The Oxidation of Partially Acylated Myoinositols

Frederick Kurzer, Dennis Chapman

Royal Free Hospital School of Medicine, University of London, London NW3, England

Z. Naturforsch. **51b,** 68–78 (1996); received May 17, 1995

Tetrakisacylmyoinositols, Pentakisacylmyoinositols, Acylated Myoinososes-2, Mass Spectra, Myoinositol Esters

1,3,4,6-Tetrakis- and 1,3,4,5,6-pentakis-acylmyoinositols are obtained by the controlled catalyzed acylation of myoinositol. The extent of the substitution depends both on the reaction conditions and the structure of the acylating agent, including steric factors. Chromic acid oxidation converts the acylmyoinositols into the corresponding 2-ketones. Under electron impact, the compounds undergo stepwise deacylation.

Introduction

The design of targeted syntheses involving cyclitols [1,2] is impeded by difficulties arising from the full substitution by hydroxy groups of their alicyclic nucleus, necessitating more or less elaborate procedures for the protection of selected groups. In the six-membered pattern, conformational differences provide a means of steering reactions into a particular course, based on contrasting reactivities of axial versus equatorial hydroxyls in the cyclohexane ring [3], acylation [4] occurring preferentially at equatorial, and oxidation at axial hydroxy-groups [1a,5].

Myoinositol (**1**) conforms in both respects to this general behaviour. Esterification (and hydrolysis) occurs more rapidly at its equatorial hydroxyls [1a], while dehydrogenation by oxygen in the presence of a platinum catalyst [6] or suitable microorganisms (especially Acetobacter suboxidans) [7] is confined to its 2-ax-hydroxy group, affording myoinosose-2 (**14,** R = H) [8]. γ-Irradiation also forms the 2-monoketone as the primary product, though not in isolable quantities [9]. Mild bromine oxidation produces chiefly moderate amounts of diketones [10]. In contrast to these stereospecific dehydrogenations, the action of other oxidizing agents (including permanganate [11], periodate [12], nitric acid [13], dimethyl sulphoxide [14] and photolytic oxygen [15]) commonly effect more deep-seated changes, tending to aromatization [13,14], quinone formation [13], ring cleavage [11,12,15] and complete degradation [11,12,15]. A singular case is the action of hot concentrated nitric acid, which converts myoinositol into DL-epi-inosose in moderate yield [8,16], involving the anomalous preferential oxidation of an equatorial hydroxy group.

Results and Discussion

Our exploratory experiments aimed at restricting the action of conventional oxidizing agents to the 2-ax-hydroxy group of myoinositol by employing equimolar (or lower) proportions of oxidant under restrained conditions, as an effective approach to the 2-monoketone, were not successful. Thus, an equivalent of aqueous chromic acid, hypobromite, permanganate or hydrogenperoxide-ferrous sulphate (Fenton's reagent) was rapidly consumed in completely degrading a portion of the total available myoinositol, leaving most of the remainder unaffected and recoverable (*e.g.* as hexaacetate). Attention was therefore directed to the production and oxidation of suitable partially acylated myoinositols, with the results reported below.

Acylation

Substitution at all six hydroxyl-groups of myoinositol occurs readily on treatment with acyl halides or anhydrides in the presence of zinc chloride [17] or sulphuric or perchloric acid [1c]. The required partial acylation, with preservation of the free 2-ax-hydroxy-group, has now been effected in pyridine, in the presence of 4-dimethylaminopyridine as catalyst. The latter catalyzes acylations up

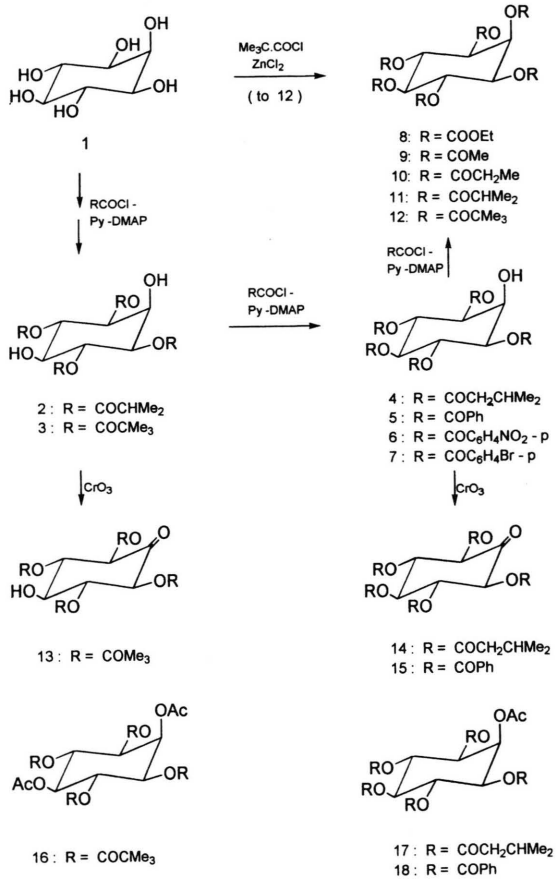
* Reprint requests to Dr. F. Kurzer.

0932–0776/96/0100–0068 $06.00

to 10^4 times more effectively than pyridine itself [18], thus making the use of milder conditions accessible. Applied under specified conditions to acyl halides incorporating sufficiently bulky head groups, the procedure afforded partially acylated products retaining their free 2-ax-hydroxy group in satisfactory and reproducible yields.

Thus, 1,3,4,6-tetrakispivaloylmyoinositol (**3**) was readily obtained by the catalyzed action of pivaloyl chloride under controlled conditions (temperature, rate of addition). Reaction did not proceed beyond the tetrasubstitution stage, in spite of the necessary use of a large excess (12 mol) of the acylating agent. The remaining free 2- and 5-hydroxy groups (of **3**) underwent acetylation by acetic anhydride-zinc chloride [17] as expected, resulting in **16**. This procedure was also used for preparing the hexakispivaloyl compound **12** for comparison. The structure of **3** was confirmed by the symmetrical distribution of its acyl-substituents, as shown by its ^{13}C NMR spectrum: The four pivaloyl groups produce only two low-field carbonyl singlets (δ 176.7, 176.3 ppm), while their (trimethyl)methyl moieties give rise to one pair of singlets (C of CMe_3, at 38.2, 38.1 ppm) and one pair of quartets (δ 26.9, 26.7 ppm), the latter originating collectively from the triple groups of the equivalent methyl entities. The four doublets of the cyclohexane ring carbons, two of them of double relative intensity, are assigned in accordance with the mapped spectrum of the parent compound **1** [19].

Isobutyroyl chloride, having comparable molecular dimensions, similarly produced the 1,3,4,6-tetrakisacyl derivative (**2**) as the major product (35–40%), together with some 1,3,4-tris-acyl compound (15–18%), formulated in accordance with the known [20] descending reactivity towards acylation and tosylation of the hydroxyl groups of **1**. With isovaleroyl chloride, however, acylation continued to the 1,3,4,5,6-penta-substituted stage **4**; here, replacement of *all* the equatorial hydroxy-groups may be promoted by the reduced steric hindrance operating between the bulky head groups of the substituents, due to their increased distance from the central cyclohexane ring. This apparent steric influence is further emphasized by the behaviour of linear aliphatic acyl halides, which effected hexa-acylation (to **9–11**). Ethyl chloroformate, described as a reagent of choice



[21] for preferentially acylating equatorial over axial hydroxy groups, did not differentiate between them in the present instance, giving **8** in low yield.

In the aromatic series, the catalyzed acylation afforded 1,3,4,5,6-pentakisaroylmyoinositols (**5–7**) as sole products consistently in high yield (80–90% for **5, 6**). The use of smaller proportions of acylating agent at lower temperatures still effected penta-acylation, though in diminished yields. The structure of the pentakisbenzoyl-compound **5** (and that of its isovaleroyl-analogue **4**) was confirmed by their ^{13}C NMR spectra (see Experimental). Both compounds underwent further mono-acetylation (to **18** and **17**, respectively). Attempts to obtain a monobenzoyl derivative of **1** by the use of a large excess of myoinositol at 0–10 °C were unsuccessful, the benzoyl chloride being recovered as the anhydride.

Oxidation

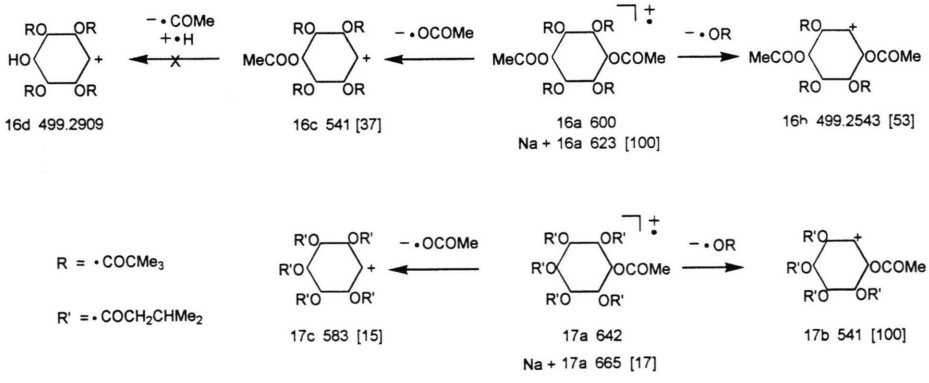
The remaining free 2-ax-hydroxy-group of the foregoing acylated myoinositols readily underwent oxidation. The action of Fieser's chromic acid reagent [22] converted the reactants (**3–5**) into the corresponding 2-ketones (**13–15**) in good yield, contrasting with the difficulty of accomplishing this reaction with the parent compound (see above). The 2-ax-5-eq-dihydroxy compound **3** gave the monoketone **13**, even though more than sufficient oxidant was employed to produce the 2,5-diketone, thus illustrating again the greater susceptibility to oxidation of axial over equatorial hydroxy groups in cyclohexane. The pentakisisovaleroyl-2-ketone **14** was converted into the parent inosose-2 (**14**, R = H) by alkaline hydrolysis, but the well-documented difficulty [6,8] of isolating this compound as its phenylhydrazone, especially on the small scale, impaired the yields (35%).

Mass Spectra

Under electron impact, cyclohexanol [23] and cyclohexanone [24] as well as the inositols [25] are ring-cleaved, with the production of such fragments as $CH_2{=}CH{-}CH{=}OH^+$ [23] of $CH_2{=}CH{-}C{=}O^+$ [24] from the former, and of $HOCH{=}CH{-}CH{=}OH^+$ (*m/z* 73) from the latter [25]. In contrast, the present myoinositol esters underwent a multi-stage fission, with prevailing retention of their alicyclic ring structure: their base peaks correspond almost invariably to the intact molecular ion, while subsequent prominent signals indicate the sequential removal of their peripheral substituents as acyl-or acyloxy entities, or elimination of the elements of the appropriate carboxylic acid, and occasional loss of water. While the sequence of these events is clear, there remains some uncertainty concerning the precise position isomerism of the intermediate ionic fragments, depending on *which* of two or more identical acyl groups is removed preferentially in any fission stage. These uncertainties are reduced, but not entirely removed, by a comparison of the mass spectra of acylmyoinositols with those of their analogues incorporating a differentiating structural element, such as a keto group (*e.g.* in **13–15**) or an acyl group distinct from the others (*e.g.* in **16–18**).

Thus, pentakisisovaleroylmyoinositol (**4**) and its corresponding 2-ketone (**14**) give rise to a matching series of signals consistently 2 mass units apart (Table I), suggesting a strictly parallel fragmentation sequence for both structures, and the consequent likely retention of the 2-keto- and hence the 2-hydroxy-group (in **14** and **4** respectively) and their immediate structural environment during the fission. The same consistency, though over a narrower range, is seen in the case of the pentakisbenzoyl pair of compounds (**5, 15**).

The initial fragmentation stage of mixed acetylacylmyoinositols (**16, 17**) provides the following information (Scheme 1): The ion radical **17a** of the 2-acetyl-1,3,4,5,6-pentakisisovaleroyl derivative **17** undergoes simultaneous loss of an isovaleroyloxy- or acetoxy-moiety, yielding **17b** and **17c** respectively. The former is the greatly predominating fission, **17b** producing the base peak (compared with a 15% abundance of **17c**). In the 2,5-diacetyl-1,3,4,6-tetrakispivaloyl compound **16**, the acetyl groups are again preferentially retained, favouring



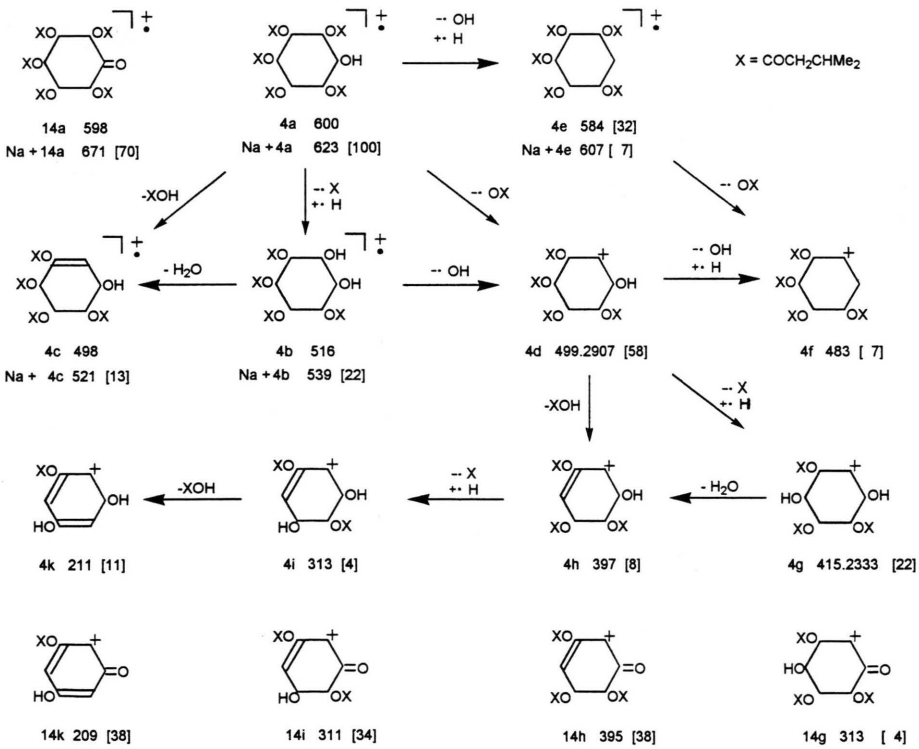
Scheme 1.

	4		**14**		**5**		**15**
m/z	Abundance	*m/z*	Abundance	*m/z*	Abundance	*m/z*	Abundance
623	100	621	70	723	100	721	45
607	7	605	4	619	3	617	9
539	22	537	2	601	6	599	18
521	13	519	8	579	13	577	12
499	58	497	100	481	6	479	20
483	7	481	5				
415	22	413	14				
397	7	395	38				
313	4	311	34				
211	11	209	38				

Table I. Correspondence of ion fragments of acylmyoinositols (**4, 5**) and their 2-ketones (**14, 15**).

the formation of **16b**. Its possible formulation as **16d** ($C_{26}H_{43}O_9$, *m/z* 499.2909), which would arise from **16a** by loss of an acetoxy and acetyl fragment, is excluded by high-resolution measurement of its exact mass ($C_{25}H_{39}O_{10}$, found: *m/z* 499.2543). Provided that these observed effects are not due to differences in the bulk of the acyl groups concerned, they suggest a tendency for the preferred, though not exclusive, removal of the substituents from the sides rather than the apexes of the chair conformations.

On the basis of the foregoing considerations, a specimen fragmentation scheme is tentatively proposed for the pentakisisovaleroyl derivative **4** as a representative pattern (Scheme 2). The spectrum is dominated by the molecular ion **4a**, which produces the base peak, and by species arising therefrom by loss of an acyloxy or acyl radical, forming **4d** and **4b**, respectively. Subsequent comparable steps account for all the significant signals, finally yielding $C_{11}H_{15}O_4^+$ formulated as the dihydroxyisovaleroyl species **4k**. The molecular formulae of



Scheme 2.

the key-intermediates **4d** and **4g** (which feature also significantly in the mass spectra of **3, 12** and **17**) were confirmed by measurement of their accurate masses. The ketone **14** corresponding to **4** undergoes a precisely parallel degradation, the last four stages of which (**14g–14k**, formed incidentally in greater abundance than **4g–4k**), are included in Scheme 2 for comparison.

The proposed scheme accounts satisfactorily for the salient features of the fragmentation process. With the reservation that the adopted position isomerism of the structures may be subject to minor modification, it may serve as model for constructing analogous schemes for the other compounds of the series, from the numerical data and assignments recorded in the Experimental Part.

It is noteworthy that the proposed fragmentation schemes for the acylmyoinositols share their essential characteristics with those of monosaccharide esters [26]. In particular, the degradation of peracetylpyranoses [27, 28] and analogues [29] is characterized by the rapid loss of acetyl and acetoxy moieties, as well as acetic acid, with marked initial retention of the cyclic structure [27]; however, the pyranose nucleus appears to undergo significant parallel and subsequent ring fission [27, 28] that is not prominent in the homocyclic acylmyoinositol structure.

Experimental

Melting points are uncorrected. Light petroleum had b.p. 60–80 °C. Analysis specimens were desolvated at 100–120 °C in a vacuum for 2–4 h, if necessary.

Infrared spectra were measured on a Unicam 1000 instrument, using KBr discs. Unassigned peaks are not recorded except for selected compounds (**3, 13, 5, 15**).

Mass spectra were determined using a VG-ZAB-2F instrument operating at 70 eV. Numbers in square brackets denote the intensity of the peaks relative to the base peak [100]. Molecular formulae were confirmed and ion fragments identified, in appropriate cases, by the determination of accurate molecular weights by the fast atom bombardment technique, involving the use of a 3-methylnitrobenzene-sodium matrix.

^{13}C NMR spectra were determined on a Bruker WM 250 Fourier transform instrument equipped with an Aspect 3000 data system, at 62.89 MHz. The solvent was deuterio-dimethyl sulphoxide. The numerical data recorded refer to the proton noise decoupled chemical shifts and first order multiplicities of the individual signals. Chemical shifts are given in δ (ppm) downfield from $SiMe_4$ as internal standard.

1,3,4,6-Tetrakispivaloylmyoinositol (**3**)

A stirred solution of myoinositol (3.6 g, 0.02 mol) and 4-dimethylaminopyridine (0.3 g) in pyridine (80 ml), preheated to 90 °C, was treated dropwise during 1 h with pivaloyl chloride (28.9 g, 0.24 mol; *ca.* 20 drops/min), the mixture being kept at 90–95 °C by heating as necessary. Stirring at this temperature was continued for 1 h, and the reaction mixture containing crystalline solid added to ice (350 g) – concentrated hydrochloric acid (80 ml). The precipitated oil was extracted with ether, the ethereal extracts washed with M sodium hydroxide (removal of pivaloic acid) and with water to neutrality. Removal of the ether gave a crystalline solid enveloped in a resin. Dissolution in boiling ethanol (30+20+10 ml) deposited microcrystalline **3**, m.p. 260–264 °C (sintering from 250 °C, somewhat rate-dependent) (3.8–4.6 g, 35–42%).

$C_{26}H_{44}O_{10}$ (516.6)
Calcd C 60.45 H 8.6%,
Found C 60.8 H 8.7% M 516.

IR: 3500 vs (OH), 3000, 2980 vs, 1490 vs, 1480 ms (CH_3, CH_2), 1745–1720 vs vbr (C=O ester), 1405 s, 1375 s (CMe_3), 1295–1280 vs, 1180–1135 vs mult (C–O ester), 1235 m, 1040 s, 1010 m cm^{-1}.

m/z: 1056 [7] (M×2+23,Na+1), 539 [100] ($M^{+\cdot}$+23), 540 [28] (corresp. to C_{26}), 516 [45] (M), 500 [28] (M-17, OH+1, H), 438 [17] (M+23–101, $Me_3C.COO$), 432 [10] (M-85, $Me_3C.CO$+1); 415.2337 [47] ($C_{21}H_{35}O_8$, M-101), 399 [5] (500–101 or 415–17+1), 348 [6] (M-2×85+2×1), 331 [20] (415–85+1), 247 [5] (415–2×85+2×1), 211 [4] (331–102, $Me_3C.COOH$ – 18, H_2O).

^{13}C NMR: 176.7 s, 176.3 s (CO at C-1,3 and C-4,6); 71.4 d, 71.2 d (double relative intensity; CH respectively of C-1,3 and C-4,6, ring); 69.5 d, 66.6 d (CH respectively of C-5 and C-2, ring); 38.2 s, 38.1 s (C of Me_3C at C-1,3 and C-4,6 or vice versa); 26.9 q, 26.7 q (Me_3 of Me_3C at C-1,3 and C-4,6 or vice versa).

2,5-Bisacetyl-1,3,4,6-tetrakispivaloylmyoinositol (**16**)

A stirred suspension of **3** (0.52 g, 0.001 mol) and anhydrous zinc chloride (1 g) in acetic anhydride (12 ml) was kept at 75–80 °C for 45 min, its colour

changing gradually to dark brown. It was quenched with water (50 ml) and stirred, when the precipitated oil changed to a pale brown solid (0.52 g, 87%), yielding **16** as microprisms, m.p. 296–300 °C (from acetone – ethanol).

$C_{30}H_{48}O_{12}$ (600.7)
Calcd C 60.0 H 8.05% M 623.3043 (incldg. Na)
Found C 60.6 H 8.2% M 623.3040

IR: 3460 m blunt (H_2O); 2990 vs, 2950 s sh, 2880 m sh, 1485 vs, 1470 s (CH_3,CH_2); 1770–1750 vs (C=O); 1400 s, 1375 vs (CMe_3), 1285 vs, 1240–1215 vs mult (C–O), 1175–1140 vvs mult, 1040 vs cm^{-1}.

m/z: 623 [100] ($M^{+\cdot}$+23,Na), 624 [33] (C_{30}), 581 [4] (M+23–43, MeCO+1,H), 541 [37] (M-59, MeCOO), 521 [4] (M+23–102, $Me_3C.COOH$), 499 [52] (M–101, Me_3COO), 499.2543 (for $C_{25}H_{39}O_{10}$), 457 [12] (499–43+1), 415 [26] (457–43+1), 415.2333 (for $C_{21}H_{35}O_8$), 373 [6] (457–85, $Me_3C.CO$+1), 289 [18] (373–85+1), 211 [9] (415–2×102).

1,3,4,6-Tetrakispivaloylmyoinososе-2 (**13**)

To a stirred solution of **3** (1.63 g, 0.003 mol) in glacial acetic acid (50 ml) at 90 °C, chromium-(VI)oxide (0.60 g, 0.006 mol, equivalent to 0.009 g.atoms available oxygen) was added. The mixture was stirred at this temperature for 20 mins, the oxidant dissolving gradually. The deep olivegreen liquid was added to ice-water (150 ml) containing sodium metabisulphite (1–2 g). The resulting finely divided precipitate gave, on crystallization from acetone-ethanol (*ca.* 25 and 10 ml per g, and partial evaporation), opaque microprisms of **13** (1.05–1.15 g, 70–75%), m.p. 250–254 °C (sintering and turning brown from 220 °C, decomposing to a dark brown mass).

$C_{26}H_{42}O_{10}$ (514.6)
Calcd C 60.7 H 8.2%,
Found C 60.3 H 8.6% M 514.

IR: 3480 ms (OH), 2995 vs, 2980 s sh, 2895 ms sh, 1490 s, 1470 ms (CH_3,CH_2), 1780 vs sh, 1760–1740 vs br (C=O ester and ring), 1290–1280 vs, 1170–1130 vvs mult (C–O ester), 1410 ms, 1375 ms br (CMe_3), 1040 s, 980 s, 900 m, 810 w, 765 m cm^{-1}.

m/z 537 [100] ($M^{+\cdot}$+23,Na), 538 [29] (C_{26}), 515 [25] (M+1), 497 [21] (M-17, OH), 435 [20] (M+23–102, $Me_3C.COOH$), 413 [44] (M-101, $Me_3C.COO$), 329 [59] (413–85, $Me_3C.CO$+1,H), 311 [20] (329–18, H_2O, or 413–102), 227 [30] (329–102), 209 [62] (311–102 or 227–18).

The *2',4'-dinitrophenylhydrazone* of **13**, obtained (35%) as described for **14** (below) formed yellow microneedles, m.p. 208–210 °C (decomp) (from ethanol).

$C_{32}H_{46}N_4O_{13}$ (694.75)
Calcd C 55.3 H 6.7 N 8.1%,
Found C 55.6 H 6.6 N 7.8%.

Tetrakis-1,3,4,6- (**2**) and *tris-1,3,4-isobutyrylmyoinositol*

To a stirred solution of **1** (1.80 g, 0.01 mol) and 4-dimethylaminopyridine (0.2 g) in pyridine (45 ml), isobutyryl chloride (6.4 g, 0.06 mol) was added dropwise at 80–85 °C over 45 min. The liquid, clearing after a temporary appearance of resin, was set aside for 1 h, then stirred into ice – concentrated hydrochloric acid (250 and 45 ml). The precipitated viscous resin coagulated on stirring, so that the turbid aqueous phase could be decanted (AP, below). The resin was stirred with fresh water, and disintegrated to a granular precipitate (1.4–1.6 g, 30–35%), which gave **2** as microprisms, m.p. 168–172 °C (from ethanol – light petroleum). – The turbid aqueous phase AP deposited a granular precipitate, which was collected within 1–2 h, and identified as **2** (*ca.* 5%) (filtrate: F).

$C_{22}H_{36}O_{10}$ (460.5)
Calcd C 57.4 H 7.9%,
Found C 57.8 H 8.0%.

IR: 3500–3350 vs with max. at 3480 (OH), 3000 vs, 2950 s sh, 2900 ms sh, 1480 s (CH_3,CH_2), 1770–1720 vs (C=O ester), 1400 s, 1360 s d (CMe_2), 1280 vs (C–O ester), 1210–1070 vs vb mult, 980 m (sharp) (the last the only difference from the IR spectrum of the tris-compound).

m/z: 942 [7] (2×M+23, Na-1), 483 [100] ($M^{+\cdot}$+23), 484 [24] (C_{22}), 443 [12] (M-17, OH), 413 [4] (M+23–71, C_3H_7CO+1,H), 395 [7] (413–18, H_2O), 373 [14] (443–71+1 or M-87, C_3H_7COO), 303 [2] (373–71+1), 285 [2] (377–88, C_3H_7COOH or 303–18).

The aqueous filtrate F slowly deposited crystalline solid (0.6–0.7 g, 15–18%), which gave opaque white *1,3,4-trisisobutyrylmyoinositol,* m.p. 200–202 °C (from a little ethanol).

$C_{18}H_{30}O_9$ (390.4)
Calcd C 55.4 H 7.7%,
Found C 55.1 H 7.7%.

IR: 3480 vs vbr (OH), 2995 s, 2960 ms sh, 2790 sh, 1480 s (CH_3,CH_2), 1760 s – 1735 vs (C=O ester), 1390 s, 1360 s (CMe_2), 1270 vs, 1225 s, 1205 vs (C–O ester), 1170, 1165 vs d cm^{-1}.

m/z: 413 [100] ($M^{+\cdot}$+23, Na), 414 [19] (C_{18}), 395 [7] (M+23–18, H_2O), 373 [22] (M-17, OH), 343 [3] (M+23–71, C_3H_7CO+1), 325 [7] (M+23–88, C_3H_7COOH), 303 [12] (373–71+1 or M-87, C_3H_7COO), 285 [2] (303–18).

In this example, the molar proportion of R.COCl had to be kept low, since the usual large excess (12 moles) under identical conditions produced the hexakis-derivative **11**, m.p. 179–181 °C (yield 90%). Lit. [17] m.p. 181 °C (For IR, *m/z*, see below).

1,3,4,5,6-Pentakis-isovaleroylmyoinositol (**4**)

The use of isovaleroyl chloride (16.9 g, 0.14 mol) in the procedure described for **3** above (temperature kept at 95–90 °C for the first, and 90–85 °C for the second half hour; stirring at 80 °C continued for 20 min) gave a pink to brown liquid which was filled with a crystalline precipitate on cooling. Its addition to ice-concentrated hydrochloric acid produced a soft resin, converted on stirring with fresh water to a buff granular solid (*ca.* 12 g). Its solution in ethanol (30 ml) gave opaque microprisms (6–6.5 g, 50–54%) of **4**, m.p. 200–202 °C (sintering from 196 °C). Spontaneous evaporation of the motherliquors gave a resin enveloping some solid; preferential removal of the former with cold ethanol gave more **4** (10–15%).

$C_{31}H_{52}O_{11}$ (600.8)
Calcd C 62.0 H 8.7%,
Found C 61.9 H 8.7%.

IR: 3520 s vbr (OH), 2980 vs, 2880 ms, 1475 ms (CH_3,CH_2), 1765–1740 vs vbr (C=O ester), 1375 s (CMe_2), 1300 vs, 1200, 1190, 1170 vs mult (C–O ester) cm^{-1}.

For *m/z*, see Table I and Scheme 2.

^{13}C NMR: 171.3 s, 171.0 s (double relative intensity; CO at C-1,3 and C-4,6); 170.8 s (CO at C-5); 70.7 d, 68.9 d (double relative intensity; CH respectively of C-1,3 and C-4,6, ring); 70.1 d, 66.2 d (CH respectively of C-5 and C-2, ring); 42.5 t, 42.3 t (double relative intensity, CH_2 of CH_2CHMe_2 at C-1,3 and C-4,6 or *vice versa*); 42.2 t (CH_2 at C-5); 25.0 d, 24.9 d (double relative intensity, CH of CH_2CHMe_2 at C-1,3 and C-4,6 or *vice versa*); 24.7 d (CH at C-5); 21.95 q, 21.9 q (double relative intensity, CH_3 of CH_2CHMe_2 at C-1,3 and C-4,6 or *vice versa*); 22.0 q (CH_3 of CH_2CHMe_2 at C-5).

2-Acetyl-1,3,4,5,6-pentakis-isovaleroylmyoinositol (**17**)

A solution of **4** (0.60 g, 0.001 mol) in acetic anhydride (15 ml) was stirred with anhydrous zinc chloride (1 g) at 80–75 °C for 45 min and the dark brown liquid added to warm water. The crystalline precipitate gave prisms (0.41 g, 64%) of **17**, m.p. 102–105 °C (from very little ethanol).

$C_{33}H_{54}O_{12}$ (642.8)
Calcd C 61.7 H 8.5%,
Found C 61.5 H 8.7%.

IR: 3480 m br blunt (H_2O), 2980 vs – 2900 s, 1475 s (CH_3,CH_2), 1775–1750 vs br (C=O, ester), 1375 vs (CMe_2), 1230 vs, 1210–1160 vs mult, 1130–1100 vs br (C–O, ester) cm^{-1}.

m/z: 665 [17] ($M^{+\cdot}$+23,Na), 666 [6] (C_{33}), 583 [18] (M-59, MeCOO), 541 [100] (M-101, C_4H_9COO), 542 [31] (C_{28}), 499 [11] (541–43, MeCO+1,H), 457 [25] (541–85, C_4H_9CO+1), 441 [2] (541–101+1), 415 [4] (457–43+1 or 499–85+1), 399 [4] (499–101+1 or 441–43+1), 331 [2] (415–85+1), 313 [2] (415–102, C_4H_9COOH, or 331–18, H_2O), 211 [9] (313–102).

1,3,4,5,6-Pentakis-isovaleroylmyoinososе-2 (**14**)

A solution of **4** (2.4 g, 0.004 mol) in glacial acetic acid (35 ml) was stirred at 85–80 °C with suspended chromium(VI)oxide (0.67 g, 0.0067 mol; 0.01 g-atom of available oxygen), so as to crush and gradually dissolve the oxidant. The brown liquid was kept at 70 °C for another 15 min, allowed to cool and stirred into water containing sodium metabisulphite (1 g). The precipitated finely divided solid (*ca.* 2 g) gave silky needles of **14** (yield 60%), m.p. 118–124 °C (from ethanol).

$C_{31}H_{50}O_{11}$ (598.7)
Calcd C 62.2 H 8.4%,
Found C 62.7 H 8.4%.

IR: 3450 ms br blunt (H_2O), 2970 vs, 2880 ms, 1475 s (CH_3,CH_2), 1780–1755 vs mult (C=O ester and ketone), 1380 ms (CMe_2), 1205–1160 vs mult, 1125–1110 vs mult (C–O ester) cm^{-1}.

For *m/z*, see Table I and Scheme 2.

To a boiling solution of **14** (0.30 g, 0.0005 mol) in ethanol (15 ml) 2,4-dinitrophenylhydrazine (0.12 g, 0.0006 mol) was added, followed by concentrated hydrochloric acid (6 drops), and boiling of the resulting orange solution continued for 5 min. The yellow solid (0.35 g) which separated slowly gave bright-yellow needles of the *2',4'-dinitrophenylhydrazone of* **14**, m.p. 192–196 °C (decomp) (from ethanol).

$C_{37}H_{54}N_4O_{14}$ (778.8)
Calcd C 57.05 H 7.0 N 7.2%,
Found C 56.9 H 7.1 N 6.9%.

Myoinososе-2 (**14**, R = H)

The foregoing penta-acyl ketone **14** (1.8 g, 0.003 mol), dissolved in ethanol (25 ml), was treated with a solution of sodium (0.46 g, 0.02 g-atom) in methanol (20 ml) and boiled under reflux for 1 h. The solution was distilled to small volume (*ca.* 10 ml), diluted with water (10 ml), acidified with 5 M hydrochloric acid, and extracted with ether (removal of isovaleric acid). The aqueous phase was again concentrated (to 12–15 ml), and gave, on addition of glacial acetic acid (2 ml) and phenylhydrazine (0.75 g) and immediate chilling and stirring, myoinososе-2 phenylhydrazone, m.p. 172–175 °C (decomp) (0.28 g, 35%). Lit. [6,8] m.p. 174–176 °C.

$C_{12}H_{16}N_2O_5$ (268.2)
Calcd N 10.45%,
Found N 10.2 %.

1,2,3,4,5,6-Hexakis-acylmyoinositols

The use, in the foregoing catalyzed procedure, of acyl chlorides terminating in smaller acyl groups resulted exclusively in hexakisacyl derivatives in variably moderate yields. Each of the following known [17] compounds had the correct percentage composition.

Hexakisacetylmyoinositol (**9**). – (12 moles RCOCl, 40–50 °C, 1 + 3 h, yield 40%), m.p. 214–216 °C (from ethanol), Lit. [17] m.p. 212 °C.

IR: 3480 s (H_2O), 3000, 2980 w d, 1445 m (CH_3), 1785–1745 vs br (C=O ester), 1250–1220 vs mult (C–O ester), 1380 vs br, 1055 vs cm^{-1}.

m/z: 455 [100] ($M^{+\cdot}$ + 23, Na), 456 [20] (C_{18}), 413 [8] (M + 23 – 43, CH_3CO + 1, H), 395 [7] (M + 23 – 60, CH_3COOH), 373 [8] (M-59, CH_3COO), 353 [3] (413–60), 331 [3] (373–43 + 1), 271 [2] (373–60), 211 [4] (271–60).

^{13}C NMR: 169.7 s, 169.1 s (CO at C-2 and C-5); 169.3 s, 169.2 s (double relative intensity, CO at C-1,3 and C-4,6); 70.0 d, 67.6 d (CH respectively of C-5 and C-2, ring); 68.9 d, 68.1 d (double relative intensity, CH respectively of C-1,3 and C-4,6, ring); 20.3 q, 20.1 q (CH_3 at C-2 and C-5); 20.25 q, 20.2 q (double relative intensity, CH_3 at C-1,3 and C-4,6).

Hexakispropionylmyoinositol (**10**). – (12 moles RCOCl, 60–65 °C, 1.5 + 1 h, yield 47%), m.p. 112–113 °C (from ethanol – light petroleum); Lit. [17] m.p. 100 °C.

IR: 3500–3400 s br (H_2O), 3000 vs, 2860 s, 2800 m sh, 1470 s (CH_3, CH_2), 1780–1750 vs (C=O ester), 1210–1160 vs mult (C–O ester), 1090 vs, 1070 s cm^{-1}.

m/z 539 [48] ($M^{+\cdot}$ + 23, Na), 540 [13] (C_{24}), 465 [5] (M + 23 – 74, C_2H_5COOH), 443 [100] (M-73, C_2H_5COO), 444 [23] (C_{21}), 387 [18] (M-73–57, C_2H_5CO + 1, H), 331 [4] (M-73–2×57 + 2), 313 [5] (387–74 or 331–18, H_2O), 257 [4] (313–57 + 1), 239 [14] (313–74), 183 [25] (239–57 + 1).

Hexakis-n-butyrylmyoinositol. – (12 moles RCOCl, 60–70 °C, addition 1.5 h, stirring at ambient temperature, 1.5 h, yield 17%), m.p. 88–92 °C (from ethanol-light petroleum). Lit. [17] m.p. 81 °C.

IR: 3500–3420 ms br (H_2O), 2980 vs, 2940 s sh, 2890 s, 1470 s (CH_3, CH_2), 1770–1745 vs (C=O ester), 1255 s, 1200–1160 vs mult (C–O ester), 1390–1345 s mult, 1110 vs–1090 s br cm^{-1}.

m/z 623 [20] ($M^{+\cdot}$ + 23, Na), 624 [6] (C_{30}), 535 [2] (M + 23 – 88, C_3H_7COOH), 513 [100] (M-87, C_3H_7COO), 514 [28] (C_{26}), 443 [29] (M-87–71, C_3H_7CO + 1, H), 373 [7] (M-87–2×71 + 2), 355 [5] (443–88 or 373–18, H_2O), 285 [3] (373–88), 267 [14] (355–88), 215 [2] (285–71 + 1), 197 [21] 267–71 + 1), 127 [7] (197–71 + 1), 109 [7] (197–88 or 127–18).

Hexakis-isobutyrylmyoinositol (**11**). For preparation, see **2**, above.

IR: 2990 vs, 2945 s sh, 2890 m sh, 1485 s (CH_3, CH_2), 1775–1740 vs (C=O ester), 1395 s, 1355 s (CMe_2), 1260 s, 1200 vs br (C–O ester), 1170–1120 vbr mult cm^{-1}.

m/z 623 [54] ($M^{+\cdot}$ + 23, Na), 624 [18] (C_{30}), 553 [12] (M + 23 – 71, *i*-C_3H_7CO + 1, H), 513 [100] (M-87, *i*-C_3H_7COO), 514 [28] (C_{26}), 443 [28] (M-71–87 + 1), 427 [4] (443–17, OH + 1), 373 [5] (M-87–2×71 + 2), 355 [4] (443–88, *i*-C_3H_7COOH or 373–18, H_2O), 267 [9] (373–88).

Hexakis-ethoxycarbonylmyoinositol (**8**). – (12 moles EtOOC.Cl, 20–30 °C for 15 min, room temperature 1 h, yield 12%), m.p. 114–116 °C (from ethanol-light petroleum). Lit. [30] m.p. 131–135 °C.

IR: 3450 s br (H_2O), 3000 s, 2960 m sh, 1485 ms, 1455 ms (CH_3, CH_2), 1785–1730 vs mult (C=O ester), 1320–1240 vs mult (C–O ester), 1385 vs cm^{-1}.

m/z 635 [45] ($M^{+\cdot}$ + 23, Na), 636 [12] (C_{24}), 563 [100] (635–73, COOEt + 1, H), 564 [23] (C_{21}), 523 [8] (540, M-73 + 1 – 17, OH), 491 [4] (563–73 + 1), 473 [8] (491–18, H_2O), 451 [7] (523–73 + 1 or 468, M-2×72–17), 385 [5] (473–89, EtOOC.O + 1), 361 [3] (451–90, EtOOC.OH), 289 [3] (361–73 + 1), 199 [4] (289–90), 109 [26] (199–90).

1,2,3,4,5,6-Hexakispivaloylmyoinositol (**12**)

A suspension of **1** (1.80 g, 0.01 mol) and anhydrous zinc chloride (2 g) in pivaloyl chloride (14.5 g, 0.12 mol) was boiled under reflux for 1.5 h. The resulting suspended sponge-like yellow mass, nearly solidifying on cooling, was taken up in successive portions of ether (with addition of M-hydrochloric acid, removal of zinc salt), the ethereal layer washed with 1.5 M sodium hydroxide (removal of pivaloic acid) and to neutrality with water. Removal of the solvent gave **12** (3.1 g, 45%) as massive prisms, m.p. 228–232 °C (from ethanol). – More prolonged boiling (2.5 h) did not improve yields, and caused some resinification.

$C_{36}H_{60}O_{12}$ (684.9)
Calcd C 63.1 H 8.8%,
Found C 63.6 H 8.9%.

IR: 3480 w br (H_2O), 3000 vs, 2960 ms sh, 2890 m sh, 1485 vs, 1470 s sh (CH_3, CH_2), 1760–1715 vs mult (C=O ester), 1410 s, 1375 s d (CMe_3), 1290 vs br (C–O ester), 1180–1120 vs mult cm^{-1}. The IR spectra of **12** and **3** are almost identical except, in the former, of a doublet at 920, 910 cm^{-1}, and the absence of the sharp hydroxyl absorption at 3500 cm^{-1}.

m/z 707 [47] ($M^{+\cdot}$+23,Na), 708 [18] (C_{36}), 623 [25] (M+23–85, $Me_3C.CO$+1,H), 605 [3] (M+23–102, $Me_3C.COOH$), 583 [100] (M-101, $Me_3C.COO$), 584 [32] (C_{31}), 516 [28] (M-2×85+2), 499 [51] (516–17, OH or 583–85+1), 415.2333 [20] ($C_{21}H_{35}O_8$, 516–101), 397 [3] (415–18, H_2O), 331 [7] (415–85+1), 313 [4] (331–18), 295 [12] (313–18), 247 [3] (331–85), 211 [17] (313–102).

Aromatic Series

1,3,4,5,6-Pentakisbenzoylmyoinositol (**5**)

To a stirred solution of **1** (3.6 g, 0.02 mol) and 4-dimethylaminopyridine (0.2 g) in pyridine (40 ml), benzoyl chloride (22.5 g, 0.16 mol) was added at room temperature dropwise during 25–30 min. The rising temperature was kept at *ca.* 50 °C by external cooling. Stirring at room temperature was continued for another 30 min and the resulting paste treated with ice concentrated hydrochloric acid (300 and 60 ml). The separated viscous material hardened and broke up to white granules on being stirred for 1–2 h. This was boiled with ethanol (80 ml, removal of benzoic acid) and the undissolved fraction (m.p. 248–252 °C, *ca.* 12.5 g, 90%) crystallized from acetone – ethanol (250 and 100 ml), producing successive crops of **5**, m.p. 256–260 °C (sintering from *ca.* 245, clearing at 270 °C, somewhat rate-dependent) (total 11.2–11.9 g, 80–85%, lustrous prisms, disintegrating to a white opaque powder on drying).

$C_{41}H_{32}O_{11}$ (700.7)
Calcd C 70.3 H 4.6%,
Found C 70.4 H 4.6%.

The compound is formed as a byproduct in the production of the hexakis- [31], m.p. 269 °C and 1,3,4,5-tetrakisbenzoylmyoinositol [32], and by reduction of the corresponding pentabenzoylinosose-2 [33], m.p. 260 °C.

IR: 3480–3420 s vbr (OH), 3080 w, 2980 w (CH=), 1750–1730 vs d (C=O ester), 1320 s sh, 1290–1250 vs vbr (C–O ester), 710 vs, 685 ms (Ph), 1000 mw, 975 mw, 940 mw, 920 w (diagnostic quartet), 1610 ms, 1590 m, 1500 mw, 1455 s, 1180 s, 1120–1090 vs mult, 1030 s cm^{-1}.

m/z 723 [100] ($M^{+\cdot}$+23,Na), 724 [45] (C_{41}), 701 [2] (M+1), 683 [6] (M–OH), 619 [3] (M+23–105, PhCO+1,H), 601 [6] (M+23–122, PhCOOH), 579 [13] (M-121, PhCOO), 560 [2] (M-122–18, H_2O), 481 [6] (601–121+1), 457 [7] (579–122), 438 [4] (560–122), 334 [25] (438–105+1), 230 [16] (334–105+1).

^{13}C NMR: 165.3 s, 165.0 s (double relative intensity, CO at C-1,3 and C-4,6 or *vice versa*), 164.9 s (CO at C-5); 72.0 d, 70.6 (double relative intensity, CH respectively of C-1,3 and 4,6), 71.1 d, 66.8 d (CH respectively of C-5 and C-2); Aromatic signals: 133.7 d, 133.6 d (double relative intensity, C-4′ at C-1,3 and C-4,6 or *vice versa*), 133.8 d (C-4′ at C-5), 129.0 s, 128.6 s (double relative intensity, C-1′ at C-1,3 and C-4,6 or *vice versa*), 128.4 s (C-1′ at C-5), 129.2 d, 128.9 d, 128.8 d, 128.75 d, 128.7 d, 128.6 d (collectively assigned to C-2′ and C-3′ of pairs of Ph at C-1,3 and C-2,4 and Ph at C-5).

The use of smaller proportions of benzoyl chloride under more restrained conditions gave in each case the same product **5** in diminished yields. – In experiments employing 1 or 2 moles of benzoyl chloride at 0–10 °C, the solid product was dibenzoyl anhydride (80 or 90% on the basis of the benzoyl chloride used), m.p. 38–40 °C (from benzene – light petroleum).

2-Acetyl-1,3,4,5,6-pentakisbenzoylmyoinositol (**18**)

This was prepared from **5** by the zinc chloride – anhydride procedure (described for **17** above), and formed opaque microprisms (95%) m.p. 256–259 °C (from acetone – ethanol). Lit. [33] m.p. 166–167 °C.

$C_{43}H_{34}O_{12}$ (742.0)
Calcd C 69.5 H 4.6%,
Found C 69.9 H 4.6%.

IR: 3460 m vbr blunt (H_2O), 3080, 2990 w (CH_3, CH=), 1750–1730 vs (C=O ester), 1320 ms, 1285 vs mult, 1230 ms (C–O ester), 710 vs, 690 ms (Ph), 1120–1095 vs mult cm^{-1} (almost identical with IR of **5**, but lacking the "diagnostic quartet").

m/z 765 [100] ($M^{+\cdot}$+23,Na), 766 [47] (C_{43}), 683 [28] (M-59, MeCOO), 621 [64] (M-121, PhCOO), 622 [26] (C_{36}), 579 [6] (683–105, PhCO+1,H).

1,3,4,5,6-Pentakisbenzoylmyoinososе-2 (**15**)

A solution of **5** (1.05 g, 0.0015 mol) in glacial acetic acid (35 ml) at 95 °C was stirred with chromium(VI)oxide (0.15 g, 0.0015 mol, 0.0023 g-atom O) for 20 min, the oxidant dissolving gradually. The brown liquid was set aside for 30 min, then stirred into ice water containing sodium metabisulphite (1 g). The finely divided precipitate (1.0 g, 95%, m.p. *ca.* 218–222 °C) was crystallized from nitrobenzene – ethanol (5 ml each, recovery 90%) or acetone – benzene (100 and 20 ml) giving felted needles of **15**, m.p. 218–224 °C. Very sparingly soluble in ethanol, acetone.

$C_{41}H_{30}O_{11}$ (698.7)
Calcd C 70.5 H 4.3% M 721.1686 (includg.Na),
Found C 71.0 H 4.5% M 721.1682.

IR: 3450 ms (H_2O), 1780 ms sh (CO ring), 1750–1735 vs (C=O ester), 1280–1270 vs vbr, 1120–1100 vs, 1075 vs (C–O ester), 710 vs, 690 m (Ph), 3080 m, 2980, 2940 mw d, 1610 ms, 1590 m, 1460 ms, 1325 ms, 1185 ms, 1145 s sh, 1030 s, 975 ms, 665 w cm^{-1}.

m/z 721 [100] ($M^{+\cdot}$+23,Na), 722 [45] (C_{41}), 617 [19] (M+23–105, PhCO+1), 599 [38] (M+23–122, PhCOOH or 617–18, H_2O), 577 [26] (M-121, PhCOO or 594, *i.e.* M-105+1, – 17 OH), 479 [45] (599–121+1), 462 [90] (479–17).

1,3,4,5,6-Pentakis(p-nitrobenzoyl)myoinositol (**6**)

was obtained as **5** (0.01 molar scale), using *p*-nitrobenzoyl chloride (0.06 mol), at 60–70 °C (addition 10 min, further heating in this range for 20 min, continued stirring 30 min). The crude precipitate gave, after extraction with 0.5 M sodium hydroxide and washing with hot water, an ivory product (m.p. *ca.* 275 °C, 8.5 g, 92%). Crystallization from nitrobenzene – ethanol (6 and 1 ml per g, recovery 70%) gave **6**, m.p. 278–285 °C (decomp., rate-dependent). Almost insoluble in the usual solvents.

$C_{41}H_{27}O_{21}N_5$ (925.7)
Calcd C 53.2 H 2.9 N 7.6%,
Found C 53.5 H 3.0 N 8.0%.

IR: 3460 s vbr (OH), 1760–1730 vs vbr (C=O ester), 1545–1530 vs (arom. NO_2, asym), 1360–1345 vs, 1325 s (arom. NO_2, sym), 1290–1250 vs mult (C–O ester), 870 vs, 845 s (1,4-disub. Ar), 780 mw, 715 vs (Ar), 1125–1090 vs mult, 1015 s cm^{-1}.

1,3,4,5,6-Pentakis(p-bromobenzoyl)myoinositol (**7**)

was prepared as the foregoing example. The crude product (4.9 g, 45%) gave **7** as a microcrystalline powder, m.p. 298–304 °C (decomp., rate dependent) (from acetone – ethanol, 25 and 5 ml per g, recovery 75%).

$C_{41}H_{27}Br_5O_{11}$ (1095.3)
Calcd C 45.0 H 2.5%,
Found C 45.1 H 2.5%.

IR: 3460 s vbr (OH), 1750–1720 vs (C=O), 1290–1260 vs mult, 1180 s, 1120–1090 vs mult (C–O), 850 s (1,4-disub Ar), 760 vs, 685 w (Ar), 1600 vs, 1020 vs cm^{-1}.

Acknowledgements

We thank Mrs. J. E. Hawkes and Mr. J. Cobb, of the University of London NMR Spectroscopy Service at King's College, London, for the production of the ^{13}C NMR spectra. We are also indebted to Dr. D. Carter, of the School of Pharmacy, University of London, for performing the mass spectrometric measurements.

[1] T. Posternak: The Cyclitols, Holden-Day Inc., San Francisco (1965);
a) p. 25, b) p. 151–156, c) p. 65.
[2] R. J. Ferrier (ed.): Carbohydrate Chemistry, Chapters on Cyclitols, Special Periodical Report, Royal Society of Chemistry, London, Vol. 26, 1994 and preceding volumes (from 1968).
[3] D. H. R. Barton, Experentia **6,** 316 (1950); J. Chem. Soc. **1953,** 1027.
[4] G. Vavon, Bull. Soc. Chim. Fr. [4] **49,** 937 (1931); E. Eliel, C. A. Lukach, J. Am. Chem. Soc. **79,** 5986 (1957).
[5] G. Vavon, B. Jacubovicz, Bull. Soc. Chim. Fr. **53,** 581 (1933); E. L. Eliel, L. A. Pilato, J. C. Richer, Chem. Ind. (London) **1961,** 2007; J. Schreiber, A. Eschenmoser, Helv. Chim. Acta **38,** 1529 (1955); Angew. Chem. **67,** 278 (1955).
[6] K. Heyns, H. Paulsen, Chem. Ber. **86,** 833 (1953).
[7] T. Posternak, Helv. Chim. Acta **24,** 1045 (1941); B. Magasanik, E. Chargaff, J. Biol. Chem. **174,** 173 (1948); for summary, see ref. 1b.
[8] T. Posternak, Biochem. Prep. **2,** 57 (1952).
[9] W. J. Criddle, E. Ward, J. Chem. Soc. (B) **1970,** 40, and refs. given therein.
[10] A. J. Fatiadi, Carbohydr. Res. **8,** 135 (1968).
[11] S. Posternak, T. Posternak, Helv. Chim. Acta **12,** 1165 (1929); **18,** 1283 (1935).
[12] T. Posternak, Helv. Chim. Acta **27,** 457 (1944); P. Fleury, G. Poirot, Y. Fieviet-Guinard, Annl. Pharm. Fr. **5,** 209 (1947); S. J. Angyal, D. J. McHugh, J. Chem. Soc. **1957,** 1423.
[13] O. Gelormini, N. E. Artz, J. Am. Chem. Soc. **52,** 2483 (1930); P. W. Preisler, L. Berger, ibid. **64,** 67 (1942).
[14] A. J. Fatiadi, Chem. Commun. **1967,** 441.
[15] W. J. Criddle, B. Jones, E. Ward, Chem. Ind. (London) **1967,** 1833.
[16] T. Posternak, Helv. Chim. Acta **19,** 1333 (1936).
[17] H. Müller, J. Chem. Soc. **91,** 1780 (1907); F. A. Hoglan, E. Bartow, Ind. Eng. Chem. **31,** 749 (1939).
[18] G. Höfle, W. Steglich, H. Vorbrüggen, Angew. Chem., Int. Ed. Eng. **17,** 569 (1978).
[19] L. F. Johnson, W. Jankowski: Carbon-13 NMR Spectra. Wiley-Interscience, New York (1972), Spectrum No. 196.
[20] T. Suami, S. Ogawa, K. Ohashi, S. Oki, Bull. Chem. Soc. Jpn. **44,** 2824 (1971); ibid. **45,** 3660 (1972).
[21] L. F. Fieser, M. Fieser: Reagents for Organic Synthesis, Wiley, New York (1967), Vol. 1. p. 366, L. F. Fieser, J. E. Herz, M. W. Klohs, M. A. Romero, T. Utne, J. Am. Chem. Soc. **74,** 3309 (1952).
[22] L. F. Fieser, J. Am. Chem. Soc. **75,** 4386 (1953).
[23] H. Budzikiewicz, Z. Pelah, C. Djerassi, Monatsh. Chem. **95,** 158 (1964).
[24] J. Seibl, T. Gäumann, Z. Anal. Chem. **197,** 33 (1963); Helv. Chim. Acta **46,** 2857 (1963); D. H. Williams, H. Budzikiewicz, Z. Pelah, C. Djerassi, Monatsh. Chem. **95,** 166 (1964).
[25] A. Buchs, E. Charollais, Helv. Chim. Acta **56,** 207 (1973).
[26] N. K. Kochetkov, O. S. Chizhov, in R. L. Whistler, J. N. BeMiller (eds): Methods in Carbohydrate Chemistry, Academic Press, New York, Vol. VI, p. 540 (1972).
[27] K. Biemann, D. C. DeJongh, H. K. Schnoes, J. Am. Chem. Soc. **85,** 1783, 2289 (1963).
[28] A. F. Pavlenko, N. I. Belogortseva, Yu. S. Ovodov, Khim. Prir. Soedin. **1982,** 31 (C.A. **97,** 6665 (1982)); D. R. Müller, B. Domon, W. J. Richter, Spectrosc. Int. J. **7,** 11 (1989).
[29] T. Fugiwara, K. Arai, Carbohydrate Res. **87,** 11 (1980); ibid. **101,** 287 (1982).
[30] C. Moldavskii, J. Chim. Ukraine **1,** 408 (1925); C. A. **20,** 2831 (1926).
[31] E. G. Griffin, J. M. Nelson, J. Am. Chem. Soc. **37,** 1552 (1915).
[32] Y. Watanabe, T. Shinohara, T. Fujimoto, S. Ozaki, Chem. Pharm. Bull. Jpn. **38,** 562 (1990).
[33] N. Z. Stanacev, M. Kates, J. Org. Chem. **26,** 912 (1961).