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Acetyl Substituted Benzenes.

Useful Cores for the Synthesis of Dendrimeric Polyketones

Enrique Díez-Barra*, Raquel González, Antonio de la Hoz, Ana Rodríguez and Prado Sánchez-Verdú.

Facultad de Química. Universidad de Castilla-La Mancha. 13071 Ciudad Real. Spain.

Abstract. Benzylation of acetyl substituted benzenes is an efficient route to dendrimeric polyketones. A benzyl bromide possessing a masked carbonyl group is the key reagent for the dendrimeric growth. π-Stacking in the crystals of the first generation from 1,4-diacetylbenzene is observed. © 1997 Elsevier Science Ltd.

The synthesis of dendrimers is an objective of permanent interest in the nineties. A huge number of reports about synthetic methodologies, new properties, chiral dendrimers and dendrimers containing metal sites have been published.[1] Ethers, esters, amides and amines are the main functional groups used for the dendrimeric growth and several functional groups have been attached to the surface of the dendrimers. While a lot of effort has been focused on the functionalization of the surface of the dendrimers, not much work has been done on the modification of the internal functional groups.

Dendrimeric polyketones, which have not yet been described, are substrates with enormous possibilities given the reactivity of the carbonyl moiety.

We have planned the synthesis of dendrimeric polyketones in which a divergent synthesis starting from acetophenone **1**, 1,4-diacetylbenzene **2** and 1,3,5-triacetylbenzene **3**, is employed and which profits from the efficient double benzylation of acetophenone under phase transfer catalysis conditions.[2]

Reactions of **1**, **2** and **3** with benzyl bromide afforded the first generation compounds (**4**, **5** and **6**) in satisfactory yields.[2,3] Reaction of **3** with *p*-bromobenzyl bromide afforded the corresponding first generation compound **7**, which possesses six bromine atoms on the surface. Compound **5** crystallises on a monoclinic system ($P2_1/n$) with two formula units per unit cell.[4] The asymmetric unit comprises one independent half-molecule. Two π-stacking between the phenyl groups, **A**.....**B** and **A**.....**A** (**A'** and **B'** are the related with **A** and **B** by a centre of symmetry) can be identified, which, according to Hunter[5], are stabilising interactions (**A**.....**B**,

SICD = 3.7909(2) Å, R_{xy}: 1.02 Å, dihedral angle: 79.99(8)°; A.....A, SICD = 3.7912(14) Å, R_{xy}: 3.10 Å, dihedral angle: 38.25(9)°)(Figure).

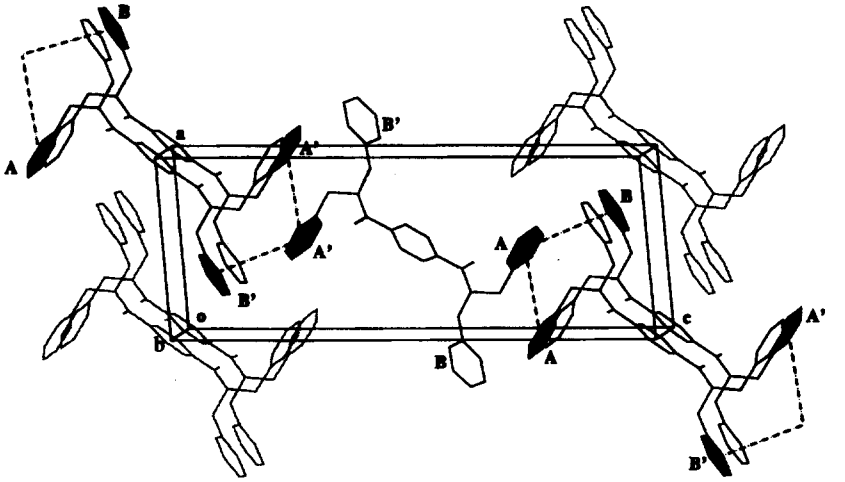
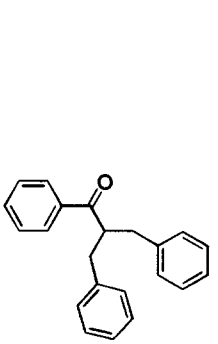


Figure. Packing diagram of **5**. Hydrogen atoms are omitted for clarity



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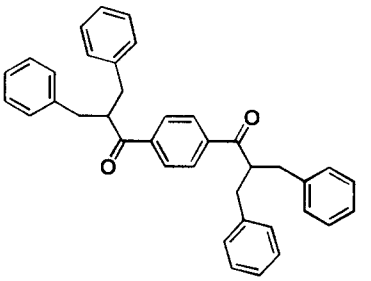
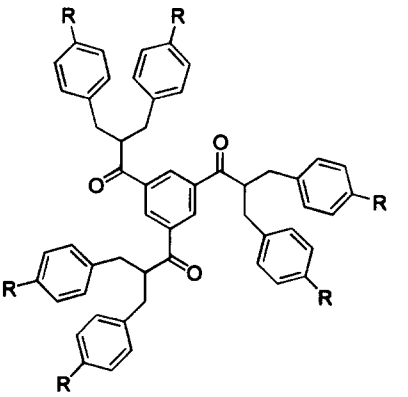


5

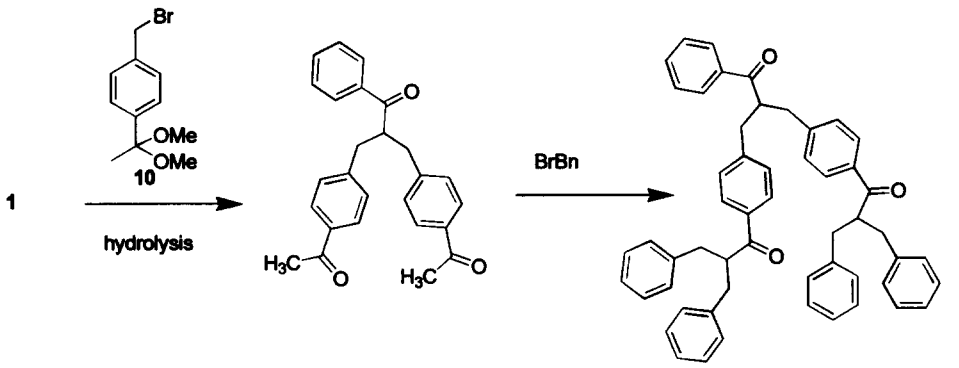


6, R = H
7, R = Br
8, R = $COCH_3$

Dendrimeric growth requires the presence of an acetyl group on the surface. Two alternative routes were tested: i) Friedel-Crafts acylation of the first generation compounds, compound **6** was converted to the corresponding hexaacetylated compound **8** using acetyl chloride and Al Cl_3 in dichloromethane (yield 45%) and compound **4** was acylated in the same conditions to afford compound **9** (yield 60%) , and ii) the use of a benzyl

bromide bearing a masked carbonyl group, **10**. Compound **10**, 4-bromomethylacetophenone dimethyl acetal was prepared by a careful radical bromination of 4-methylacetophenone and subsequent acetalization.[6]

Alkylation of **1** with **10** following the general procedure[3] and subsequent hydrolysis using montmorillonite clay K-10 in carbon tetrachloride at room temperature afforded the first generation compound bearing the acetyl groups, which permit further growth. Benzylation of **9** afforded the second generation compound from acetophenone **11** in 12% yield (**11**, M= 744, three carbonyls groups, seven phenyl groups).



9 **11**

In conclusion a new class of dendrimers, dendrimeric polyketones, possessing a large number of phenyl moieties and with different surface functionalities have been prepared. The methodology used represents a versatile route, by modification of the surface functionalities, to a wide number of dendrimers. Studies on next generation, compounds, new surface groups and modifications to the internal carbonyl groups are in progress.

Acknowledgement. Financial support from the Spanish DGICYT (MAT95-1965-E) is gratefully acknowledged.

References and Notes

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2. Díez-Barra, E.; de la Hoz A.; Loupy, A.; Martínez-González, A.; Martínez-Merino, V.; Merino, S.; Paugam R.; Sánchez-Verdú, P.; Sansoulet, J.; Torres, J. *Tetrahedron*, **1997**, *53*, 3659.
3. *General procedure*: Benzylations of 1,4-diacetylbenzene or 1,3,5-triacetylbenzene were performed by stirring a mixture of the appropriate ketone, benzyl bromide, finely ground potassium hydroxide and tetrabutylammonium bromide as catalyst, at room temperature for 24 hours in the absence of solvent. The crude products were extracted with dichloromethane and purified by column chromatography. **5**, 60%, mp 166-7°C (methanol) ^{1}H-NMR (δ, $CDCl_3$): 2.79 (dd, *J*=6.1 and 13.5), 3.07 (dd, *J*=8.1 and 13.5), 3.93 (tt, *J*=6.1 and 8.1), 7.08-7.25 (m), 7.55 (s). ^{13}C-NMR (δ, $CDCl_3$): 38.29, 51.03, 126.33, 127.91, 128.39, 128.89, 139.10, 140.23, 203.10.; **6**, 40%, mp 178-179°C (toluene). ^{1}H-NMR (δ, $CDCl_3$): 2.79 (dd, *J*=6.1 and 13.5),

3.01 (dd, *J*=8.3 and 13.5), 3.84 (tt, *J*=6.1 and 8.3), 7.04-7.19 (m), 7.91 (s). ^{13}C-NMR (δ, $CDCl_3$): 38.40, 50.73, 126.41, 128.43, 128.95, 130.85, 137.69, 138.88, 201.93. MS, m/z (%): 745 (M+1) (30), 653 (13), 549 (8.6), 137 (13.7), 136 (14), 91 (100).; **7**, 35%, mp 70-1°C (methanol). ^{1}H-NMR (δ, $CDCl_3$): 2.75 (dd, *J*=6.1 and 13.7), 2.97 (dd, *J*=8.3 and 13.7), 3.81 (tt, *J*=6.1 and 8.3), 6.95 (d, *J*=8.5), 7.30 (d, *J*=8.5), 7.95 (s). ^{13}C-NMR (δ, $CDCl_3$): 37.73, 50.31, 120.47, 130.66, 130.96, 131.60, 137.52, 200.96. MS, m/z (%): 1224.93 (M+13) (7), 1222.93 (M+11) (30), 1220.90 (M+9) (74), 1218.89 (M+7) (100), 1216.88 (M+5) (85), 1214.88 (M+3) (44), 1212.87 (M+1) (11); **8**, 45%, mp 104-5°C.^{1}H-NMR (δ, $CDCl_3$): 2.51 (s), 2.82 (dd, *J*=6.1 and 13.7), 3.08 (dd, *J*=8.1 and 13.7), 3.95 (tt, *J*=6.1 and 8.1), 7.18 (d, *J*=8.1), 7.80 (d, *J*=8.1), 8.10 (s). MS, m/z (%): 997 (M+1) (100), 865 (14), 717 (10).; **9**, 30%, mp 107-8°C (methanol). ^{1}H-NMR (δ, $CDCl_3$): 2.54 (s), 2.85 (dd, *J*=6.1 and 13.5), 3.20 (dd, *J*=8.1 and 13.5), 4.06 (tt, *J*=6.1 and 8.1), 7.23 (d, *J*=8.1), 7.35 (dd, *J*=7.3 and 7.6), 7.49 (tt, *J*=1.3 and 7.6), 7.73 (dd, *J*=1.3 and 7.3), 7.82 (d, *J*=8.1). ^{13}C-NMR (δ, $CDCl_3$): 26.50, 38.16, 49.55, 128.00, 128.56, 128.60, 129.19, 133.17, 135.49, 136.83, 144.74, 197.59, 202.01.; **11**, 12%, mp 104-5°C(toluene-n-hexane). ^{1}H-NMR (δ, $CDCl_3$): 2.71 (dd, *J*=6.2 and 13.8), 2.75 (ddd, *J*=2.7, 6.2 and 13.7), 3.06 (dd, *J*=7.6 and 13.7), 3.07 (ddd, *J*=2.7, 7.6 and 13.8), 3.92 (dddd, *J*=6.2, 6.2, 7.6 and 7.6), 7.05-7.66 (m). ^{13}C-NMR (δ, $CDCl_3$): 38.00, 38.19, 49.54, 50.36, 126.18, 127.98, 128.31, 128.35, 128.52, 128.94, 129.04, 133.11, 135.68, 136.83, 139.45, 144.45, 202.10, 202.74. MS, m/z (%): 746.38 (M+2) (17), 745.38 (M+1) (29), 653.30 (6), 91.04 (100), 77.01 (17).

4. Crystal data for **5**: Colourless (0.20 x 0.34 x 0.23 mm) monoclinic crystals with space group $P2_1/n$ and lattice constants a= 9.424(2), b= 6.0240(10), c= 25.7000(10) Å. beta = 94.84(10)°, V = 1453.8(4) Å^{-3}, Z = 4, Dc = 1.194 gr cm^{-3}, μ= 0.072 mm^{-1}. Reflexions were collected at 25°C on a Nonius CAD-4 diffractometer equipped with graphite monochromated radiation (λ = 0.7107 cm^{-1}), 6657 Friedel pairs collected (2<Ξ<28), 3494 reflexions with I>2σI. Data were recorded for Lorentz and polarisation effects and absorption correction was not necessary. Data/parameters 3494/181. The structure was solved by direct methods (SIR 92)[7] and refinement on F^2 was carried out by full-matrix least squares analysis (SHELXL-93).[8] Anisotropic temperature parameters were considered for all non-hydrogen atoms, while hydrogen atoms were included but not refined. Final disagreement indices are R = 0.045, Rw = 0.0674, GOF = 0.770, largest diff. Peak and hole 0.130 and -0.177 e Å^{-3}.
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6. To a solution of 4-methylacetophenone (45 mmol) in acetonitrile (150 mL) was added NBS (1 equivalent). After the reaction was complete, the solvent was evaporated and carbon tetrachloride (100 mL) was added. The solid succinimide, which floats upon the surface, was filtered off and the solvent was removed by using a rotary evaporator. The crude product was purified by recrystallization from ethyl acetate/n-hexane (yield 70%). ^{1}H-NMR (δ, $CDCl_3$): 2.60 (s), 4.50 (s), 7.49 (d, *J* = 8.1 Hz), 7.94 (d, *J* = 8.1 Hz). Acetalization was performed following literature procedures,[9] (yield 90%), **10**: ^{1}H-NMR (δ, $CDCl_3$): 1.52 (s), 3.18 (s), 4.50 (s), 7.37 (d, *J*=8.3), 7.47 (d, *J*=8.3); ^{13}C-NMR (δ, $CDCl_3$): 26.51, 33.77, 49.20, 102.01, 127.92, 129.16, 137.47, 143.74.
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