SYNTHESIS OF 3-ARYL-4-ACETYL-1H-PYRAZOLO[3,4-b]PYRIDINES AND 3-ARYL-4-ACETYL-1H-PYRAZOLO[4,3-c]PYRIDINES

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Abstract ——— 4-Acetyl-2-chloro-3-lithiopyridine ethylene glycol ketal and 2-acetyl-4-chloro-3-lithiopyridine ethylene glycol ketal were reacted with aromatic aldehydes and oxidation of the resulting alcohols provided the corresponding 3-aroylpyridines. These intermediates were transformed by hydrazine hydrate to 4-acetyl-3-aryl-1H-pyrazolo[3,4-b]- and -[4,3-c]pyridine ethylene glycol ketals, which afforded the title compounds, respectively, by acid hydrolysis.

Polysubstituted derivatives of 1H-pyrazolo[3,4-b]pyridine have been extensively studied as potentially biologically active compounds especially with the aim to find new inhibitors of xanthine oxidases[1]. Probably due to their inaccessibility, the series of polysubstituted 1H-pyrazolo[4,3-c]pyridines are less documented but some derivatives have also been described[2].

However, 4-acetyl-3-aryl-1H-pyrazolo[3,4-b]pyridines are yet unknown. As a new example of the possible use of 4-acetyl-2-chloropyridine ethylene glycol ketal as the starting material for building various polyheterocyclic systems, we wish to report the synthesis of these new 1H-pyrazolo[3,4-b]pyridine derivatives. Further, we describe also the synthesis of the isomeric 4-acetyl-3-aryl-1H-pyrazolo[4,3-b]pyridines from 2-acetyl-4-chloropyridine ethylene glycol ketal.

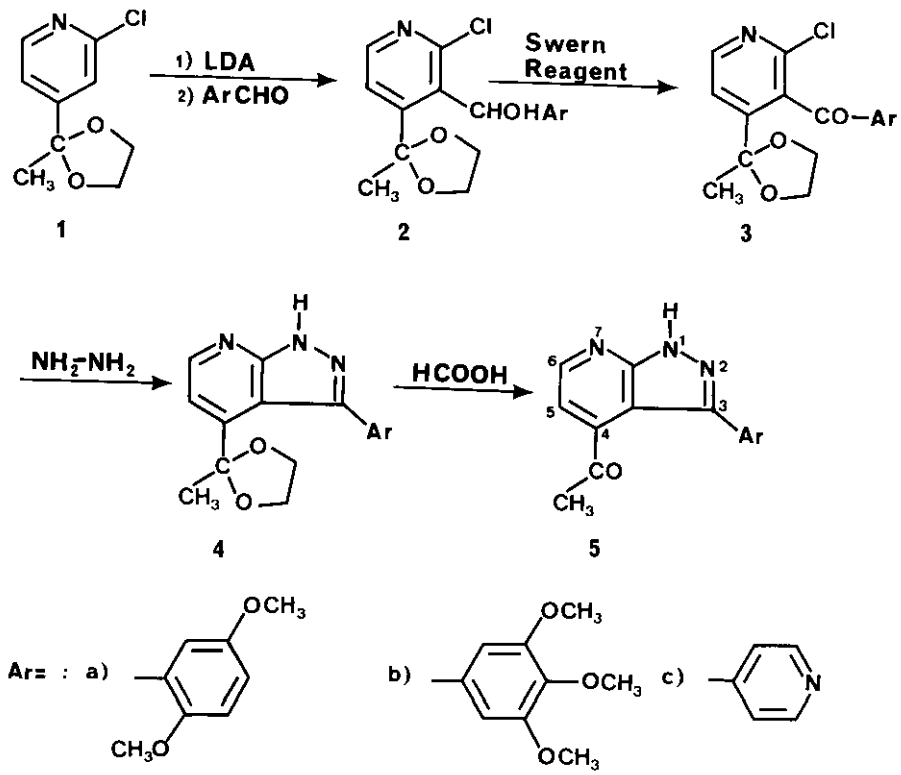
1) 4-Acetyl- 3-aryl-1H-pyrazolo[3,4-b]pyridines

As already described in previous papers from this laboratory[3,4], lithiation of 4-acetyl-2-chloropyridine ethylene glycol ketal **1**[5] provided the corresponding 3-lithiopyridine which condensed with 2,5-dimethoxybenzaldehyde to afford alcohol **2a** in good yield. Compounds **2b** and **2c** have now been obtained under the same conditions, and oxidation of **2** a-c by Swern reagent gave aryl ketones **3** a-c in 42-53 % overall yields.

These chloroketones were treated with hydrazine hydrate to give the expected pyrazolo[3,4-b]pyridine ketals **4** a-c, which were transformed by acid hydrolysis to corresponding 4-acetyl-3-aryl-1H-pyrazolo[3,4-b]pyridines

5 a-c. 4-Acetyl-2-chloropyridine ethylene glycol ketal 1 was thus proved to be a convenient starting material for the synthesis of this new class of 1H-pyrazolo[3,4-b]pyridine derivatives.

Scheme I



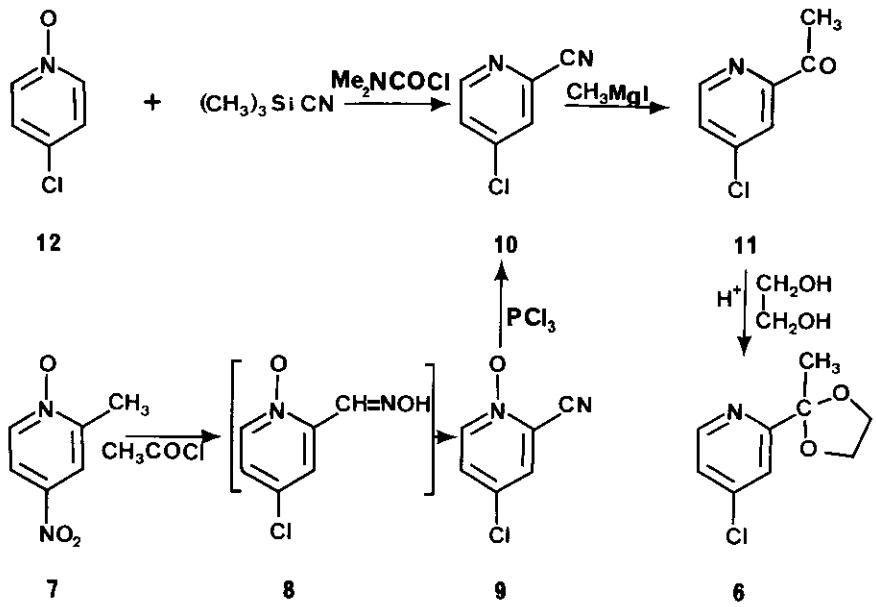
1 2 3 4 5

2) 4-Acetyl-3-aryl-1H-pyrazolo [4,3-c] pyridines

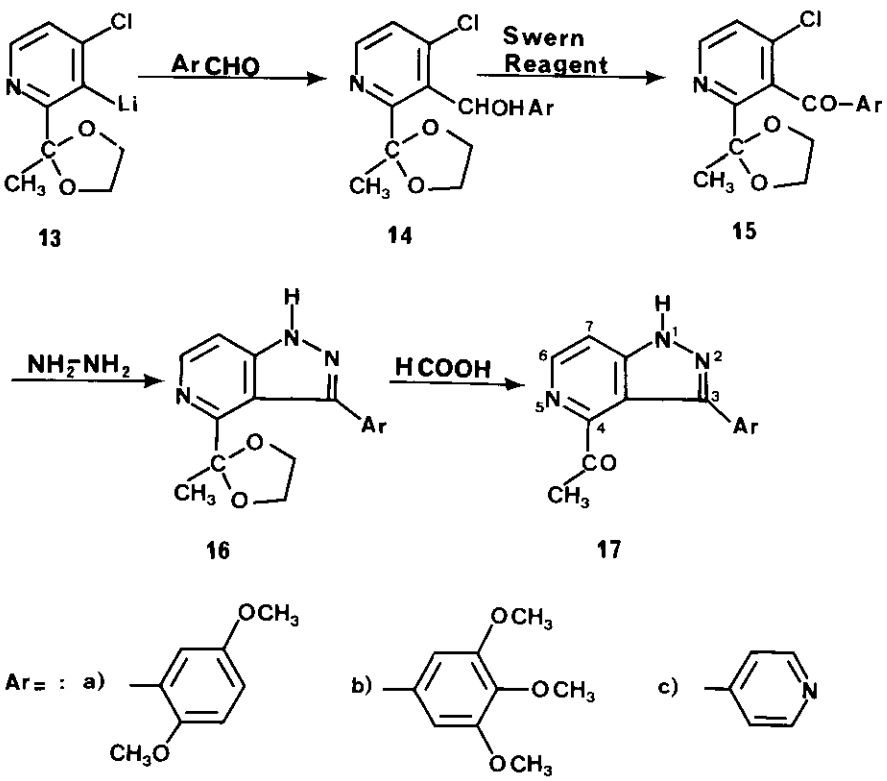
Preceding results allowed us to think that it would be possible to obtain the related 4-acetyl-3-aryl-1H-pyrazolo[4,3-c]pyridines 17 starting from 2-acetyl-4-chloropyridine ethylene glycol ketal 6. This key conpound, however, was not yet described. We have prepared 6 by various transformations summarized in Scheme II.

In order to prepare 4-chloro-2-cyanopyridine 10, a precursor of 2-acetyl-4-chloropyridine 11, 4-chloropyridine N-oxide 12[9] was treated with dimethyl sulfate and potassium cyanide[7] to give 10 in 38.6 % yield (literature[7]: 55 %). Then two other routes were explored. The reaction of 4-nitro-α-picoline N-oxide 7 with acetyl chloride led to 4-chloro-2-cyanopyridine N-oxide 9 through the transient oxime 8[9], and deoxygenation of 9 with phosphorus trichloride gave 10[7] ; the overall yield was only 31.5 % yield. On the other hand, the one-step deoxygenative cyanation[8] of 4-chloropyridine N-oxide 12[9] by means of trimethylsilyl cyanide and N,N-

Scheme II



Scheme III



dimethylcarbamoyl chloride afforded 10 in a satisfactory yield of 85 %. The transformation of 10 into 2-acetyl-4-chloropyridine 11 was effected by the reaction with methylmagnesium iodide in 74 % yield. The ketone 11 was converted to the corresponding ketal 6 in 90 % yield upon treatment with ethylene glycol and p-toluenesulfonic acid (Scheme II).

Lithiation of the chloro ketal 6 with lithium diisopropylamide took place at the 3 position, giving 2-acetyl-4-chloro-3-lithiopyridine ethylene glycol ketal 13 as expected. According to transformations summarized in Scheme III, which is identical with those of Scheme I for preparation of 1H-pyrazolo[3,4-b]pyridine derivatives 5, 4-acetyl-3-aryl-1H-pyrazolo[4,3-c]pyridines 17 a-c were then obtained in good yields. Thus, our results show that 4-acetyl-2-chloropyridine ethylene glycol ketal 1 and 2-acetyl -4-chloropyridine ethylene glycol ketal 6 are convenient starting materials in the synthesis of 4-acetyl-3-aryl-1H-pyrazolo[3,4-b]- and -[4,3-c]pyridines which are two new classes of 1H-pyrazolo[3,4-b]- and -[4,3-c]pyridine derivatives.

EXPERIMENTAL SECTION

4-Chloro-2-cyanopyridine 10 ——— Treatment of 4-chloropyridine N-oxide 12[9] with dimethyl sulfate and potassium cyanide[7] gave 10 in a 38.6 % yield. Two new techniques have then been worked out.

Method A : 4-Nitro-α-picoline N-oxide 7[10] (21.5 g, 0.14 mol) was added to acetyl chloride (100 ml) at room temperature under stirring. An exothermic reaction was observed and the mixture was stirred at room temperature for 2 h, then at 55-65°C for 7 h and cooled. After 15 h, the mixture was filtered and the filtrate was evaporated, giving an oily residue which was taken up in water (100 ml) and neutralized with solid sodium carbonate. The resulting precipitate was collected, washed with cold toluene and air dried (a). The aqueous filtrate was extracted with chloroform, and the residue from the extract was dissolved in the minimum amount of boiling toluene, filtered and cooled (freezer) to give a second crop of the expected product (b). The solid obtained (a + b) was recrystallized from toluene to afford 7.61 g (35.2 %) of 4-chloro-2-cyanopyridine N-oxide 9, mp 130°C. A solution of 9 (10 g, 64 mmol) in chloroform (50 ml) was treated with phosphorus trichloride (10 ml) at room temperature for 2 h and at reflux for 2 h. The mixture was poured in cold water (100 ml) and neutralized with solid sodium carbonate, and the usual work up gave 8.06 g (90 %) of 4-chloro-2-cyanopyridine 10 as colorless needles (cyclohexane), mp 84-85°C, in agreement with literature[7].

Method B : 4-Chloropyridine-N-oxide 12[9] (32.06 g, 0.248 mol) was dissolved in dry dichloromethane (450 ml) and trimethylsilyl cyanide (25 g, 0,252 mole) was added at once under stirring. After 5 min, N,N-dimethylcarbamoyl chloride (26.6 g, 0.248 mol) was added dropwise and the mixture was stirred at room temperature for 8 days. A 10 % aqueous solution of potassium carbonate (350 ml) was added dropwise and the mixture was stirred 15 min. The product was distilled (bp_{20} = 120°C) and crystallized from cyclohexane or hexane, giving 29.2 g (85 %) of colorless crystals, in all respects identical to the compound obtained by method A.

2-Acetyl-4-chloropyridine 11 ——— To a stirred solution of methylmagnesium iodide [from methyl iodide, (142 g, 1 mol), magnesium (24.3 g, 1 mol) and dry diethyl ether (300 ml)], a solution of nitrile **10** (34.6 g, 0.25 mole) in dry diethyl ether (300 ml) was added dropwise. The resulting mixture was kept at room temperature for 3 h and poured in cold aqueous 1M ammonium chloride solution (1.5 l). After acidification to pH 1 with concentrated hydrochloric acid, the mixture was stirred for 15 h, neutralized with 28 % ammonia and treated as usual. The product was distilled (bp_{12} 96-98°C), giving 28.9 g (74 %) of a colorless oil, which progressively crystallized on standing at room temperature, mp 30°C. Anal. Calcd for C_7H_6ClNO : C, 54.01 ; H, 3.85 ; N, 9.00. Found : C, 53.74 ; H, 4.03 ; N, 9.17. ^{1}H Nmr ($CDCl_3$) : δ = 2.69 (s, 3H, CH_3); 7.45 (dd, 1H, 5-H, J_{5-6}= 5.3 Hz, J_{5-3}= 2Hz). 8.00 (d, 1H, 3-H, J = 2 Hz); 8.56 (d, 1H, 6-H, J = 5.3 Hz).

2-Acetyl-4-chloropyridine Ethylene Glycol Ketal 6 ——— A mixture of the ketone **11** (27.3 g, 175 mmol), ethylene glycol (34 g, 0.5 mol), p-toluenesulfonic acid (34.5 g, 200 mmol) and benzene (300 ml) was heated at reflux for 5 h under stirring with a Dean-Stark apparatus and kept at room temperature for 15 h. The resulting mixture was poured into 1M aqueous sodium hydroxide solution (500 ml) under stirring and worked up as usual. The crude product was distilled to give 31.6 g (90 %) of a colorless liquid, bp_{12} 134-136°C. Anal. Calcd for $C_9H_{10}ClNO_2$: C, 54.13 ; H, 5.01 ; N, 7.01. Found : 53.90 ; H, 5.23 ; N, 6.78. ^{1}H Nmr ($CDCl_3$) : δ = 2.61 (s, 3H, CH_3); 3.83-4.07 (m, 4H, CH_2 CH_2); 7.18 (dd, 1H, 5-H, J_{5-6} = 5.3 Hz, J_{5-3} = 1.8 Hz); 7.53 (d, 1H, 3-H, J = 1.8 Hz); 8.48 (d, 1H, 6-H, J = 5.3 Hz).

Alcohols 2 (a-c) and 14 (a-c) ; General Procedure ——— To anhydrous tetrahydrofuran (THF, 100 ml) cooled in ice and maintained under argon, a 1.6 N solution of n-butyllithium in hexane (15 ml, 24 mmol) and anhydrous diisopropylamine (3.36 ml, 24 mmol) were added successively under stirring. This mixture was maintained at 0°C for 1 h, then cooled down to - 70°C and 4-acetyl-2-chloropyridine ethylene glycol ketal **1**[5] or 2-acetyl-4-chloropyridine ethylene glycol ketal **6** (4 g, 20 mmol in 10 ml THF) was added at once. After 4 h under stirring at -70°C a solution of the required aldehyde (20 mmol/ in THF (20 ml) was added dropwise.

The resulting mixture was stirred at -70°C for 2 h, then at room temperature for 15 h, and poured into water (200 ml) and extracted with dichloromethane (3 x 80 ml). The combined organic layers are washed with brine, dried over magnesium sulfate and evaporated under reduced pressure. The residue was taken up in boiling cyclohexane (**2a**, **14b**) or ethyl acetate (**2b**, **2c**, **14a**, **14c**) and the resulting solid (after 18 h at room temperature) was recrystallized from the same solvent to give colorless microcrystals (Table).

Ketones 3 (a-c) and 15 (a-b) ; General Procedure ——— To a cooled flask (-70°C) maintained under argon, dry dichloromethane (5 ml), oxalyl chloride (560 mg, 4.4 mmol), dimethyl sulfoxide (748 mg, 9.6 mmol) in dichloromethane (2 ml) were added successively. The heterogeneous mixture was stirred for 10 min and a solution of the required alcohol (1 mmol) in dichloromethane (5 ml) was added at once. After stirring for 4 h at -70°C,

triethylamine (1.8 ml) was added and the mixture was left to reach room temperature for 15 h. It was then poured into water (100 ml) and extracted with dichloromethane (3 x 60 ml). The residue from the extract was recrystallized from cyclohexane to give colorless microcrystals (Table).

2-Acetyl-4-chloro-3-isonicotinoylpyridine Ethylene Glycol Ketal 15c ——— Under the preceeding conditions, alcohol **14c** was mainly recovered and only trace of the expected ketone **15c** was obtained. Consequently, this alcohol was oxidized by an alterative technique, using manganese dioxide. Thus, a mixture of the alcohol **14c** (1 g, 3.3 mmol), chloroform (70 ml) and manganese dioxide (5 g, 57 mmol) was heated at reflux for 24 h under stirring and filtered. Insoluble material was washed with hot chloroform, and the residue from the chloroform solutions was recrystallized from cyclohexane to give pale yellow microcrystals (Table).

4-Acetyl-3-aryl-1H-pyrazolo[3,4-b]pyridine Ethylene Glycol Ketals 4(a-c) and 4-Acetyl-3-aryl-1H-pyrazolo[4,3-c]pyridine Ethylene Glycol Ketals 16 (a-c); General Procedure ——— A mixture of the ketone **3** (a-c) or **15** (a-c) (1 mmol) and hydrazine hydrate (5 ml) was heated at reflux for 1 h (**15c**), 6 h (**3b**, **3c**, **15a**) or 18 h (**3a**, **15b**) and evaporated to dryness under reduced pressure. The resulting solid residue of 1H-pyrazolopyridine was recrystallized from ethanol (**4a**, **16a**, **16c**) or toluene (**4c**). For compounds **4b** and **16b**, the residues were chromatographed on a silica gel column with dichloromethane-ethanol (95 : 5). Evaporation of solvent afforded a solid which was recrystallized from cyclohexane (**4b**) or cyclohexane-ethyl acetate (1 : 1) (**16b**) to provide colorless crystals (Table).

4-Acetyl-3-aryl-1H-pyrazolo[3,4-b]pyridines 5 (a-c) and 4-Acetyl-3-aryl-1H-pyrazolo[4,3-c]pyridines 17 (a-c); General Procedure ——— A mixture of ketal **4** (a-c) or **16** (a-c) (1 mmol) and 50 % aqueous formic acid (10 ml) was heated at reflux for 7 h, poured into water (50 ml) and basified with solid potassium carbonate. To obtain compounds **5c** and **17c**, the aqueous solution was then saturated with sodium chloride. The resulting precipitate was collected, air dried and recrystallized from toluene (**5a**, **5b**, **17a**, **17b**) or ethyl acetate (**5c**, **17c**) to give pale yellow or yellow crystals (Table).

TABLE

Alcohols 2 (a-c), 14 (a-c), ketones 3 (a-c), 15 (a-c), 4-acetyl-3-aryl-1H-pyrazolopyridine ethylene glycol ketals 4 (a-c), 16 (a-c) and 4-acetyl-3-aryl-1H-pyrazolopyridines 5 (a-c), 17 (a-c).

Compd	mp (°C)	Yield (%)	Analytical Data C	H	N	Cl[a,b]	^{1}H-Nmr (solvent)[c] δ (ppm)
2a	92[4]	72					
2b	142	73	a) 57.65	5.60	3.54	8.96	($CDCl_3$) : 1.74 (s, 3H, CH_3), 3.36-4.10 (m, 4H, CH_2CH_2),
			b) 57.78	5.49	3.49	8.84	3.78 + 3.68 (2s, 3 x 3H, 3', 5'-$(OCH_3)_2$ + 4'-OCH_3), 4.30 (m, 1H, CHOH), 6.43 (s, 2H, 2'-H + 6'-H), 6.59 (m, 1H, CH-OH), 7.58 (d, 1H, 5-H, J_{5-6} = 5 Hz), 8.39 (d, 1H, 6-H, J = 5 Hz).
2c	180	73	a) 58.73	4.93	9.13	11.56	($CDCl_3$) : 1.76 (s, 3H, CH_3), 3.40-4.16 (m, 5H, CH_2CH_2 +
			b) 58.89	4.90	9.18	11.69	CH-OH), 6.74 (br s, 1H, CHOH), 7.35 (d, 2H, 3'-H + 5'-H, $J_{3'-2'}$= 5.5 Hz), 7.65 (d, 1H, 5-H, J_{5-6} = 5.5 Hz), 8.46 (d, 1H, 6-H, J = 5.5 Hz), 8.63 (d, 2H, 2'-H + 6'-H, J = 5.5 Hz).
14a	148	70	a) 59.10	5.51	3.83	9.69	($CDCl_3$) : 1.77 (s, 3H, CH_3), 3.60-4.10 (m, 4H, CH_2-CH_2),
			b) 59.25	5.37	3.98	9.93	3.72 (s, 2 x 3H, $(OCH_3)_2$), 4.40 (d, 1H, CH-OH, J = 7.5 Hz), 6.66-6.82 (4H, 6'-H + 4'-H + 3'-H + CH-OH, J = 7.5 Hz), 7.27 (d, 1H, 5-H, J_{5-6} = 5 Hz), 8.46 (d, 1H, 6-H, J = 5 Hz).
14b	134	51	a) 57.65	5.60	3.54	8.96	($CDCl_3$) : 1.80 (s, 3H, CH_3), 3.07-3.98 (m, 4H, CH_2-CH_2),
			b) 57.42	5.59	3.27	9.13	3.77 + 3.86 (2 s, 3 x 3H, 3', 5'-$(OCH_3)_2$+ 4'-OCH_3), 4.63 (d, 1H, CHOH, J = 11.3 Hz), 6.44 (s, 2H, 2'-H + 6'-H), 6.58 (d, 1H, CH-OH, J = 11.3 Hz), 7.36 (d, 1H, 5-H, J_{5-6} = 5.1 Hz), 8.55 (d, 1H, 6-H, J = 5.1 Hz).
14c	240	52	a) 58.73	4.93	9.13	11.56	($CDCl_3$) : 1.79 (s, 3H, CH_3), 3.06-4.10 (m, 4H, CH_2-CH_2),
			b) 58.69	4.88	9.09	11.43	4.51 (d, 1H, CHOH, J = 9Hz), 6.66 (d, 1H, CHOH, J = 9 Hz), 7.12 ; 7.20 (m, 3H, 3'-H + 5'-H + 5-H), 7.37 (d, 1H, 6-H, J_{6-5} = 5 Hz), 8.57 (dd,2H, 2'-H + 6'-H, $J_{2',3'}$ = 6.2 Hz, $J_{2',5'}$ = 1.5 Hz)
3a	119	85	a) 59.43	4.99	3.85	9.74	($CDCl_3$) : 1.63 (s, 3H, CH_3), 3.30-4.04 (m, 4H, CH_2-CH_2),
			b) 59.58	5.18	4.05	9.98	3.48 (s, 3H, 2'-OCH_3), 3.87 (s, 3H, 5'-OCH_3), 6.86 (d, 1H, 3'-H, $J_{3'-4'}$= 9Hz), 7.13 (dd, 1H, 4'-H, J = 9 Hz, J = 3.2 Hz), 7.40 (d, 1H, 5-H, J_{5-6} = 5.3 Hz), 7.68 (d, 1H, 6'-H, $J_{6'-4'}$= 3.2 Hz), 8.38 (d, 1H, 6-H, J = 5.3 Hz).

3b	120	72	a) 57.95	5.12	3.56	9.00	($CDCl_3$) : 1.69 (s, 3H, CH_3), 3.30-4.10 (m,4H, CH_2CH_2),
			b) 57.94	5.12	3.85	9.32	3.88 + 3.99 (2s, 3 x 3H, 3', 5'-$(OCH_3)_2$ + 4'-OCH_3), 7.05 (s, 2H, 2'-H + 6'-H), 7.52 (d, 1H, 5-H, J_{5-6} = 5.1 Hz), 8.53 (d, 1H, 6-H, J = 5.1 Hz).
3c	139	59	a) 59.12	4.30	9.19	11.64	($CDCl_3$) : 1.70 (s, 3H, CH_3), 3.30-4.10 (m, 4H, CH_2CH_2),
			b) 58.93	4.43	9.15	11.53	7.59 (d, 1H, 5-H, J_{5-6} = 5.1 Hz), 7.74 (m, 2H, 3'-H + 5'-H), 8.68 (d, 1H, 6-H, J = 5.1 Hz), 8.95 (m, 2H, 2'-H + 6'-H).
15a	124	85	a) 59.43	4.99	3.85	9.74	($CDCl_3$) : 1.70 (s, 3H, CH_3), 3.40-4.00 (m, 2H, CH_2CH_2),
			b) 59.60	4.77	3.75	9.26	3.47 (s, 3H, 2'-OCH_3), 3.87 (s, 3H, 5'-OCH_3), 6.86 (d, 1H, 3'-H, $J_{3'-4'}$= 9 Hz), 7.13 (dd, 1H, 4'-H, J = 9 Hz, J = 3.2 Hz), 7.30 (d, 1H, 5-H, J_{5-6} = 5,2 Hz), 7.66 (d, 1H, 6'-H, $J_{6'-4'}$= 3.2 Hz), 8.54 (d, 1H, 6-H, J = 5.2 Hz)
15b	146	74	a) 57.95	5.12	3.56	9.00	($CDCl_3$) : 1.73 (s, 3H, CH_3), 3.30-4.04 (m, 4H, CH_2CH_2),
			b) 58.08	4.97	3.63	9.12	3.86 + 3.96 (2s, 3 x 3H, 3', 5'-$(OCH_3)_2$ + 4'-OCH_3), 6.98 (s, 2H, 2'-H + 6'-H), 7.38 (d, 1H, 5-H, J_{5-6} = 5.2 Hz), 8.66 (d, 1H, 6-H, J = 5.2 Hz).
15c	102	90.5	a) 59.12	4.30	9.19	11.64	($CDCl_3$) : 1.69 (s, 3H, CH_3), 3.30-3.96 (m, 4H, CH_2-CH_2),
			b) 58.92	4.31	9.42	11.75	7.42 (d, 1H, 5-H, J_{5-6}= 5.2 Hz), 7.56 (dd, 2H, 3'-H + 5'-H, $J_{3'-2'}$= 6Hz, $J_{3'-5'}$ = 1.5 Hz), 8.68 (d,1H,6-H, J = 5.2 Hz), 8.83 (dd, 2H, 2'-H + 6'-H, J = 6 Hz, J = 1.5 Hz).
4a	155	76.5	a) 62.00	6.50	10.85[d]		($CDCl_3$) : 1.57 (s, 3H, CH_3), 3.50-3.96 (m, 4H, CH_2-CH_2),
			b) 61.78	6.27	10.86		3.71 + 3.82 (2s, 2 x 3H, 2', 5'-$(OCH_3)_2$), 6.92-6.98 (m, 3H, 3'-H + 4'-H + 6'-H), 7.35 (d, 1H, 5-H, J_{5-6} = 5.1 Hz), 8.57 (d, 1H, 6-H, J = 5.1 Hz).
4b	150	56	a) 61.44	4.70	11.32		($CDCl_3$) : 1.52 (s, 3H, CH_3), 3.60-4.20 (m, 4H, CH_2CH_2),
			b) 61.21	5.61	11.36		3.94 + 3.97 (2s, 3 x 3H, 3', 5'-$(OCH_3)_2$ + 4'-OCH_3), 6.97 (s, 2H, 2'-H + 6'-H), 7.52 (d, 1H, 5-H, J_{5-6} = 4.9 Hz), 8.68 (d, 1H, 6-H, J = 4.9 Hz).
4c	>270	84	a) 63.82	5.00	19.85		($CDCl_3$) : 1.53 (s, 3H, CH_3), 3.57-3.99 (m, 4H, CH_2-CH_2),
			b) 63.48	4.80	20.08		7.43 (d, 1H, 5H, J_{5-6} = 4.8 Hz), 7.54 (dd, 2H, 3'-H + 5'-H, $J_{3'-2'}$ = 6.2 Hz, $J_{3'5'}$ = 1.5 Hz), 8.64 (d, 1H, 6-H, J = 4.8 Hz), 8.73 (dd, 2H, 2'-H + 6'-H, J = 6.2, J = 1.5 Hz).

16a	262	62.5	a) 63.33	5.61	12.31	(DMSO-d_6) : 1.43 (s, 3H, CH_3), 3.14-3.58 (m, 4H, CH_2-CH_2), 3.51 + 3.66 (2s, 2 x 3H, 2', 5'-$(OCH_3)_2$), 6.75-6.89 (m, 3H, 3'-H + 4'-H + 6'-H), 7.44 (d, 1H, 7-H, J_{7-6} = 5.9 Hz), 8.22 (d, 1H, 6-H, J = 5.9 Hz).
			b) 63.09	5.43	12.41	
16b	262	58	a) 61.44	4.70	11.32	($CDCl_3$) : 1.62 (s, 3H, CH_3), 3.57-4.08 (m, 4H, CH_2CH_2), 3.86 + 3.89 (2s, 3 x 3H, 3', 4', 5'-$(OCH_3)_3$), 6.87 (s, 2H, 2'-H + 6'-H), 7.33 (d, 1H, 7-H, J_{7-6} = 6 Hz), 8.47 (d, 1H, 6-H, J = 6 Hz), 11.13 (br s, 1H, NH).
			b) 61.77	5.38	11.28	
16c	>270	90	a) 63.82	5.00	19.85	(DMSO-d_6) : 1.60 (s, 3H, CH_3), 3.12-3.80 (m, 4H, CH_2-CH_2), 7.48 (dd, 2H, 3'- H + 5'-H, $J_{3'-2'}$= 6 Hz, $J_{3'5'}$ = 1.5 Hz), 7.63 (d, 1H, 7-H, J_{7-6}= 5.8 Hz), 8.39 (d, 1H, 6-H, J = 5.8 Hz), 8.68 (dd, 2H, 2'-H + 6'-H, J = 6 Hz, J = 1.5 Hz).
			b) 63.60	4.80	19.76	
5a	190	79	a) 64.63	5.09	14.14	($CDCl_3$): 2.32 (s, 3H, CH_3), 3.60 + 3.87 (2s, 2 x 3H, 2', 5'-$(OCH_3)_2$), 6.88 (d, 1H, 3'-H, $J_{3'-4'}$= 8.6 Hz), 7.03 (dd, 1H, 4'-H, $J_{4'-6'}$= 2.8 Hz, J = 8.6 Hz), 7.30 (d, 1H, 6'-H, J = 2.8 Hz), 7.31 (d, 1H, 5-H, J_{5-6} = 4.8 Hz), 8.72 (d, 1H, 6-H, J = 4.8 Hz).
			b) 64.87	4.96	14.32	
5b	137	51	a) 62.37	5.24	12.84	($CDCl_3$) : 2.20 (s, 3H, CH_3), 3.94 (s, 3 x 3H, 3', 4', 5-(O$CH_3)_3$), 6.86 (s, 2H, 2'- H + 6'-H), 7.16 (d, 1H, 5-H, J_{5-6} = 4.9 Hz), 8.74 (d, 1H, 6-H, J = 4.9 Hz).
			b) 62.40	5.39	12.80	
5c	250	81	a) 65.53	4.23	23.52	(DMSO. d_6) : 2.65 (s, 3H, CH_3), 7.48 (dd, 2H, 3'-H + 5'-H, $J_{3'-2'}$= 6 Hz, $J_{3'5'}$ = 1.5 Hz), 7.67 (d, 1H, 5-H, J_{5-6} = 4.5 Hz), 8.66 (dd, 2H, 2'-H + 6'-H, J = 6 Hz, J = 1.5 Hz), 8.81 (d, 1H, 6-H, J = 4.5 Hz).
			b) 65.32	3.95	23.31	
17a	>270	74	a) 64.63	5.09	14.14	(DMSO-d_6) : 2.64 (s, 3H, CH_3), 3.58 + 3.81 (2s, 2 x 3H, 2', 5'-$(OCH_3)_2$), 6.97-7.12 (m, 3H, 3'-H + 4'-H + 6'-H), 7.78 (d, 1H, 7-H, J_{7-6} = 5.7 Hz), 8.44 (d, 1H, 6-H, J = 5.7 Hz).
			b) 64.35	4.93	14.06	
17b	138	56	a)62.37	5.24	12.84	($CDCl_3$) : 2.63 (s, 3H, CH_3), 3.90 + 3.94 (2s, 3 x 3H, 3', 4', 5'-$(OCH_3)_3$), 6.78 (s, 2H, 2'-H + 6'-H), 7.50 (d, 1H, 7-H, J_{7-6} = 6 Hz), 8.51 (d, 1H, 6-H, J = 6 Hz).
			b) 62.46	5.37	12.58	

17c	262	56	a) 65.53	4.23	23.52	(DMSO-d_6) : 2.76 (s, 3H, CH_3), 7.51 (dd, 2H, 3'-H + 5'-H, $J_{3'2'}$ = 6 Hz, $J_{3'5'}$ = 1.5 Hz), 7.90 (d, 1H, 7-H, J_{7-6} = 5.6 Hz), 8.56 (d, 1H, 6-H, J = 5.6 Hz), 8.67 (dd, 2H, 2'-H + 6'-H, J = 6 Hz, J = 1.5 Hz).
			b) 65.62	4.15	23.30	

a - Calculed

b - Found

c - ^1H Nmr spectra were recorded at 100 MHz on a Varian XL 100 spectrometer.

d - Calculed for $C_{18}H_{19}N_3O_4$, C_2H_5OH

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Received, 22nd May, 1989