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An expedient route to *p-tert*-butylthiacalix[4]arene 1,3-diethers via Mitsunobu reactions

István Bitter* and Viktor Csokai

Department of Organic Chemical Technology, Budapest University of Technology and Economics, H-1521 Budapest, Hungary

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Abstract—Regioselective distal dialkylation of *p-tert*-butylthiacalix[4]arene with alcohols was performed under the Mitsunobu protocol using the DEAD/TPP system. The method provides a versatile tool for obtaining 1,3-diethers with different functional groups in the alkyl chains.

The large number of calixarene derivatives is partly ascribed to the regio- and conformation selective reactions developed during the last decades.[1,2] Among these, the partial *O*-alkylation and acylation, along with aromatic nitration, halogenation, formylation, etc. of calix[4]arenes provide important synthetic tools for designing supramolecules of great variety. Similar regioselective reactions, at least with the same efficiency, have not been found in thiacalixarene chemistry. The lack of regio- and stereoselectivity in the weak base (K_2CO_3, Et_3N) mediated partial *O*-alkylation and acylation reactions of thiacalix[4]arenes can be attributed to the substantially reduced differences between the OH acidities[3] and the 15% larger cavity as compared with a calixarene counterpart. As a consequence, tetraalkylation of thiacalix[4]arenes takes place easily in the presence of different bases,[4–7] but the stereochemical outcome of the alkylation strongly depends on the base used and the upper rim substitution (*tert*-butyl versus H).[7] 1,3-Diethers or diesters, however, cannot be obtained simply by following the 1,3-dialkylation or diacylation procedure described for calix[4]arenes. Actually, only a few 25,27-dialkoxythiacalix[4]arenes (methoxy, propoxy and ethoxycarbonylmethoxy)[8,9] and several partially acylated derivatives have been prepared in moderate yields and selectivities[10–13] so far.

Recently studies conducted in our laboratory to synthesize thiacalix[4]monocrowns[9] revealed, that unlike calixarenes, only biscrowns could be obtained by the ring closure of thiacalixarenes with tetra- and pentaethylene glycol derivatives in the presence of K_2CO_3. Therefore the temporary protection of two distal OH groups was required prior to cyclization. Due to the difficulties of 1,3-disubstitution in the thiacalixarene series mentioned above, we failed to introduce regioselectively any protecting group either on alkylation or acylation. Thus, we did not succeed in synthesizing diametrically bridged thiacalix[4]monocrowns with unsubstituted 26,28-OH groups.

To overcome the problems in base mediated alkylations, the Mitsunobu reaction[14] appeared to be an attractive alternative to *O*-alkylation. This reaction has already been utilized in calixarene chemistry in particular cases to obtain glycosyl calixarenes[15] and for the alkylation of calix[4]arenes with benzylic and allylic alcohols,[16] but to our knowledge, it is unprecedented in thiacalixarene chemistry. The alkylation of phenols with alcohols effected by the triphenylphosphine/diethyl azodicarboxylate (TPP/DEAD) system is well-documented in the literature.[17] In recent papers the Mitsunobu reaction has been used to synthesize chiral synthons for macrocyclic frameworks[18] and for the selective monoalkylations of 1,1′-bi-2-naphthol.[19] The success of the latter reaction prompted us to explore the possibility of regioselective *O*-alkylations of thiacalix[4]arenes under standard Mitsunobu conditions.

First, compound **1** was treated with a tenfold excess of MeOH using 2.2 mol of TPP/DEAD in THF at ambient temperature. After 24 h a single product spot was detected by TLC (hexane–EtOAc = 9:1) besides unreacted starting **1** which was almost entirely consumed after 72 h. By increasing the molar ratio of TPP/

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* Corresponding author. Tel.: 36-1-463-1379; fax: 36-1-463-3648; e-mail: ibitter@mail.bme.hu

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DEAD: **1** to three, the reaction took place in 24 h affording **2a** in 80% yield. The reaction was repeated with a series of primary alcohols resulting in the formation of 1,3-dialkoxythiacalix[4]arenes **2b–h** (Scheme 1).[20] Under these conditions the reaction generally stops at disubstitution and the tri- or tetraalkoxy products could not be isolated. This protocol seems to be especially effective with long chain alcohols and glycol monoethers, where the alkylating agents (halogenides or tosylates) derived from them react sluggishly in base-mediated reactions. It was disappointing that benzyl and allyl alcohol did not give single products, inseparable mixtures of compounds of different degrees of alkylation were formed. By decreasing the molar ratio of reagents to 2.2, the dibenzyl derivative **2l** was detected but we failed to isolate it in analytically pure form even after chromatography. To achieve temporary protection of the 25,27-OH groups in the thiacalixarene skeleton, attempts were made to introduce the readily removable bulky phthalimidomethyl group with *N*-hydroxymethyl-phthalimide. Although this reaction was successful and compound **2k** was obtained in an excellent yield in a relatively fast reaction using 2.2 equiv. of reagents, it proved to be unstable during further, alkali carbonate-mediated alkylation with BnBr. However, the Mitsunobu benzylation of **2k** helped to solve this problem (see later).

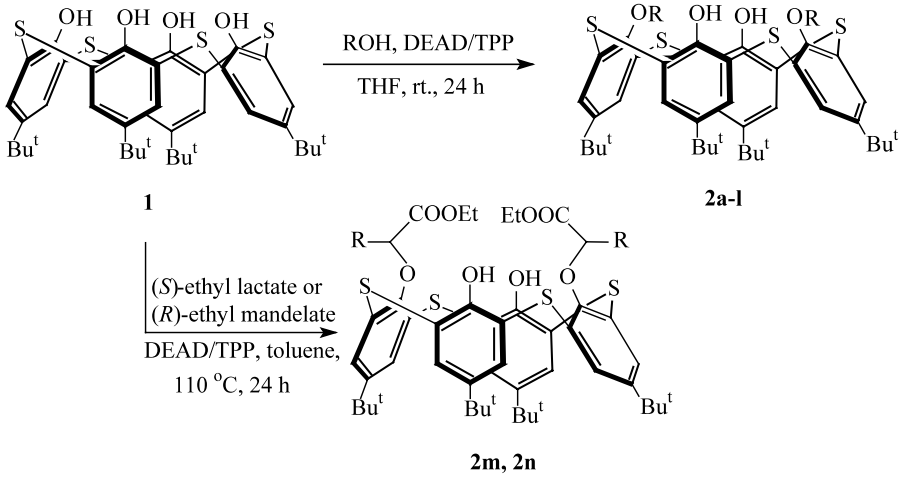
As was expected, secondary alcohols gave poor results under mild reaction conditions but at elevated temperatures (110°C, 24 h in toluene) (*S*)-ethyl lactate and (*R*)-ethyl mandelate cleanly afforded the chiral diesters **2m**,**n** in good yields with possible inversion of configuration (the optical purities were not determined) (Scheme 1). The sterically hindered (–)-menthol proved to be unreactive even under vigorous conditions.

Unexpectedly, great differences in the reactivities and in the outcome of the reaction were observed with halohydrins. 6-Bromohexanol and diethylene glycol monochlorohydrin reacted sluggishly to afford diethers **2g** and **2h** with lower yields as compared to the other long chain alcohols. 3-Chloropropanol, however, gave a substantial quantity of the tetraalkylated product **4** at ambient temperature when a threefold excess of reagents was used. Decreasing the molar ratio of TPP/DEAD: **1** to 2.2, diether **2j** could be isolated but only in 30% yield.[20] On the contrary, 2-bromoethanol behaved similarly to the other alcohols and resulted solely in diether **2i**. However, if the molar ratio of TPP/DEAD: **1** was increased to 6, tetraethers **3** and **4** were formed exclusively in excellent yields. It is worth noting that peralkylation of **1** by *n*-octanol affording **5** could also be attained but only at elevated temperatures (110°C, toluene). These examples represent an acceptable alternative for the tetraalkylation of thiacalixarenes.

The conformations of the compounds prepared were proved by NMR measurements. The extremely simple ^{1}H NMR spectra of diethers **2** showed the presence of one conformer. Two pairs of singlets observed for the aromatic and Bu^t protons appeared at 7.70–6.90 and 1.37–0.70 ppm, respectively, indicating a C_{2v} symmetry in the *cone* conformation, analogous to literature results.[8,9]

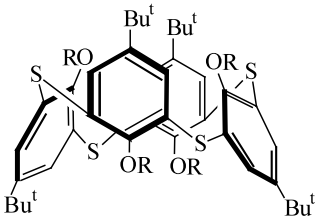
Tetraethers **3**, **4** and **5** were assigned the 1,3-*alternate* conformer on the basis of chemical shifts and literature analogy.[21] The Bu^t and aromatic protons in the 1,3-*alt* conformation are deshielded while those of the *cone* are shielded by the attached phenyl rings. Consequently, two singlets at lower field are expected for the 1,3-*alt* conformation (7.2–7.4, 1.2–1.3 ppm), while these are at higher field for the *cone* conformation (6.8–7.0, 0.75–0.85 ppm). Furthermore, the OCH_2 and CH_2Br moieties of 1,3-*alt*-**3** are shielded by the adjacent phenyl rings so that these protons should give resonances at higher field (t, 4.11, t, 2.56) than those of *cone*-**2i** (t, 4.90, t, 3.98) (Fig. 1).

The success of peralkylation involves the possibility of preparing tetraethers with two different alkyl groups. These after all, were utilized in the synthesis of dibenzyl **2l**. The easily accessible **2k** was cleanly dibenzylated by BnOH (THF, rt, 48 h) affording compound **6** which, unexpectedly, exists in the *partial cone* conformation



2	R (yield)
a	Me (80%)
b	*n*-Bu (27%)
c	*n*-Oct (67%)
d	$PhOCH_2CH_2$ (63%)
e	2-Naphth$(OCH_2CH_2)_2$ (50%)
f	$Me(OCH_2CH_2)_2$ (46%)
g	$(OCH_2CH_2)_2Cl$ (43%)
h	$(CH_2)_6Br$ (29%)
i	CH_2CH_2Br (89%)
j	$(CH_2)_3Cl$ (30%)
k	phthalimidomethyl (80%) Bn
m	(*R*)-Me (54%)
n	(*S*)-Ph (72%)

Scheme 1. Synthesis of thiacalix[4]arene 1,3-diethers via Mitsunobu reactions.

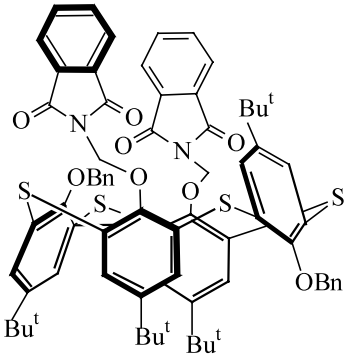


	R(yield)
3	$(CH_2)_2Br$ (90 %)
4	$(CH_2)_3Cl$ (93 %)
5	*n*-Oct (40 %)

Figure 1. Thiacalix[4]arene tetraethers.

exclusively in $CDCl_3$. The ^1H NMR spectrum of **6** reflects the lower symmetry when compared to the 1,3-*alternate* **3**–**5**. The three singlets (1.57, 1.19 and 0.8 ppm in a 1:1:2 ratio) for the Bu^t groups, the two singlets (4.99 and 4.97 ppm) for the OCH_2Ph groups and the splitting of the aromatic signals into two doublets (7.65 and 7.25 ppm with *meta* coupling $J=2.6$ and 2.2 Hz, respectively) and two singlets (8.02 and 7.38 ppm) are all indicative of the *paco* structure **6**, similar to another literature example.[7]

After removing the phthalimidomethyl protecting groups from **6** by simple base treatment (toluene/EtOH, K_2CO_3, 1 h reflux), **2l** was cleanly obtained in 60% overall yield.[20] This protection–deprotection route is expected to work efficiently in the synthesis of diethers not available by direct alkylation.



6 (68%)

In spite of the two literature examples,[15,16] the scope of Mitsunobu alkylation has not been utilized fully in calixarene chemistry. To illustrate the advantages of this method, we have prepared 25,27-bis(2-bromoethoxy)-26,28-dihydroxycalix[4]arene at ambient temperature in a yield of 55% (not optimized) using 2-bromoethanol in THF under the Mitsunobu protocol.[20] This compound has already been synthesized by Zhang et al. in a 48 h reaction by the K_2CO_3 mediated alkylation of calix[4]arene with an enormous excess of 1,2-dibromoethane (100 ml/12 mmol calixarene!) in boiling MeCN, and a similar yield was reported.[22]

Intermediates **2g**–**j**, **3** and **4**, by replacement of the terminal halogen atoms with nucleophiles, may have potential in the synthesis of various novel thiacalixarenes. Actually, a recent attempt has failed to synthesize **3** with the standard K_2CO_3-mediated alkylation of **1** with 1,2-dibromoethane.[21] Instead, intramolecular cyclizations between the proximal OH groups took place resulting in the formation of a molecular basket doubly capped by ethylene bridges. We have attained the same result when **2i** was treated with K_2CO_3 in boiling MeCN. Compounds **3** and **4** provide the possibility of accessing koilands where the central 1,3-*alt*-thiacalixarene core is fused with two (thia)calix units through connecting chains.

In conclusion, we have demonstrated for the first time the selective *O*-alkylation of *p*-*tert*-butylthiacalix[4]arene with a series of alcohols under the Mitsunobu protocol, thus opening a simple access to intermediates containing reactive functional groups which are not available by other methods. Furthermore, a useful protecting group has also been introduced into thiacalixarene chemistry.

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20. NMR spectra were recorded at 298 K in $CDCl_3$ at 500/125 MHz on a Bruker-Avance DRX-500 instrument. *General procedure for the synthesis of diethers* **2**. To the stirred mixture of **1** (0.72 g, 1 mmol), TPP (0.8 g, 3 mmol), ROH (10 mmol) in 20 ml dry THF, a 40% toluene solution of DEAD (1.3 ml, 3 mmol) was added under ice-cooling and allowed to react at ambient temperature for 24 h. The solvent was then removed under reduced pressure and the residue was triturated with hot MeOH (20 ml) and filtered to give white solids which were recrystallized or purified by chromatography on silica (eluent: hexane–EtOAc = 9:1 unless otherwise stated).

Compound 2a. Mp 246–248°C, (lit.[9] mp 246–248°C); ^{1}H and ^{13}C NMR data are identical with those of the sample prepared by alkylation of **1** with MeI.[9]

Compound 2b. Mp 222–224°C (EtOAc–MeOH); ^{1}H NMR: δ 7.96 (s, 2H, O*H*), 7.67 (s, 4H, Ar*H*), 6.96 (s, 4H, Ar*H*), 4.50 (t, 4H, J = 6.58, OCH_2), 2.00 (p, 4H, J = 7.07, CH_2), 1.63 (m, 4H, CH_2), 1.35 (s, 18H, Bu^t), 1.05 (t, 6H, J = 7.35, CH_3), 0.80 (s, 18H, Bu^t); ^{13}C NMR: δ 156.6, 156.1, 147.9, 142.7, 134.5, 133.0, 129.1, 122.4 (Ar), 75.9, (OCH_2), 34.4 (C(CH$_3$)$_3$), 34.2 (C(CH$_3$)$_3$), 32.4 (CH$_2$), 31.7 (C(CH$_3$)$_3$), 31.0 (C(CH$_3$)$_3$), 19.3 (CH$_2$), 14.3 (CH$_3$); FAB-MS m/z: 831.6 [M+H]$^+$, 870.6 [M+K]$^+$, 1091.9 [M+Cs]$^+$; anal. calcd for $C_{48}H_{64}O_4S_4$ (832.15): C, 69.20; H, 7.69, found: C, 68.77; H, 7.71%.

Compound 2c. Mp 220–222°C; ^{1}H NMR: δ 7.94 (s, 2H, O*H*), 7.67 (s, 4H, Ar*H*), 6.96 (s, 4H, Ar*H*), 4.49 (t, 4H, J = 6.73 OCH_2), 2.03 (m, 4H, CH_2), 1.58 (m, 4H, CH_2), 1.42 (m, 4H, CH_2), 1.35 (s, 18H, Bu^t), 1.31 (t, 6H, CH_3), 1.26 (m, 4H, CH_2), 0.89 (m, 8H, CH_2), 0.81 (s, 18H, Bu^t); ^{13}C NMR: δ 156.8, 156.3, 148.1, 142.9, 134.7, 133.1, 129.3, 122.6 (Ar), 76.4, (OCH_2), 34.6 (C(CH$_3$)$_3$), 34.4 (C(CH$_3$)$_3$), 32.3 (CH$_2$), 31.9 (C(CH$_3$)$_3$), 31.2 (C(CH$_3$)$_3$), 32.3, 30.4, 29.9, 29.7, 26.2, 23.1 (CH$_2$), 14.5 (CH$_3$); anal. calcd for $C_{56}H_{80}O_4S_4$ (944.79): C, 71.15; H, 8.47, found: C, 70.79; H, 8.42%.

Compound 2d. Mp 208–209°C; ^{1}H NMR: δ 8.17 (s, 2H, O*H*), 7.71 (s, 4H, Ar*H*), 7.28 (t, 4H, Ar*H*), 6.98 (s, 4H, Ar*H*), 6.96 (d, 4H, J = 8.20, Ar*H*), 6.92 (t, 2H, Ar*H*), 4.87 (t, 4H, J = 4.15, CH_2), 4.20 (t, 4H, J = 4.20, CH_2), 1.37 (s, 18H, Bu^t), 0.82 (s, 18H, Bu^t); ^{13}C NMR: δ 158.9, 156.1, 156.0, 148.2, 142.8, 134.9, 132.9, 129.5, 129.4, 122.4, 121, 114.9 (Ar), 72.9, 67.3 (OCH_2), 34.4 (C(CH$_3$)$_3$), 34.2 (C(CH$_3$)$_3$), 31.7 (C(CH$_3$)$_3$), 31.0 (C(CH$_3$)$_3$); FAB-MS m/z: 959.2 [M+H]$^+$, 1044 [M+Rb]$^+$, 1091.9 [M+Cs]$^+$; anal. calcd for $C_{56}H_{64}O_6S_4$ (960.19): C, 69.98; H, 6.66, found: C, 69.59; H, 6.71%.

Compound 2e. Mp 156–158°C (eluent: hexane–EtOAc = 8:2); ^{1}H NMR: δ 8.10 (s, 2H, O*H*), 7.68 (d, 2H, J = 7.95 Ar*H*), 7.63 (m, 4H, Ar*H*), 7.61 (s, 4H, Ar*H*), 7.37 (t, 2H, J = 7.40 Ar*H*), 7.28 (t, 2H, J = 7.35 Ar*H*), 7.12 (d, 2H, Ar*H*), 7.11 (s, 2H, Ar*H*), 6.92 (s, 4H, Ar*H*), 4.78 (t, 4H, J = 4.50, OCH_2), 4.30 (t, 4H, J = 4.50, OCH_2), 4.13 (t, 4H, J = 4.50, OCH_2), 4.05 (t, 4H, J = 4.50, OCH_2), 1.31 (s, 18H, Bu^t), 0.77 (s, 18H, Bu^t); ^{13}C NMR: δ 157.0, 156.1, 148.1, 142.7, 134.8, 134.7, 132.9, 129.4, 123.7, 122.3, 119.2, 107.1 (Ar), 73.8 (ArOCH_2), 70.9, 70.0, 67.8 (OCH_2), 34.4 (C(CH$_3$)$_3$), 34.2 (C(CH$_3$)$_3$), 31.7 (C(CH$_3$)$_3$), 30.9 (C(CH$_3$)$_3$), FAB-MS m/z: 1149 [M+H]$^+$, 1171 [M+Na]$^+$, 1187 [M+K]$^+$, 1234.8 [M+Rb]$^+$, 1280.8 [M+Cs]$^+$; anal. calcd for $C_{68}H_{76}O_8S_4$ (1148.65): C, 71.05; H, 6.62, found: C, 70.68; H, 6.55%.

Compound 2f. Mp 148–150°C (eluent: hexane–EtOAc = 8:2); ^{1}H NMR: δ 8.04 (s, 2H, O*H*), 7.68 (s, 4H, Ar*H*), 6.95 (s, 4H, Ar*H*), 4.76 (t, 4H, J = 4.65, OCH_2), 4.08 (t, 4H, J = 4.68, CH_2), 3.84 (m, 4H, J = 4.68, CH_2), 3.66 (t, 4H, J = 4.65, OCH_2), 3.40 (s, 6H, OCH_3), 1.35 (s, 18H, Bu^t), 0.80 (s, 18H, Bu^t); ^{13}C NMR: δ 156.13, 156.1, 148.0, 142.7, 134.8, 132.8, 129.3, 122.3 (Ar), 73.8 (ArOCH_2), 72.2 (OCH_3), 70.8, 70.7, 59.2 (CH$_2$), 34.3 (C(CH$_3$)$_3$), 34.2 (C(CH$_3$)$_3$), 31.7 (C(CH$_3$)$_3$), 30.9 (C(CH$_3$)$_3$); FAB-MS m/z: 946.3 [M+Na]$^+$, 962.4 [M+K]$^+$, 1008.1 [M+Rb]$^+$, 1056 [M+Cs]$^+$; anal. calcd for $C_{50}H_{68}O_8S_4$ (924.45): C, 64.91; H, 7.36, found: C, 64.63; H, 7.31%.

Compound 2g. Mp 215–217°C (eluent: hexane–EtOAc = 95:5); ^{1}H NMR: δ 8.02 (s, 2H, O*H*), 7.66 (s, 4H, Ar*H*), 6.93 (s, 4H, Ar*H*), 4.73 (t, 4H, J = 4.50, ArOCH_2), 4.09 (t, 4H, J = 4.63, ClCH_2), 3.93 (t, 4H, J = 5.95, OCH_2), 3.74 (t, 4H, J = 6.00, OCH_2), 1.33 (s, 18H, Bu^t), 0.78 (s, 18H, Bu^t); ^{13}C NMR: δ 155.9, 155.8, 148.0, 142.7, 134.8, 132.8, 129.1, 122.1 (Ar), 73.6 (ArOCH_2), 71.5, 70.6, 69.9 (CH$_2$), 34.2 (C(CH$_3$)$_3$), 34.0 (C(CH$_3$)$_3$), 31.5 (C(CH$_3$)$_3$), 30.8 (C(CH$_3$)$_3$); FAB-MS m/z: 933.6 [M+H]$^+$, 954.6 [M+Na]$^+$, 970.5 [M+K]$^+$, 1016.6 [M+Rb]$^+$, 1064.4 [M+Cs]$^+$; anal. calcd for $C_{48}H_{62}O_6S_4Cl_2$ (932.19): C, 61.78; H, 6.65, found: C, 61.43; H, 6.70%.

Compound 2h. Mp 278–280°C; ^{1}H NMR: δ 7.92 (s, 2H, O*H*), 7.69 (s, 4H, Ar*H*), 6.97 (s, 4H, Ar*H*), 4.50 (t, 4H, J = 6.50, OCH_2), 3.47 (t, 4H, J = 6.80, BrCH_2), 2.04 (m, 4H, J = 7.10, CH_2), 4.05 (t, 4H, J = 7.00 CH_2), 1.61–1.65 (m, 8H, CH_2), 1.36 (s, 18H, Bu^t), 0.82 (s, 18H, Bu^t); ^{13}C NMR: δ 156.3, 155.8, 147.8, 142.6, 134.4, 132.8, 128.9, 122.2, (Ar), 75.8 (ArOCH_2), 34.5 (C(CH$_3$)$_3$), 34.4 (C(CH$_3$)$_3$), 33.3 (CH$_2$), 31.8 (C(CH$_3$)$_3$), 31.1 (C(CH$_3$)$_3$), 30.1, 28.4, 25.4 (CH$_2$); FAB-MS m/z: 1047.9 [M+H]$^+$, 1069.9 [M+Na]$^+$; anal. calcd for $C_{52}H_{70}O_4S_4Br_2$ (1047.13): C, 59.60; H, 6.69, found: C, 59.68; H, 6.64%.

Compound 2i. Mp 212–214°C; ^{1}H NMR: δ 7.76 (s, 2H, O*H*), 7.70 (s, 4H, Ar*H*), 6.98 (s, 4H, Ar*H*), 4.90 (t, 4H, J = 6.18, OCH_2), 3.98 (t, 4H, J = 6.18 BrCH_2), 1.37 (s, 18H, Bu^t), 0.82 (s, 18H, Bu^t); ^{13}C NMR: δ 155.8, 155.7, 148.6, 143.1, 134.6, 133, 129.1, 122.2 (Ar), 74.4, 67.3 (CH$_2$), 34.4 (C(CH$_3$)$_3$), 34.3 (C(CH$_3$)$_3$), 31.7 (C(CH$_3$)$_3$), 30.9 (C(CH$_3$)$_3$); FAB-MS m/z: 934.1 [M+H]$^+$; anal. calcd for $C_{44}H_{54}O_4S_4Br_2$ (932.51): C, 56.64; H, 5.79, found: C, 56.82; H, 5.74%.

Compound 2j. (Molar ratio of TPP/DEAD:**1** = 2.2). Mp 288–290°C; ^{1}H NMR: δ 7.75 (s, 2H, O*H*), 7.59 (s, 4H, Ar*H*), 6.93 (s, 4H, Ar*H*), 4.53 (t, 4H, J = 5.63, ArOCH_2), 3.90 (t, 4H, J = 6.45, ClCH_2), 2.40 (t, 4H, J = 6.16 (CH_2), 1.23 (s, 18H, Bu^t), 0.75 (s, 18H, Bu^t); ^{13}C NMR: δ 156.2, 155.9, 148.4, 143.0, 134.6, 133.3, 128.9, 122.1 (Ar), 72.9 (ArOCH_2), 42.1 (ClCH_2), 34.4 (C(CH$_3$)$_3$), 34.2

($C(CH_3)_3$), 33.5 (CH_2), 31.7 ($C(CH_3)_3$), 30.9 ($C(CH_3)_3$); FAB-MS m/z: 872.9 $[M+H]^+$; anal. calcd for $C_{46}H_{58}O_4S_4Cl_2$ (872.09): C, 63.28; H, 6.65, found: C, 62.62; H, 6.59%.

Compound 2k. (Molar ratio of TPP/DEAD:**1** = 2.2, 6 h). Mp 320–322°C; ^1H NMR: δ 7.92 (m, 4H, phthalimide Ar*H*), 7.76 (m, 4H, phthalimide Ar*H*), 7.52 (s, 4H, Ar*H*), 7.29 (s, 2H, O*H*), 7.19 (s, 4H, Ar*H*), 6.15 (s, 4H, OCH_2N), 1.25 (s, 18H, Bu^t), 0.96 (s, 18H, Bu^t); ^{13}C NMR: δ 167.3 (*C*O), 155.7, 154.8, 148.3, 142.5, 134.4, 134.2, 133.5, 131.9, 129.1, 123.9, 121.4 (Ar), 77.2 69.7 ($ArOCH_2$), 34.1 ($C(CH_3)_3$), 34.0 ($C(CH_3)_3$), 31.3 ($C(CH_3)_3$), 30.9 ($C(CH_3)_3$); FAB-MS m/z: 1038.9 $[M+H]^+$, 1061.8 $[M+Na]^+$, 1077.8 $[M+K]^+$, 1123.7 $[M+Rb]^+$, 1171.6 $[M+Cs]^+$; anal. calcd for $C_{58}H_{58}O_8N_2S_4$ (1038.58): C, 67.03; H, 5.59, found: C, 66.52; H, 5.50%.

Compound 2l. (Obtained quantitatively by treatment of **6** with K_2CO_3 in a 1:1 mixture of toluene/EtOH under 1 h reflux). Mp 288–290°C; ^1H NMR: δ 7.98 (s, 2H, O*H*), 7.68 (s, 4H, Ar*H*), 7.62 (d, 4H, J = 7.3, Bn*H*), 7.33–7.29 (m, 6H, Bn*H*), 6.96 (s, 4H, Ar*H*), 5.49 (s, 4H, $ArOCH_2$), 1.34 (s, 18H, Bu^t), 0.79 (s, 18H, Bu^t); FAB-MS m/z: 899.5 $[M+H]^+$; anal. calcd for $C_{54}H_{60}O_4S_4$ (900.34): C, 71.97; H, 6.66, found: C, 71.78; H, 6.63%.

Compound 2m. (Molar ratio of TPP/DEAD:**1** = 2.2, toluene, 110°C, 24 h). Mp 178–179°C; $[\alpha]_D = -10$ (*c* 1, $CHCl_3$); ^1H NMR: δ 7.68 (d, 4H, J = 9.95 Ar*H*), 7.56 (s, 2H, O*H*), 7.03 (s, 4H, Ar*H*), 5.15 (q, 2H, J = 6.68, O*CH*), 4.29 (q, 4H, J = 6.85, OCH_2), 1.89 (d, 6H, J = 6.70, CH_3), 1.35 (s, 18H, Bu^t), 1.32 (t, 6H, CH_3), 0.85 (s, 18H, Bu^t); ^{13}C NMR: δ 171.6, 156.0, 155.7, 147.6, 142.4, 134.5, 132.9, 129.0, 122.3 (Ar), 74.8 (ArO*C*H), 61.4 (OCH_2), 34.1 ($C(CH_3)_3$), 33.9 ($C(CH_3)_3$), 31.4 ($C(CH_3)_3$), 30.7 ($C(CH_3)_3$), 18.6, 14.1 (CH_3); FAB-MS m/z: 920.7 $[M+H]^+$, 944 $[M+Na]^+$, 959.9 $[M+K]^+$, 1005.9 $[M+Rb]^+$, 1053.9 $[M+Cs]^+$; anal. calcd for $C_{50}H_{64}O_8S_4$ (920.42): C, 65.19; H, 6.95, found: C, 64.72; H, 6.88%.

Compound 2n. (Molar ratio of TPP/DEAD:**1** = 2.2, toluene, 110°C, 24 h). Mp 201–203°C; $[\alpha]_D = +76.8$ (*c* 1, $CHCl_3$); ^1H NMR: δ 7.63 (m, 4H, Ar*H*), 7.55 (d, 2H, J = 2.43, Ar*H*), 7.48 (d, 2H, J = 2.46, Ar*H*), 7.42 (s, 2H, O*H*), 7.32 (m, 6H, Ar*H*), 6.90 (d, 2H, J = 2.52, Ar*H*), 6.85 (d, 2H, J = 2.45, Ar*H*), 6.00 (s, 2H, O*CH*), 4.22 (q, 4H, J = 7.15, OCH_2), 1.20 (s, 18H, Bu^t), 1.16 (t, 6H, J = 7.09, CH_3), 0.72 (s, 18H, Bu^t); ^{13}C NMR: δ 170.1, 156.0, 155.5, 147.6, 142.3, 134.5, 132.9, 129.0, 122.1 (Ar), 85.4 (OCH_2), 61.7 (ArO*C*H), 34.1 ($C(CH_3)_3$), 33.9 ($C(CH_3)_3$), 31.4 ($C(CH_3)_3$), 30.7 ($C(CH_3)_3$), 14.6 (CH_3); FAB-MS m/z: 1045.8 $[M+H]^+$, 1067.9 $[M+Na]^+$, 1083.9 $[M+K]^+$, 1129.8 $[M+Rb]^+$, 1177.7 $[M+Cs]^+$; anal. calcd for $C_{60}H_{68}O_8S_4$ (1043.58): C, 69.00; H, 6.52, found: C, 68.55; H, 6.44%.

Compound 3. (molar ratio of TPP/DEAD:**1** = 6, 24 h). Mp 326–328°C; ^1H NMR: δ 7.36 (s, 8H, Ar*H*), 4.11 (t, 8H, J = 8.03, OCH_2), 2.56 (t, 8H, J = 8.00, $BrCH_2$), 1.31 (s, 36H, Bu^t); ^{13}C NMR: δ 153.4, 147.5, 128.1, 127.4 (Ar), 76.6, 67.3 (CH_2), 34.7 ($C(CH_3)_3$), 31.6 ($C(CH_3)_3$); anal. calcd for $C_{48}H_{60}O_4S_4Br_4$ (1144.19): C, 48.25; H, 5.25, found: C, 48.02; H, 5.19%.

Compound 4. (molar ratio of TPP/DEAD:**1** = 6, 24 h). Mp 354°C (hexane–EtOAc = 95:5); ^1H NMR: δ 7.37 (s, 8H, Ar*H*), 4.00 (t, 8H, J = 6.78, $ArOCH_2$), 3.20 (t, 8H, J = 6.65, $ClCH_2$), 1.49 (m, 8H, CH_2), 1.31 (s, 36H, Bu^t); ^{13}C NMR: δ 156.6, 146.6, 128.3, 127.6 (Ar), 66.2 ($ArOCH_2$), 42.3, 34.6 (CH_2), 32.4 ($C(CH_3)_3$), 31.5 ($C(CH_3)_3$); anal. calcd for $C_{52}H_{68}O_4S_4Cl_4$ (1024.43): C, 60.92; H, 6.64, found: C, 60.47; H, 6.60%.

Compound 5. (Molar ratio of TPP/DEAD:**1** = 6, toluene, 110°C, 24 h). Mp 220–222°C (hexane–EtOAc = 95:5); ^1H NMR: δ 7.27 (s, 8H, Ar*H*), 3.78 (t, 8H, J = 7.70, $ArOCH_2$), 1.24 (s, 36H, Bu^t), 1.23 (m, 8H, CH_2), 1.19 (m, 16H, CH_2), 1.13–1.05 (m, 16H, CH_2), 0.98 (m, 8H, J = 6.50, CH_2), 0.85 (t, 12H, J = 6.75, CH_3); ^{13}C NMR: δ 156.9, 145.1, 127.9, 127.4 (Ar), 68.7 ($ArOCH_2$), 34.4 ($C(CH_3)_3$), 32.1 (CH_2), 31.5 ($C(CH_3)_3$), 29.9, 29.8, 29.1, 26.1, 22.8, (CH_2), 14.3 (CH_3); anal. calcd for $C_{72}H_{112}O_4S_4$ (1168.74): C, 73.93; H, 9.58, found: C, 73.46; H, 9.52%.

Compound 6. (Molar ratio of TPP/DEAD:**1** = 4, THF, rt, 24 h). Mp 234–236°C (hexane–EtOAc = 95:5); ^1H NMR: δ 8.02 (s, 2H, Ar*H*), 7.90 (m, 4H, phthalimide Ar*H*), 7.75 (m, 4H, phthalimide Ar*H*), 7.65 (d, 2H, J = 7.15, Bn*H*), 7.38 (s, 2H, Ar*H*), 7.35–7.29 (m, 6H, Bn*H*), 7.25 (d, 2H, J = 2.6, Ar*H*), 7.04 (d, 2H, J = 7.25, Bn*H*), 6.89 (d, 2H, J = 2.2, Ar*H*), 5.71 (s, 4H, OCH_2N), 4.99 (s, 2H, OCH_2), 4.97 (s, 2H, OCH_2), 1.57 (s, 9H, Bu^t), 1.19 (s, 9H, Bu^t), 0.80 (s, 18H, Bu^t); ^{13}C NMR: δ 167.1 (*C*O), 159.9, 156.8, 156.4, 146.6, 146.1, 144.9, 137.4, 137.1, 136.1, 134.2, 134.1, 133.7, 133.0, 132.0, 130.3, 130.2, 129.6, 128.5, 128.3, 128.1, 128.0, 127.8, 127.1, 123.6 (Ar), 76.0, 72.2, 69.6 ($ArOCH_2$), 34.7, 34.3, 34.1 ($C(CH_3)_3$), 31.6, 31.5, 31.1 ($C(CH_3)_3$); FAB-MS m/z: 1219.7 $[M+H]^+$; anal. calcd for $C_{72}H_{70}O_8S_4N_2$ (1218.40): C, 70.92; H, 5.75, found: C, 70.78; H, 5.70%.

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