; N, 3.1. $C_{25}H_{25}NO_6S$ requires C, 64.2; H, 5.4; N, 3.0%); λ_{max}(EtOH) 215 (4.42) and 258 nm (4.15); ν_{max}(Nujol) 3 650–2 500vbr, 1 735, 1 710, 1 600, 1 370, 1 290, 1 205, 1 180, 1 130, 1 025, 750, and 680 cm^{-1}; δ_H(90 MHz) 1.83 (3 H, s, 5-Me), 2.24 (3 H, s, Ar*Me*), 2.35–1.98 (2 H, br m, 6-H_2), 3.09 (1 H, m, 1-H), 3.54 (1 H, dd, $J_{1,2}$ 3.4, $J_{2,3}$ 5.8 Hz, 2-H), 3.66 (3 H, s, OMe), 4.05 (1 H, br m, 3-H), 5.50 (1 H, br s, 4-H), 5.49 (1 H, vbr, OH), and 7.09–8.00 (9 H, m, ArH); δ_C(22.5 MHz) 21.40 (Ar*Me*), 23.35 (5-Me), 29.42 (C-6), 35.59 (C-3), 42.26 and 43.77 (C-2 and -1), 52.06 (OMe), 113.93 (C-7′), 119.29 and 120.26 (C-4 and -4′), 123.14 (C-5′), 123.41 (C-3′), 124.38 and 124.65 (C-2′ and -6′), 126.82 (2 × C-2″), 129.69 (2 × C-3″), 130.40 (C-3′a), 135.27, 135.43, and 135.54 (C-5, -7′a, and -1″), 144.70 (C-4″), 173.63 (1-CO), and 173.90 (2-CO); *m*/*z* 469 (M^+, 65%), 435 (34), 360 (14), 337 (14), 270 (29), 208 (45), and 182 (100).

Method B. A stirred mixture of the anhydride (**5**) (2 g, 4.6 mmol) in methanol (10 ml), 1,2-dimethoxyethane (DME) (40 ml), and disodium hydrogen phosphate (20 g) was treated with sodium amalgam (5%; 11 g, 23 mmol) to afford the monoester (**14**) (1.5 g, 70%) and the unprotected monoester (**27**) (0.2 g, 14%), m.p. 173–175 °C (from Et_2O), after flash chromatography.

(1RS,2SR,3SR)-*Dimethyl* 5-*Methyl*-3-(1′-*tosylindol*-3′-*yl*)*cyclohex*-4-*ene*-1,2-*dicarboxylate* (**16**).—A solution of the monoester (**14**) (0.5 g, 1.07 mmol) in anhydrous methanol (10 ml), and BF_3·MeOH (20%; 1.13 ml, 2.14 mmol) was heated to reflux for 5 days. Work-up and purification of the crude product by chromatography yielded the diester (**16**) (58 mg, 12%) as a white powder, m.p. 75–76 °C; λ_{max}(EtOH) 212 (4.34) and 255 nm (4.07); ν_{max}(Nujol) 1 730, 1 720, 1 590, 1 470, 1 380, 1 190, 785, and 715 cm^{-1}; δ_H(90 MHz) 1.85 (3 H, br s, 5-Me), 2.31 (3 H, s, Ar*Me*), 2.32 (2 H, m, 6-H_2), 2.85 (3 H, s, 2-CO_2Me), 3.13 (1 H, m, 1-H), 3.51 (1 H, m, 2-H), 3.69 (3 H, s, 1-CO_2Me), 4.00 (1 H, br m, 3-H), 5.47 (1 H, br s, 4-H), and 7.09–8.04 (9 H, m, ArH); δ_C(22.5 MHz) 21.51 (Ar*Me*), 23.46 (5-Me), 29.42 (C-6), 35.75 (C-3), 42.09 and 43.99 (C-1 and -2), 50.44 (2-CO_2*Me*), 52.01 (1-CO_2*Me*), 113.71 (C-7′), 119.67 and 120.21 (C-4 and -4′), 123.03, 123.46, and 123.79 (C-2′, -5′, and -6′), 124.60 (C-3′), 126.82 (2 × C-2″), 129.80 (2 × C-3″), 130.23 (C-3′a), 135.16 and 135.43 (C-5, -7′a, and -1″), 144.75 (C-4″), 171.46 (2-CO), and 173.79 (1-CO); *m*/*z* 481 (M^+, 64%), 450 (M − CH_2O, 9), 421 (M − CH_3OH − CO, 14), 362 (30), 301 (28), 269 (91), 265 (100), 254 (41), 234 (49), 208 (72), and 182 (83).

(1RS,2SR,3SR)-1-*Ethyl Hydrogen* 5-*Methyl*-3-(1′-*tosylindol*-3′-*yl*)*cyclohex*-4-*ene*-1,2-*dicarboxylate* (**15**).—The procedure was similar to method B in the preparation of compound (**14**). Reaction of the anhydride (**5**) (200 mg, 0.46 mmol) in ethanol and dimethoxyethane with sodium amalgam yielded the ester (**15**) (143 mg, 65%) as a pale yellow solid, m.p. 89–91 °C; ν_{max}(Nujol) 3 500–2 700vbr, 1 725, 1 700, 1 600, 1 380, 1 175, 1 130, 980, 750, and 680 cm^{-1}; δ_H(90 MHz) 1.20 (3 H, t, *J* 7 Hz, OCH_2Me), 1.83 (3 H, br s, 5-Me), 2.25 (3 H, s, Ar*Me*), 2.30–2.71 (2 H, m, 6-H_2), 3.07 (1 H, ddd, $J_{1,2}$ 3.06, $J_{1,6}$ 5.91 and 10.72 Hz, 1-H), 3.53 (1 H, dd, $J_{1,2}$ 3.06, $J_{2,3}$ 6.57 Hz, 2-H), 4.14 (2 H, q, *J* 7.0 Hz, OCH_2Me), 4.22 (1 H, br m, 3-H), 4.60 (1 H, vbr s, OH), 5.49 (1 H, br s, 4-H), and 7.09–8.00 (9 H, m, ArH); δ_C(22.5 MHz) 14.09 (OCH_2Me), 21.40 (Ar*Me*), 23.35 (5-Me), 29.42 (C-6), 35.29 (C-3), 42.31 and 43.72 (C-2 and -1), 61.00 (OCH_2Me), 113.93 (C-7′), 119.29 (C-4′), 120.26 (C-4), 123.14 (C-5′), 123.52 (C-3′), 124.44 and 124.65 (C-2′ and -6′), 126.82 (2 × C-2″), 129.69 (2 × C-3″), 130.45 (C-3′a), 135.27, 135.43, and 135.65 (C-5, -7′a, and -1″), 144.70 (C-4″), 173.19 (CO), and 173.63 (CO); *m*/*z* 481 (*M*$^+$, 91%), 435 (*M* − H_2O − CO, 48), 363 (35), 271 (47), 208 (52), 182 (100), 167 (45), 155 (32), 116 (25), and 91 (48).

(7RS,11SR,12SR)-*Methyl* 9-*Methyl*-6-*oxo*-5-*tosyl*-6,7,8,11-*tetrahydro*-7,11-*methano*-5H-*cyclo*-*oct*[b]*indole*-12-*carboxylate* (**10**).—A stirred solution of the monoester (**14**) (98 mg, 0.21 mmol) in anhydrous $CHCl_3$ (1 ml) and PPE (182 mg, 0.42 mmol) was refluxed for 0.5 h. The resulting brown solution was cooled, poured into water (25 ml), and diethyl ether (25 ml) was added. The organic layer was washed successively with water and brine, dried, and evaporated to dryness. Chromatography of the residue on silica gel with diethyl ether as eluant yielded the *keto ester* (**10**) (59 mg, 62%) as a yellow solid, m.p. 170–171 °C (Found: *M*$^+$, 449.1294. $C_{25}H_{23}NO_5S$ requires *M*, 449.1295); λ_{max}(EtOH) 305 nm (3.81); ν_{max}(Nujol) 1 730, 1 675, 1 600, 1 545, 1 380, 1 195, and 705 cm^{-1}; δ_H(90 MHz) 1.51 (3 H, br s, 9-Me), 2.38 (3 H, s, Ar*Me*), 2.03–2.52 (2 H, br m, 8-H_2), 3.18 [1 H, t (dd), $J_{7,12}$ 2.63, $J_{11,12}$ 2.63 Hz, 12-H], 3.42 (1 H, m, 7-H), 3.50 (3 H, s, OMe), 4.09 (1 H, m, collapses to a d, $J_{10,11}$ 5.3 Hz on irradiation at δ 3.18, 11-H), 5.83 (1 H, br d, $J_{10,11}$ 5.3 Hz, collapses to a br s on irradiation at δ 4.09, 10-H), 7.22–8.23 (7 H, m, ArH), and 8.28 (1 H, d, *J* 7.0 Hz, 4-H); δ_C(22.5 MHz) 21.56 (Ar*Me*), 22.70 (9-Me), 31.15 (C-11), 33.75 (C-8), 43.77 and 47.02 (C-7 and -12), 52.11 (OMe), 116.31 (C-4), 121.08 (C-10), 122.97 (C-1), 123.89 (C-2), 125.90 (C-11a), 127.79 (2 × C-2′), 129.31 (2 × C-3′), 129.42 (C-3 and C-11b), 130.61 (C-5a), 134.24 (C-9), 136.95 (C-1′), 142.75 (C-4a), 144.43 (C-4′), 172.22 (CO), and 182.01 (C-6); *m*/*z* 449 (*M*$^+$, 100%), 385 (42), 362 (12), 298 (21), 294 (*M* − $C_7H_7SO_2$, 34), 266 (44), 234 (67), and 206 (43).

(7RS,11SR,12SR)-*Ethyl* 9-*Methyl*-6-*oxo*-5-*tosyl*-6,7,8,11-*tetrahydro*-7,11-*methano*-5H-*cyclo*-*oct*[b]*indole*-12-*carboxylate* (**11**).—The procedure was similar to the preparation of compound (**10**). The keto ester (**15**) (122 mg, 0.25 mmol) yielded the keto ester (**11**) (56 mg, 48%) as a yellow solid, m.p. 68–69 °C; ν_{max}(Nujol) 1 730, 1 675, 1 600, 1 550, 1 375, 1 180, 1 190, 1 090, 750, and 680 cm^{-1}; δ_H(90 MHz) 0.99 (3 H, t, *J* 7.0 Hz, OCH_2Me), 1.52 (3 H, s, 9-Me), 2.38 (3 H, s, Ar*Me*), 2.04–2.67 (2 H, br m, 8-H_2), 3.16 [1 H, t (dd), $J_{7,12}$ 2.62, $J_{11,12}$ 2.62 Hz, 12-H], 3.47 (1 H, br d, *J* 6.6 Hz, 7-H), 3.95 (2 H, q, *J* 7.0 Hz, OCH_2Me), 3.99 (1 H, br m, 11-H), 5.83 (1 H, br d, $J_{11,12}$ 6.12 Hz, collapses to a s on irradiation at δ 3.99, 10-H), 7.23–8.15 (7 H, m, ArH), and 8.28 (1 H, d, *J* 7.9 Hz, 4-H); δ_C(22.5 MHz) 13.87 (OCH_2Me), 21.56 (Ar*Me*), 22.70 (9-Me), 31.20 (C-11), 33.80 (C-8), 43.88 and 47.08 (C-7 and -12), 61.00 (OCH_2Me), 116.20 (C-4), 121.02 (C-10), 123.03 (C-1), 123.84 (C-2), 125.95 (C-11a), 127.85 (2 × C-2′), 132.31 (2 × C-3′ and C-3), 134.24 (C-9 and -11b), 137.00 (C-1′), 140.20 (C-5a), 142.69 (C-4a), 144.43 (C-4″), 171.73 (CO), and 187.11 (C-6); *m*/*z* 463 (*M*$^+$, 100%), 399 (55), 363 (20), 307 (43), 298 (32), 280 (55), 234 (85), 208 (35), 207 (43), 206 (100), and 91 (45).

(1RS,2SR,3SR)-3-(1′-*Methoxyindol*-3′-*yl*)-5-*methylcyclohex*-4-*ene*-1,2-*dicarboxylic Anhydride* (**21**).—A solution of the diene (**7**) (37 g, 17.4 mmol) and maleic anhydride (2.56 g, 26 mmol) in anhydrous benzene (100 ml) was warmed at 80 °C for 1 h. Removal of the solvent and column chromatography on silica gel with diethyl ether–light petroleum (1:1) as eluant afforded the adduct (**21**) as a white solid (4.76 g, 88%), m.p. 94–95 °C (from Et_2O–light petroleum); λ_{max}(EtOH) 222 (4.32), 275 (3.52), 290 (3.56), and 298 nm (3.52); ν_{max}(Nujol) 3 040, 1 855, 1 780, 1 450, 1 380, 1 230, 1 220, 1 000, 950, 905, and 745 cm^{-1}; δ_H(90 MHz) 1.87 (3 H, s, 5-Me), 2.29 and 2.80 (2 H, ABq, *J* 16.19 Hz, 6-H_2), 3.42–3.52 (2 H, m, 1- and 2-H), 4.04 (4 H, s, OMe and 3-H), and 7.01–7.59 (5 H, m, ArH); δ_C(22.5 MHz) 23.36 (Me), 27.52 (C-6), 32.34 (C-3), 40.03 and 45.13 (C-1 and -2), 65.98 (OMe), 108.57 (C-7′), 109.05 (C-3′), 118.80 (C-4′), 120.00 (C-4), 122.65 (C-5′), 122.87 (C-6′), 123.03 (C-3′a), 124.17 (C-2′), 132.56 (C-7′a), 135.76 (C-5), 170.87 (2-CO), and 174.01 (1-CO); *m*/*z* 311 (*M*$^+$, 40%), 281 (*M* − OCH_2, 10), 213 (*M* − $C_4H_2O_3$, 20), 182 (100), 167 (45), and 116 (13).

(1RS,2SR,3SR)-1-*Methyl Hydrogen* 3-(1′-*Methoxyindol*-3′-*yl*)-5-*methylcyclohex*-4-*ene*-1,2-*dicarboxylate* (**22**) *and* (1RS,2SR,3SR)-3-(1′-*Methoxyindol*-3′-*yl*)-5-*methylcyclohex*-4-*ene*-1,2-*dicarboxylic Acid* (**23**).—A stirred solution of the anhydride (**21**) (0.93 g, 3 mmol), absolute methanol (2.43 ml, 60 mmol), and 2M-HCl (2.25 ml) in THF (30 ml) was heated under reflux for 2 h. The resulting solution was cooled, poured into water, and extracted with dichloromethane (100 ml). The extract was washed successively with water and brine, dried, and evaporated to dryness. Chromatography of the residue on silica gel with diethyl ether as eluant gave, first, the acid ester (**22**) (0.44 g, 42.5%). Recrystallization from diethyl ether–light petroleum gave *compound* (**22**) as white needles, m.p. 164–167 °C (Found: *M*$^+$, 343.1419. $C_{19}H_{21}NO_5$ requires *M*, 343.1418); λ_{max}(EtOH) 221 (4.54), 276 (3.71), and 290 nm (3.76); ν_{max}(Nujol) 3 180–2 560vbr, 1 740, 1 710, 1 450, 1 255, 1 200, 1 170, 950, and 740 cm^{-1}; δ_H(90 MHz) 1.80 (3 H, s, 5-Me), 2.13–2.91 (2 H, m, 6-H_2), 3.00 (1 H, ddd, $J_{1,6}$ 6.13 and 10.94, $J_{1,2}$ 3.50 Hz, 1-H), 3.54 (1 H, dd, $J_{1,2}$ 3.06, $J_{2,3}$ 6.57 Hz, 2-H), 3.67 (3 H, s, CO_2Me), 3.90 (3 H, s, OMe), 4.07 (1 H, br s, 3-H), 5.49 (1 H, br s, 4-H), and 7.05–7.60 (4 H, m, ArH); δ_C(22.5 MHz) 23.35 (5-Me), 29.31 (C-6), 35.75 (C-3), 42.31 and 44.80 (C-1 and -2), 51.95 (CO_2Me), 65.05 (OMe), 108.45 (C-7′), 112.41 (C-3′), 118.80 (C-4′), 119.67 (C-4), 121.51 and 121.62 (C-2′ and -5′), 122.38 (C-6′), 123.46 (C-3′a), 112.40 (C-7′a), 134.51 (C-5), 173.73 (CO), and 175.95 (CO); *m*/*z* 343 (*M*$^+$, 49%), 266 (*M* − C_6H_5, 18), 208 (34), 182 (100), 167 (47), 116 (10), and 93 (13).

Further elution furnished the diacid (**23**) (0.10 g, 10%), m.p. 160–162 °C (from CH_2Cl_2–Et_2O); ν_{max}(Nujol) 3 430, 3 500–2 500vbr, 1 710, 1 450, 1 210, and 1 180, 950, and 740 cm^{-1}; δ_H(90 MHz, [$^2H_6$]acetone) 1.79 (3 H, br s, 5-Me), 2.18 (1 H, br dd, $J_{1,6}$ 5.69, $J_{6,6}$ 22.75 Hz, 6-H), 2.49 (1 H, br dd, $J_{1,6}$ 11.21, $J_{6,6}$ 22.75 Hz, 6-H), 3.15 (1-H, ddd, $J_{1,2}$ 3.5, $J_{1,6}$ 5.69 and 11.21 Hz, 1-H), 3.59 (1-H, dd, $J_{1,2}$ 3.5, $J_{2,3}$ 6.12 Hz, 2-H), 3.99 (3-H, s, OMe), 4.16 (1 H, br s, 3-H), 5.52 (1 H, br s, 4-H), 6.37 (2 H, vbr, exchangeable with D_2O, 2 × OH), and 6.93–7.71 (5 H, m, ArH); δ_C(22.5 MHz; [$^2H_6$]acetone) 23.57 (5-Me), 30.17 (C-6), 36.46 (C-3), 42.47 and 45.45 (C-1 and -2), 65.82 (OMe), 108.89 (C-7′), 113.98 (C-3′), 120.05 (C-4 and -4′), 122.49 and 122.65 (C-2′ and -5′), 122.81 (C-6′), 122.65 (C-3′a), 133.37 (C-7′a), 134.95 (C-5), 174.00 (2-CO), and 175.52 (1-CO); *m*/*z* 329 (*M*$^+$, 33%), 311 (*M* − H_2O, 10), 299 (*M* − CH_2O, 23), 231 (10), 254 (17), 208 (43), 182 (100), and 167 (46).

Methyl 5-*Methoxy*-9-*methyl*-6-*oxo*-5,6,6aβ,7β,8,10aβ-*hexa*-

hydroindeno[2,1-b]*indole-7-carboxylate* (**24**) *and* (7RS,11SR,-12SR)-*Methyl 5-Methoxy-9-methyl-6-oxo-6,7,8,11-tetrahydro-7,11-methano-5H-cyclo-oct*[b]*indole-1,2-carboxylate* (**25**).—A solution of monoester (**22**) (0.7 g, 2.04 mmol) and PPE (1.70 g, 4.08 mmol) in anhydrous chloroform (2.5 ml) was refluxed for 0.5 h. The solution was cooled and diethyl ether (50 ml) was added. The organic layer was washed successively with water and brine, dried, and evaporated to dryness. Successive flash chromatography of the residue on silica gel with diethyl ether–light petroleum (1:1) as eluant afforded, first, the ketone (**24**) (0.32 g, 48%) as a pale yellow powder. Recrystallization from diethyl ether gave an analytical sample of *compound* (**24**), m.p. 146–147.5 °C (Found: C, 70.1; H, 6.0; N, 4.3. $C_{19}H_{19}NO_4$ requires C, 70.14; H, 5.89; N, 4.31%); λ_{max}(EtOH) 205 (4.46), 234 (4.40), and 300 nm (4.44); ν_{max}(Nujol) 1 720, 1 680, 1 610, 1 560, 1 530, 1 390, 1 190, and 790 cm^{-1}; δ_H(90 MHz) 1.62 (3 H, s, 9-Me), 2.16 (2 H, br d, *J* 7.88 Hz, 8-H_2), 2.88 (1 H, td, $J_{6a,7}$ 4.81, $J_{7,8}$ 7.88 Hz, 7-H), 3.83 (3 H, s, CO_2Me), 3.91 (1 H, dd, $J_{6a,7}$ 5.25, $J_{6a,10a}$ 5.25 Hz, 6a-H), 4.16 (4 H, m + s, 10a-H and OMe), 5.68 (1 H, br s, 10-H), and 7.07–7.43 (4 H, m, ArH); δ_C(22.5 MHz) 23.78 (9-Me), 28.22 (C-8), 36.46 (C-10a), 40.79 and 51.84 (C-7 and -6a), 52.76 (CO_2Me), 66.31 (OMe), 110.73 (C-4), 118.86 (C-10b), 120.91 (C-10), 121.24 (C-1), 121.51 (C-2), 127.69 (C-3), 133.59 (C-10c), 133.86 (C-9), 140.69 (C-5a), 143.83 (C-4a), 173.63 (7-CO), and 191.02 (C-6); *m/z* 325 (M^+, 41%), 294 ($M - OCH_3$, 15), 266 ($M - C_2H_3O_2$, 13), 238 (23), 235 ($M - C_7H_6$, 25), 234 ($M - C_7H_7$, 100), 207 (27), 206 (37), and 59 (16).

Further elution gave the isomeric *ketone* (**25**) (0.11 g, 16%) as a white solid. Recrystallization of compound (**25**) from dichloromethane–diethyl ether yielded white prisms, m.p. 200–201 °C (Found: M^+, 325.1312. $C_{19}H_{19}NO_4$ requires *M*, 325.1313); ν_{max}(Nujol) 1 720, 1 645, 1 610, 1 525, 1 465, 1 440, 1 280, 1 235, 1 200, 1 050, and 790 cm^{-1}; δ_H(90 MHz) 1.57 (3 H, s, 9-Me), 2.21 (1 H, br d, *J* 18.81 Hz, 8-H), 2.61 (1 H, dd, $J_{7,8}$ 7.43, $J_{8,8}$ 18.81 Hz, 8-H), 3.25 (1 H, dd, $J_{7,12}$ 2.84, $J_{11,12}$ 2.84 Hz, 12-H), 3.47 (1 H, d, *J* 8.46 Hz, 7-H), 3.52 (3 H, s, CO_2Me), 4.00 (1 H, m, 11-H), 4.10 (3 H, s, OMe), 5.93 (1 H, br d, *J* 4.81 Hz, 10-H), and 7.06–7.73 (4 H, m, ArH); δ_C(22.5 MHz) 22.81 (9-Me), 31.04 (C-11), 33.26) (C-8), 43.93 and 48.43 (C-7 and -12), 52.01 (CO_2Me), 65.71 (OMe), 109.76 (C-4), 119.56 (C-11a), 120.97 (C-10), 121.19 (C-1), 124.87 (C-2), 125-95 (C-11b), 127.58 (C-3), 130.94 (C-5a), 132.62 (C-9), 135.76 (C-4a), 172.81 (12-CO), and 189.12 (C-6); *m/z* 325 (M^+, 100%), 295 ($M - CH_2O$, 15), 266 ($M - C_2H_3O_2$, 22), 234 ($M - C_7H_7$, 46), 208 (32), 207 (30), 206 (53), 180 (19), and 144 (23).

(1RS,2SR,3SR)-3-(*Indol-3′-yl*)-5-*methylcyclohex-4-ene*-1,2-*dicarboxylic Acid* (**26**).—A solution of the anhydride (**5**) (5 g, 11.5 mmol) in methanol (90 ml), KOH (16.8 g), and water (10 ml) was heated under reflux for 1 h. The resulting solution was cooled, poured into water (50 ml), and diethyl ether (100 ml) was added. The aqueous layer was acidified with dil. HCl and was extracted with diethyl ether. The combined extracts were washed successively with water and brine, dried, and evaporated to dryness to yield the diacid (**26**) (3.6 g, 97%) as a pale yellow powder, m.p. 133–134 °C; λ_{max}(EtOH) 221 (4.86), 270 (4.17), and 288 nm (4.13); ν_{max}(Nujol) 3 400, 3 350–2 850br, 3 020, 1 700br, 1 220, and 730 cm^{-1}; δ_H(90 MHz) 1.78 (3 H, s, 5-Me), 2.17–2.34 and 2.57–2.68 (2 H, m, 6-H_2), 3.05 (1 H, m, 1-H), 3.51 (1 H, m, 2-H), 4.16 (1 H, br m, 3-H), 5.52 (1 H, br s, 4-H), 6.28 (2 H, vbr, 2 × CO_2H), 6.87 (1 H, d, *J* 1.97 Hz, 2′-H), 6.95–7.62 (4 H, m, ArH), and 8.00 (1 H, br s, NH); δ_C(22.5 MHz) 23.48 (5-Me), 29.85 (C-6), 36.13 (C-3), 42.15 and 45.18 (C-1 and -2), 111.65 (C-7′), 166.07 (C-3′), 118.91 and 118.99 (C-4′ and -4), 121.56 (C-5′), 122.73 and 123.19 (C-2′ and -6′), 127.50 (C-3′a), 133.94 and 136.76 (C-5 and -7′a), 175.20 (2-CO), and 176.28 (1-CO); *m/z* 299 (M^+, 77%), 281 ($M - H_2O$, 39), 254 ($M - CHO_2$, 29), 208 (52), 183 ($M - C_4H_4O_4$, 81), 182 ($M - C_4H_4O_4 - H$, 100), and 168 (81).

(1RS,2SR,3SR)-1-*Methyl Hydrogen* 3-(*Indol-3′-yl*)-5-*methylcyclohex-4-ene*-1,2-*dicarboxylate* (**27**) *and Dimethyl* 3-(*Indol-3′-yl*)-5-*methylcyclohex-4-ene*-1,2-*dicarboxylate* (**28**).—*Method A*. A solution of the diacid (**26**) (6.57 g, 22 mmol) in anhydrous methanol (220 ml) containing BF_3·MeOH (20%; 24.66 ml, 44 mmol) was heated under reflux for 1 h. The resulting green solution was cooled, poured into water, and extracted with diethyl ether. The combined extracts were washed successively with water and brine, dried, and evaporated to dryness. Flash chromatography of the residue on silica gel with diethyl ether–light petroleum (7:3) as eluant yielded, first, the *monoester* (**27**) (5.27 g, 73%) as a yellow solid, m.p. 173–175 °C (from Et_2O) (Found: C, 69.2; H, 6.3; N, 4.5. $C_{18}H_{19}NO_4$ requires C, 69.0; H, 6.1; N, 4.5%); λ_{max}(EtOH) 220 (4.52), 280 (3.72), and 290 nm (3.62); ν_{max}(Nujol) 3 400, 3 500–2 600vbr, 1 720, 1 270, 1 220, 1 190, 765, and 750 cm^{-1}; δ_H(90 MHz) 1.79 (3 H, br s, 5-Me), 2.08–2.35 and 2.54–2.87 (2 H, m, 6-H_2), 3.12 (1 H, ddd, $J_{1,2}$ 3.94, $J_{1,6}$ 6.78 and 10.83 Hz, 1-H), 3.55 (1 H, dd, $J_{1,2}$ 3.94, $J_{2,3}$ 6.12 Hz, 2-H), 3.69 (3 H, s, OMe), 4.16 (1 H, br m, 3-H), 5.50 (1 H, br s, 4-H), 6.40 (1 H, vbr, exchangeable with D_2O, OH), 6.84 (1 H, d, *J* 2.63 Hz, collapses to a s in D_2O, 2′-H), 7.01–7.28 (3 H, m, 4′-, 5′-, and 6′-H), 7.47 (1 H, m, 7′-H), and 8.14 (1 H, br s, exchangeable with D_2O, NH); δ_C(22.5 MHz) 23.40 (5-Me), 29.20 (C-6), 35.65 (C-3), 42.31 and 44.91 (C-2 and -1), 52.06 (OMe), 111.33 (C-7′), 115.99 (C-3′), 118.48 and 119.34 (C-4 and -4′), 121.89 (C-5′), 122.05 (C-6′), 122.65 (C-2′), 126.98 (C-3′a), 133.97 (C-5), 136.08 (C-7′a), 174.22 (1-CO), and 176.50 (2-CO); *m/z* 313 (M^+, 100%), 268 ($M - CO_2H$, 22), 208 (61), 183 (44), 182 (61), 168 (56), 167 (22), and 117 (36).

Further elution furnished the diester (**28**) (1.2 g, 16%) as a pale yellow solid, m.p. 80–83 °C; ν_{max}(Nujol) 3 360, 3 040, 1 720, 1 380, 1 190, 1 160, and 740 cm^{-1}; δ_H(90 MHz) 1.82 (3 H, br s, 5-Me), 2.10–2.38 and 2.62–2.80 (2 H, m, 6-H_2), 3.01 (1 H, m, 1-H), 3.05 (3 H, s, 2-CO_2Me), 2.59 (1 H, m, 2-H), 3.66 (3 H, s, 1-CO_2Me), 4.14 (1 H, br m, 3-H), 5.56 (1 H, br s, 4-H), 6.87 (1 H, d, *J* 1.75 Hz, 2′-H), 6.97–7.32 (3 H, m, 4′-, 5′-, and 6′-H), 7.57 (1 H, m, 7′-H), and 8.44 (1 H, br s, NH); δ_C(22.5 MHz) 23.35 (5-Me), 29.62 (C-6), 35.97 (C-3), 42.20 and 44.96 (C-1 and -2), 50.60 (2-CO_2Me), 51.84 (1-CO_2Me), 111.33 (C-7′), 116.15 (C-3′), 118.75 and 119.02 (C-4 and -4′), 121.62 (C-5′), 122.27 (C-2′ and -6′), 126.93 (C-3′a), 133.86 (C-7′a), 136.30 (C-5), 172.54 (2-CO), and 174.33 (1-CO); *m/z* 327 (M^+, 19%), 255 (24), 208 (50), 144 (100), and 117 (50).

Method B. A mixture of the anhydride (**5**) (0.5 g, 1.15 mmol) in DME (10 ml), methanol (5 ml), disodium hydrogen phosphate (5 g), and sodium amalgam (5%; 5 g, 10.8 mmol) was stirred at room temperature for 1.5 h. The resulting mixture was poured into water, acidified with dil. HCl, and extracted with diethyl ether. The combined extracts were washed successively with water and brine, dried, and evaporated to dryness. The crude product was chromatographed on silica gel with diethyl ether as eluant to yield the monoester (**27**) (295 mg, 82%).

Methyl 9-*Methyl-6-oxo-5,6aβ,7β,8,10aβ-hexahydroindeno*-[2,1-b]*indole-7-carboxylate* (**29**).—To a solution of PPE (0.75 g, 1.88 mmol) in anhydrous $CHCl_3$ (1 ml) was added dropwise a solution of the monoester (**27**) (0.3, 0.94 mmol) in anhydrous $CHCl_3$ (2 ml). After being refluxed for 0.5 h, the resulting solution was poured into water and extracted with diethyl ether. Work-up and purification of the reaction product by chromatography on silica gel yielded the *keto* ester (**29**) (189 mg, 68%) as needles (from CH_2Cl_2–Et_2O), m.p. 227–229 °C (Found: C, 73.1; H, 6.0; N, 4.6. $C_{18}H_{17}NO_3$ requires C, 73.2; H, 5.8; N, 4.7%); λ_{max}(EtOH) 205 (4.39), 231 (4.29), and 303 nm (4.35); ν_{max}(Nujol) 3 220, 3 080, 1 730, 1 670, 1 620, 1 570, 1 540, 1 330, 1 200, 760, 750, and 740 cm^{-1}; δ_H(90 MHz) 1.62 (3 H, br s, 9-Me), 2.15 (2 H, br d, *J* 7.44 Hz, 8-H_2), 2.92 (1 H, m, 7-H), 3.87 (3 H, s, OMe), 4.00 [1 H, t (dd), $J_{6a,7}$ 5.3, $J_{6a,10a}$ 5.3 Hz, 6a-H),

4.26 (1 H, br m, 10a-H), 5.75 (1 H, br s, 10-H), 7.17–7.79 (4 H, m, ArH), and 9.72 (1 H, br s, NH); δ_C[22.5 MHz; $CDCl_3$ and $(CD_3)_2SO$] 23.67 (9-Me), 28.12 (C-8), 36.30 (C-10a), 40.90 (C-7), 51.63 (C-6a), 52.49 (OMe), 114.03 (C-4), 120.32 (C-1), 121.19 (C-10), 121.56 (C-2), 122-38 (C-10b), 126.93 (C-3), 132.89 (C-9), 136.41 (C-10c), 144.05 (C-5a), 147.84 (C-4a), 173.90 (7-CO), and 193.29 (C-6); *m/z* 295 (M^+, 100%), 264 (M − OMe, 16), 236 ($M - C_2H_3O_2$, 71), 235 ($M - CH_3OH$ − CO, 91), 220 (27), and 208 (71).

(1RS,2SR,3SR)-2-*Methyl Hydrogen* 3-(*Indol-3′-yl*)-5-*methylcyclohex*-4-*ene*-1,2-*dicarboxylate* (**30**).—A mixture of the diester (**28**) (1.10 g, 3.2 mmol) in THF (32 ml), 3M-aq. KOH (32 ml), and tetrabutylammonium hydrogen sulphate (cat.) was heated under reflux for 2 h. Work-up and purification by chromatography afforded *monoester* (**30**) (517 mg, 52%) as a white solid, m.p. 79–81 °C (Found: M^+, 313.1312. $C_{18}H_{19}NO_4$ requires M, 313.1313); λ_{max}(EtOH) 219 (4.17), 280 (3.42), and 288 nm (3.32); ν_{max}(Nujol) 3 390, 3 030, 1 710, 1 450, 1 220, 1,180, and 750 cm^{-1}; δ_H(90 MHz) 1.83 (3 H, 5-Me), 2.22–2.40 and 2.68–2.81 (2 H, m, 6-H_2), 3.05 (1 H, m, 1-H), 3.09 (3 H, s, OMe), 3.56 (1 H, dd, $J_{1,2}$ 3.3, $J_{2,3}$ 6.4 Hz, 2-H), 4.19 (1 H, m, 3-H), 5.55 (1 H, br s, 4-H), 6.89 (1 H, d, J 1.8 Hz, collapses to a s in D_2O, 2′-H), 6.98–7.34 (3 H, m, 4′-, 5′-, and 6′-H), 7.56 (1 H, m, 7′-H), 8.23 (1 H, br s, exchangeable with D_2O, NH), and 9.78 (1 H, vbr, exchangeable with D_2O, CO_2H); δ_C(22.5 MHz) 23.35 (5-Me), 29.47 (C-6), 35.81 (C-3), 41.77 and 44.75 (C-2 and -1), 50.98 (OMe), 111.22 (C-7′), 116.09 (C-3′), 118.75 and 119.18 (C-4, and -4′), 121.78 (C-5′), 122.05 (C-6′), 122.49 (C-2′), 126.82 (C-3′a), 133.92 (C-5), 136.19 (C-7′a), 172.98 (2-CO), and 179.04 (1-CO); *m/z* 313 (M^+, 100%), 254 ($M - C_2H_3O_2$, 27), 208 (48), 183 (36), 182 (52), 168 (50), and 119 (39).

(7RS,11SR,12SR)-*Methyl* 9-*Methyl*-6-*oxo*-6,7,8,11-*tetrahydro*-7,11-*methano*-5H-*cyclo-oct*[b]*indole*-12-*carboxylate* (**31**).—To a solution of PPE (0.55 g, 1.28 mmol) in anhydrous $CHCl_3$ (0.5 ml) was added dropwise a solution of the monoester (**30**) (0.2 g, 0.64 mmol) in anhydrous $CHCl_3$ (1.5 ml). The resultant solution was heated under reflux for 0.5 h, cooled, then poured into water. The aq. layer was extracted with diethyl ether. The combined extracts were washed successively with water and brine, dried, and evaporated to dryness. Chromatography of the residue on silica gel with diethyl ether–light petroleum as eluant gave the *ester* (**31**) (140 mg, 74%) as a yellow solid, m.p. 247–248.5 °C (from CH_2Cl_2–Et_2O) (Found: M^+, 295.1209. $C_{18}H_{17}NO_3$ requires M, 295.1207); λ_{max}(EtOH) 205 (4.48), 236 (4.41), and 315 nm (4.42); ν_{max}(Nujol) 3 250, 3 040, 1 720, 1 640, 1 620, 1 560, 1 520, 1 370, 1 330, 1 260, 1 230, 1 200, 1 150, 1 030, 1 000, and 740 cm^{-1}; δ_H[90 MHz; $(CD_3)_2SO$] 1.53 (3 H, br s, 9-Me), 2.00 (1 H, br d, $J_{8,8}$ 18.82 Hz, 8-H), 2.50–2.77 (1 H, br dd, $J_{7,8}$ 7.0, $J_{8,8}$ 18.82 Hz, 8-H), 3.25–3.36 (2 H, m, 7- and 12-H), 3.43 (3 H, s, OMe), 4.10 (1 H, m, 11-H), 5.96 (1 H, d, $J_{10,11}$ 6.57 Hz, 10-H), 6.97–7.43 (3 H, m, 1-, 2-, and 3-H), 7.75 (1 H, br d, J 7.9 Hz, 4-H), and 11.62 (1 H, br s, NH); δ_C(22.5 MHz; [$^2H_6$]acetone) 22.54 (9-Me), 30.39 (C-11), 32.34 (C-8), 42.80 and 48.16 (C-7 and -12), 51-68 (OMe), 112.95 (C-4), 119.94 and 120.91 (C-1 and -10), 123.89 (C-11a), 135.57 (C-2), 126.28 (C-3), 129.09 (C-11b), 131.37 (C-9), 132.56 (C-5a), 138.25 (C-4a), 172.76 (12-CO), and 190.31 (6-CO); *m/z* 295 (M^+, 100%), 208 (54), and 144 (31).

(1RS,2SR,3SR)-3-(*Indol-3′-yl*)-5-*methylcyclohex*-4-*ene*-1,2-*dicarboxylic Anhydride* (**32**).—A stirred solution of the freshly prepared crude diene (**8**)[3] and maleic anhydride (2.8 g, 28.2 mmol) in anhydrous benzene (10 ml) was stirred at room temperature for 1 h and warmed at 60 °C for 1 h. Removal of solvent and successive chromatography on silica gel with diethyl ether–light petroleum (3:1) as eluant gave the adduct (**32**) (1.16 g, 30%) as a yellow solid, m.p. 86–90 °C; λ_{max}(EtOH) 22 (4.53), 280 (3.85), and 290 nm (3.81); ν_{max}(Nujol) 3 360br, 1 750, 1 700, 1 610, and 790 cm^{-1}; δ_H(90 MHz) 1.85 (3 H, s, 5-Me), 4.03 (1 H, br m, 3-H), 3.59–3.23 (2 H, m, 1- and 2-H), 4.03 (1 H, br m, 3-H), 5.87 (1 H, br s, 4-H), 6.89 (1 H, d, J 2.4 Hz, 2′-H), 6.99–7.58 (4 H, m, ArH), and 8.11 (1 H, br s, NH); δ_C(22.5 MHz) 23.32 (5-Me), 27.74 (C-6), 32.56 (C-3), 40.25 and 45.10 (C-1 and -2), 111.54 (C-7′), 113.11 (C-3′), 118.40 (C-4′), 119.61 (C-4), 122.35 (C-5′), 123.46 and 124.44 (C-2′ and -6′), 126.44 (C-3′a), 135.84 (C-5), 136.55 (C-7′a), 171.11 (2-CO), and 174.28 (1-CO); *m/z* 281 (M^+, 84%), 218 (27), 194 (23), 183 ($M - C_4H_2O_3$, 95), 182 ($M - C_4H_2O_3$ − H, 100), and 168 (100).

(1RS,2SR,3SR)-1-*Methyl Hydrogen* 3-(1′-*Benzylindol*-3′-*yl*)-5-*methylcyclohex*-4-*ene*-1,2-*dicarboxylate* (**35**).—To a solution of the anhydride (**32**) (1.16 g, 4.1 mmol) and TBAHS (1.39 g, 4.1 mmol) in benzene (41 ml) at 0 °C was added dropwise aq. NaOH (50%; 4.1 ml). The resulting mixture was vigorously stirred at room temperature for 10 min and benzyl bromide (0.58 ml, 4.92 mmol) was added dropwise. The resulting pale brown solution was stirred at room temperature for 0.5 h, poured into water, and extracted with diethyl ether. The ethereal layer was discarded and the aq. layer was acidified by dil. HCl and extracted with diethyl ether. The combined extracts were washed successively with water and brine, dried, and evaporated to give compound (**33**) as a pale yellow-brown solid (0.502 g) which was used for the following reaction without further purification.

The crude anhydride (**33**), anhydrous methanol (13 ml), and BF_3·MeOH (20%; 2.19 ml, 12.3 mmol) were heated under reflux for 2 h. Usual work-up and purification by chromatography on a silica gel column eluted with diethyl ether–light petroleum (7:3) yielded the monoester (**35**) (0.745 g, 45%) as a brown, amorphous solid, m.p. 167–169 °C; ν_{max}(Nujol) 3 500–2 550vbr, 1 700br, 1 380, and 740 cm^{-1}; δ_H(90 MHz) 1.79 (3 H, s, 5-Me), 2.08–3.34 and 2.56–2.88 (2 H, m, 6-H_2), 3.09 (1 H, m, 1-H), 5.42 (1 H, m, 2-H), 3.61 (3 H, s, OMe), 4.16 (1 H, br m, 3-H), 5.04 (2 H, br s, NCH_2Ph), 5.58 (1 H, br s, 4-H), 6.77 (1 H, s, 2′-H), 6.86–7.22 and 7.53–7.62 (9 H, m, ArH); δ_C(22.5 MHz) 23.35 (5-Me), 29.31 (C-6), 35.70 (C-3), 42.36 and 44.91 (C-2 and -1), 49.73 (C-1″), 51.84 (OMe), 109.86 (C-7′), 115.39 (C-3′), 118.64 and 119.07 (C-4 and -4′), 121.62 (C-5′), 122.11 (C-2′), 126.33 (C-3″), 126.77 (C-6′), 127.25 (C-3′a), 127.69 (C-5″), 128.66 (C-4″), 134.08 (C-2″), 136.25 (C-5), 137.76 (C-7′a), 173.84 (1-CO), and 176.33 (2-CO).

Methyl 5-*Benzyl*-9-*methyl*-6-*oxo*-5,6aβ,7β,8,10aβ-*hexahydroindeno*[2,1-b]*indole*-7-*carboxylate* (**37**).—The monoester (**35**) (127.6 mg, 0.32 mmol), anhydrous $CHCl_3$ (1.2 ml), and PPE (0.28 g, 0.64 mol) were heated under reflux for 0.5 h. Work-up and purification of the reaction product by chromatography afforded the *keto ester* (**37**) (78 mg, 63%), m.p. 152.5–153 °C (from Et_2O) (Found: M^+, 385.1674. $C_{25}H_{23}NO_3$ requires M, 385.1676); λ_{max}(EtOH) 204 (4.40), 235 (4.14), and 304 nm (4.17); ν_{max}(Nujol) 3 080, 3 050, 3 030, 1 735, 1 685, 1 600, 1 540, 1 470, 1 385, 1 220, 1 200, 1 185, 785, 765, and 740 cm^{-1}; δ_H(90 MHz) 1.62 (3 H, s, 9-Me), 2.16 (2 H, br d, J 8.1 Hz, 8-H_2), 2.89 (1 H, td, $J_{6a,7}$ 5.03, $J_{7,8}$ 7.88 Hz, 7-H), 3.82 (3 H, s, OMe), 3.91 [1 H, t(dd), $J_{6a,7}$ 5.47, $J_{6a,10a}$ 5.47 Hz, 6a-H], 4.18 (1 H, br m, 10a-H), 5.32 and 5.67 (2 H, ABq, J 15.9 Hz, PhCH_2N), 5.74 (1 H, br s, 10-H), 6.96–7.31 (8 H, m, ArH), and 7.73 (1 H, br d, J 7.22 Hz, 4-H); δ_C(22.5 MHz) 23.81 (9-Me), 28.17 (C-8), 35.97 (C-10a), 41.04 (C-7), 47.54 (NCH_2), 51-79 (C-6a), 52.93 (OMe), 111.95 (C-4), 120.59 (C-1), 121.27 and 121.73 (C-2 and -10), 122.68 (C-10b), 126.96 (C-3), 127.17 (2 × C-3′), 127.50 (C-5′), 128.61 (2 × C-4′), 133.46 (C-9), 136.30 (C-10c), 137.17 (C-2′), 144.05 (C-5a), 146.89 (C-4a), 173.82 (7-CO), and 193.21 (C-6); *m/z* 385 (M^+, 100%), 326 ($M - C_2H_3O_2$, 33), 325 ($M - CH_3OH$ − CO, 40), 298 (18), 234 (29), and 91 (92).

(1RS,2SR,3SR)-5-*Methyl*-3-(1′-*methylindol*-3′-*yl*)*cyclohex*-4-*ene*-1,2-*dicarboxylic Anhydride* (**34**).—To a solution of the anhydride (**32**) (0.7 g, 2.46 mmol) and TBAHS (0.84 g, 2.46 mmol) in benzene (25 ml) at 0 °C was added dropwise aq. NaOH (50%; 2.5 ml). The resulting mixture was vigorously stirred at room temperature for 10 min and iodomethane (0.43 g, 2.95 mmol) was added dropwise. After being stirred at room temperature for 0.5 h, the resulting solution was poured into water, and extracted with diethyl ether. The ethereal layer was discarded and the aqueous layer was acidified with dil. HCl and extracted with diethyl ether. Usual work-up gave compound (**34**) (0.54 g, 65%) as a pale pink, amorphous powder, m.p. 88–91 °C; ν_{max}(Nujol) 3 040, 1 845, 1 725, 1 460, 1 375, 1 250, 980, and 740 cm^{-1}; δ_H(90 MHz) 1.83 (3 H, br s, 5-Me), 2.30 (1 H, br dd, $J_{1,6}$ 7.1, $J_{6,6}$ 14.87 Hz, 6-H), 2.70 (1 H, br d, $J_{6,6}$ 14.87 Hz, 6-H), 3.38 (2 H, m, 1- and 2-H), 3.66 (3 H, s, NMe), 4.00 (1 H, br s, 3-H), 5.87 (1 H, br s, 4-H), 6.82 (1 H, s, 2′-H), and 6.98–7.56 (4 H, m, ArH); δ_C(22.5 MHz) 23.29 (5-Me), 27.63 (C-6), 32.50 (NMe), 32.73 (C-3), 40.14 and 45.13 (C-1 and -2), 109.48 (C-7′), 111.65 (C-3′), 118.59 and 119.13 (C-4 and -4′), 121.94 (C-5′), 124.60 (C-2′), 127.04 (C-3′a), 128.07 (C-6′), 135.54 (C-5), 137.17 (C-7′a), 170.97 (2-CO), and 174.22 (1-CO); *m*/*z* 295 (M^+, 96%), 222 (20), 197 ($M - C_4H_2O_3$, 100), 196 (84), 182 (80), 167 (20), and 158 (23).

(1RS,2SR,3SR)-1-*Methyl Hydrogen* 5-*Methyl*-3-(1′-*methylindol*-3′-*yl*)*cyclohex*-4-*ene*-1,2-*dicarboxylate* (**36**).—A solution of the anhydride (**34**) (165 mg, 0.56 mmol) in THF (5 ml), dil. HCl (0.39 ml), and methanol (0.9 ml) was heated under reflux for 2 h. Usual work-up and purification by chromatography on a silica gel column eluted with diethyl ether–light petroleum (3:2) yielded the monoester (**36**) (93 mg, 51%) as a white solid, m.p. 167–172 °C; λ_{max}(EtOH) 223 (4.59) and 288 nm (3.77); ν_{max}(Nujol) 3 280br, 1 740, 1 700, 1 370, 1 210, 1 155, 940, and 750 cm^{-1}; δ_H(90 MHz) 1.79 (3 H, br s, 5-Me), 2.09–2.35 and 2.53–2.82 (2 H, br m, 6-H_2), 3.10 (1 H, ddd, $J_{1,2}$ 3.5, $J_{1,6}$ 6.1 and 11.3 Hz, 1-H), 3.59 (3 H, s, NMe), 3.65 (3 H, s, OMe), 3.62 (1 H, m, 2-H), 4.15 (1 H, br m, 3-H), 5.51 (1 H, br s, 4-H), 6.78 (1 H, s, 2′-H), 6.96–7.29 (3 H, m, 4′-, 5′-, and 6′-H), and 7.54 (1 H, s, 7′-H); δ_C(22.5 MHz) 23.23 (5-Me), 29.14 (C-6), 32.17 (NMe), 35.64 (C-3), 42.25 and 44.96 (C-2, and -1), 51.73 (OMe), 109.10 (C-7′), 114.62 (C-3′), 118.52 and 118.69 (C-4 and -4′), 121.29 (C-5′), 122.15 (C-2′), 126.97 (C-6′), 127.30 (C-3′a), 133.64 (C-7′a), 136.72 (C-5), 173.73 (1-CO), and 176.16 (2-CO); *m*/*z* 327 (M^+, 100%), 282 ($M - CO_2H$, 27), 222 (23), 197 (70), 196 (60), and 182 (57).

Methyl 5,9-*Dimethyl*-6-*oxo*-5,6,6aβ,7β,8,10aβ-*hexahydroindeno*[2,1-b]*indole*-7-*carboxylate* (**38**).—To a solution of PPE (245 mg, 0.56 mmol) in anhydrous $CHCl_3$ (0.3 ml) was added a solution of the monoester (**36**) (93 mg, 0.28 mmol) in anhydrous $CHCl_3$ (0.7 ml). After being refluxed for 0.5 h, the resulting solution was worked up. Chromatography of the residue on silica gel with diethyl ether–light petroleum (3:2) afforded the *keto ester* (**38**) (65 mg, 74%) as pale yellow prisms (from Et_2O), m.p. 150–151 °C (Found: M^+, 309.1365. $C_{19}H_{19}NO_3$ requires *M*, 309.1364); λ_{max}(EtOH) 204 (4.49), 234 (4.51), and 304 nm (4.49); ν_{max}(Nujol) 3 030, 1 735, 1 680, 1 610, 1 550, 1 380, 1 260, 1 220, 1 200, 1 160, 970, and 750 cm^{-1}; δ_H(90 MHz) 1.61 (3 H, br s, 9-Me), 2.14 (2 H, br d, *J* 7.9 Hz, 8-H_2), 2.88 (1 H, td, $J_{6a,7}$ 5.3, $J_{7,8}$ 8.3 Hz, 7-H), 3.83 (3 H, s, NMe), 3.84 (3 H, s, OMe), 3.89 (1 H, m, 6a-H), 4.01 (1 H, br m, 10a-H), 5.71 (1 H, br s, 10-H), 7.07–7.50 (3 H, m, 1-, 2-, and 3-H), and 7.72 (1 H, m, 4-H); δ_C(22.5 MHz) 23.73 (9-Me), 28.11 (C-8), 30.06 (NMe), 35.91 (C-10a), 40.90 (C-7), 51-08 (C-6a), 52.92 (OMe), 111.05 (C-4), 120.32 (C-1), 121.35 and 121.56 (C-2 and -10), 122.27 (C-10b), 126.82 (C-3), 133.21 (C-9), 136.46 (C-10c), 144.59 (C-5a), 146.27 (C-4a), 173.79 (7-CO), and 193.40 (C-6); *m*/*z* 309 (M^+, 100%), 250 ($M - CO_2CH_3$, 82), 249 (82), 243 (36), and 222 (91).

(1RS,2SR,3SR)-2-*Benzyl* 1-*Methyl* 3-(*Indol*-3′-*yl*)-5-*methylcyclohex*-4-*ene*-1,2-*dicarboxylate* (**39**) *and* (1RS,2SR,3SR)-2-*Benzyl* 1-*Methyl* 3-(1′-*Benzylindol*-3′-*yl*)-5-*methylcyclohex*-4-*ene*-1,2-*dicarboxylate* (**40**).—To a mixture of the monoester (**27**) (0.2 g, 0.64 mmol) and TBAHS (0.22 g, 0.64 mmol) in benzene (6.4 ml) at 0 °C was added aq. NaOH (50%; 0.64 ml). After addition of benzyl bromide (0.09 ml, 0.768 mmol), the resulting pale yellow solution was stirred at room temperature for 1 h. Neutralization of the reaction with dil. HCl and work-up gave a pale yellow oil. Chromatography of the crude product on silica gel with diethyl ether–light petroleum (1:5) as eluant afforded compound (**40**) (0.141 g, 45%) as a white solid, m.p. 90–95 °C; ν_{max}(film) 3 040, 3 020, 1 720br, 1 610, 1 540, 1 470, 1 460, 1 440, 1 200, 1 170, 1 020, 910, 740, and 700 cm^{-1}; δ_H(90 MHz) 1.84 (3 H, br s, 5-Me), 2.20–2.46 and 2.73–2.86 (2 H, br m, 6-H_2), 3.05 (1 H, m, 1-H), 3.61 (3 H, s, OMe), 3.68 (1 H, m, 2-H), 4.17 (1 H, br m, 3-H), 4.50 (2 H, ABq, *J* 12.58 Hz, PhCH_2O), 5.15 (2 H, s, PhCH_2N), 5.58 (1 H, br s, 4-H), 6.59 (2 H, m, ArH), 6.91 (1 H, s, 2′-H), 7.02–7.33 (13 H, m, ArH), and 7.66 (1 H, m, 7′-H).

Further elution with diethyl ether–light petroleum (1:1) furnished compound (**39**) (53 mg, 20%) as pale yellow prisms (from Et_2O), m.p. 156–157 °C; λ_{max}(EtOH) 218 (4.53), 280 (3.81), and 288 nm (3.74); ν_{max}(Nujol) 3 350, 3 040, 1 715, 1 690, 1 225, 1 190, and 750 cm^{-1}; δ_H(90 MHz) 1.84 (3 H, br s, 5-Me), 2.22–2.40 and 2.70–2.83 (2 H, br m, 6-H_2), 3.13 (1 H, m, 1-H), 3.61 (3 H, s, OMe), 3.68 (1 H, m, 2-H), 4.15 (1 H, br m, 3-H), 4.55 (2 H, ABq, *J* 15.97 Hz, PhCH_2), 5.57 (1 H, br s, 4-H), 6.55 (2 H, m, ArH), 6.84 (1 H, d, *J* 2.6 Hz, 2′-H), 7.37–7.01 (6 H, m, ArH), 7.62 (1 H, m, 7′-H), and 7.98 (1 H, br s, NH); δ_C(22.5 MHz) 23.46 (5-Me), 29.58 (C-6), 35.97 (C-3), 42.31 and 44.69 (C-1 and -2), 51.84 (OMe), 65.55 (Ph*C*H_2), 111.27 (C-7′), 116.53 (C-3′), 118.91 and 119.40 (C-4 and -4′), 121.89 (C-5′ and -6′), 122.16 (C-2′), 126.98 (C-3′a), 127.42, 127.63, and 128.01 (2 × C-3″, 2 × C-4″, C-5″), 134.30 (C-7′a), 135.76 (C-2″), 136.30 (C-5), and 171.62 (2-CO); *m*/*z* 403 (M^+, 100%), 312 (33), 268 (50), 206 (73), 183(73), 183 (37), 182 (47), 168 (50), 116 (53), and 91 (67).

Methyl 9-*Methyl*-6-*oxo*-5-*tosyl*-5,6,6aβ,7β,8,10aβ-*hexahydroindeno*[2,1-b]*indole*-7-*carboxylate* (**2**).—To a solution of the keto ester (**29**) (0.2 g, 0.68 mmol) in benzene (2.04 ml) containing TBAHS (23 mg, 0.068 mmol) at 0 °C was added dropwise 50% aq. NaOH (0.68 ml). After the mixture had been vigorously stirred at room temperature for 5 min, a solution of tosyl chloride (0.19 g, 1.02 mmol) in benzene (2.75 ml) was added. Work-up and recrystallization of the crude product from dichloromethane–diethyl ether afforded the title keto ester (**2**) (0.29 g, 95%) as needles, m.p. 196–197 °C (Found: C, 66.7; H, 5.1; N, 3.2. $C_{25}H_{23}NO_5S$ requires C, 66.8; H, 5.1; N, 3.1%); λ_{max}(EtOH) 234 (4.10), 241 (3.99), and 293 nm (4.09); ν_{max}(Nujol) 3 040, 3 020, 1 745, 1 710, 1 440, 1 380, 1 220, 1 185, 1 130, 750, and 680 cm^{-1}; δ_H(90 MHz) 1.58 (3 H, s, 9-Me), 2.12 (2 H, br d, *J* 7.9 Hz, 8-H_2), 2.34 (3 H, s, Ar*Me*), 2.87 (1 H, m, 7-H), 3.85 (3 H, s, OMe), 3.94 (1 H, m, 6a-H), 4.10 (1 H, br m, 10a-H), 5.59 (1 H, br s, 10-H), 7.18–7.72 (5 H, m, 1-, 2-, 3-, and 2 × 2′- or 3′-H), 7.97 (2 H, 1/2 ABq, *J* 8.3 Hz, 2 × 3′- or 2′-H), and 8.26 (1 H, d, *J* 7.9 Hz, 4-H); δ_C(22.5 MHz) 21.50 (Ar*Me*), 23.67 (9-Me), 28.16 (C-8), 35.48 (C-10a), 40.51 (C-7), 51.89 (C-6a), 52.70 (OMe), 115.65 (C-4), 119.61 (C-1), 121.56 (C-10), 123.99 (C-2), 124.21 (C-10b), 127.41 (2 × C-2′ and C-3), 129.19 (C-10c), 129.29 (2 × C-3′), 135.05 and 135.59 (C-9 and C-1′), 143.01 (C-5a), 145.07 (C-4′), 155.04 (C-4a), 173.29 (7-CO), and 189.11 (C-6); *m*/*z* 449 (M^+, 15%), 294 ($M - C_7H_7SO_2$, 40), 234 (93), 207 (28), 206 (35), and 91 (100).

X-Ray Study of Compound (**24**).—Intensity data were collected on an Enraf-Nonius CAD4 diffractometer with graphite monochromated Mo-K_α radiation (0.710 73 Å). Crystal data and a summary of data collection and structure refinement

Table 3. Crystallographic details for compound (**24**).

Formula	$C_{19}H_{19}NO_4$
Formula mass	325.36
Crystal system	Monoclinic
a (Å)	9.946(1)
b (Å)	11.218(3)
c (Å)	14.956(2)
β (°)	92.37(1)
V (Å^3)	1 667.4(7)
Space group	$P2_1/c$
Z	4
D_x (g cm^{-3})	1.296
μ (cm^{-1})	0.85
Crystal colour/shape	Colourless prisms
Crystal dimensions	0.10 × 0.35 × 0.39
Collection range	$2\theta_{max}$ 50°, $h, k \pm l$
Scan mode and scan speed (° min^{-1})	$\omega/2\theta$, 1.1–5.5
Scan width (°)	0.70 + 0.34 tan θ
No. of independent reflections	3 096
No. of reflections with $F_o > 3\sigma(F_o)$, m	2 074
No. of parameters, p	226
R^a	0.046
$R_w{}^a$	0.068
S^a	1.813
Residual extrema in final difference map (e Å^{-3})	−0.19, +0.63

^{a} $R = \Sigma||F_o| - |F_c||/\Sigma|F_o|$. $R_w = [w(|F_o| - |F_c|)^2/\Sigma w|F_o|^2]^{\frac{1}{2}}$, with $w = 4F_o^2/[\sigma^2(F_o^2) + (0.055F_o^2)^2]$. $S = [\Sigma w(|F_o| - |F_c|)^2/(m - p)]^{\frac{1}{2}}$.

Table 4. Positional parameters for compound (**24**), with esds in parentheses.

Atom	x	y	z
O(1)	−0.200 6(2)	0.335 5(2)	0.325 6(1)
O(2)	0.123 9(2)	0.258 9(2)	0.302 0(1)
O(3)	0.425 7(2)	0.318 2(1)	0.325 6(1)
O(4)	0.421 8(2)	0.122 7(2)	0.299 8(1)
N	−0.134 2(2)	0.351 5(2)	0.407 6(1)
C(1)	−0.142 9(3)	0.364 6(2)	0.645 7(2)
C(1a)	−0.101 5(2)	0.353 9(2)	0.557 5(1)
C(2)	−0.276 3(3)	0.386 4(2)	0.659 0(2)
C(3)	−0.370 1(3)	0.397 4(2)	0.587 3(2)
C(4)	−0.333 4(2)	0.388 0(2)	0.499 8(2)
C(4a)	−0.198 9(2)	0.367 0(2)	0.486 2(2)
C(5a)	−0.001 3(2)	0.325 1(2)	0.427 4(1)
C(5b)	0.022 7(2)	0.328 3(2)	0.516 9(1)
C(6)	0.115 5(2)	0.288 9(2)	0.379 7(1)
C(6a)	0.230 7(2)	0.293 3(2)	0.450 4(2)
C(7)	0.338 0(2)	0.198 1(2)	0.438 0(2)
C(8)	0.282 8(3)	0.074 7(2)	0.456 4(2)
C(9)	0.2113(3)	0.069 7(2)	0.542 9(2)
C(10)	0.163 9(3)	0.165 7(2)	0.581 4(2)
C(10a)	0.164 5(2)	0.289 6(2)	0.542 1(1)
C(11)	−0.169 7(3)	0.429 9(3)	0.265 7(1)
C(12)	0.196 2(4)	−0.053 5(3)	0.581 3(1)
C(13)	0.397 6(2)	0.205 7(2)	0.346 9(1)
C(14)	0.473 1(3)	0.338 5(3)	0.237 4(2)
H(6a)	0.275(3)	0.370(3)	0.443(2)
H(7)	0.410(3)	0.214(3)	0.482(2)
H(10a)	0.206(3)	0.348(3)	0.583(2)

parameters are given in Table 3. Atomic scattering factors were taken from ref. 16. Calculations were carried out on a MicroVax II computer using the Structure Determination Package (SDP).[17]

The structure was solved by direct methods with MULTAN 82[18] from which all the non-hydrogen atoms were located. Hydrogen atoms H(6a), H(7), and H(10a) were found in a subsequent difference Fourier map. Refinement was by full-matrix least-squares. All the non-hydrogen atoms were refined anisotropically; the positional parameters of H6(a), H(7), and H(10a) were also refined but the rest of the hydrogen atoms were kept at calculated positions with fixed isotropic temperature factors. The final R-values are given in Table 3, fractional co-ordinates in Table 4,, and selected torsion angles in Table 5.*

Table 5. Selected torsion angles (°).

H(6a)–C(6a)–C(10a)–H(10a)	−21(3)
H(6a)–C(6a)–C(7)–H(7)	+57(3)

* *Supplementary data* (see Instructions for Authors, section 5.6.3, in the January issue). Tables of bond lengths, bond angles, and thermal parameters are available on request from the Cambridge Crystallographic Data Centre.

Acknowledgements

This work was supported by the World Health Organization Special Programme of Research in Human Reproduction. We thank the University of Hong Kong for a studentship (to T.-T. W.) and the Croucher Foundation for a studentship (to W.-T. W).

References

1 K. F. Cheng, T. Y. Chan, T. F. Lai, and Y. C. Kong, *J. Chem. Soc., Perkin Trans. 1*, 1988, 3317.
2 K. F. Cheng, T. Y. Chan, T. T. Wong, and T. F. Lai, *J. Chem. Soc., Perkin Trans. 1*, 1990, 1555.
3 Y. C. Kong, K. F. Cheng, R. C. Cambie, and P. G. Waterman, *J. Chem. Soc., Chem. Commun.*, 1985, 47.
4 Y. C. Kong, K. H. Ng, K. H. Wat, A. Wong, I. F. Saxena, K. F. Cheng, P. P. H. But, and H. T. Chang, *Planta Med.*, 1985, **51**, 304.
5 G. Schranim, H. Grotsch, and W. Pollmann, *Angew. Chem., Int. Ed. Engl.*, 1962, **1**, 1.
6 R. M. Trost, H. C. Arndt, P. E. Strege, and T. R. Veeboeven, *Tetrahedron Lett.*, 1976, 347.
7 K. F. Cheng, T. T. Wong, W. L. Chan, and Y. C. Kong, unpublished results.
8 W. C. Still, M. Kahn, and A. Mitra, *J. Org. Chem.*, 1978, **43**, 2923.
9 K. F. Cheng, Y. C. Kong, and T. Y. Chan, *J. Chem. Soc., Chem. Commun.*, 1985, 48.
10 I. Ribas, J. Sara, and L. Casteds, *Tetrahedron*, 1973, **29**, 3617.
11 T. Imanishi, A. Nagaki, N. Yagi, and M. Hanaobe, *Chem. Pharm. Bull.*, 1981, **29**, 901.
12 J. H. Adams, J. R. Lewis, and J. G. Paul, *Synthesis*, 1979, 429.
13 G. Burkhardt, M. P. Klein, and M. Calvin, *J. Am. Chem. Soc.*, 1965, **87**, 591.
14 J. R. Van Wazer and S. Norval, *J. Am. Chem. Soc.*, 1966, **88**, 4415.
15 M. Yokoyama, M. Kodera, and T. Imamoto, *J. Org. Chem.*, 1984, **49**, 75.
16 'International Tables for X-Ray Crystallography,' Kynoch Press, Birmingham, 1974, vol. 4, pp. 99–149.
17 'Enraf-Nonius Structure Determination Package,' SDP, Enraf-Nonius, Delft, The Netherlands, 1985.
18 P. Main, S. J. Fiske, S. E. Hull, L. Lessinger, G. Germain, J. P. Declercq, and M. M. Woolfson, 'MULTAN 82, A System of Computer Programs for the Automatic Solution of Crystal Structures,' Universities of York and Louvain, 1982.

Paper 0/01108H
Received 13*th March* 1990
Accepted 2*nd May* 1990