Reactivity of Carbocyclic Four-membered Radicals for the Preparation of Carbocyclic Analogues of Oxetanocins

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New carbocyclic four-membered *C*-nucleosides have been synthesized from the corresponding carboxylic acids and heteroaromatic compounds by the use of the Barton radical reaction. These carbocyclic nucleosides are analogues of oxetanosyl and cyclobutyl *N*-nucleosides which exhibit potent antiviral activities. The present synthetic routes provide a method for the preparation of cyclobutyl *C*-nucleosides.

Recently, new nucleoside analogues, which possess potent antiviral activities, have attracted considerable attention. Among these, four-membered nucleosides are some of the most interesting target compounds in view of their chemical and physiological properties (Fig. 1). Thus, the isolation of oxetanocin-A (OXT-A),[1] which possesses potent antibacterial, antitumour and antiviral activity prompted an extensive study for the preparation of oxetanosyl *N*-nucleosides such as OXT-H, OXT-X, OXT-G and 2-amino-OXT-A.[2]

Carbocyclic analogues of the oxetanocins, in which a methylene group replaces the oxygen atom in the oxetane ring, have become important, powerful anti-viral agents in recent years,[3] sometimes exhibiting high activity against the herpes and HIV viruses.[4] Furthermore, oxetanosyl *C*-nucleoside, which contains a maleimide group, was reported as a showdomycin analogue, exhibiting the expected biological activity.[5] However, the four-membered oxetane ring is generally unstable with respect to the five-membered ring found in ribofuranosyl nucleosides. Alternatively, cyclobutyl nucleosides, *i.e.*, carbocyclic nucleosides, are more stable to acid-catalysed ring opening and so their formation is easier. In addition, *C*-nucleosides are expected to show different biological activities from *N*-nucleosides due to the extra stability of the glycosidic bond.[6] As part of our study concerning the synthesis of *C*-nucleosides,[7] we now report the synthesis of new cyclobutyl *C*-nucleosides by the use of a radical coupling reaction *via* the cyclobutyl radical using Barton's method.

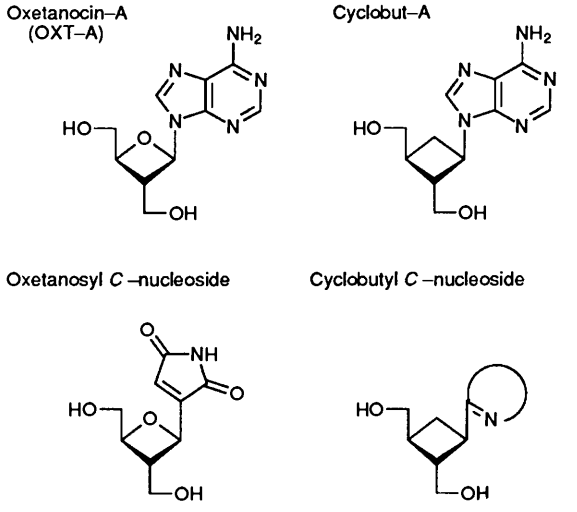
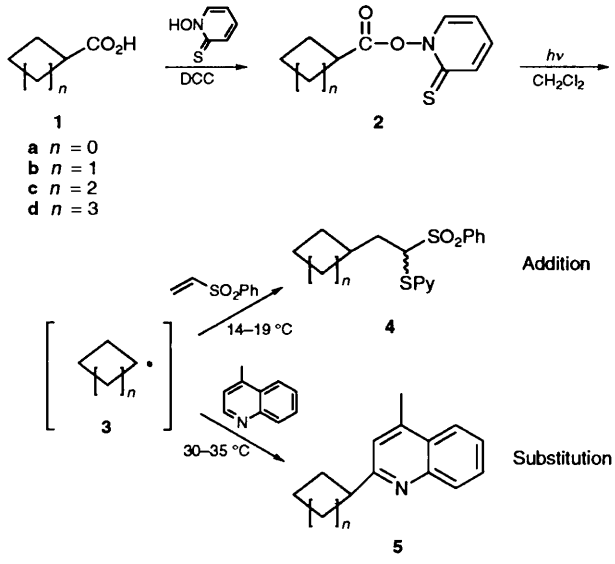


Fig. 1 Oxetanosyl and cyclobutyl nucleosides



Scheme 1

Results and Discussion

Reactivity of Cyclobutyl Radical.—For a preliminary study, the reactivities of cyclobutyl radical **3b** towards various electron-deficient compounds, such as phenyl vinyl sulfone and 4-methylquinoline, were compared with those of other carbocyclic radicals, such as cyclopropyl **3a**, cyclopentyl **3c** and cyclohexyl **3d** radicals. Thus, the radicals **3** were formed from the corresponding carboxylic acids by the Barton reaction[8] and their reactivity towards phenyl vinyl sulfone (addition reaction) and protonated 4-methylquinoline (substitution reaction) were performed under identical reaction conditions to give compounds **4** and **5**, respectively.

The results shown in Fig. 2 suggested that the cyclobutyl radical **3b** was rather reactive towards electron-deficient substrates and showed a reactivity similar to that of other cyclic and acyclic carbon radicals,[8] despite the relative increase in s-orbital character. Our present results support the low nucleophilicity of the radical **3a** in contrast with that of **3b**; Ingold[9] and Giese[10] have already studied the reactivity of **3a**. This result indicated that radical coupling could be used for the preparation of cyclobutyl *C*-nucleosides from the corresponding carboxylic acids and heteroaromatic compounds.

Preparation of Cyclobutyl C-Nucleosides.—The starting materials, 2,3-bis(benzyloxymethyl)cyclobutanecarboxylic acid **11a** and 2,3-bis(benzoyloxymethyl)cyclobutanecarboxylic acid

11b were prepared from sodium cyanide and diethyl maleate in racemic form (Scheme 2). 3,4-Bis(benzyloxymethyl)cyclopentanone **8**[11,12] was formylated with methyl formate and sodium methoxide. Then, the ketone was treated with toluene-*p*-sulfonyl azide under basic conditions to afford the corresponding 2-diazo derivative **9** in 91% yield.[13] Irradiation with a high-pressure mercury lamp gave the ring-contracted product **10** in quantitative yield, *via* the Wolff rearrangement. Oxidation of the benzyl groups of **10** into benzoyl groups was achieved with ruthenium(IV) oxide in good yield.[14] The resultant benzoyl-protected, methyl ester was subsequently hydrolysed under acidic conditions to give the corresponding carboxylic acid **11b** in 72% yield. Compound **11a** was obtained by the hydrolysis of compound **10** with sodium hydroxide.

The carboxylic acid **11b** was treated with *N*-hydroxypyridine-2-thione in the presence of dicyclohexylcarbodiimide (DCC) in THF at room temp. to give the Barton ester **12b** as an unstable yellow oil. In order to examine the nucleophilicity of the radical **13b**, the thiohydroxamic ester **12b** was irradiated with a tungsten lamp in the presence of phenyl vinyl sulfone to give the product **15b** in 38% yield.

The ester **12b** was also irradiated without an electrophile to give the corresponding pyridyl sulfide **14b** in 64% yield. This result suggested that the radical **13b** is formed in moderate yield, but that the reactivity was lower than that of the anomeric radicals such as the 2-deoxyribosyl radical.[7]

Compound **12b** was then irradiated in the presence of various heteroaromatic compounds to give the corresponding *C*-nucleoside derivatives **16b** in moderate yields, as shown in Table 1. From the ^{1}H NMR, COSY and NOESY spectra, the major products **16b-i**, **ii**, **v** with 4-methylquinoline, methyl nicotinate and pyrimidine were estimated to be present in the β-form. The yields of compound **16b** were dependent on the heteroaromatic compounds used, although why **16b-iii** was not formed from benzothiazole is unclear. The reactivity of the carbon-centred radical toward both protonated benzothiazole and protonated 4-methylquinoline was very similar.[15] However, the reactivity of ribofuranosyl radical to protonated benzothiazole was lower than that to protonated 4-methylquinoline,[7] whilst compound **13a** exhibited the same reactivity as that of **13b**. Thus, **16a-i** and **16a-v** were obtained in moderate yields

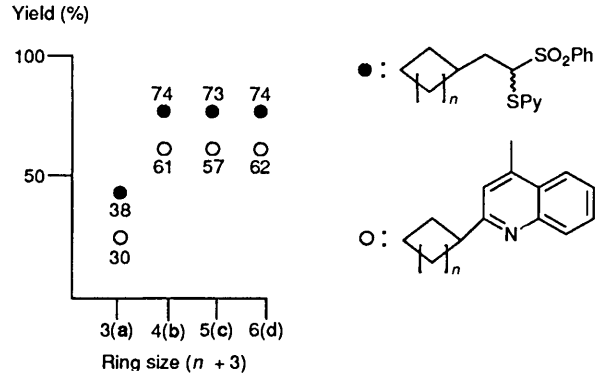
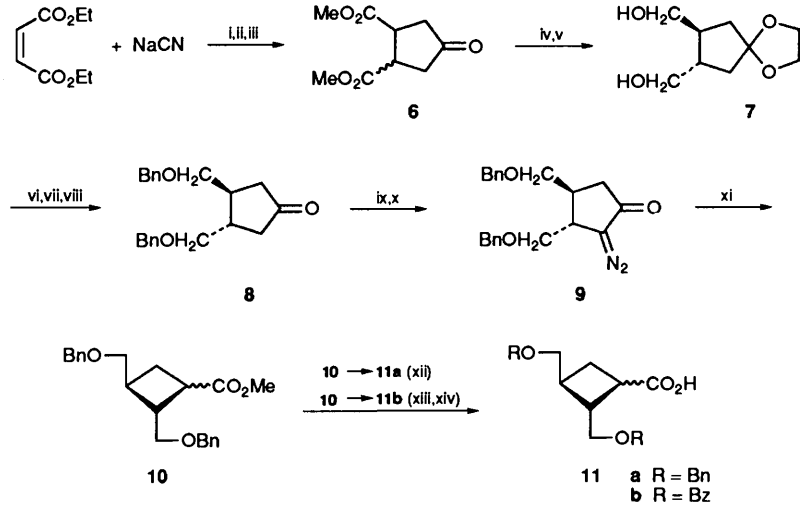
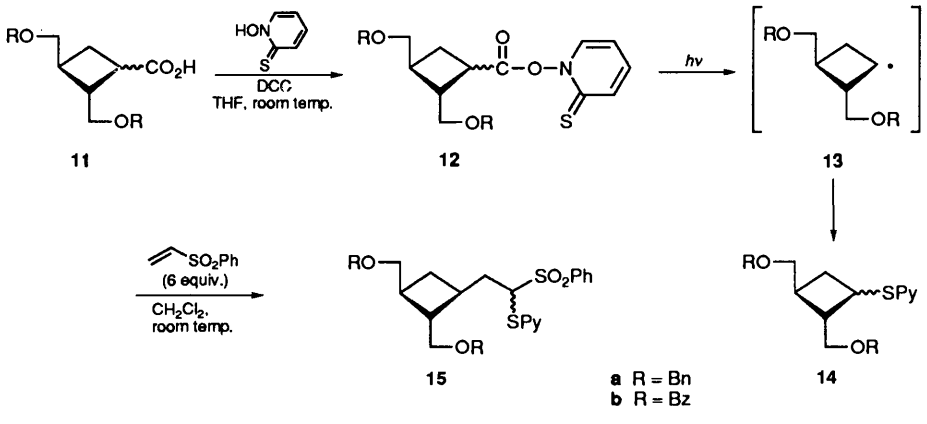


Fig. 2 Reactivities of the radical **3**

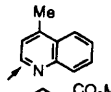
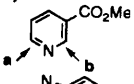
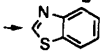
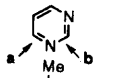
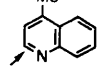
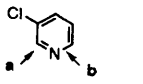


Scheme 2 Synthesis of the starting material. *Reagents and conditions:* i, MeOH, reflux; ii, HCl, heat; iii, MeOH, H^+, heat; iv, $HOCH_2CH_2OH$, TsOH, C_6H_6, heat; v, $LiAlH_4$, THF, −78 °C; vi, NaH–DMF; vii, BnBr; viii, HCl, THF; ix, HCO_2Me, MeONa, diethyl ether; x, TsN_3, Et_3N; xi, *hν*, MeOH; xii, NaOH; xiii, RuO_2–$NaIO_4$, CCl_4–MeCN–H_2O; xiv, HCl, 1,4-dioxane.

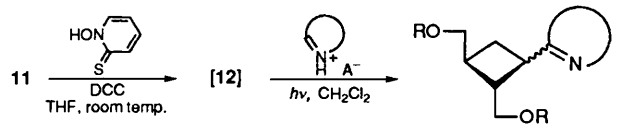


Scheme 3 Addition to phenyl vinyl sulfone

Table 1 Reaction of the cyclobutane derivative **11** with heteroaromatic compounds

Base (7 equiv.)[a]	R	Temp. (°C)	Yield (%)[b]
i 	Bz	31–42	41 (**16b**–i)
ii 	Bz	30–35	24 (**16b**–ii) (**a**:**b** = 58:42)
iii 	Bz	0–3	trace (**16b**–iii)
iv 	Bz	33–37	30 (**16b**–iv) (almost **a**)
i 	Bn	32–38	41 (**16a**–i)
v 	Bn	30–35	52 (**16a**–v) (**a**:**b** = 34:18)

[a] → = C–C bond forming position. [b] Isolated yield.



HA = Camphorsulfonic acid

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by the same method. Compound **16b** could easily be deprotected to give compound **17b** in high yield.

The key step for the synthesis of cyclobutyl *C*-nucleosides is the radical coupling reaction of the cyclobutyl radical **13** with several heteroaromatic compounds. This procedure has advantages such as the short synthetic route towards *C*-nucleosides containing a cyclobutyl ring as a sugar moiety, facile deprotection and its application to various heteroaromatic compounds.

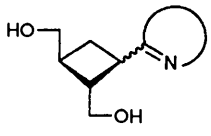

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Fig. 3

Experimental

Elemental analyses were performed on a Perkin-Elmer 240 elemental analyser at the Chemical Analysis Center of Chiba University. IR spectra were recorded on a HITACHI 215 spectrometer. ^1H and ^{13}C NMR were measured [deuteriochloroform with tetramethylsilane (TMS) as the internal reference] using JEOL MH-100, JNM-FX-270, JNM-GSX-400 and JNM-GSX-500 spectrometers. Chemical shifts (δ) are expressed in ppm from TMS and J values are given in Hz. Carbon signals were assigned by DEPT and INEPT. 2D-NMR (COSY and NOESY) data were recorded on JEOL JNM-GSX-400 and JNM-GSX-500 spectrometers. Mass spectra were obtained on HITACHI M-60 and JEOL HX-110 mass spectrometers. TLC analysis was performed on thin layer analytical plates of Kieselgel 60 F_{254} (E. Merck, Darmstadt) and Wakogel B-5F. Silica gel column chromatography was carried out on Wakogel C-200 or C-300. Reactions were carried out under dry, oxygen-free argon atmosphere unless otherwise stated.

Typical Procedure for the Addition to Phenyl Vinyl Sulfone.—To a solution of cyclobutanecarboxylic acid (0.102 g, 1.00 mmol) in dry THF (4 cm^3) were added *N*-hydroxypyridine-2-thione (0.153 g, 1.20 mmol) and 1,3-dicyclohexylcarbodiimide (DCC) (0.283 g, 1.30 mmol; 95%) at 0 °C. After the mixture had been stirred in the dark for 1.5 h at room temperature the precipitated 1,3-dicyclohexylurea was removed by filtration and then added to a flask containing phenyl vinyl sulfone (0.840 g, 5.00 mmol) and washed with dry dichloromethane (5 cm^3). The filtrate was then irradiated with a 500 W tungsten lamp for 0.5 h at 15–18 °C after which it was quenched with hydrazine hydrate (0.700 g), stirred for 15 min at room temperature and then extracted with diethyl ether. The organic layer was separated, dried (Na_2SO_4), filtered and then concentrated. The residue was purified by column chromatography on silica gel (dichloromethane–diethyl ether, 10:1) to give the product **4b** in 74% yield (0.309 g).

2-Cyclopropyl-1-(2-pyridylsulfanyl)ethyl phenyl sulfone **4a**. M.p. 75–76 °C (Et_2O–hexane); ν_{max}(Nujol)/cm^{-1} 1300, 1290, 1145, 1080, 780 and 750; δ_H 8.21 (1 H, d, $J_{5',6'}$ 4.7, Py-6'-H), 7.93 (2 H, d, J_{ortho} 8.0, Ph), 7.48–7.27 (4 H, m, Ph and Py-4'-H), 7.00 (1 H, d, $J_{3',4'}$ 8.0, Py-3'-H), 6.90 (1 H, dd, $J_{4',5'}$ 6.3 and $J_{5',6'}$ 4.7, Py-5'-H), 5.83 (1 H, dd, J_{vic} 9.8 and J_{vic} 4.6, CH), 2.20–2.00 (2 H, m, CH_2), 1.10–0.95 (1 H, m, 1''-H), 0.60–0.40 (2 H, m), 0.35–0.10 (1 H, m) (Found: C, 60.2; H, 5.3; N, 4.3%) [Calc. for $C_{16}H_{17}NO_2S_2$: C, 60.16; H, 5.36; N, 4.39%] [Found: *m/z* (HRMS, FAB), 319.0704. Calc. for $C_{16}H_{18}NO_2S$: 319.0700].

2-Cyclobutyl-1-(2-pyridylsulfanyl)ethyl phenyl sulfone **4b**. M.p. 79 °C (Et_2O–hexane); ν_{max}(Nujol)/cm^{-1} 1495, 1300, 1140, 1080, 775, 740, 725 and 690; δ_H 8.19 (1 H, d, $J_{5',6'}$ 5.1, Py-6'-H), 7.88 (2 H, d, J_{ortho} 6.5, Ph), 7.46–7.23 (4 H, m, Ph- and Py-4'-H), 6.94 (1 H, d, $J_{3',4'}$ 8.5, Py-3'-H), 6.88 (1 H, dd, $J_{4',5'}$ 7.8 and $J_{5',6'}$ 5.1, Py-5'-H), 5.62 (1 H, dd, J_{vic} 11.4 and J_{vic} 2.8, CH), 2.68–2.53 (1 H, m, CH_2), 2.51–2.40 (1 H, m, CH_2), 2.12–1.90 (3 H, m), 1.90–1.62 (4 H, m) (Found: C, 61.5; H, 5.6; N, 4.2. Calc. for $C_{17}H_{19}NO_2S_2$: C, 61.23; H, 5.74; N, 4.20%).

2-Cyclopentyl-1-(2-pyridylsulfanyl)ethyl phenyl sulfone **4c**. M.p. 77–78 °C (Et_2O–hexane); ν_{max}(Nujol)/cm^{-1} 1290, 1150, 1080, 780, 755, 730 and 690; δ_H 8.20 (1 H, d, $J_{5',6'}$ 4.8, Py-6'-H), 7.90 (2 H, d, J_{ortho} 7.0, Ph), 7.45–7.25 (4 H, m, Ph and Py-4'-H), 6.95 (1 H, d, $J_{3',4'}$ 8.2, Py-3'-H), 6.90 (1 H, dd, $J_{4',5'}$ 7.6 and $J_{5',6'}$ 4.8, Py-5'-H), 5.75 (1 H, dd, J_{vic} 11.7 and J_{vic} 2.9, CH), 2.32–2.08 (2 H, m, CH_2), 2.08–1.93 (1 H, m, 1''-H), 1.90–1.70 (2 H, m), 1.70–1.44 (4 H, m) and 1.30–1.08 (2 H, m) (Found: C, 62.45; H, 5.8; N, 4.0. Calc. for $C_{18}H_{21}NO_2S_2$: C, 62.21; H, 6.09; N, 4.03%). [Found: *m/z* (HRMS, FAB), 347.1017 (M + H). Calc. for $C_{18}H_{22}NO_2S_2$ 347.1013].

2-Cyclohexyl-1-(2-pyridylsulfanyl)ethyl phenyl sulfone **4d**. M.p. 78–80 °C (Et_2O–hexane) (lit.,[16] m.p. 76–78 °C).

Typical Procedure for the Substitution Reaction.—To a solution of cyclobutanecarboxylic acid (0.102 g, 1.00 mmol) in dry THF (4 cm^3) were added *N*-hydroxypyridine-2-thione (0.153 g, 1.20 mmol) and dicyclohexylcarbodiimide (DCC) (0.282 g, 95%, 1.30 mmol) at 0 °C. After being stirred for 1.5 h at room temp. in the dark, the reaction mixture was filtered into a flask containing 4-methylquinolinium camphor-10-sulfonate (2.250 g, 6.00 mmol) and washed with dichloromethane (4 cm^3) under an argon atmosphere. After the yellow solution of the ester was irradiated with a 500 W tungsten lamp for 2 h at 30–35 °C, the reaction mixture was quenched with sat. aq. $NaHCO_3$, extracted with dichloromethane, dried over Na_2SO_4, filtered and concentrated. The residue was chromatographed (dichloromethane–diethyl ether, 20:1) to give the product **5b** in 61% yield (0.117 g).

2-*Cyclopropyl*-4-*methylquinoline* **5a**. Oil; ν_{max}(neat)/cm^{-1} 1590, 1550, 1500, 1440, 1400, 1290, 1190, 1165, 1080, 1020, 955, 850 and 760; δ_H 7.96 (1 H, dd, $J_{7,8}$ 8.6 and $J_{6,8}$ 1.1, 8-H), 7.90 (1 H, dd, $J_{5,6}$ 8.6 and $J_{5,7}$ 1.1, 5-H), 7.63 (1 H, ddd, $J_{7,8}$ 8.6, $J_{6,7}$ 7.3 and $J_{5,7}$ 1.1, 7-H), 7.44 (1 H, ddd, $J_{5,6}$ 8.6, $J_{6,7}$ 7.3 and $J_{6,8}$ 1.1, 6-H), 6.99 (1 H, d, $J_{long\ range}$ 1.1, 3-H), 2.74 (3 H, s, -Me), 2.19 (1 H, m, 1′-H) and 1.17–1.04 (4 H, m, 2′-H and 3′-H); *m*/*z* (EI) 182 (M^+, 59%) (Found: C, 85.0; H, 7.2; N, 7.6. Calc. for $C_{13}H_{13}N$: C, 85.21; H, 7.15; N, 7.64%).

2-*Cyclobutyl*-4-*methylquinoline* **5b**. Oil; ν_{max}(neat)/cm^{-1} 1590, 1500, 1435, 1400, 860 and 760; δ_H 8.06 (1 H, br d, $J_{7,8}$ 8.1, 8-H), 7.93 (1 H, br d, $J_{5,6}$ 8.1, 5-H), 7.65 (1 H, ddd, $J_{7,8}$ 8.1, $J_{6,7}$ 6.8 and $J_{5,7}$ 1.4, 7-H), 7.48 (1 H, ddd, $J_{5,6}$ 8.1, $J_{6,7}$ 6.8 and $J_{6,8}$ 1.4, 6-H), 7.19 (1 H, s, 3-H), 3.82 (1 H, quin, J_{vic} 8.9, 1′-H), 2.68 (3 H, s, -Me), 2.50–2.41 (4 H, m, 2′-H and 4′-H) and 2.19–1.93 (2 H, m, 3′-H); *m*/*z* (EI) 197 (M^+, 100%) (Found: C, 84.9; H, 7.8; N, 7.2. Calc. for $C_{14}H_{15}N$: C, 85.24; H, 7.66; N, 7.10%).

2-*Cyclopentyl*-4-*methylquinoline* **5c**. Oil; ν_{max}(neat)/cm^{-1} 1590, 1550, 1530, 1500, 1440, 1400, 860 and 760; δ_H 8.04 (1 H, br d, $J_{7,8}$ 8.1, 8-H), 7.93 (1 H, br d, $J_{5,6}$ 8.1, 5-H), 7.66 (1 H, ddd, $J_{7,8}$ 8.1, $J_{6,7}$ 7.0 and $J_{5,7}$ 1.4, 7-H), 7.48 (1 H, ddd, $J_{5,6}$ 8.1, $J_{6,7}$ 7.0 and $J_{6,8}$ 1.4, 6-H), 7.17 (1 H, s, 3-H), 3.38–3.27 (1 H, m, 1′-H), 2.67 (3 H, s, -Me), 2.21–2.14 (2 H, m, cyclopentyl-H) and 1.90–1.73 (6 H, m, cyclopentyl-H); *m*/*z* (EI) 211 (M^+, 26%) (Found: C, 85.3; H, 8.2; N, 6.7. Calc. for $C_{15}H_{17}N$: C, 85.26; H, 8.11; N, 6.63%).

2-*Cyclohexyl*-4-*methylquinoline* **5d**. Oil; ν_{max}(neat)/cm^{-1} 2880, 2825, 1590, 1550, 1500, 1440, 1400, 1330, 1170, 1025, 950, 860 and 760; δ_H 8.04 (1 H, dd, $J_{7,8}$ 8.1 and $J_{6,8}$ 1.4, 8-H), 7.94 (1 H, dd, $J_{5,6}$ 8.1, $J_{5,7}$ 1.4, 5-H), 7.64 (1 H, ddd, $J_{7,8}$ 8.1, $J_{6,7}$ 7.3 and $J_{5,7}$ 1.4, 7-H), 7.48 (1 H, ddd, $J_{5,6}$ 8.1, $J_{6,7}$ 7.3 and $J_{6,8}$ 1.4, 6-H), 7.17 (1 H, s, 3-H), 2.87 (1 H, tt, J_{vic} 11.7 and J_{vic} 3.8, 1′-H), 2.68 (3 H, s, -Me) and 2.04–1.31 (10 H, m, cyclohexyl-H); *m*/*z* (EI) 225 (M^+, 28%) (Found: C, 85.3; H, 8.6; N, 6.5. Calc. for $C_{16}H_{19}N$: C, 85.28; H, 8.50; N, 6.22%).

Preparation of 2,3-*Bis*(*benzyloxymethyl*)*cyclobutanecarboxylic Acid* **11a** *and* 2,3-*Bis*(*benzoyloxymethyl*)*cyclobutanecarboxylic Acid* **11b**.—Compound **10** was prepared by the literature method.[9–12]

Methyl 2,3-*bis*(*benzyloxymethyl*)*cyclobutanecarboxylate* **10**. Colourless oil (99%); ν_{max}(neat)/cm^{-1} 2840, 1720, 1430, 1350, 1190, 1090, 740 and 700; δ_H 7.35–7.25 (10 H, m, Ph), 4.52 (0.8 H, s, minor-CH_2Ph), 4.50 (2.4 H, d, J_{gem} 11.8, major-CH_2Ph), 4.44 (0.8 H, s, minor-CH_2Ph), 3.65 (1.8 H, s, major-Me), 3.59 (1.2 H, s, minor-Me), 3.57–3.53 (1.6 H, m, minor-CH_2OBn), 3.51–3.43 (2.4 H, m, major-CH_2OBn), 3.22 (0.4 H, dt, $J_{1',4'b}$ 9.3 and $J_{1',2'}$ 5.8, minor-1′-H), 2.94 (0.6 H, dt, $J_{1',4'b}$ 9.3 and $J_{1',2'} = J_{1',4'a}$ 8.8, major-1′-H), 2.78–2.75 (0.4 H, m, minor-2′-H), 2.59 (0.6 H, ddd, J_{vic} 13.7, $J_{1',2'} = J_{2',3'}$ 8.8 and J_{vic} 5.2, major-2′-H), 2.53–2.44 (0.8 H, m, minor-3′-H and 4′a-H), 2.45 (0.6 H, dd, $J_{2',3'}$ 8.8 and J_{vic} 6.1, major-3′-H), 2.23 (0.6 H, dt, J_{gem} 11.0 and $J_{1',4'a}$ 8.8, major-4′a-H), 1.95 (0.6 H, dt, J_{gem} 11.0 and $J_{1',4'b} = J_{3',4'b}$ 9.3, major-4′b-H) and 1.94–1.88 (0.4 H, m, minor-4′b-H) [Found: *m*/*z* (HRMS, FAB), 355.1909, (M + H). Calc. for $C_{22}H_{27}O_4$ 355.1909].

Methyl 2,3-*bis*(*benzoyloxymethyl*)*cyclobutanecarboxylate*. Oil; ν_{max}(neat)/cm^{-1} 2915, 1705, 1445, 1430, 1265, 1200, 1170, 1110, 1015 and 715; δ_H 8.06–8.00 (4 H, m, Ph), 7.58–7.54 (2 H, m, Ph), 7.47–7.42 (4 H, m, Ph), 4.50–4.32 (4 H, m, CH_2O), 3.65 (1.8 H, s, major-Me), 3.61 (1.2 H, s, minor-Me), 3.37 (0.4 H, dt, $J_{1',4'b}$ 9.9 and $J_{1',2'}$ 6.3, minor-1′-H), 3.03 (0.6 H, dt, $J_{1',4'b}$ 9.6 and $J_{1',2'} = J_{1',4'a}$ 8.8, major-1′-H), 3.08–3.00 (0.4 H, m, minor-2′-H), 2.94 (0.6 H, dd, $J_{1',2'}$ 8.8 and J_{vic} 5.8, major-2′-H), 2.95–2.86 (0.4 H, m, minor-3′-H), 2.68–2.60 (1 H, m, major-3′-H, minor-4′a-H), 2.36 (0.6 H, dt, J_{gem} 11.3 and $J_{1',4'a}$ 8.8, major-4′a-H), 2.17 (0.6 H, dt, J_{gem} 11.3 and $J_{1',4'b}$ 9.6, major-4′b-H) and 2.11–2.05 (0.4 H, m, minor-4′b-H) [Found: *m*/*z* (HRMS, FAB) 383.1495 (M + H). Calc. for $C_{22}H_{23}O_6$ 383.1495].

To a solution of the methyl ester **10** (0.34 g, 0.88 mmol) in 1,4-dioxane (5 cm^3) was added HCl (1 cm^3, 2 mol dm^{-3}) and heated for one day at 60 °C. The solution was diluted with diethyl ether, filtered, dried over Na_2SO_4, filtered and finally concentrated. The residue was purified by column chromatography on silica gel (ethyl acetate–hexane–acetic acid, 50 : 50 : 1) to give the carboxylic acid **11** in 72% yield (0.23 g).

2,3-*Bis*(*benzoyloxymethyl*)*cyclobutanecarboxylic Acid* **11b**. Oil; ν_{max}(neat)/cm^{-1} 3640–2200, 1790–1625, 1595, 1580, 1490, 1450, 1180, 1075, 1030, 920, 810, 720 and 690; δ_H 8.06–7.99 (4 H, m, Ph), 7.62–7.37 (6 H, m, Ph), 4.53–4.32 (4 H, m, CH_2O), 3.39 (0.4 H, td, $J_{1',4'b}$ 9.1 and $J_{1',2'}$ 5.5, minor-1′-H), 3.09–3.02 (0.4 H, m, minor-2′-H), 3.05 (0.6 H, dt, $J_{1',4'b}$ 9.3 and $J_{1',2'} = J_{1',4'a}$ 8.8, major-1′-H), 2.96 (0.6 H, tt, $J_{1',2'} = J_{2',3'}$ 8.8 and J_{vic} 5.2, major-2′-H), 2.94–2.89 (0.4 H, m, minor-3′-H), 2.68 (0.6 H, tq, $J_{2',3'} = J_{3',4'a}$ 8.8 and $J_{3',4'b} = J_{vic}$ 5.8, major-3′-H), 2.60 (0.4 H, ddd, J_{gem} 12.4, $J_{1',4'a}$ 9.3 and $J_{3',4'a}$ 5.8, minor-4′a-H), 2.38 (0.6 H, dt, J_{gem} 11.5 and $J_{1',4'a} = J_{3',4'a}$ 8.8, major-4′a-H), 2.18 (0.6 H, dt, J_{gem} 11.5 and $J_{1',4'b}$ 9.3, major-4′b-H) and 2.12–2.05 (0.4 H, m, minor-4′b-H) [Found: *m*/*z* (HRMS, FAB), 369.1338 (M + H). Calc. for $C_{21}H_{21}O_6$ 369.1338].

Preparation of 2-[2,3-*Bis*(*benzoyloxymethyl*)*cyclobutyl*]-1-(2-*pyridylsulfanyl*)*ethyl Phenyl Sulfone* **15b**.—To a solution of the acid **11b** (0.225 g, 0.50 mmol) in dry THF (3 cm^3) were added *N*-hydroxypyridine-2-thione (0.070 g, 0.55 mmol) and DCC (0.125 g, 0.60 mmol) at 0 °C. After the mixture had been stirred for 3 h at room temp. in the dark, the precipitated 1,3-dicyclohexylurea was filtered off and washed with dry dichloromethane (5 cm^3) under an argon atmosphere. To the filtrate was added phenyl vinyl sulfone (0.420 g, 2.50 mmol) and the mixture was irradiated with a 500 W tungsten lamp for 3 h at 0 °C. After the reaction mixture had been quenched by the addition of hydrazine hydrate (0.5 g) the solution was stirred for 15 min at room temp. and then extracted with diethyl ether. The organic layer was dried (Na_2SO_4), filtered, and concentrated. The residue was purified by column chromatography on silica gel (ethyl acetate–hexane, 1 : 2) to give the product sulfone **15b** (R_f 0.4) in 38% yield (0.066 g); ν_{max}(neat)/cm^{-1} 3040, 2930, 1715, 1600, 1580, 1575, 1560, 1450, 1420, 1320, 1310, 1275, 1150, 1125, 1120, 1080, 1030, 770, 735, 730, 720 and 700; δ_H 8.17 (0.4 H, dd, $J_{5',6'}$ 4.0 and $J_{4',6'}$ 1.6, minor-Py-6′-H), 8.11 (0.6 H, dd, $J_{5',6'}$ 4.0 and $J_{4',6'}$ 1.7, major-Py-6′-H), 8.05–7.97 (4 H, m, Ph), 7.89–7.79 (2 H, m, $PhSO_2$), 7.60–7.19 (10 H, m, $PhSO_2$-, Ph- and Py-4′-H), 6.94–6.80 (2 H, m, Py-3′-H and 5′-H), 5.68 (1 H, m, CH), 4.58–4.25 (4 H, m, CH_2O), 2.72–2.02 (6 H, m, 1″-H, 2″-H, 3″-H, 4″-H and CH_2), 1.75–1.54 (1 H, m, CH_2) (Found: C, 65.3; H, 5.15; N, 2.2. Calc. for $C_{33}H_{31}NO_6S_2$: C, 65.87; H, 5.19; N, 2.33%).

Preparation of 2,3-*Bis*(*benzoyloxymethyl*)*cyclobutyl Pyridyl Sulfide* **14**.—To a solution of **11b** (0.225 g, 0.50 mmol) in dry THF (3 cm^3) were added *N*-hydroxypyridine-2-thione (0.070 g, 0.55 mmol) and DCC (0.125 g, 0.60 mmol) at 0 °C. After the mixture had been stirred at room temperature for 3 h in the dark, precipitated 1,3-dicyclohexylurea was filtered off and washed with dry dichloromethane (5 cm^3) under an argon atmosphere. The filtrate was irradiated for 3 h at 0 °C. After the reaction mixture had been quenched, the reaction mixture was extracted with ether and the extract dried (Na_2SO_4) filtered, and concentrated. The residue was purified by column chromatography on silica gel (eluent, ethyl acetate–hexane 1 : 2) to give the product **14** (0.035 g, 64%); ν_{max}(neat)/cm^{-1} 3270, 3030, 2920, 2840, 1725, 1715, 1710, 1640, 1600, 1580, 1550, 1490, 1450, 1415, 1315, 1255, 1180, 1125, 1070, 1030, 770, 735, 730, 720, 695 and 680; δ_H 8.33 (1 H, ddd, $J_{5,6}$ 4.9, $J_{3,6}$ 2.2 and $J_{4,6}$ 1.1, Py-6-H), 8.06–7.99 (4 H, m, Ph), 7.90–7.87 (1 H, ddd, $J_{3,4}$ 7.8, $J_{4,5}$ 7.3

and $J_{4,6}$ 1.1, Py-4-H), 7.58–7.50 (2 H, m, Ph), 7.45–7.33 (4 H, m, Ph), 7.11 (1 H, ddd, $J_{3,4}$ 7.8, $J_{3,6}$ 2.2 and $J_{3,5}$ 1.1, Py-3-H), 6.91 (1 H, ddd, $J_{4,5}$ 7.3, $J_{5,6}$ 4.9 and $J_{3,5}$ 1.1, Py-5-H), 4.61–4.29 (5 H, m, CH_2O and 1'-H), 2.85–2.68 (2 H, m, 2'-H and 3'-H), 2.08–1.78 (1 H, m, 4'a-H) and 1.62–1.16 (1 H, m, 4'b-H) [Found: m/z (HRMS, FAB), 434.1419 (M + H). Calc. for $C_{25}H_{24}NO_4S$: 434.1424].

Typical Procedure for the Preparation of C-*Nucleosides.*—To a solution of the acid **11b** (0.185 g, 0.50 mmol) in dry THF (3 cm^3) were added *N*-hydroxypyridine-2-thione (0.067 g, 0.55 mmol) and DCC (0.124 g, 95%, 0.60 mmol) at 0 °C. After being stirred for 1.5 h at room temp. in the dark, the mixture was filtered into a solution of 4-methylquinolinium camphor-10-sulfonate (1.31 g, 3.5 mmol) in dichloromethane (4 cm^3) under an argon atmosphere. The yellow solution of the ester was stirred and irradiated with a 500 W tungsten lamp for 2.5 h at 30–33 °C, then the mixture was quenched with sat. aq. $NaHCO_3$, extracted with dichloromethane, dried over Na_2SO_4, filtered and finally concentrated. The residue was chromatographed (ethyl acetate–hexane, 1:3–1:1) and further purified by PLC on silica gel (ethyl acetate–hexane, 1:1) to give the β-form of **16b–i** in 41% yield (0.052 g).

2-[2,3-*Bis*(*benzoyloxymethyl*)*cyclobutyl*]-4-*methylquinoline* **16b–i**. ν_{max}(neat)/cm^{-1} 2900, 1710, 1600, 1505, 1450, 1375, 1320, 1260, 1180, 1120, 1075, 1030, 770, 715 and 695; δ_H 8.08 (2 H, dd, J_{ortho} 8.1 and J_{meta} 1.3, Ph), 8.04 (1 H, d, $J_{7,8}$ 8.4, 8-H), 7.94 (2 H, dd, J_{ortho} 8.1 and J_{meta} 1.3, Ph), 7.96–7.93 (1 H, m, 5-H), 7.68 (1 H, ddd, $J_{7,8}$ 8.4, $J_{6,7}$ 7.0 and $J_{5,7}$ 1.5, 7-H), 7.54 (1 H, tt, J_{ortho} 7.3 and J_{meta} 1.3, Ph), 7.51 (1 H, ddd, $J_{5,6}$ 8.4, $J_{6,7}$ 7.0 and $J_{6,8}$ 1.5, 6-H), 7.50–7.49 (1 H, m, Ph), 7.40 (2 H, dt, J_{ortho} 7.9 and J_{meta} 1.5, Ph), 7.34 (2 H, dt, J_{ortho} 7.9 and J_{meta} 1.5, Ph), 7.17 (1 H, s, 3-H), 4.54 (2 H, d, J_{vic} 5.9, 2'-CH_2O), 4.50 (1 H, dd, J_{gem} 11.0 and J_{vic} 5.3, 3'-CH_2O), 4.46 (1 H, dd, J_{gem} 11.0 and J_{vic} 5.9, 3'-CH_2O), 3.61 (1 H, dd, $J_{1',4'b}$ 9.7 and $J_{1',2'}$ 8.8, 1'-H), 3.17 (1 H, tt, $J_{1',2'} = J_{2',3'}$ 8.8 and J_{vic} 5.9, 2'-H), 2.77 (1 H, tdd, $J_{2',3'}$ 8.8, J_{vic} 5.9 and J_{vic} 5.3, 3'-H), 2.61 (3 H, s, Me), 2.58 (1 H, dt, J_{gem} 11.0 and $J_{3',4'a}$ 8.6, 4'a-H) and 2.49 (1 H, dt, J_{gem} 11.0 and $J_{1',4'b}$ 9.7, 4'b-H); NOE was not observed; δ_C 166.7, 166.6 (benzoyl CO), 162.1 (base C-2), 147.9 (base C-8a), 144.3 (base C-4), 132.9–128.3 (Ph), 129.8 (base C-8), 129.0 (base C-7), 127.1 (base C-4a), 125.6 (base C-5), 123.5 (base C-6), 120.8 (base C-3), 67.2 (2'-CH_2O), 66.9 (3'-CH_2O), 43.6 (C-1'), 42.1 (C-2'), 33.8 (C-3'), 27.1 (C-4') and 18.6 (base Me) [Found: *m/z* (HRMS, FAB), 466.2022. Calc. for $C_{30}H_{28}NO_4$] (M + H). (Found: C, 76.95; H, 5.8; N, 2.9. Calc. for $C_{30}H_{27}NO_4$: C, 77.40; H, 5.85; N, 2.93%).

Methyl 6-[2,3-*Bis*(*benzoyloxymethyl*)*cyclobutyl*]*nicotinate* **16b–iia**. ν_{max}(neat)/cm^{-1} 2920, 1720, 1705, 1590, 1450, 1430, 1410, 1310, 1265, 1210, 1110, 1070, 1025, 965, 745, 715 and 690; δ_H 9.17 (1 H, dd, $J_{4,6}$ 2.2 and $J_{3,6}$ 0.6, 2-H), 8.16 (1 H, dd, $J_{3,4}$ 8.0 and $J_{4,6}$ 2.2, 4-H), 8.07 (2 H, dd, J_{ortho} 8.2 and J_{meta} 1.4, Ph), 7.94 (2 H, dd, J_{ortho} 8.2 and J_{meta} 1.4, Ph), 7.56 (1 H, tt, J_{ortho} 7.4 and J_{meta} 1.4, Ph), 7.54 (1 H, tt, J_{ortho} 7.4 and J_{meta} 1.4, Ph), 7.43 (2 H, dd, J_{ortho} 8.2 and J_{ortho} 7.4, Ph), 7.39 (2 H, dd, J_{ortho} 8.2 and J_{ortho} 1.4, Ph), 7.25 (1 H, d, $J_{3,4}$ 8.0, 5-H), 4.49 (2 H, d, J_{vic} 5.5, 2'-CH_2O), 4.43 (1 H, dd, J_{gem} 11.3 and J_{vic} 5.5, 3'-CH_2O), 4.43 (1 H, dd, J_{gem} 11.3 and J_{vic} 6.1, 3'-CH_2O), 3.95 (3 H, s, CO_2Me), 3.52 (1 H, dd, $J_{1',2'}$ 9.1 and $J_{1',4'a}$ 8.5, 1'-H), 3.08 (1 H, ddt, $J_{1',2'}$ 9.1, $J_{2',3'}$ 7.8 and J_{vic} 5.5, 2'-H), 2.75 (1 H, m, 3'-H), 2.53 (1 H, dt, J_{gem} 10.7 and $J_{1',4'a}$ 8.5, 4'a-H), 2.32 (1 H, dd, J_{gem} 10.7 and $J_{1',4'b}$ 9.6, 4'b-H); NOE (1'-H↔3'-H, base-CO_2Me↔3'-CH_2O) was observed; δ_C 166.6 (base CO), 166.6, 166.5 (benzoyl CO), 165.9 (base C-2), 150.8 (base C-6), 137.3 (base C-4), 133.1–128.3 (Ph), 121.4 (base C-5), 119.7 (base C-3), 67.2 (2'-CH_2O), 66.4 (3'-CH_2O), 52.3 (base-Me), 43.9 (C-1'), 41.6 (C-2'), 33.7 (C-3') and 27.6 (C-4') [Found: *m/z* (HRMS, FAB): 460.1751. Calc. for $C_{27}H_{26}NO_6$: 460.1759].

Methyl 2-[2,3-*Bis*(*benzoyloxymethyl*)*cyclobutyl*]*nicotinate* **16b–iib**. ν_{max}(neat)/cm^{-1} 2920, 1710, 1595, 1580, 1560, 1425, 1310, 1280, 1175, 1115, 1070, 1025, 770, 720, 690 and 680; δ_H 8.71 (1 H, dd, $J_{5,6}$ 4.7 and $J_{4,6}$ 1.9, 6-H), 8.10 (1 H, dd, $J_{4,5}$ 8.0 and $J_{4,6}$ 1.9, 4-H), 8.08 (2 H, dd, J_{ortho} 8.5 and J_{meta} 1.4, Ph), 7.93 (2 H, dd, J_{ortho} 8.3 and J_{meta} 1.4, Ph), 7.54 (1 H, dt, J_{ortho} 7.4 and J_{meta} 1.4, Ph), 7.51 (1 H, dt, J_{ortho} 7.7 and J_{meta} 1.4, Ph), 7.41 (2 H, dd, J_{ortho} 8.5 and J_{ortho} 7.4, Ph), 7.38 (2 H, dd, J_{ortho} 8.3 and J_{ortho} 1.4, Ph), 7.20 (1 H, dd, $J_{4,5}$ 8.0 and $J_{5,6}$ 4.7, 5-H), 4.47 (1 H, dd, J_{gem} 11.3 and J_{vic} 5.8, 3'-CH_2O), 4.45 (2 H, d, J_{vic} 5.8, 2'-CH_2O), 4.43 (1 H, dd, J_{gem} 11.3 and J_{vic} 6.1, 3'-CH_2O), 4.27 (1 H, dd, $J_{1',4'b}$ 9.6 and $J_{1',2'}$ 8.8, 1'-H), 3.84 (3 H, s, CO_2Me), 3.38 (1 H, ddt, $J_{2',3'}$ 9.1, $J_{1',2'}$ 8.8 and J_{vic} 5.8, 2'-H), 2.73 (1 H, tdd, $J_{3',4'}$ 10.4, $J_{2',3'}$ 9.1 and J_{vic} 6.1, 3'-H), 2.57 (1 H, dd, J_{gem} 10.4 and $J_{1',4'a}$ 8.5, 4'a-H) and 2.20 (1 H, dd, J_{gem} 10.4 and $J_{1',4'b}$ 9.6, 4'b-H); NOE was not observed; δ_C 166.9 (base CO), 166.7, 166.6 (benzoyl CO), 162.2 (base C-2), 152.0 (base C-6), 138.0 (base C-4), 132.8–128.3 (Ph), 125.1 (base C-3), 120.9 (base C-5), 67.6 (2'-CH_2O), 66.7 (3'-CH_2O), 52.3 (base-Me), 42.2 (C-1'), 38.7 (C-2'), 33.7 (C-3') and 28.5 (C-4') [Found: *m/z* (HRMS, FAB), 460.1757 (M + H) Calc. for $C_{27}H_{26}NO_6$ 460.1759].

4-[2,3-*Bis*(*benzoyloxymethyl*)*cyclobutyl*]*pyrimidine* **16b–iva**. ν_{max}(neat)/cm^{-1} 3040, 2920, 1715, 1595, 1580, 1545, 1465, 1450, 1390, 1315, 1280, 1180, 1115, 1075, 1030, 725, 695 and 685; δ_H 9.16 (1 H, d, $J_{2,5}$ 1.3, 2-H), 8.57 (1 H, d, $J_{5,6}$ 5.1, 6-H), 8.07 (2 H, dd, J_{ortho} 8.4 and J_{meta} 1.3, Ph), 7.94 (2 H, dd, J_{ortho} 8.4 and J_{meta} 1.3, Ph), 7.56 (1 H, tt, J_{ortho} 7.3 and J_{meta} 1.3, Ph) 7.55 (1 H, tt, J_{ortho} 7.3, J_{meta} 1.3, Ph), 7.46–7.39 (4 H, m, Ph), 7.18 (1 H, dd, $J_{5,6}$ 5.1 and $J_{2,5}$ 1.3, 5-H), 4.49 (2 H, d, J_{vic} 5.7, 2'-CH_2O), 4.47 (1 H, dd, J_{gem} 11.0 and J_{vic} 5.5, 3'-CH_2O), 4.42 (1 H, dd, J_{gem} 11.0 and J_{vic} 6.2, 3'-CH_2O), 3.42 (1 H, q, $J_{1',2'}$ 9.0, 1'-H), 3.07 (1 H, tt, $J_{1',2'}$ 9.0 and J_{vic} 5.7, 2'-H), 2.76 (1 H, tdd, $J_{3',4'a}$ 8.6, J_{vic} 6.2 and J_{vic} 5.5, 3'-H), 2.51 (1 H, dt, J_{gem} 11.0 and $J_{3',4'a}$ 8.6, 4'a-H) and 2.31 (1 H, dt, J_{gem} 11.0 and $J_{1',4'b}$ 9.5, 4'b-H); NOE (1'-H↔2'-CH_2O, 2-H↔3'-CH_2O) was observed; δ_C 170.4 (base C-4), 166.5 (benzoyl CO), 159.0 (base C-2), 156.7 (base C-6), 133.1–128.4 (Ph), 119.4 (base C-5), 66.9 (2'-CH_2O), 66.2 (3'-CH_2O), 43.5 (C-1'), 40.9 (C-2'), 33.7 (C-3') and 26.9 (C-4') [Found: *m/z* (HRMS, FAB), 403.1657 (M + H) Calc. for $C_{24}H_{23}N_2O_4$ 403.1656]. [Found: C, 71.5; H, 5.55; N, 6.9. Calc. for $C_{24}H_{22}N_2O_4$: C, 71.62; H, 5.51; N, 6.96].

2-[2,3-*Bis*(*benzoyloxymethyl*)*cyclobutyl*]*pyrimidine* **16b–ivb**. ν_{max}(neat)/cm^{-1} 2930, 1710, 1670, 1560, 1520, 1450, 1430, 1320, 1260, 1185, 1110, 1075, 1030, 810 and 720; δ_H 8.67 (2 H, d, $J_{4,5} = J_{5,6}$ 4.7, 4-H and 6-H), 8.07 (2 H, dd, J_{ortho} 8.2 and J_{meta} 1.4, Ph), 7.97 (2 H, dd, J_{ortho} 8.2 and J_{meta} 1.4, Ph), 7.54 (1 H, tt, J_{ortho} 7.4 and J_{meta} 1.4, Ph), 7.53 (1 H, tt, J_{ortho} 7.4 and J_{meta} 1.4, Ph), 7.41 (2 H, dd, J_{ortho} 8.2 and J_{meta} 7.4, Ph), 7.39 (2 H, dd, J_{ortho} 8.2 and J_{meta} 7.4, Ph), 7.13 (1 H, t, $J_{4,5} = J_{5,6}$ 4.7, 5-H), 4.53 (1 H, dd, J_{gem} 11.3 and J_{vic} 5.5, 2'-CH_2O), 4.48 (1 H, dd, J_{gem} 11.3 and J_{vic} 5.8, 2'-CH_2O), 4.45 (2 H, dd, J_{vic} 6.0 and J_{vic} 6.2, 3'-CH_2O), 3.67 (1 H, dd, $J_{1',4'b}$ 9.6 and $J_{1',4'a}$ 8.5, 1'-H), 3.17 (1 H, tt, $J_{1',2'}$ 8.8 and J_{vic} 5.5, 2'-H), 2.82–2.74 (1 H, m, 3'-H), 2.58 (1 H, dt, J_{gem} 11.0 and $J_{1',4'a}$ 8.5, 4'a-H) and 2.32 (1 H, dt, J_{gem} 11.0 and $J_{1',4'b}$ 9.6, 4'b-H); NOE (1'-H↔3'-H) was observed [Found: *m/z* (HRMS, FAB), 403.1663. Calc. for $C_{24}H_{23}N_2O_4$: 403.1656].

2-[2,3-*Bis*(*benzyloxymethyl*)*cyclobutyl*]-4-*methylquinoline* **16a–i**. ν_{max}(neat)/cm^{-1} 2900, 1710, 1600, 1505, 1450, 1375, 1320, 1260, 1180, 1120, 1075, 1030, 770, 715 and 695; δ_H 8.28–8.10 (1 H, br s, 8-H), 7.94 (1 H, d, $J_{5,6}$ 8.4, 5-H), 7.70 (1 H, t, $J_{6,7}$ 7.5, 7-H), 7.53 (1 H, t, $J_{6,7}$ 7.5, 6-H), 7.37–7.23 (11 H, m, 3-H and Ph), 4.55 (2 H, d, $J_{long\ range}$ 0.7, CH_2Ph), 4.52 (2 H, d, $J_{long\ range}$ 2.0, CH_2Ph), 3.70–3.59 (1 H, m, 1'-H), 3.69 (1 H, d, J_{vic} 5.7, 2'-CH_2OBn), 3.68 (1 H, d, J_{vic} 6.2, 2'-CH_2OBn), 3.60 (2 H, d, J_{vic} 4.4, 3'-CH_2OBn), 2.88–2.81 (1 H, m, 2'-H), 2.62 (3 H, s, Me), 2.57–2.51 (2 H, m, 3'-H and 4'a-H) and 2.32–2.24 (1 H, m, 4'b-H); NOE was not observed [Found: *m/z* (HRMS, FAB),

438.2437 (M + H) Calc. for $C_{30}H_{32}NO_2$: 438.2431] (Found: C, 82.6; H, 7.2; N, 3.1. Calc. for $C_{30}H_{31}NO_2$: C, 82.34; H, 7.14; N, 3.20%).

2-[2,3-*Bis*(*benzyloxymethyl*)*cyclobutyl*]-3-*chloropyridine* **16a–va**. ν_{max}(neat)/cm^{-1} 2840, 1570, 1440, 1350, 1205, 1095, 800, 740 and 700; δ_H 8.47 (1 H, dd, $J_{5,6}$ 4.7 and $J_{4,6}$ 1.6, 6-H), 7.58 (1 H, dd, $J_{4,5}$ 8.0 and $J_{4,6}$ 1.6, 4-H), 7.34–7.24 (10 H, m, Ph), 7.05 (1 H, dd, $J_{4,5}$ 8.0, $J_{5,6}$ 4.7, 5-H), 4.52 (2 H, s, CH_2Ph), 4.50 (2 H, s, CH_2Ph), 3.82 (1 H, q, $J_{1',2'}$ 9.0, 1'-H), 3.62 (1 H, dd, J_{gem} 9.5, J_{vic} 6.0, 3'-CH_2O), 3.59 (2 H, d, J_{vic} 5.3, 2'-CH_2O), 3.54 (1 H, dd, J_{gem} 9.5 and J_{vic} 6.9, 3'-CH_2O), 2.90 (1 H, ddd, $J_{2',3'}$ 13.9, $J_{1',2'}$ 9.0 and J_{vic} 5.3, 2'-H), 2.62–2.54 (1 H, m, 3'-H), 2.47 (1 H, dt, J_{gem} 9.9 and $J_{1',4'a}$ 8.4, 4'a-H) and 1.97 (1 H, dt, J_{gem} 9.9 and $J_{1',4'b}$ 9.5, 4'b-H); NOE (1'-H↔3'-H, 1'H↔2'-CH_2OBn) was observed (Found: *m/z* (HRMS, FAB), 408.1722, (M + H). Calc. for $C_{25}H_{27}ClNO_2$: 408.1729] (Found: C, 73.9; H, 6.6; N, 3.2. Calc. for $C_{25}H_{26}ClNO_2$: C, 73.61; H, 6.42; N, 3.43%).

6-[2,3-*Bis*(*benzyloxymethyl*)*cyclobutyl*]-3-*chloropyridine* **16a–vb**. ν_{max}(neat)/cm^{-1} 2835, 2320, 1605, 1470, 1445, 1410, 1355, 1150, 1095, 840, 740 and 700; δ_H 8.49 (1 H, s, 2-H), 8.31 (1 H, d, $J_{5,6}$ 6.0, 4-H), 7.56 (1 H, d, $J_{5,6}$ 6.0, 5-H), 7.35–7.23 (10 H, m, Ph), 4.51 (2 H, s, CH_2Ph), 4.49 (2 H, s, CH_2Ph), 3.61 (1 H, dd, J_{gem} 9.5 and J_{vic} 4.8, 2'-CH_2O), 3.57 (1 H, q, $J_{1',4'b}$ 9.2, 1'-H), 3.50 (1 H, dd, J_{gem} 9.5 and J_{vic} 6.6, 2'-CH_2O), 3.48 (1 H, d, J_{vic} 4.8, 3'-CH_2O), 3.47 (1 H, d, J_{vic} 4.8, 3'-CH_2O), 2.71 (1 H, tdd, $J_{1',2'}$ = $J_{2',3'}$ 8.8, J_{vic} 6.0 and J_{vic} 4.8, 2'-H), 2.57 (1 H, dt, J_{gem} 10.4 and $J_{1',4'a}$ 8.4, 4'a-H), 2.48 (1 H, ddt, $J_{3',4'}$ 13.4, $J_{2',3'}$ 8.8 and J_{vic} 4.8, 3'-H) and 1.97 (1 H, dt, J_{gem} 10.4 and $J_{1',4'b}$ 9.2, 4'b-H); NOE was not observed [Found: *m/z* (HRMS, FAB), 408.1725. Calc. for $C_{25}H_{27}ClNO_2$: 408.1729].

Typical Procedure for the Deprotection.—Compound **16b–iva** (0.050 g, 0.13 mmol) was dissolved in dry methanol (12 cm^3) saturated with ammonia at 0 °C. After the solution had been stirred for 1 day at room temp. in a sealed tube, the reaction mixture was concentrated and purified by PLC (dichloromethane–methanol, 10:1) to give compound **17–iva** in 91% yield (0.022 g).

2-[2,3-*Bis*(*hydroxymethyl*)*cyclobutyl*]-4-*methylquinoline* **17–i**. δ_H 7.96 (1 H, d, $J_{7,8}$ 8.3, 8-H), 7.93 (1 H, d, $J_{5,6}$ 8.3, 5-H), 7.66 (1 H, dd, $J_{7,8}$ 8.3 and $J_{6,7}$ 6.9, 7-H), 7.50 (1 H, dd, $J_{5,6}$ 8.3 and $J_{6,7}$ 6.9, 6-H), 7.10 (1 H, s, 3-H), 3.83 (1 H, dd, J_{gem} 10.2 and J_{vic} 6.1, 2'-CH_2O), 3.78 (1 H, dd, J_{gem} 10.2 and J_{vic} 8.5, 2'-CH_2O), 3.70 (1 H, dd, J_{gem} 10.8 and J_{vic} 5.2, 3'-CH_2O), 3.61 (1 H, dd, J_{gem} 10.8 and J_{vic} 6.9, 3'-CH_2O), 3.40 (1 H, dt, $J_{1',4'b}$ 9.6 and $J_{1',2'}$ 9.1, 1'-H), 2.67 (3 H, s, base-Me), 2.62 (1 H, dddd, $J_{1',2'}$ 9.1, J_{vic} 8.5, J_{vic} 6.1 and $J_{2',3'}$ 5.8, 2'-H), 2.52 (1 H, dt, J_{gem} 10.2 and $J_{3',4'a}$ 7.7, 4'a-H), 2.33 (1 H, ddd, $J_{3',4'a}$ 7.7, J_{vic} 6.9 and J_{vic} 5.2, 3'-H) and 2.03 (1 H, dt, J_{gem} 10.3 and $J_{1',4'b}$ 9.6, 4'b-H) [Found: *m/z* (HRMS, FAB), 258.1492 (M + H). Calc. for $C_{16}H_{20}NO_2$: 258.1493].

4-[2,3-*Bis*(*hydroxymethyl*)*cyclobutyl*]*pyrimidine* **17–iv**. δ_H 9.10 (1 H, d, $J_{2,5}$ 0.8, 2-H), 8.64 (1 H, d, $J_{5,6}$ 5.2, 6-H), 7.19 (1 H, dd, $J_{5,6}$ 5.2 and $J_{2,5}$ 0.8, 5-H), 4.35 (1 H, br s, 2'-OH), 3.77 (1 H, dd, J_{gem} 10.4 and J_{vic} 7.2, 2'-CH_2O), 3.71 (1 H, dd, J_{gem} 10.5 and J_{vic} 4.7, 3'-CH_2O), 3.68 (1 H, dd, J_{gem} 10.4 and J_{vic} 8.8, 2'-CH_2O), 3.54 (1 H, dd, J_{gem} 10.5 and J_{vic} 8.0, 3'-CH_2O), 3.40 (1 H, br s, 3'-OH), 3.23 (1 H, td, $J_{1',4'a}$ = $J_{1',4'b}$ 10.2 and $J_{1',2'}$ 9.1, 1'-H), 2.51 (1 H, ddt, $J_{1',2'}$ = $J_{2',3'}$ 9.1, J_{vic} 8.8 and J_{vic} 7.2, 2'-H), 2.42 (1 H, dt, J_{gem} = $J_{1',4'a}$ 10.2 and $J_{3',4'a}$ 8.0, 4'a-H), 2.33 (1 H, ttd, $J_{2',3'}$ = $J_{1',4'b}$ 9.1, J_{vic} = $J_{3',4'a}$ 8.0 and J_{vic} 4.7, 3'-H) and 1.98 (1 H, dt, J_{gem} = $J_{1',4'b}$ 10.2 and $J_{3',4'b}$ 9.1, 4'b-H) [Found: *m/z* (HRMS, FAB), 195.1149. Calc. for $C_{10}H_{15}N_2O_2$: 195.1133].

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