An Efficient Method for Preparation of Chiral Macrocyclic Bisamides Starting from Diol Derivatives of D-Mannitol and L-Tartaric Acid

Daniel T. Gryko,[a] Piotr Piątek,[b] Janusz Jurczak*[ab]

[a] Institute of Organic Chemistry, Polish Academy of Sciences, 01-224 Warsaw, Poland

[b] Department of Chemistry, University of Warsaw, 02-093 Warsaw, Poland

Fax +48(22)6326681; E-mail jurczak@ichf.edu.pl

Received 2 April 1998; revised 17 July 1998

Abstract: Starting from various 1,2- and 1,4-diol derivatives of D-mannitol and L-tartaric acid, eight chiral macrocyclic bisamides were obtained via C_2-elongation of diols with *tert*-butyl bromoacetate followed by macrocyclization of the resultant diesters with primary α,ω-diamines.

Key words: chiral diazacoronands, cyclic bisamides, macrocyclisation, high pressure, transesterification

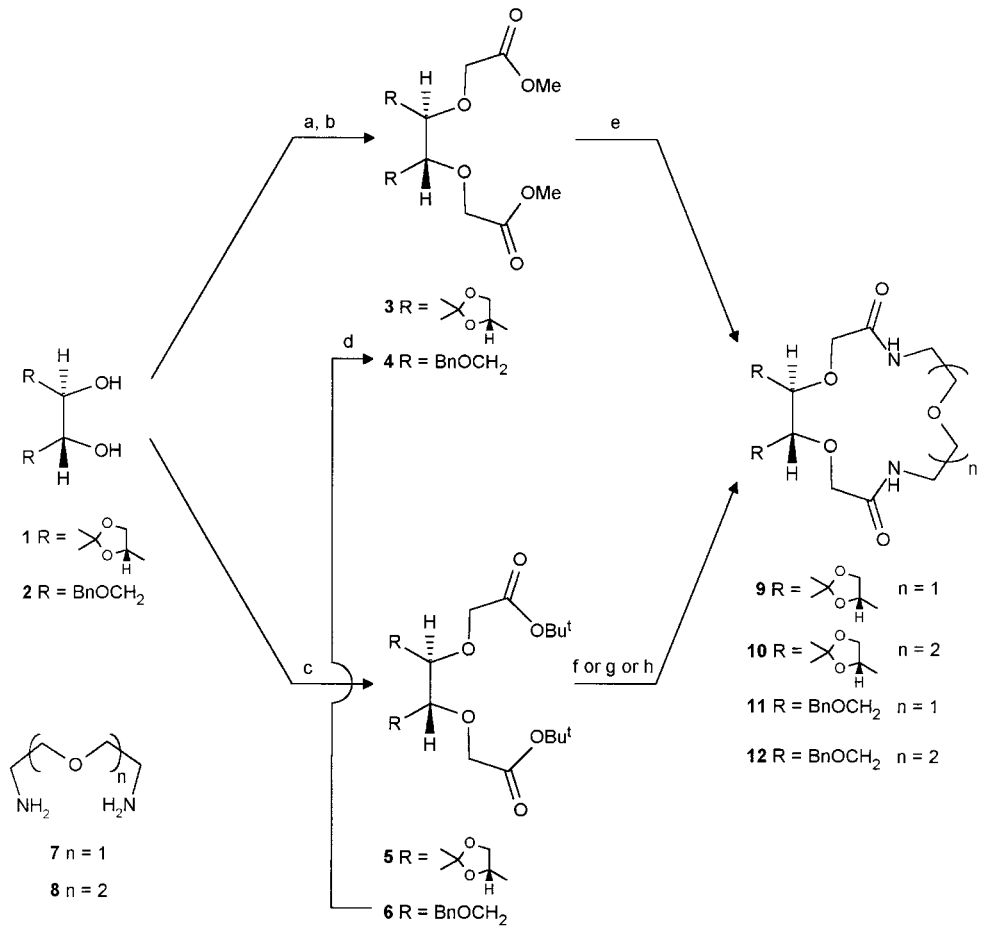
The strategies of preparation of highly elaborated macrocyclic compounds are based on elongation of the selected starting material with the successive, usually two-carbon fragments. To achieve this, reactions with allyl bromide followed by reductive ozonolysis,[1, 2] as well as reactions with chloroacetic[3, 4] or bromoacetic[5, 6] acid are applied. Recently, we have reported that dimethyl α,ω-dicarboxylates react with primary α,ω-diamines in methanol at room temperature with no need for using the high-dilution technique.[7–10] Obviously, to obtain the more complex diazacoronand derivatives by our method, it would be advantageous to elongate the diol with the -CH_2CO_2Me unit within one step. Such an increase in performance of the proposed strategy is particularly significant in the case of the optically active compounds. This results from the presence of various, often unstable functional or protective groups as well as from the expense of diols, which are often prepared from tartaric acid or sugars in several stages.

As a part of our extensive studies on methodology of the synthesis of chiral macrocyclic bisamides being the convenient precursors of the respective diazacoronands, we decided to prepare the series of chiral compounds **9–12** and **18–21**, differing in the ring size, starting from D-mannitol and L-tartaric acid. According to the strategy adopted from the literature, the substrate esters **3–6** and **15–17** should be prepared by elongation of the respective diols with bromoacetic acid and then esterification of the resultant acids. This method was verified for two diols, **1** and **2** (Scheme 1). Unfortunately, in the case of ester **3**, the yield was merely 8%, in spite of the application of a very mild method of esterification. A much better yield (49%) was achieved in the synthesis of ester **4**, but here some problems with purification of the product occurred.

Being aware of disadvantages of this two-step procedure recommended in the literature, we attempted to prepare the methyl esters immediately by elongation of the respective diols with methyl bromoacetate. In spite of testing various reaction conditions, we did not obtain the desired compounds. In this situation, we decided to apply the two-phase method of C_2-elongation of diols using *tert*-butyl bromoacetate, previously described by us,[11] to obtain esters **5**, **6**, **15**, and **16**. After slight modification of the reaction conditions, we obtained *tert*-butyl esters **5**, **6**, **15**, and **16** in very good yield (Schemes 1 and 2, Table 2). The main advantages of this method are: one-stage reaction, use of relatively safe reactants, short reaction time, easy workup, high yield, and crystallizable products. Prolongation of the reaction time results in reduction of yield. It is noteworthy that substitution of $BrCH_2CO_2t$-Bu with $ClCH_2CO_2t$-Bu proved unsuccessful. Similarly, application of methyl or ethyl bromoacetate did not lead to the desired products.

The synthesis of macrocyclic bisamides was initially performed using methyl esters **3** and **4**. These esters react with amines **7** and **8** under normal conditions to give bisamides **9**, **10**, **11**, and **12**, although, as expected, the yields are lower than in the case of dimethyl 3,6-dioxaoctanodioate,[9] the unsubstituted analogue of esters **3** and **4** (Scheme 1, Table 1). It would seem reasonable that bulky, labile benzyl groups disorder the preorganization much more than the more rigid dioxolanes, but the yields of the respective bisamides do not differ markedly each other.

We knew from the previous studies[12] that *tert*-butyl esters did not react with α,ω-diamines under normal conditions. Because of its inconvenience, we discarded the two-stage process, i.e., transesterification followed by macrocyclization under normal conditions. We found that *tert*-butyl esters **5**, **6**, **15**, and **16** reacted with α,ω-diamines in methanol under pressure of 12 kbar to afford optically active bisamides **9**, **10**, **12**, **18**, and **19** in 47–80% yield (Schemes 1 and 2, Table 1). It seems that the high-pressure macrocyclization proceeds in two stages. Transesterification is the first stage, and the resulting dimethyl ester reacts with α,ω-diamine in the second stage. To verify this hypothesis, we performed two experiments. In the first one, we reacted ester **3** with amine **8** under pressure of 12 kbar. The respective bisamide **10** was obtained in 48% yield, almost identical as in case of the reaction of *tert*-butyl ester **5** under pressure of 12 kbar. Next, *tert*-butyl ester **6** was transesterified in methanol under normal pressure. In spite of prolonged reaction time (72 h), only traces of



Scheme 1 a) NaH, THF, $BrCH_2CO_2H$, reflux; b) ClO_2Me, NMM, MeOH, r.t.; c) $BrCH_2CO_2t$-Bu, $NaOH_{aq}$, $(Bu)_4NCl$, PhMe, r.t.; d) Et_3N, MeOH, r.t., 12 kbar; e) 7 or 8, MeOH, r.t.; f) 7 or 8, MeOH, r.t., 12 kbar; g) 7 or 8, DBU, MeOH, r.t.; h) 8, DBU, LiBr, MeOH, r.t.

products **4** were observed. Then we modified the reaction conditions by adding catalytic amounts of triethylamine (Scheme 1). Now dimethyl ester **4** was isolated in 91% yield. This allows conclusion that primary amines **7** and **8** are both transesterification catalysts and substrates in the macrocyclization reaction.

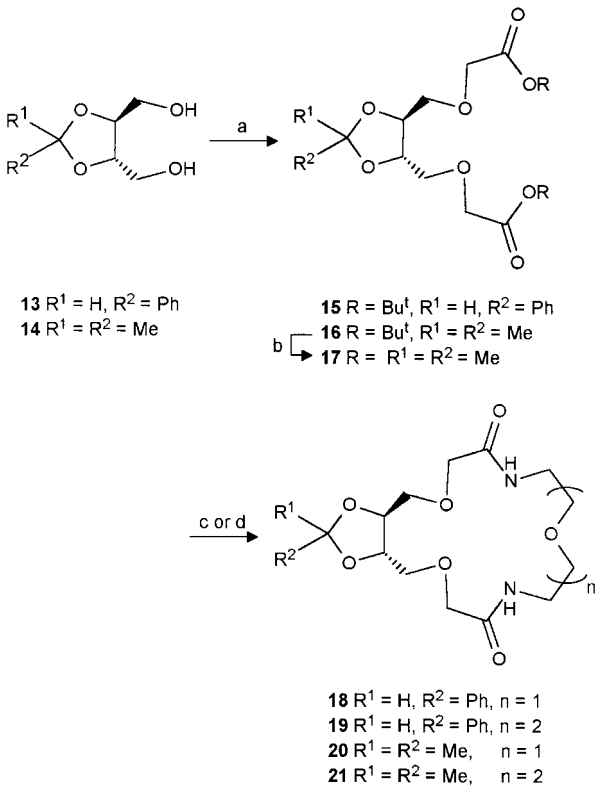
Table 1 Yields (%) of Bisamides **9–12** and **18–21**

Bisamide	From Dimethyl Esters 7 days[a] (Method A)	From *tert*-Butyl Esters 12 kbar, 72 h,[a] (Method B)	From *tert*-Butyl Esters DBU, 21 days,[a] (Method C)
9	30	57	42
10	39	48	52
11	34	–	56
12	35	64	59
18	–	65	57
19	–	80	62
20	–	–	41
21	–	–	33

[a] MeOH, r.t.

Having in perspective the necessity for preparation of diazacoronands in multigram scale, we looked for a catalyst which could enable amidation of *tert*-butyl esters under normal pressure. We needed the transesterification catalyst to be simultaneously a strong base and a weak nucleophile. Unlike the acid catalyst, such a compound would not inactivate the amine and would accelerate the amidation reaction itself, which is catalyzed by bases.[13] Our choice was 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), which was already used for transesterification in the synthesis of various esters.[14–16] Thus, we performed reaction of *tert*-butyl ester **5** and amine **8** in methanol in the presence of 20 mol% DBU at room temperature. After three weeks, we isolated cyclic bisamide **10** in 52% yield (Scheme 1). It is noteworthy that unlike DBU, triethylamine, 1,4-diazabicyclo[2.2.2]octane (DABCO), or 4-dimethylaminopyridine (DMAP) are not effective catalysts in this reaction.

In absence of primary amine, the *tert*-butyl esters undergo conversion to the dimethyl esters, e.g., ester **16** can be converted directly to dimethyl ester **17** in 90% yield (Scheme 2). The same conversion can be effected by heating the ester with one equivalent of DBU at reflux for 8 h.



Scheme 2 a) $BrCH_2CO_2t$-Bu, $NaOH_{aq}$, $(Bu)_4NCl$, PhMe, r.t.; b) MeOH, DBU, reflux; c) **7** or **8**, MeOH, r.t., 12 kbar; d) **7** or **8**, DBU, MeOH, r.t.

The successful experiment of preparation of bisamide **10** from ester **5** in the presence of DBU prompted us to prepare other bisamides in this way. Table 1 shows the results of reaction of the *tert*-butyl esters with amines in the presence of DBU. The yields are in the range of 40% to 60%. One can easily note that the yields for the *tert*-butyl esters and DBU are in each case at least by 10% higher than the yields for the methyl esters. The most probable explanation is overlapping of two factors. The first of them is the increase of conversion to 100% using DBU. The second one is the quasi-high-dilution condition caused by slow transesterification of the *tert*-butyl esters during the reaction course.

The disadvantage of this method is long reaction time. It was avoided by us via addition of anhydrous LiBr. The DBU/LiBr system has been used as a strong basic transesterification catalyst by Seebach et al.[17] Thus, an addition of DBU/LiBr to the mixture of di-*tert*-butyl ester and diamine in methanol should accelerate both reaction steps. Thanks to the use of the DBU/LiBr system, we shorten the reaction time from three weeks to 24 hours. The reaction of di-*tert*-butyl ester **5** with diamine **8** in anhydrous methanol in the presence of one equivalent of DBU and 10 equivalents of LiBr afforded bisamide **10** in the yield of 61% (the highest from among all methods).

The method presented here enables two-stage transformation of diols to macrocyclic bisamides in the average total yield of about 40%.

Melting points were taken on a Kofler type (Boetius) hot-stage apparatus and are not corrected. Optical rotations were measured using a JASCO DIP-360 polarimeter with thermally jacketed 10 cm cell. ^{1}H NMR spectra were recorded with a Varian Gemini (200 MHz) and/or a Bruker AM500 (500 MHz) spectrometer in $CDCl_3$ using TMS as an internal standard. ^{13}C NMR spectra were recorded using also a Varian Gemini (50 MHz) and/or a Bruker AM500 (125 MHz) spectrometers. All chemical shifts are quoted in parts per million relative to TMS ($\delta = 0.00$ ppm), and coupling constants (J) are measured in Hertz. HRMS experiments were performed on an AMD-604 Intectra instrument using the electron impact (EI) technique. Column chromatography was carried out on silica gel (Kieselgel-60, 200–400 mesh). Methanol was freshly distilled from Mg/I_2 under Ar. THF was freshly distilled from Na under Ar. LiBr was dried at 180°C under high vacuum and stored in a desiccator over P_2O_5. α,ω-Diamine **8** was purchased from Fluka. α,ω-Diamine **7** [18] and diols **1**,[19] **2**,[20] **13**[21,22] and **14**[20] were prepared according to the literature procedures.

Dimethyl Esters (3 and 4); General Procedure

A solution of diol (19 mmol) in THF (50 mL) was dropwise added to a vigorously stirred suspension of NaH, (1.83 g, 76 mmol) in THF (400 mL), and the mixture was refluxed over a period of 1 h. Then a solution of bromoacetic acid (5.35 g, 38 mmol) in THF (100 mL) was dropwise added over a period of 4 h, and the mixture was refluxed over a period of 8 h. After cooling, H_2O (30 mL) was added, THF was evaporated, and the residue was carefully acidified to pH = 6.9–7.0, using diluted HCl_{aq}. Then water was evaporated at 30°C, and the residue was suspended in MeOH (100 mL). *N*-Methylmorpholine (NMM, 4.1 g, 40 mmol) was added, and the suspension was cooled down to 0 °C. To the vigorously stirred suspension, methyl chloroformate (3.6 g, 40 mmol) was dropwise added, and the mixture was left standing at r.t. for a period of 12 h. Then MeOH was evaporated, sat. $NaHCO_3$ (40 mL) was added to the residue, and the aqueous suspension was extracted with $CHCl_3$ (4 × 50 mL). The combined extracts were washed with H_2O (50 mL) and dried (Na_2SO_4). The filtrate was evaporated to leave the diester as an oil. Crude diester **5** was then recrystallized from MeOH, while crude diester **6** was then chromatographed on a silica gel column using hexane/EtOAc as an eluent (Table 2).

Di-*tert*-butyl Esters (5, 6, 15 and 16); General Procedure

A solution containing diol (16.6 mmol) and tetrabutylammonium chloride (10.8 mmol) in toluene (250 mL) was added to solution of aq NaOH (35%, 250 mL). The mixture was cooled to 10 °C, under vigorous stirring. Then *tert*-butyl bromoacetate (51 mmol) was added in one portion. The water bath was removed and mixture was very vigorously stirred for 30 min. Next, H_2O (100 mL) and hexane (100 mL) were added and the mixture was stirred for another 5 minutes. Phases were separated and organic phase was dried (Na_2SO_4). The filtrate was evaporated to leave the diester as a pale yellow oil. Crude product was then chromatographed on a silica gel column using hexane/EtOAc as an eluent (Table 2).

Bisamides (9–12 and 18–21); General Procedures

Method A (standard conditions): An equimolar 0.1 M methanolic solution (1.5 mmol) of α,ω-diamine and dimethyl α,ω-dicarboxylate was left at ambient temperature over a period of 7 days. Then the solvent was evaporated and the residue was chromatographed on a silica gel column using 0.5–3% mixtures of MeOH in $CHCl_3$.

Method B (under high pressure): An equimolar solution of the dimethyl α,ω-dicarboxylate (0.5 mmol) and the appropriate α,ω-diamine (0.5 mmol) in 5 mL of MeOH was filled into a Teflon ampoule, placed in a high-pressure vessel filled with ligroin as a transmission medium and compressed (12 kbar) at r.t. for 48 h.[8,23] After decompression, the mixture was transferred quantitatively to a

Table 2 Compounds **3–6**, **9–12** and **15–21** Prepared[a,b]

Product	Yield[c] (%)	mp (°C)	$[\alpha]_D^{23}$ (*c*, $CHCl_3$)	^1H NMR ($CDCl_3$/TMS) δ, *J* (Hz)	^{13}C NMR ($CDCl_3$/TMS) δ	HRMS *m/z*
3	8.4	111	+ 10.1 (1.3)	1.31 (s, 6 H), 1.4 (s, 6 H), 3.7 (s, 6 H), 3.7–4.3 (m, 8 H), 4.34 (s, 2 H), 4.37 (s, 2 H)	24.9, 26.5, 51.7, 65.9, 69.1, 76.4, 80.7, 108.4, 170.6	Calcd for $C_{18}H_{31}O_{10}$ $(M + H)^+$ 407.1917 Found 407.1908
4	49.0[d,e] 91.0[f]	colourless oil	+ 8.5 (2.5)	3.6–3.9 (m, 6 H), 3.70 (s, 6 H), 4.35 (s, 4 H), 4.51 (s, 2 H), 4.52 (s, 2 H), 7.2–2.4 (m, 10 H)	51.7, 68.3, 70.6, 73.5, 80.0, 127.7, 127.8, 128.4, 138.2, 171.2	Calcd for $C_{24}H_{31}O_8$ $(M + H)^+$ 447.2019 Found 447.2015
5	79.2	83–86	+ 7.1 (1.05)	1.35 (s, 6 H), 1.42 (s, 6 H), 1.47 (s, 18 H), 3.7–3.9 (m, 2 H), 4.0–4.2 (m, 4 H), 4.17 (d, AB/2, 2 H, *J* = 16.2), 4.28 (d AB/2, 2 H, *J* = 16.2), 4.3–4.5 (m, 2 H)	25.0, 26.5, 28.1, 66.2, 69.8, 76.3, 80.6, 81.4, 108.3, 169.2	Calcd for $C_{23}H_{39}O_{10}$ $(M - CH_3)^+$ 475.2543 Found 475.2542
6	38.5	56–58	+ 3.1 (1.0)	1.45 (s, 18 H), 3.5–3.9 (m, 6 H), 4.20 (d AB/2, 2 H, *J* = 16.5), 4.24 (d AB/2, 2 H, *J* = 16.5), 4.46 (d, AB/2, 2 H, *J* = 11.8), 4.55 (d AB/2, 2 H, *J* = 11.8), 7.2–7.4 (m, 10 H)	28.3, 69.3, 70.7, 73.6, 79.0, 81.5, 127.6, 127.9, 128.5, 138.4, 170.2	Calcd. for $C_{30}H_{42}O_8Na$ $(M + Na)^+$ 553.2777 Found 553.2771
9	[g]	colourless oil	–14.9 (1.0)	1.34 (s, 6 H), 1.40 (s, 6H), 3.4–3.7 (m, 8 H), 3.7–3.9 (m, 4 H), 4.0–4.1 (m, 4 H), 4.16 (d AB/2, 2 H, *J* = 14.8), 4.20 (d, AB/2, 2 H, *J* = 14.8), 7.23 (br t, 2 H)	25.2, 26.7, 38.2, 69.8, 70.6, 74.7, 78.6, 109.5, 168.8	Calcd. for $C_{20}H_{35}N_2O_9$ $(M + H)^+$ 447.2343 Found 447.2338
10	[g]	66–68	+ 2.2 (1.0)	1.33 (s, 6 H), 1.39 (s, 6 H), 3.55 (s, 8 H), 3.6–3.7 (m, 8 H), 3.9–4.0 (m, 2 H), 4.1–4.2 (m, 2 H), 4.17 (d AB/2, 2 H, *J* = 14.8), 4.21 (d AB/2, 2 H, *J* = 14.8), 7.09 (br t, 2 H)	25.0, 26.6, 38.3, 66.8, 69.7, 70.6, 72.0, 74.9, 80.3, 109.1, 168.7	Calcd. for $C_{22}H_{38}N_2O_{10}$ $(M)^+$ 490.2526 Found 490.2528
11	[g]	colourless oil	+ 54.5 (0.95)	3.3–3.8 (m, 14 H), 3.93 (d AB/2, 2 H, *J* = 15.0), 4.20 (d AB/2, 2 H, *J* = 15.0), 4.47 (s, 4 H), 7.19 (br t, 2 H), 7.2–7.4 (m, 10 H)	38.0, 68.1, 68.8, 69.3, 73.6, 78.6, 127.9, 128.0, 128.5, 137.3, 169.3	Calcd. for $C_{26}H_{34}N_2O_7$ $(M)^+$ 486.2366 Found 486.2368
12	[g]	colourless oil	+ 4.3 (1.0)[j]	3.3–3.7 (m, 16 H), 3.73 (m, 2 H), 4.01 (d AB/2, 2 H, *J* = 15.3), 4.17 (d AB/2, 2 H, *J* = 15.3), 4.48 (d AB/2, 2 H, *J* = 11.9), 4.51 (d AB/2, 2 H, *J* = 11.9), 7.2–7.4 (m, 10 H), 7.23 (t, 2 H, *J* = 5.1)	38.4, 68.7, 69.7, 70.4, 70.8, 73.5, 78.8, 127.7, 127.9, 128.5, 137.5, 169.4	Calcd for $C_{28}H_{38}N_2O_8$ $(M)^+$ 530.2641 Found 530.2641
15	84.5	65–67	+ 1.4 (1.05)	1.47 (s, 9 H), 1.48 (s, 9 H), 3.81 (d, 4 H, *J* = 4.4), 4.06 (d, 4 H, *J* = 4.5), 4.4–4.8 (m, 2 H), 5.98 (s, 1 H), 7.2–7.6 (m, 5 H)	28.1, 69.0, 71.4, 77.5, 78.0, 81.7, 104.1, 126.8, 128.3, 129.3, 137.4, 169.4	Calcd for $C_{23}H_{34}O_8$ $(M)^+$ 438.2254 Found 438.2248
16	85.7	colourless oil	– 9.6 (1.2)	1.43 (s, 6 H), 1.48 (s, 18 H), 3.6–3.8 (m, 4 H), 4.04 (s, 4 H), 4.0–4.2 (m, 2 H)	26.9, 28.0, 69.2, 71.6, 77.1, 81.5, 109.7, 169.3	Calcd for $C_{18}H_{31}O_8$ $(M - CH_3)^+$ 375.2019 Found 375.2014
17	90.0[h] 92.5[i]	colourless oil	–9.8 (1.0)	1.42 (s, 6 H), 3.75 (s, 6 H), 3.7–3.8 (m, 4 H), 4.0–4.1 (m, 2 H), 4.19 (s, 4 H)	26.9, 51.8, 68.7, 71.8, 77.0, 109.8, 170.6	Calcd. for $C_{16}H_{22}O_6$ $(M + H)^+$ 307.1393 Found 307.1390
18	[g]	colourless oil	+ 30.0 (0.9)	3.4–3.8 (m, 12 H), 4.04 (d AB/2, 2 H, *J* = 15.2), 4.10 (d AB/2, 2 H, *J* = 15.2), 4.35 (m, 2 H), 5.98 (s, 1 H), 6.86 (br t, 2 H), 7.3–7.5 (m, 5 H)	38.5, 38.5, 69.5, 69.6, 70.9, 71.1, 71.9, 77.2, 77.4, 103.9, 126.3, 128.4, 129.6, 137.1, 168.7, 168.8	Calcd for $C_{19}H_{26}N_2O_7$ $(M)^+$ 394.1740 Found 394.1734
19	[g]	colourless oil	– 2.0 (1.0)	3.4–3.7 (m, 12 H), 3.80 (m, 4 H), 4.09 (s, 2 H), 4.12 (d AB/2, 2 H, *J* = 15.0), 4.29 (m, 2 H), 5.97 (s, 1 H), 7.16 (br t, 1 H), 7.19 (br t, 1 H), 7.3–7.5 (m, 5 H)	36.6, 38.7, 70.1, 70.2, 70.6, 70.7, 71.2, 71.4, 71.4, 77.3, 78.0, 104.1, 126.5, 128.4, 129.6, 136.9, 169.2, 169.2	Calcd for $C_{21}H_{30}N_2O_8$ $(M)^+$ 438.2002 Found 438.2003
20	[g]	105–108	+ 34.3 (1.0)	1.41 (s, 6 H), 3.4–3.6 (m, 8 H), 3.70 (m, 4 H), 4.06 (s, 4 H), 4.12 (m, 2 H), 6.88 (br t, 2 H)	27.2, 38.4, 69.4, 71.0, 72.0, 77.1, 109.8, 168.9	Calcd for $C_{14}H_{23}N_2O_7$ $(M - CH_3)^+$ 331.1505 Found 331.1510
21	[g]	colourless oil	–14.9 (1.1)	1.41 (s, 6 H), 3.4–3.6 (m, 8 H), 3.63 (s, 4 H), 3.6–3.8 (m, 4 H), 4.0–4.1 (m, 2 H), 4.09 (d AB/2, 4 H, *J* = 15.1), 7.06 (br t, 2 H)	26.8, 38.6, 70.1, 70.6, 71.3, 71.4, 77.2, 109.8, 169.2	Calcd for $C_{17}H_{31}N_2O_8$ $(M + H)^+$ 391.2080 Found 391.2079

[a] All compounds are hygroscopic and many of them are labile oils available only in small quantities.
[b] The chemical purity of all compounds was confirmed by ^1H and ^{13}C NMR spectra.
[c] All yields were based on isolated product.
[d] The yield obtained *via* elongation using bromoacetic acid.
[e] The yield of crude product.
[f] The yield obtained from **6** *via* transesterefication
[g] Yields are given in Table 1.
[h] The yield obtained from **16** *via* transesterification in method I
[i] The yield obtained from **16** *via* transesterification in method II
[j] $[\alpha]_D^{23}$ = + 4.3 (1.3, $CHCl_3$)[5]

round-bottomed flask and the solvent was evaporated. The residue was chromatographed on a silica gel column using 0.5–3% mixtures of MeOH in $CHCl_3$.

Method C (with DBU): An equimolar 0.1 M methanolic solution (1.5 mmol) of α,ω-diamine and dimethyl α,ω-dicarboxylate containing DBU (20 mol%) was left at ambient temperature over a period of 21 days. Then the solvent was evaporated and the residue was chromatographed on a silica gel column using 0.5–3% mixtures of MeOH in $CHCl_3$.

Method D (with DBU and LiBr): An equimolar 0.1 M methanolic solution (1.5 mmol) of α,ω-diamine and dimethyl α,ω-dicarboxylate containing DBU (100 mol%) and anhyd LiBr (1000 mol%) was left at ambient temperature over a period of 24 h. Then the solvent was evaporated and the residue was chromatographed on a silica gel column using 0.5–3 % mixtures of MeOH in $CHCl_3$.

Transesterification Procedures

Methyl 2-[((4*S*,5*S*)-2,2-Dimethyl-5-{[(methyloxycarbonyl)-methoxy]methyl}-1,3-dioxolan-4-yl)methoxy]acetate (17)
Method I: A reaction mixture containing di-*tert*-butyl ester **16** (390 mg, 1 mmol), DBU (610 mg, 4 mmol) and MeOH (100 mL) was allowed to stand at r.t. for 4 weeks. Then MeOH was removed under reduced pressure and oily residue was chromatographed on a silica gel column using $CHCl_3$. *Method II*: A mixture containing di-*tert*-butyl ester **16** (390 mg, 1 mmol), DBU (610 mg, 4 mmol) and MeOH (100 mL) was refluxed for 8 h. Then MeOH was removed under reduced pressure and oily residue was chromatographed under above-mentioned conditions (Table 2).

Methyl 2-({(1*R*,2*R*)-3-(Benzyloxy)-1-[(benzyloxy)methyl]-2-[(methyloxycarbonyl)methoxy]propylo}oxy)acetate (4)
Di-*tert*-butyl ester **6** (530 mg, 1 mmol), Et_3N (10 mg, 0.2 mmol) and MeOH (5 mL) was filled into a Teflon ampoule, placed in a high-pressure vessel filled with ligroin as a transmission medium and compressed (12 kbar) at r.t. for 72 h. After decompression, the mixture was transferred quantitatively to a round-bottomed flask and the solvent was evaporated. The residue was chromatographed on a silica gel column using $CHCl_3$ as an eluent (Table 2).

Acknowledgement

This work was supported by the State Committee for Scientific Research (Project 3T09A13409) and by Warsaw University (BST-562/18/97).

References

(1) Curtis, W.D.; Laidler, D.A.; Stoddart, J.F.; Jones, G.H. *J. Chem. Soc., Perkin Trans. 1*, 1**977**, 1756.
(2) Mani, N.S.; Kanakamma, P.P. *Tetrahedron Lett*. **1994**, *35*, 3629.
(3) Bako, P.; Fenichel, L.; Toke, L. *Liebigs Ann*. **1990**, 1161.
(4) Montanari, F.; Tundo, P. *Tetrahedron Lett*.**1979**, 5055.
(5) Ando, N.; Yamamoto, Y.; Oda, J.; Inouye, Y. *Synthesis* **1978**, 688.
(6) Rastetter, W.H.; Phillion, D.P. *J. Org. Chem*. **1981**, *46*, 3204.
(7) Jurczak, J.; Kasprzyk, S.; Sałański, P.; Stankiewicz, T. *J. Chem. Soc., Chem. Commun*., **1991**, 956.
(8) Jurczak, J.; Kasprzyk, S.; Sałański, P.; Stankiewicz, T. *High Press. Res*. **1992**, *11*, 139.
(9) Jurczak, J.; Stankiewicz, T.; Sałański, P.; Kasprzyk, S.; Lipkowski, P. *Tetrahedron* **1993**, *49*, 1478.
(10) Gryko, D.T.; Piątek, P.; Jurczak, J. *Tetrahedron* **1997**, *53*, 7957.
(11) Pietraszkiewicz, M.; Jurczak, J. *Tetrahedron* **1984**, *40*, 2967.
(12) Gryko, D.T.; *Ph. D. Thesis*, Institute of Organic Chemistry of the Polish Academy of Sciences, Warsaw, 1997.
(13) Bunnet, J.F.; Davis,G.T. *J. Am. Chem. Soc.* **1960**, *82*, 665.
(14) Green, M.J., Eur. Pat. 0110629, 17th Nov. **1983** (*Chem. Abstr.* **1984**, *101*, 170717k); Green, M.J., Eur. Pat. 0150962, 17th Jan. 1985 (*Chem. Abstr.*:**1986**, *104*, 129505p).
(15) Babtistella, L.H.B.; Dos Santos, J.F.; Ballabio, C.; Marsaioli, A.J. *Synthesis* **1989**, 436.
(16) Ishikawa, T.; Ohsumi,Y.; Kawai, T. *Bull. Chem. Soc. Jpn.* **1990**, *63*, 819.
(17) Seebach, D.; Thaler, A.; Blaser, D.; Ko, S.Y. *Helv. Chim. Acta* **1991**, *74*, 1102.
(18) Dietrich, B.; Lehn, J.-M.; Sauvage, J.-P. *Tetrahedron Lett*. **1969**, *10*, 2885.
(19) Kierstead, R.W.; Faraone, A.; Mennona, F.; Mullin, J.; Guthrie, R.W.; Crowley, H.; Simko, B.; Blaber, L.C. *J. Med. Chem.* **1983**, *26*, 1561.
(20) Mash, E.A.; Nelson, K.A.; Van Deusen, S.; Hemperly, S.B. *Org. Synth.* Vol.68, 92.
(21) Byun, H.-S.; Bittman, R. *Synth. Commun*. **1993**, *23*, 3201.
(22) Curtis, W.D.; Laidler, D.A.; Stoddart, J.F.; Jones, G.H. *J. Chem. Soc., Perkin Trans. 1* **1977**, 1756.
(23) Jurczak, J.; Chmielewski, M.; Filipek, S. *Synthesis* **1979**, 41