Tetrahedron 64 (2008) 11661–11665

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Cation template assisted oligoethylene glycol desymmetrization by intramolecular Cannizzaro reaction of topologically remote aldehydes

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ARTICLE INFO

Article history:
Received 2 June 2008
Received in revised form 3 October 2008
Accepted 8 October 2008
Available online 14 October 2008

Dedicated to Professor Luis Castedo on the occasion of his 70th birthday

Keywords:
Oligoethylene glycol desymmetrization
Cannizzaro reaction
Cation template

ABSTRACT

Oligoethylene glycol chains containing 2–5 ethylene glycol units, and possessing a benzyl alcohol and a benzoic acid end groups, can be quantitatively obtained by intramolecular Cannizzaro reaction of the corresponding remote benzaldehyde end groups. The process is quite effective if a complex with an appropriate cation is formed to allow the two aldehyde groups to be spatially confined near enough each other for the intramolecular redox process.

1. Introduction

The development of supramolecular chemistry and, more recently, nanochemistry and nanotechnology, has relied on the design of effective chemical tools with a view to connecting chemical subunits in order to construct more complex and extensively developed superstructures; the ability to connect units lying at well-defined distances can help develop useful devices.[1] Immobilizing (bio)chemical substrates onto solid surfaces and controlled skeletal growth of chemical architecture for the construction of, for example, (bio)sensors, require the use of accurately defined spaces.[2]

A number of chemical species have been tested as potential spacers. Oligoethylene glycols (OEGs) are especially attractive for this purpose by virtue of their unusual, frequently amphiphilic properties in solution, which have promoted their widespread use in this context. The ability to prepare OEG chains of a specific length possessing a high chemical flexibility, thanks to their bearing two different functional groups at the ends of the chain, is a major current challenge for organic chemists and a growing demand of the scientific community.[3] Meeting such a demand will require developing effective chemical methodologies to desymmetrize specific OEG derivative chains.

Desymmetrizing symmetric compounds involves altering them in such a way as to suppress one or more elements of symmetry of their structures. Some chemical[4] and biological methods[5] have already proved effective for this purpose and raised the demand for new desymmetrizing technologies for use in large-scale industrial processes.

The pharmaceutical sector has made great efforts at developing chemical methodologies and transformation procedures for desymmetrizing pairs of equivalent chemical groups in compounds such as diols and diamines, among others.[6] For structural reasons, however, the end groups in these molecules usually lie at relatively close positions precluding far-reaching conformational rearrangement. As a result, large polymeric (oligomeric) materials, where the equivalent groups are normally located at the two ends of the macromolecule, require using special methodologies for desymmetrizing their topologically remote functional groups.

Derivatization with one stoichiometric equivalent of a protecting-group reagent generally yields a statistical proportion of the monosubstituted product in addition to disubstituted and unreacted starting material, thereby requiring tedious purification and detracting from products' yields.[7–9]

The intrinsic nature of the Cannizzaro reaction makes it the ideal candidate for desymmetrizing nonenolizable dialdehydes via an intramolecular process. We have conducted basic and applied research into this process[10] with a view to developing a standardized procedure for application to various OEG derivatives as a general method for desymmetrizing these oligomeric materials. Previously,

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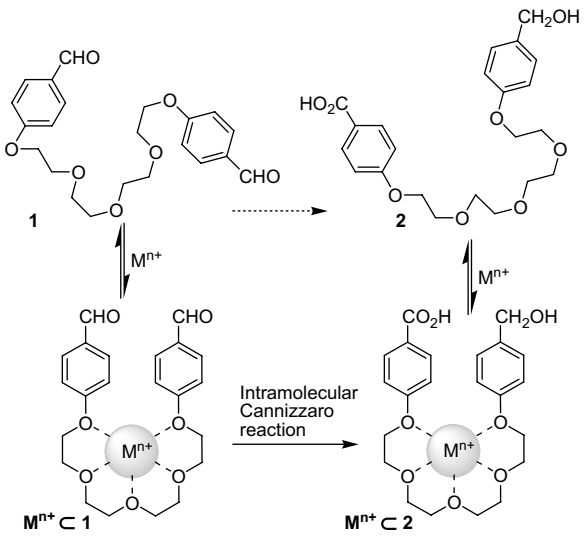
0040-4020/$ – see front matter © 2008 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2008.10.015

we converted the tetraethylene glycol (TEG) chain in its dialdehyde derivative and found the intramolecular Cannizzaro reaction to be readily accomplished and provide a simple, effective method for preparing desymmetrized diaryl-TEG. It avoids the need for several protection–deprotection reactions and tedious workup while providing quantitative yields that facilitate isolation of the desired product in pure form (Scheme 1).

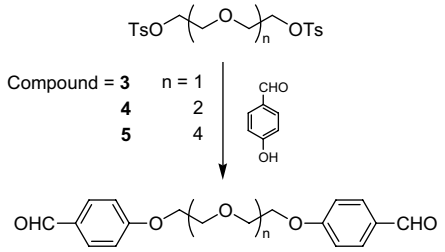


Scheme 1. Schematic depiction of the proposed desymmetrization strategy.

This paper reports the experiments we used to examine the effect of the OEG chain length on the binding efficiency of various cations with a template effect on the desymmetrization process with a view to standardizing the proposed approach as a general method for obtaining desymmetrized di-, tri-, tetra-, and pentaethylene glycol chain derivatives (DEG, TrEG, TEG and PEG, respectively) as a set of scalable, orthogonally ended functionalized spacers. In addition, we examined the influence of *ortho* and *meta* substituents in the aromatic aldehydes.

2. Results and discussion

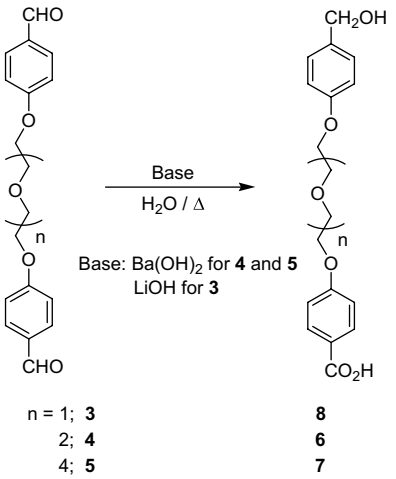
Our primary goal was to extend the ability of alkaline and/or alkaline-earth cation metals to facilitate the spatial rearrangement of remote benzene-carbaldehyde groups in such a way that the Cannizzaro reaction would operate preferentially in an intramolecular manner. We found barium cation to arrange a tetraethylene glycol chain end decorated with benzene-carbaldehyde **1** optimally in space for the Cannizzaro reaction to occur exclusively via its intramolecular pathway (Scheme 1).[10] With this in mind, we prepared a series of related oligoethylene glycols including diethylene glycol **3**, triethyleneglycol **4** and pentaethylene glycol **5** with two benzene-carbaldehyde groups at their chain ends (Scheme 2). Condensation



Scheme 2. Synthesis of the starting dialdehydes from the corresponding oligoethylene ditosylates.

of the corresponding ditosylate derivatives with 4-hydroxy benzaldehyde (4-HBA) in an alkaline medium gave the corresponding OEG, functionalized with the nonenolizable benzaldehyde moiety amenable to Cannizzaro reaction at the ends of their respective chains. This condensation reaction was achieved in yields exceeding 90% in all cases.

The triethylene and pentaethylene glycol derivatives **4** and **5** were quantitatively desymmetrized to the corresponding 1-benzyl alcohol, and ω-benzoic acid derivatives **6** and **7**, respectively (Scheme 3). The reaction was accomplished by refluxing a 0.15 M aqueous solution of the starting dialdehydes containing 1 M $Ba(OH)_2$ for 24 h. Following neutralization and extraction with organic solvents, the desymmetrized products were isolated in quantitative yields and pure enough for use in subsequent reactions.



Scheme 3. Desymmetrization of OEG-dialdehydes by intramolecular Cannizzaro reaction.

The templated influence of the cation was clearly confirmed by the results shown in Tables 1 and 2. With the triethyleneglycol **4**, a 2 M solution of the alkaline hydroxides of Table 1 provided poor yields of the corresponding desymmetrized product, **6**—the difference in yield was always recovered as starting material—, which exhibited a marked decrease in yield with increasing cation radius from Li^+ to K^+. Increasing the concentration of the bases to 4 M raised the cation concentration capable of displacing the association equilibrium in order to increase the concentration of complexed species triggering the intramolecular Cannizzaro reaction. With compound **5**, the 2 M solutions of the previous alkaline hydroxides exposed the increased complexing ability of sodium cation relative to lithium and potassium. However, raising the cation concentration to 4 M provided an increased yield of the desymmetrized product **7** as a result of the complexing equilibrium being displaced to the complexed form—mainly with potassium as cation. However, the lithium complex of this pentaethylene derivative must have retained

Table 1
Yields (%) of desymmetrized compounds **6** (from dialdehyde **4**) and **7** (from dialdehyde **5**) as a function of the alkaline base used in the intramolecular Cannizzaro reaction

Starting dialdehyde	Concentration of base (M)	Base		
		LiOH	NaOH	KOH
4	2	32	31	17
	4	92	89	89
5	2	33	88	33
	4	45	92	90

Table 2
Influence of the nature of the cation (added as a chloride salt), and its concentration, on the yield (%) of desymmetrized compound **6** as obtained by pouring dialdehyde **4** (0.15 M) over an aqueous 2 M solution of LiOH

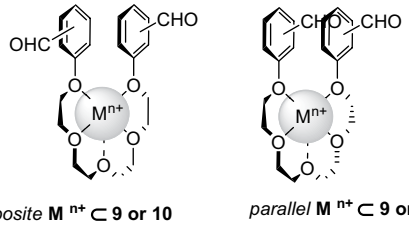
Salt Added	Concentration (M)	Yield (%) of compound **6**
LiCl	4	76
	6	83
	8	88
$BaCl_2$	1	Quantitative

a high degree of freedom, so the required arrangement of the aldehyde groups for intramolecular Cannizzaro reaction was not as stable as in the other complexes and the yield was lower as a result.

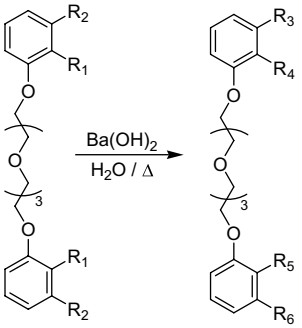
That the well-complexed forms of the starting dialdehydes were responsible for the high yields obtained in the intramolecular Cannizzaro desymmetrization was confirmed by the data of Table 2. As stated above, a 2 M solution of LiOH provided a yield of only 32% in the conversion of dialdehyde **4** into the desymmetrized product **6** (Table 1). However, adjusting the final concentration of lithium cation in this solution to 4 M by addition of LiCl raised the yield of **6** from 32 to 76%. Higher concentrations of lithium such as 6 or 8 M further increased the reaction yields up to 88%. Also, simply adjusting the barium cation concentration to 1 M with $BaCl_2$ in a 2 M LiOH solution raised the desymmetrization yield from 32% (Table 1) to a quantitative value (Table 2).

The compound with the shortest ethylene glycol chain, **3**, can also undergo intramolecular desymmetrization by Cannizzaro reaction to give **8**. However, the difficulty of dissolving the starting dialdehyde **3** in water compelled us to use a higher dilution. All desymmetrization attempts performed with a 0.15 M concentration of **3** resulted in the recovery of unreacted starting material. Compound **3** was quite insoluble in pure water; also, the water–ethanol and water–tetrahydrofuran mixtures assayed were useless to obtain the desymmetrized derivative with the alkaline (sodium and lithium) and alkaline-earth metals (barium) used. Only after treating the resulting slurry of **3** at a 0.15 M concentration with an extremely concentrated (6 M) aqueous solution of LiOH the desymmetrized product **8** was isolated, in a 42% yield, following tedious workup (8% of unreacted **3** was also recovered). This indicates that, if $\mathbf{Li}^{+}\subset\mathbf{3}$ is forced to be present, then it will be properly arranged for intramolecular Cannizzaro reaction. In fact, more dilute (0.005 M) **3** in 6 M aqueous LiOH provided a 85% yield of the desymmetrized product **8**.

All OEG-dialdehydes studied so far have been found to exhibit a relative *para* arrangement of the carbaldehyde group and the oxygen atom in the ethylene glycol chain. A unique situation is therefore possible in the complexed form as regards the relative arrangement of the two carbaldehydes (see $\mathbf{M}^{n+}\subset\mathbf{1}$ in Scheme 1). On the other hand, the two carbaldehyde groups in the *ortho* and *meta* analogs may face each other or adopt the nearest possible arrangement (Scheme 4). We examined the influence of the relative position of the carbaldehyde group with respect to the



Scheme 4. Opposite versus parallel relative arrangements of the carbaldehyde groups in the complexed forms of the *ortho* and *meta* models of tetraethylene glycols **9** and **10**.



9: R_1=CHO; R_2=H
10: R_1=H; R_2=CHO
11: R_3=R_6=H; R_4=CH_2OH; R_5=CO_2H
12: R_3=CH_2OH; R_4=R_5=H; R_6=CO_2H

Scheme 5. Desymmetrization of the tetraethylene glycols **9** (*ortho*) and **10** (*meta*) by intramolecular Cannizzaro reaction.

oligoethylene chain in order to assess the outcome of the intramolecular Cannizzaro reaction. To this end, we synthesized the two isomers of the *para*-tetraethylene glycol **1** with an *ortho*-**9** or *meta*-**10** arrangement on the aromatic ring, and reacted them under the same conditions as in the intramolecular Cannizzaro reaction of **1**. Similar to **1**, a quantitative yield of the desymmetrized derivatives **11** and **12**, respectively, was obtained for the two isomers (Scheme 5). The more relaxed opposite conformation of the complexed products **11** and **12** was comparatively less favorable for intramolecular Cannizzaro reaction than the more congested parallel conformations. However, the concurrence of the complexes **9** and **10** decisively facilitated intramolecular Cannizzaro reaction.

Neither dialcohol or diacid resulting from an intermolecular process was detected under the conditions studied in this and previous works.[10] Only desymmetrized compounds and starting material was detected. With complexed cations, the optimum situation is a vicinal arrangement of the skeletal remote atoms involved. Experiments in presence of, for example, anisaldehyde were carried out and no cross-over product has been detected, providing that cations has only template effects.[10]

3. Conclusions

In summary, we found that a scalable collection of oligoethylene glycol chains ranging from di- to pentaethylene glycol, which possess two different, orthogonally functional groups at their chain ends, can be directly synthesized and obtained with no tedious workup simply by treating their corresponding aromatic-functionalized symmetric dialdehydes under conventional Cannizzaro conditions. Such a simple procedure is effective provided by a cation templated spatially ordered arrangement of the topologically distant end groups, which induces the intramolecular redox process. The results for the *ortho*-**9** and *meta*-**10** isomers confirm that this process is general for various substitution models of the aromatic ring. Also, the regiochemistry is no limiting factor for successful desymmetrization and the intramolecular Cannizzaro reaction is applicable to various types of macromolecular systems.

4. Experimental

4.1. General methods

All reagents were purchased from commercial sources and used untreated unless otherwise stated. ^{1}H NMR and ^{13}C NMR spectra were recorded at 25 °C at 400 and 100 MHz, respectively, using

TMS as internal standard. EIMS spectra were obtained at 70 eV via direct insertion. HRMS and elementary analysis were recorded at the C.A.C.T.I. service of the University of Vigo (Spain). To exclude retention of complexed metals within the ethylene glycol chain and counter ions of desymmetrized compounds, samples were analyzed by ICP-MS and no contaminants were detected (detection limit is in parts per million). As additional purity control, HPLC analyses (Col. Kromasil 100 C18 5.0 μm, 250×3.0 mm; Mobile phase: acetonitrile–water 30:70% vol containing a 0.1% of formic acid; flow: 1.3 mL/min; detector: 254 nm) of the desymmetrized compounds were performed and only single peaks were detected for each compound. Melting points are given uncorrected. All reactions were monitored by TLC, using 60F 254 silica gel coated plates. Column chromatography was performed by using silica gel 60 (0.040–0.063 mm) at an elevated pressure.

4.2. OEG-ditosylates

Diethylene glycol and triethyleneglycol ditosylates were synthesized as described.[11] Pentaethylene glycol ditosylate was obtained from commercial sources.

4.3. OEG-Dialdehydes

An acetonitrile (400 mL) suspension of the sodium salt of the corresponding hydroxybenzaldehyde (16 mmol) containing the desired OEG-ditosylate (8 mmol) was refluxed until TLC confirmed the disappearance of the starting material. The cooled reaction mixture was then filtered off and the filtrate concentrated on a rotary evaporator. In order to remove traces of unreacted products, the crude residue obtained was dissolved in CH_2Cl_2 and extracted with 10% aqueous NaOH and, finally, pure water. The organic solution was then carefully dried with anhydrous $MgSO_4$ and the solvent evaporated to obtain the pure compound in almost quantitative yield.

*4.3.1. 1,7-Bis-(p-benzaldehyde)-1,4,7-trioxaheptane (**3**)[12]*

White solid: mp 134–136 °C; ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 3.95 (t, J=4.6 Hz, 4H), 4.23 (t, J=4.6 Hz, 4H), 7.00 (d, J=8.8 Hz, 4H), 7.81 (d, J=8.8 Hz, 4H), 9.86 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 67.7, 69.7, 114.8, 130.1, 131.9, 163.7, 190.8. EIMS m/z (%) 314 (M^+, 89), 286 (68), 149 (91), 121 (100), 77 (99).

*4.3.2. 1,10-Bis-(p-benzaldehyde)-1,4,7,10-tetraoxadecane (**4**)[13]*

White solid: mp 72–74 °C. ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 3.74 (s, 4H), 3.87 (t, J=4.7 Hz, 4H), 4.19 (t, J=4.7 Hz, 4H), 6.99 (d, J=8.8 Hz, 4H), 7.80 (d, J=8.8 Hz, 4H), 9.86 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$ ppm) δ 67.7, 69.5, 70.9, 114.8, 130.0, 131.9, 163.7, 190.8. EIMS m/z (%) 358 (M^+, 77), 149 (99), 121 (100), 77 (87). HRMS m/z calcd for $C_{20}H_{23}O_6$ $[M+H]^+$: 359.1495; found 359.1490.

*4.3.3. 1,16-Bis-(p-benzaldehyde)-1,4,7,10,13,16-hexaoxahexadecane (**5**)[14]*

White solid: mp 44–46 °C. ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 3.63 (m, 12H), 3.85 (t, J=4.5 Hz, 4H), 4.18 (t, J=4.5 Hz, 4H), 6.98 (d, J=8.4 Hz, 4H), 7.80 (d, J=8.8 Hz, 4H), 9.86 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$ ppm) δ 67.1, 68.7, 69.9, 70.1, 114.3, 129.4, 131.2, 163.2, 190.1. EIMS m/z (%) 446 (M^+, 6), 149 (99), 148 (90), 121 (100), 120 (90). HRMS m/z calcd for $C_{24}H_{31}O_8$ $[M+H]^+$: 447.2019; found 447.2010.

*4.3.4. 1,13-Bis-(o-benzaldehyde)-1,4,7,10,13,-pentaoxatridecane (**9**)[15]*

Oil. ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 3.68 (m, 8H), 3.88 (t, J=4.8 Hz, 4H), 4.21 (t, J=4.8 Hz, 4H), 6.95 (d, J=8.0 Hz, 2H), 6.99 (t, J=7.2 Hz, 2H), 7.49 (dt, J=7.2 Hz and J=2.0 Hz, 2H), 7.79 (dd, J=8.0 Hz and J=2.0 Hz, 2H), 10.48 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 67.7, 69.0, 70.1, 70.4, 112.6, 120.4, 124.5, 127.6, 135.5, 160.8, 189.3. EIMS m/z (%) 402 (M^+, 7), 149 (70), 148 (20), 121 (100), 120 (35).

*4.3.5. 1,13-Bis-(m-benzaldehyde)-1,4,7,10,13,-pentaoxatridecane (**10**)[16]*

Oil. ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 3.7 (m, 8H), 3.85 (t, J=4.8 Hz, 4H), 4.16 (t, J=4.8 Hz, 4H), 7.17 (dt, J=7.5 Hz and J=1.9 Hz, 2H), 7.40 (m, 6H), 9.93 (s, 2H). ^{13}C NMR (100 MHz, CDCl3, ppm) δ 67.2, 69.1, 70.2, 70.4, 112.6, 121.6, 123.0, 129.6, 137.3, 158.9, 191.6. EIMS m/z (%) 402 (M^+, 8), 149 (52), 148 (51), 121 (100), 77 (55).

4.4. General procedure for the desymmetrization of OEG-dialdehydes

A round-bottomed flask furnished with a condenser and a magnetic stir bar was loaded with OEG-dialdehyde (1.2 mmol of **4**, **5**, **9**, or **10**), $Ba(OH)_2 \cdot 8H_2O$ (2.52 g, 8 mmol) and H_2O (8 mL), and the solution being refluxed for 24 h. After cooling, the flask was immersed in a water–ice mixture and concentrated hydrochloric acid added to pH 2. The resulting mixture was extracted with dichloromethane, organics were dried with anhydrous $MgSO_4$, and filtered, and the solvent was removed on a rotary evaporator. The corresponding desymmetrized products **6**, **7**, **11**, and **12** were obtained almost quantitatively and in a pure enough form for most synthetic purposes. The procedure for dialdehyde **3** was identical except that an amount of 0.3 mmol of the compound was treated with a 60 mL solution of 6 M LiOH to obtain **8**.

*4.4.1. Compound **6***

Quantitative. White solid, mp 108–110 °C; ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 3.74 (s, 4H), 3.85 (m, 4H), 4.09 (m, 2H), 4.18 (m, 2H), 4.59 (s, 2H), 6.86 (m, 2H), 6.92 (d, J=8.8 Hz, 2H), 7.24 (m, 2H), 7.97 (d, J=8.8 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 65.0, 67.4, 67.6, 69.6, 69.8, 70.8, 114.6, 114.7, 121.8, 128.6, 132.2, 133.2, 158.4, 163.1, 170.0. HRMS m/z calcd for $C_{20}H_{25}O_7$ $[M+H]^+$ 377.1600, found 377.1612. Anal. calcd for $C_{20}H_{25}O_7 \cdot {}^1/_2\, H_2O$: C, 62.33; H, 6.54. Found: C, 62.56; H, 6.38.

*4.4.2. Compound **7***

Quantitative. White solid, mp 73–75 °C. ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 3.65 (m, 12H), 3.84 (m, 4H), 4.09 (m, 2H), 4.16 (m, 2H), 4.59 (s, 2H), 6.87 (m, 2H), 6.92 (d, J=9.0 Hz, 2H), 7.24 (m, 2H), 7.97 (d, J=9.0 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 64.9, 67.5, 67.6, 69.5, 69.7, 70.6, 70.8, 114.3, 114.7, 121.9, 128.6, 132.2, 133.3, 158.4, 163.1, 170.6. EIMS m/z (%) 464 (M+, 14), 446 (10), 297 (72), 165 (100), 95 (45). HRMS m/z calcd for $C_{24}H_{32}O_9$ $[M]^+$: 464.2046; found 464.2057.

*4.4.3. Compound **8***

85%. White solid, mp 175–180 °C. ^{1}H NMR (400 MHz, DMSO-d_6, ppm) δ 3.81 (m, 4H), 4.08 (t, J=4.8 Hz, 2H), 4.19 (t, J=4.8 Hz, 2H), 4.40 (d, J=5.2 Hz, 2H), 5.04 (t, J=5.2 Hz, 1H), 6.54 (s, 1H), 6.88 (d, J=8.4 Hz, 2H), 7.02 (d, J=8.4 Hz, 2H), 7.20 (d, J=8.4 Hz, 2H), 7.87 (d, J=8.4 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 62.8, 67.4, 67.8, 69.2, 69.4, 114.4, 114.6, 123.3, 128.2, 131.7, 135.0, 157.6, 162.4, 167.3. HRMS m/z calcd for $C_{18}H_{19}O_5$ $[M+H]^+$: 315.1227; found 315.1200.

*4.4.4. Compound **11***

Quantitative. Oil. ^{1}H NMR (400 MHz, CDCl3, ppm) δ 3.68 (m, 8H), 3.82 (m, 2H), 3.87 (m, 2H), 4.15 (m, 2H), 4.31 (m, 2H), 4.62 (s, 2H), 6.84 (d, J=7.6 Hz, 1H), 6.91 (t, J=7.4 Hz, 1H), 6.98 (d, J=7.6 Hz, 1H), 7.10 (t, J=7.2 Hz, 1H), 7.23 (m, 2H), 7.50 (ddd, J=7.4 Hz, 7.2 Hz and 2.0 Hz, 1H), 8.10 (dd, J=7.2 and 2.0 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 61.2, 67.4, 68.7, 69.1, 70.1, 70.2, 111.7, 113.1, 118.1, 120.6, 121.8, 128.3, 128.4, 129.8, 132.9, 134.4, 134.5, 156.4, 157.1, 165.6. EIMS

m/*z* (%) 420 (M+, 6), 402 (15), 165 (22), 121 (100), 120 (30). HRMS *m*/*z* calcd for $C_{22}H_{28}NaO_8$ $[M+Na]^+$: 443.1676; found 443.1664. Anal. calcd for $C_{22}H_{28}O_8$: C, 62.85; H, 6.71. Found: C, 62.87; H, 6.80.

4.4.5. Compound ***12***

Quantitative. Oil. ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 3.70 (m, 8H), 3.84 (m, 4H), 4.11 (m, 2H), 4.15 (m, 2H), 4.64 (s, 2H), 6.81 (d, J=8.0 Hz, 1H), 6.89 (d, J=8.0 Hz, 1H), 6.94 (s, 1H), 7.12 (d, J=8.0 Hz, 1H), 7.21 (t, J=8.0 Hz, 1H), 7.32 (t, J=8.0 Hz, 1H), 7.58 (s, 1H), 7.65 (d, J=8.0 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 64.3, 66.9, 67.2, 69.3, 69.4, 70.2, 70.3, 70.4, 112.6, 113.4, 114.8, 119.0, 120.2, 122.3, 129.1, 129.2, 130.6, 142.2, 158.3, 158.5, 169.8. EIMS *m*/*z* (%) 420 (M+, 27), 165 (37), 150 (46), 147 (53), 121 (100), 89 (32), 77 (38). HRMS *m*/*z* calcd for $C_{22}H_{28}NaO_8$ $[M+Na]^+$: 443.1676; found 443.1675. Anal. calcd for $C_{22}H_{28}O_8$: C, 62.85; H, 6.71. Found: C, 62.89; H, 6.86.

Acknowledgements

This work was supported by Spain's DGI (Project CTQ07-60190).

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