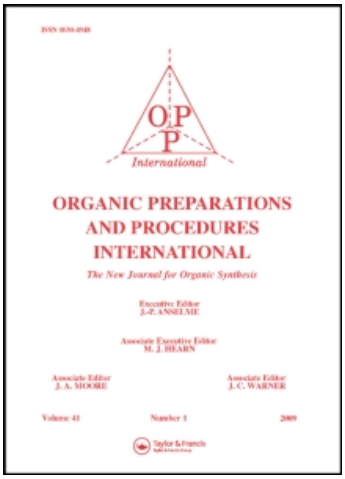


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# REACTION OF *bis*PHENOL-A DIGLYCIDYL ETHER WITH SUBSTITUTED PHENOLS

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# REACTION OF *bis*PHENOL-A DIGLYCIDYL ETHER WITH SUBSTITUTED PHENOLS

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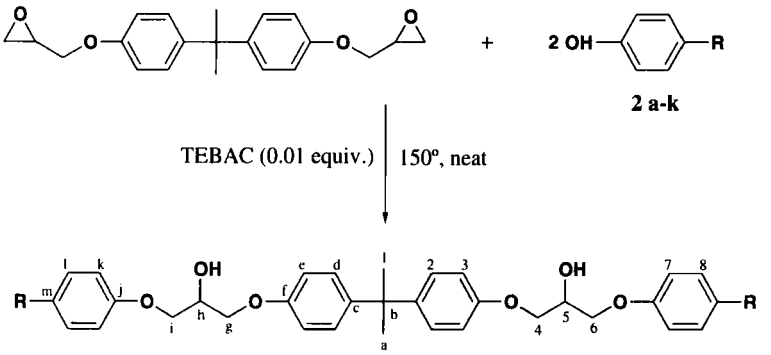
The ring opening of epoxides[1-3] with nucleophiles is an important transformation in organic synthesis leading to various 1,2-difunctionalized molecules. Epoxides also play a crucial role in materials science.[4-6] In the particular field of epoxy resins, we were interested in the development of synthetic routes allowing pure model compounds to be prepared, *i.e.* the bisphenol-A diglyceryl aryl ethers **3 a-l**. The chemo- and regioselectivity of the epoxide ring opening depends on intrinsic and




**3 a-l**

a) R = H; b) R = Me; c) R = $CO_2Me$; d) R = COMe; e) R = CHO; f) R = CN; g) R = $NO_2$
h) R = F; i) R = Cl; j) R = Br; k) R = I; l) R = $CO_2H$ (from deprotection of **3c**)

environmental factors.[7,8] Recent search for mild and selective reactions involves the use of acidic or electrophilic catalysts, such as cerium ammonium nitrate,[9] tin halide,[10] lithium trifluoromethanesulfonate,[11] ferric chloride supported on silica,[12] titanium- and zinc chloride,[13] samarium[14] and lanthanide complexes.[15] Although the reaction of epoxides with aliphatic alcohols appears well documented, the reaction with phenols is not described as extensively as expected.[1-3,16] The subject is often discussed from the industrial point of view,[17-18] without details about selectivity and potential oligomer formation.

This paper reports a systematic study of epoxide ring opening with *para*-substituted phenols, using *bis* phenol-A diglycidyl ether[19] (BADGE) **1**, a difunctional monomer of industrial interest, as substrate.

We first examined the reaction of **1** with three equivalents of phenol (**2a**) and *p*-cresol (**2b**) in basic medium (NaOH), under liquid-liquid phase-transfer conditions (Table 1, entries 1-2) as usually described for phenol alkylation with alkyl halides.[20] The reaction to give the *bis*-adducts **3** proceeded slowly, even at 60°; an unidentified gummy material formed at the interface and the yields of crude **3a-b**, after 70 h, were only 30-40%. Attempts to react the pre-formed phenolates (sodium salt; Table 1, entry 3 and potassium salt; Table 1, entry 4) in dry media, also gave very poor yields of **3**. The reaction of phenol at 130° with cesium fluoride as catalyst,[19] was inefficient (Table 1, entry 5). The use of $BF_3$ etherate as catalyst,[4] led only to degradation products (Table 1, entry 6). Thus hard basic or acidic conditions proved to be inapplicable to our purpose; in the absence of the catalyst, the reaction was not efficient either (Table 1, entry 9).

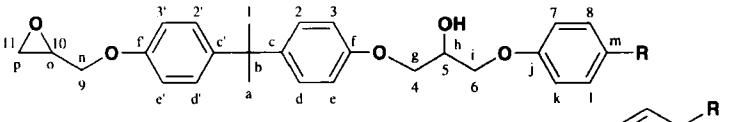
It was found that the reaction of **1** with *p*-cresol was better conducted at 130°, in the presence of a phase-transfer catalyst such as tetramethylammonium chloride (TMAC) (Table 1, entry 7). However, although *p*-cresol (more reactive than phenol) was used, about 60 to 90 minutes were still



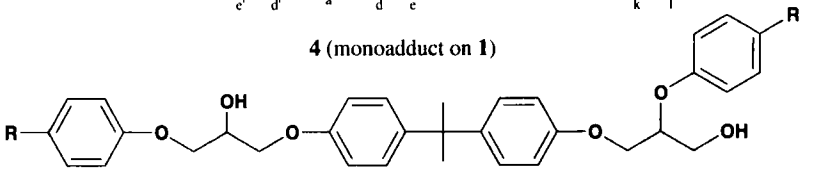
**TABLE 1**. Conditions for Epoxide Ring Opening with Phenols.

| Entry | Ar-OH (n equiv.) | Conditions | Products (% Yield) |
|---|---|---|---|
| 1 | **2a** (3 equiv.) | 50% aq. NaOH-toluene (1:1) $nBu_4N\ HSO_4$ (0.1-0.2 equiv.) 20° to 60°; 30 to 70 h | bisadduct **3a** (33)[21] |
| 2 | **2b** (3 equiv.) | idem entry 1 | bisadduct **3b** (43) |
| 3 | **2a** (2 equiv.) | NaH(2-4 equiv.), ether or THF 20° to reflux; 24 to 65 h | monoadduct **4a** (15-25) and traces of bisadduct **3a** |
| 4 | **2b** (2 equiv.) | preformed ArOK, neat, 130° 1 h to 3 h | bisadduct **3b** (<10%) |
| 5 | **2a** (2 equiv.) | CsF (0.02 equiv.), neat, 130° 1 h to 3 h | traces of bisadduct **3a**[(a)] |
| 6 | **2b** (2 equiv.) | $BF_3$.ether (2.2 equiv.), dioxane, 20°, 30 h | degradation[(a)] |
| 7 | **2b** (2-3 equiv.) | $Me_4N$ Cl (0.1 equiv.), neat, 130°, 1 h to 1 h 30 | bisadduct **3b** (≥90%)[(a)] |
| 8 | **2b** (3 equiv.) | $Ph_3PEt$ I (0.1 equiv.), neat, 130°, 1 h | bisadduct **3b** (≥85%)[(a)] |
| 9 | **2b** (2 equiv.) | neat, 130°, 5 days | mixture of epoxide **1**, mono- and *bis*-adducts, **4b** and **3b**[(a)] |
| 10 | **2c** (2 equiv.) | $Me_4N$ Cl (0.1 equiv.), neat, 130°, 10h | bisadduct **3c** (>80%) |
| 11 | **2c** (2 equiv.) | $Et_3NBn$ Cl (0.01 equiv.), neat, 150°, 2 h | bisadduct **3c** (>80%) |

a) NMR analysis of the crude mixture.



**4** (monoadduct on **1**)



**5** (monoregioisomer of **3**)

required to produce high yields (≥90%). The reaction time could not be significantly reduced without loss of yield using a soft phosphonium catalyst instead of an ammonium salt (Table 1, entry 8). As our interest was to apply the selected conditions for reacting **1** with *p*-cresol to other reactions of *para*-functionalized phenols (activated as well as deactivated), we conducted the *bis*-epoxide ring opening of **1** with the deactivated methyl *p*-hydroxybenzoate **2c** in neat conditions at 130° with 0.1 equivalent of TMAC (*i.e.*, similar to Table 1, entry 7). Compared with *p*-cresol, a tenfold increase of the reaction time was necessary to get similar yield (table 1, entry 10); this can be attributed to reduced nucleophilicity of **2c** due to the presence of an electron-withdrawing substituent on the aromatic nucleus. However, complete reaction was achieved to give **3c**, at 150° within 2 h, using a more lipophilic catalyst, *i.e.* triethylbenzylammonium chloride (TEBAC), in only 0.01 equivalent amount (Table 1, entry 11). Therefore, these conditions were used for the reaction of **1** with two equivalents of *p*-hydroxyacetophenone (**2d**), *p*-hydroxybenzaldehyde (**2e**), *p*-hydroxybenzonitrile (**2f**), *p*-nitrophenol (**2g**), *p*-fluorophenol (**2h**), *p*-chlorophenol (**2I**), *p*-bromo-phenol (**2j**) and *p*-iodophenol (**2k**) (Table 2).

**TABLE 2.** Reaction of **1** with *para*-Substituted Phenols (**2**)

| Entry | R in **2** | Time (mmol **1**)[a] | Product | Yield (%)[b] |
|---|---|---|---|---|
| 1 | $CO_2Me$ | 2 h (60 mmol) | **3c** | 72 |
| 2 | COMe | 4.5 h (29 mmol) | **3d** | 84 |
| 3 | CHO | 4.5 h (22 mmol) | **3e** | 54 |
| 4 | CN | 5.2 h (23 mmol) | **3f** | 75 |
| 5 | $NO_2$[c] | 5.5 h (12 mmol) | **3g** | 54 |
| 6 | F | 6 h ( 22 mmol) | **3h** | 66 |
| 7 | Cl | 5 h (22 mmol) | **3i** | 90 |
| 8 | Br | 5 h (21 mmol) | **3j** | 88 |
| 9 | I | 7 h (27 mmol) | **3k** | 69 |
| 10 | $CO_2H$ | deprotection of **3c** (12 mmol) | **3l** | 81 |

a) 2 Equiv. of phenol, 0.01 equiv. of TEBAC, neat, 135-150°. b) Pure fraction isolated by preparative MPLC (12-60 mmol scale). c) TMAC was used as catalyst

From the $^1$H NMR analysis of the crude mixtures, it was concluded that the *bis*-adducts **3a-k** were formed selectively in about 90-95% yields in all cases. The regioselectivity of the epoxide ring opening is thus mainly controlled by steric factors (nucleophilic attack on the less substituted carbon atom), as already mentioned for reactions involving soft[22] or resonance-stabilized[23] nucleophiles under neutral or basic conditions. HPLC Analysis of the crude mixtures revealed the presence of two side-products (less than 5% each), namely the monoadducts **4** and the mono-regioisomers **5** of the *bis*-adducts. Pure fractions of **3a-k** (Tables 1 and 2) were obtained by preparative MPLC and fully characterized (Tables 3 and 4). Typically, in the $^1$H NMR spectra of all compounds, we found H-5 at δ 4.33-4.41 (multiplet) and H-4 + H-6 at δ 4.02 to 4.24 (multiplets). In the $^{13}$C NMR spectra, the lines attributed to C-g, C-h and C-i appeared around 68-69 ppm. Samples of the side-products **4** and **5** were also recovered: in the $^1$H NMR spectra, compounds **4** were characterized by signals at δ 2.70-2.90 (2H) and 3.30-3.40 (1H) due to the epoxide moiety; compounds **5** showed a typical signal at δ 4.5 due to the C<u>H</u>-O-Aryl group.



**TABLE 3.** $^1$H NMR Data (δ) of Compounds **3** (200 MHz, $CDCl_3$ + 1% TMS).

| Cmpd | H-1(a) | OH(b) | H-4(c) | H-6(c) | H-5(c) | H-3(b) | H-7(b) | H-2(b) | H-8(b) |
|---|---|---|---|---|---|---|---|---|---|
| **3a** | 1.60 | 3.50(d) | 4.04 | to 4.15 | 4.35 | 6.80(8.7) | 6.87(8.8) | 7.11(8.8) | 7.24(e) |
| **3b** | 1.62 | 2.83(4.3) | 4.05 | to 4.16 | 4.33 | 6.81(8.8) | 6.80(8.5) | 7.12(8.8) | 7.06(8.5) |
| **3c** | 1.61 | 2.69(4.0) | 4.10 | to 4.18 | 4.37 | 6.81(8.9) | 6.92(8.8) | 7.12(8.9) | 7.97(8.8) |
| **3d** | 1.64 | 2.59(4.7) | 4.13 | 4.21 | 4.40 | 6.83(8.7) | 6.96(8.7) | 7.14(8.7) | 7.94(8.7) |
| **3e** | 1.62 | 3.52(d) | 4.11 | 4.21 | 4.38 | 6.82(8.6) | 6.98(8.7) | 7.12(8.6) | 7.78(8.7) |
| **3f** | 1.63 | 3.10(d) | 4.11 | 4.19 | 4.39 | 6.82(8.8) | 6.95(8.9) | 7.13(8.8) | 7.54(8.9) |
| **3g** | 1.64 | 2.56(5.4) | 4.14 | 4.24 | 4.41 | 6.83(8.9) | 6.99(9.3) | 7.14(8.9) | 8.21(9.3) |
| **3h** | 1.63 | 2.60(5.2) | 4.08 | to 4.13 | 4.36 | 6.83(8.9) | 6.87(8.2) | 7.13(8.9) | 6.97(8.2) |
| **3i** | 1.63 | 2.58(5.1) | 4.02 | to 4.18 | 4.36 | 6.82(8.9) | 6.85(9.0) | 7.14(8.9) | 7.24(9.0) |
| **3j** | 1.63 | 2.53(5.3) | 4.06 | to 4.19 | 4.35 | 6.81(8.9) | 6.83(8.8) | 7.14(8.9) | 7.38(8.8) |
| **3k** | 1.63 | 2.58(d) | 4.08 | to 4.13 | 4.37 | 6.76(8.9) | 6.81(8.8) | 7.12(8.9) | 7.52(8.8) |

a) singlet. b) doublet (*J* given in Hz). c) multiplet. d) broad singlet. e) doublet of doublet. For the atoms numbering, see Scheme.

Deprotection[24] of the methyl esters of **3c** was considered for preparing the *bis*-carboxyl derivative **3l**. Under classical saponification conditions ($K_2CO_3$, LiOH or KOH (10 equiv.) in $CH_3OH$-$H_2O$, 20°), the reaction was very slow (7-18 days). Acidic hydrolysis ($CF_3CO_2H$-$H_2O$, 20°) also appeared to be slow (several days) and accompanied by some degradation of **3c**. The reaction with trimethylsilyl iodide (TMSCl excess, NaI excess, $CH_3CN$, 20°) required 16 days for completion. Nucleophilic displacement with sodium iodide (2 equiv.) in refluxing DMF (4 days) was accompanied by degradation of **3c**. Lastly, the reaction of lithium iodide (8 equiv.) in pyridine[25] gave the complete deprotection after 15 h of reflux. Acidification and MPLC purification furnished pure **3l** in 81% yield.

**TABLE 4.** $^{13}C$ NMR Data (ppm) of Compounds **3** (50 MHz, $CDCl_3$ + 1% TMS)

| Cmpd | C-a | C-b | C-g | C-h | C-i | C-e | C-k | C-m | C-d | C-l | C-c | C-f | C-j |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **3a** | 30.9 | 41.6 | 68.8 | 68.7 | 68.8 | 114.0 | 114.6 | 121.1 | 127.7 | 129.4 | 143.6 | 156.3 | 158.4 |
| **3b** | 30.8 | 41.4 | 68.5 | 68.6 | 68.8 | 113.8 | 114.3 | 130.1 | 127.5 | 129.7 | 143.4 | 156.1 | 156.2 |
| **3c** | 30.9 | 41.6 | 68.5 | 68.6 | 68.8 | 113.9 | 114.0 | 123.0 | 127.8 | 131.6 | 143.7 | 156.1 | 162.1 |
| **3d** | 30.8 | 41.5 | 68.4 | 68.5 | 68.9 | 113.9 | 114.1 | 130.5 | 127.6 | 130.4 | 143.5 | 156.1 | 162.3 |
| **3e** | 30.9 | 41.6 | 69.0 | 68.4 | 69.0 | 113.9 | 114.7 | 130.1 | 127.7 | 131.9 | 143.6 | 156.0 | 163.4 |
| **3f** | 31.0 | 41.9 | 68.6 | 68.7 | 69.3 | 114.2 | 115.4 | 118.8 | 127.9 | 134.1 | 144.0 | 156.3 | 161.8 |
| **3g** | 30.9 | 41.7 | 68.3 | 68.5 | 69.4 | 113.9 | 114.6 | 141.9 | 125.9 | 127.9 | 143.9 | 156.1 | 163.4 |
| **3h** | 31.0 | 41.7 | 68.6 | 68.8 | 69.4 | 113.9 | 115.7 | 155.9 | 127.8 | 116.0 | 143.7 | 156.2 | 154.5 |
| **3i** | 30.8 | 41.5 | 68.4 | 68.5 | 69.0 | 113.8 | 115.7 | 125.8 | 127.6 | 129.2 | 143.5 | 156.0 | 156.9 |
| **3j** | 31.0 | 41.7 | 68.6 | 68.7 | 69.1 | 114.0 | 116.4 | 113.4 | 127.8 | 132.3 | 143.7 | 156.2 | 157.5 |
| **3k** | 31.0 | 41.8 | 68.6 | 68.7 | 68.9 | 114.0 | 117.0 | 83.4 | 127.8 | 138.3 | 143.8 | 156.2 | 158.4 |

For the atoms numbering, see Scheme.



In conclusion, the epoxide ring opening of bisphenol-A diglycidyl ether **1** was performed, in a chemo- and regioselective manner, using substituted phenols **2** (2 equiv.), neat at 130-150°, in the presence of triethylbenzylammonium chloride (0.01 equiv.) as catalyst, to yield the *bis*-adducts **3**. The reactions were easily conducted at the 4g to 20g scale (≈ 12 to 60 mmol) of **1**, including a preparative MPLC purification of the final products **3**. The catalytic role of halide ions in epoxide ring opening has been previously pointed out.[26-27]

## EXPERIMENTAL SECTION

The melting points were determined with an Electrothermal microscope and are uncorrected. The IR spectra were taken with a Bio-Rad FTS 135 instrument and calibrated with polystyrene. The NMR spectra were recorded on a Varian Gemini 200 apparatus (at 200 MHz for the proton and 50 MHz for the carbon). The Mass spectra were obtained on a Finnigan-MAT TSQ-70 instrument (CI mode) and with a Xenon Ion Tech 8KV (FAB mode). The microanalyses were performed at the Christopher Ingold Laboratories of the University College, London, UK. EPON 825 is the Shell epoxy resin containing the highest percentage of single molecule BADGE; this starting material has been purified (>99%) into **1** by medium pressure liquid chromatography (MPLC) on silica gel (Machery-Nagel, 15-40 µm, contains 8% of water) with hexane-EtOAc (8:2, then 7:3), in a Prochrom equipment (diameter of the column : 8 cm; pressure : 40 bars; flow rate : 120 ml/min; UV detection at 254 nm). For the HPLC analyses, we used a home-made column with MPLC grade silica gel (dimensions of the column = 250 X 46 mm; eluent = hexane-*i*PrOH (97.5:2.5); flow rate = 3 mL/min). The retention times are as follows : t ≈ 2.5 min for **2**; t = 4.5 min for **1**; t = 6 to 8 min for **4**; t = 12 to 14 min for **3**; t ≈ 23 min for **5**.

**Typical Experiment for the Preparation of the *bis*-Adduct 3c.-** A mixture of bisphenol- A diglycidyl ether **1** (20 g, 58.75 mmol, 1 equiv.), methyl *p*-hydroxybenzoate **2c** (17.87 g, 117.5 mmol, 2 equiv.) and triethylbenzylammonium chloride (TEBAC) (0.136 g, 0.587 mmol, 0.01 equiv.) was

heated at 150° for 2 h, with magnetic stirring in a flask closed with a security trap (for pressure equilibration). The crude oily mixture was dissolved in hot dichloromethane (50 ml), filtered over Celite 521 and chromatographed on silica gel (MPLC; eluent : hexane-ethyl acetate, 6:4 then 1:1) to give **3c** as a white crystalline solid. Yield: 27.3 g (72%); mp 123-128°; IR (film): 3446, 2951, 2874, 1715 (ester), 1606, 1581, 1510, 1458, 1436, 1384, 1362, 1314, 1285, 1249, 1170, 1106, 1039, 1011 $cm^{-1}$; $^1H$ NMR (see Table 3 ): δ 3.86 (s, $CO_2$Me); $^{13}C$ NMR (see Table 4 ): δ 51.8 (OMe), 166.8 (CO ester); MS ($FAB^+$) m/e 645.

*Anal.* Calcd for $C_{37}H_{40}O_{10}.H_2O$: C, 67.0; H, 6.33. Found: C, 67.22; H, 6.09

**Compounds 3a-k**.- Prepared as above, they are generally hygroscopic oils or foams:

**3a** (pale yellow viscous oil): MS ($FAB^+$) m/e 528.3; $^1H$ NMR: δ 6.39 (dd, *J* = 8.8 Hz, R=H).

*Anal.* Calcd for $C_{33}H_{36}O_6.1/2H_2O$: C,73.65; H, 6.88. Found: C,73.85; H, 7.00

**3b** (slighty white viscous oil): MS ($FAB^+$) m/e 556.2; $^1H$ NMR δ 2.27 (s, R=Me); $^{13}C$ NMR ppm 20.2 (Ar-Me).

*Anal.* Calcd for $C_{35}H_{40}O_6 \cdot 1/3H_2O$: C, 74.64; H, 7.23. Found: C, 74.86; H, 7.35

**3d** (pale yellow foam): MS ($FAB^+$) m/e 613.3; IR (film) ν 1674 $cm^{-1}$; $^1H$ NMR δ 2.56 (s, R= CO-Me); $^{13}C$ NMR ppm 26.1 (CO-Me), 196.8 (CO-Me).

*Anal.* Calcd for $C_{37}H_{40}O_8 \cdot 1/2H_2O$: C, 71.42; H, 6.59. Found: C, 71.17; H, 6.33

**3e** (pale yellow oil): MS ($FAB^+$) m/e 585 ($C_{35}H_{36}O_8$ + 1); IR (film) ν 1686 $cm^{-1}$; $^1H$ NMR δ 9.82 (s, R= CHO); $^{13}C$ NMR ppm 190.8 (H-CO).

*Anal.* : unstable, partially oxidized into **3l**

**3f** (pale yellow foam): MS ($FAB^+$) m/e 579.6; IR (film) ν 2225 $cm^{-1}$; $^{13}C$ NMR ppm 104.2 (R= CN).

*Anal.* Calcd for $C_{35}H_{34}N_2O_6.H_2O$: C, 70.89; H, 6.03; N, 4.69. Found: C, 70.91; H, 5.81; N, 4.60

**3g** (yellow foam): MS ($FAB^-$) m/e 618; IR (film) ν 1511, 1342 $cm^{-1}$.

*Anal.* Calcd for $C_{33}H_{34}N_2O_{10}$: C, 64.07; H, 5.54; N, 4.53. Found: C, 64.20; H, 5.40; N, 4.45

**3h** (colorless viscous oil): MS ($FAB^+$) m/e 564.

*Anal.* Calcd for $C_{33}H_{34}F_2O_6.H_2O$: C, 67.96; H, 6.18. Found: C, 67.70; H, 6.09

**3i** (white foam): MS (CI, $CH_4$ - $N_2O$) m/e 597, 599.

*Anal.* Calcd for $C_{33}H_{34}Cl_2O_6.1/3H_2O$: C, 65.61; H, 5.74; Cl, 11.60. Found: C, 65.87; H, 5.98; Cl, 11.36

**3j** (white amorphous solid): MS (CI, $CH_4$ - $N_2O$) m/e 685.3, 687.1.

*Anal.* Calcd for $C_{33}H_{34}Br_2O_6$: C, 57.74; H, 4.99; Br, 23.28. Found: C, 57.64; H, 4.96; Br, 23.56

**3k** (white foam): MS (CI, $CH_4$ - $N_2O$) m/e 780.1.

*Anal.* Calcd for $C_{33}H_{34}I_2O_6$: C, 50.78; H, 4.39. Found: C, 50.29; H, 4.57

**Description of a Typical Mono-adduct 4c**.- Pale yellow oil; IR (film) ν 3469, 3057, 2963, 2929, 2873, 2558, 2251, 2072, 1918, 1714, 1605, 1581, 1506, 1457, 1435, 1384, 1363, 1249, 1170, 1106, 1037, 1012 $cm^{-1}$; $^1H$ NMR (200 MHz, $CDCl_3$) δ 1.61 (s, 6H, H-1), 2.58 (d, *J* = 5.1 Hz, 1H, OH), 2.71-2.90 (m, 2H, H-11), 3.30-3.40 (m, 1H, H-10), 3.87 (s, 3H, $OCH_3$), 3.80-4.04 (m, 2H, H-9), 4.10-4.19 (m, 4H, H-4 + H-6), 4.30-4.45 (m, 1H, H-5), 6.79(d, *J* = 8.9 Hz, 2H, H-3), 6.81 (d, *J* = 8.9 Hz, 2H, H-3'), 6.92 (d, *J* = 8.7 Hz, 2H, H-7), 7.11 (d, *J* = 8.9 Hz, 2H, H-2), 7.13 (d, *J* = 8.9 Hz, 2H, H-2'),

7.97 (d, $J$ = 8.7 Hz, 2H, H-8); $^{13}C$ NMR (50 MHz, $CDCl_3$) ppm 30.9 (C-a), 41.6 (C-b), 44.6 (C-p), 50.1 (C-o), 51.7 ($O\underline{C}H_3$), 68.5 (C-h), 68.6 (C-g + C-n), 68.8 (C-i), 113.8 (C-e), 113.9 (C-e'), 114.1 (C-k), 122.9 (C-m), 127.6 (C-d), 127.7 (C-d'), 131.5 (C-l), 143.4 (C-c), 143.6 (C-c'), 156.1 (C-f), 156.2 (C-f'), 162.1 (C-j), 166.6 ($\underline{C}$=O); MS ($FAB^+$) m/e 493.

*Anal.* Calcd for $C_{29}H_{32}O_7$: C, 70.71; H, 6.54. Found: C,70.40; H, 7.05

**Preparation of the Di-acid 3l**.- A solution of di-ester **3c** (7.5 g, 11.63 mmol, 1 equiv.) and lithium iodide (12.45 g, 93.06 mmol, 8 equiv.) in dry pyridine (22 ml) was refluxed for 15 h under argon atmosphere. The crude mixture was dissolved in hot ethyl acetate and acidified with 2N HCl to reach pH1. The aqueous phase was extracted with ethyl acetate (6 x 100 ml). Drying over $MgSO_4$, concentration and chromatography on silica gel (MPLC, eluant : hexane-EtOAc-HOAc, 66.5 : 28.5 : 5; then 47.5 : 47.5 : 5) gave the di-acid **3l** as an amorphous white solid (hygroscopic material). Yield: 7.17 g (81%); mp 174-9°; IR (KBr) ν 3856, 3552, 3477, 3068, 2977, 2932, 2869, 2658, 2541, 1685, 1606, 1579, 1511, 1453, 1427, 1298, 1248, 1175, 1039 $cm^{-1}$; $^1H$ NMR (200 MHz, $CD_3OD$) δ 1.58 (s, 6H, H-1), 4.07-4.19 (m, 8H, H-4 + H-6), 4.20-4.35 (m, 2H, H-5), 6.82 (d, $J$ = 8.8 Hz, 4H, H-3), 6.99 (d, $J$ = 8.9 Hz, 4H, H-7), 7.09 (d, $J$ = 8.8 Hz, 4H, H-2), 7.95 (d, $J$ = 8.9 Hz, 4H, H-8); $^{13}C$ NMR (50 MHz, $CD_3OD$) ppm 33.3 (C-a), 44.5 (C-b), 71.6 (C-g), 72.1 (C-h), 72.4 (C-i), 117.0 (C-e), 117.2 (C-k), 126.2 (C-m), 130.6 (C-d), 134.6 (C-l), 146.7 (C-c), 159.9 (C-f), 166.0 (C-j), 171.5 ($\underline{C}$=O); MS (CI, $CH_4$ - $N_2O$) m/e 616.3.

*Anal.* Calcd for $C_{35}H_{36}O_{10}\bullet 1/2H_2O$: C, 67.13; H, 5.91. Found: C, 67.50; H, 5.65

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