Synthesis of Olefinic Crown Diamides and their Conversion into Pyrazolino Macrocycles: Promising Photoluminescent Crown Compounds

Rana N. Malhas, Yehia A. Ibrahim*

Chemistry Department, Faculty of Science, Kuwait University, P. O. Box 5969, Safat 13060, Kuwait
Fax +9654816482; E-mail: yehiaai@kuc01.kuniv.edu.kw

Received 16 May 2006; revised 19 June 2006

Abstract: Macrocyclic crown diamides with 16- or 24-membered rings containing *E*- and *Z*-olefinic double bonds were synthesized either by bisalkylation or by ring-closing metathesis (RCM) techniques. The two methods were evaluated and compared with regard to yield and to product stereochemistry. Isomerization of some *Z*-olefinic macrocycles to their corresponding *E*-isomers was achieved using Grubbs' catalyst second generation. Some of the required starting dials, diols and bishalo compounds were prepared by different routes including cross-metathesis (CM). The latter was compared with other investigated methods. Some of the olefinic macrocycles were subjected to cycloaddition reactions with diphenylnitrileimine to give the corresponding pyrazolino macrocycles. The latter showed interesting emission spectra.

Key words: ring-closing metathesis, *E*,*Z* isomerization, macrocyclic ether amides, cycloaddition, pyrazolino macrocycles

Crown compounds and azacrown compounds constitute important macrocyclic groups in supramolecular chemistry. They have been shown to exhibit important applications including selective ion separation, detection, molecular recognition, catalysis, biological applications as well as many other interesting uses in diverse fields of supramolecular chemistry.[1–3] Of particular interest are crown ethers incorporating amide groups, since such groups modify the binding properties of the crown compounds in favor of alkaline earth cations over alkali metal ions. Moreover, the number of ether oxygen atoms, amide carbonyl groups, ring size, lipophilic groups and other structural features control the selectivity towards different ions.[2–7]

During the past decade, ring-closing metathesis (RCM) has emerged as a powerful tool for the construction of small-, medium- and large-ring systems.[8] A large part of the success of this reaction has been due to the availability of well-defined catalysts such as those developed by Schrock[9] and Grubbs.[10]

In the present work the synthesis of each of the *E* and *Z* stereoisomers of macrocyclic crown diamides **2a–c**, **3a–c**, **6a–c** and **7a–c** with 16- and 24-membered rings was investigated by bisalkylation and also as *E:Z* mixtures by ring-closing metathesis using Grubbs' catalysts **I** and **II** (Figure 1).

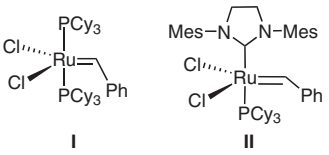


Figure 1 Grubbs' catalysts

In the present study the effect of Grubbs' catalysts **I** and **II** on the RCM reactions of **1a–c** regarding the yield and the stereoselectivity of the *E*- and *Z*-olefinic macrocyclic crown diamides was investigated. Thus, RCM of the 1,ω-dienes **1a–c** using catalysts **I** and **II** (Scheme 1) gave a mixture of the corresponding isomeric macrocycles **2a–c** and **3a–c**, in the yields and *E:Z* ratios shown in Table 1.

From Table 1 it is clear that catalyst **II** is more active and leads to higher yield of the *E*-isomer. Thus, 2.5% and 1.25% of catalyst **I** are needed to accomplish the RCM of **1a** and **1b**, respectively (entries 1 and 3). However, only 1% of catalyst **II** is needed to achieve better RCM conversions (entries 2 and 4). On the other hand, RCM of **1c** required 5% of either of the catalyst **I** or **II** to achieve 70% and 93% conversions, respectively (as monitored by TLC). Table 1 shows also the reported RCM synthesis of **6a**,**b** and **7a**,**b** from the corresponding appropriate 1,ω-dienes **5a**,**b** using catalyst **I**.[4a]

It is also concluded from these results that Grubbs' catalyst **II** not only improved the yield of the RCM product but also increased the selectivity towards the *E* isomer. Therefore, in the present study we also investigated the possibility of *Z*-to-*E* isomerization of these olefinic macrocycles. Thus, treatment of **2a** and **6a** with Grubbs' catalyst **I** showed complete recovery of unchanged starting materials. On the other hand, treatment of **2a**, **6a** and **6b** with 1% of catalyst **II** led to 92% conversion of **2a** into **3a** (entry 7), 93% conversion of **6a** into **7a** (entry 10) and 100% conversion of **6b** into **7b** (entry 11). The *Z*-to-*E* isomerization promoted by Grubbs' catalyst **II** is derived by two factors which are the more thermodynamic stability of the *E* isomer and by the reactivity of this catalyst towards polysubstituted olefins.[11]

The pure *Z* macrocycles **2a**−**c** were readily obtained in 42–50% yields via bisalkylation of the dipostassium salts **4a**−**c** with (*Z*)-1,4-dichloro-2-butene in *N*,*N*-dimethylformamide. The pure *E* isomers **3a**−**c** were similarly obtained in 68−80% yields by treatment of **4a**−**c** with (*E*)-1,4-dichloro-2-butene. Similar bisalkylation of **4a–c** with

SYNTHESIS 2006, No. 19, pp 3261–3269
Advanced online publication: 02.08.2006
DOI: 10.1055/s-2006-942540; Art ID: T07906SS

Table 1 Catalysts, Yields and *Z*/*E* Ratios of Macrocycles

Entry	Substrate	Catalyst (conditions)	Product	Yield (%)	*Z*/*E* ratio
1	**1a**	**I**[a]	**2a**, **3a**	60[4a]	1:5.7
2	**1a**	**II**[b]	**2a**, **3a**	85	1:15
3	**1b**	**I**[c]	**2b**, **3b**	100[4a]	1:1.1
4	**1b**	**II**[b]	**2b**, **3b**	100	1:1.5
5	**1c**	**I**[d]	**2c**, **3c**	70	1:1.6
6	**1c**	**II**[d]	**2c**, **3c**	93	1:4
7	**2a**	**II**[b]	**2a**, **3a**	92	1:11
8	**5a**	**I**[a]	**6a**, **7a**	100[4a]	1:7
9	**5b**	**I**[a]	**6b**, **7b**	98[4a]	1:2.3
10	**6a**	**II**[b]	**6a**, **7a**	93	1:15
11	**6b**	**II**[b]	**7b**	100	

[a] Substrate (1 mM), Grubbs' catalyst (2.5%), CH_2Cl_2 (10 mL), reflux, 2 h.
[b] Substrate (1 mM), Grubbs' catalyst (1%), CH_2Cl_2 (10 mL), reflux, 2 h.
[c] Substrate (1 mM), Grubbs' catalyst (1.25%), CH_2Cl_2 (10 mL), reflux, 2 h.
[d] Substrate (1 M), Grubbs' catalyst (5%), CH_2Cl_2 (10 mL), reflux, 2 h.

(*Z*)-1,4-bis(*o*-chloromethylphenoxy)-2-butene **8** and its *E* isomer **9** gave the corresponding *Z* macrocycles **6a–c** (11–49%) and their *E* isomers **7a–c** (39–56%), respectively.

The starting materials **8** and **9** required for the synthesis of the macrocycles **6** and **7** were obtained as outlined in Scheme 2 using two synthetic approaches.

The first synthetic approach (Scheme 2) starts with the reaction of the potassium salt of salicylaldehyde **10** with (*Z*)-1,4-dichloro-2-butene and (*E*)-1,4-dichloro-2-butene to give (*Z*)-1,4-bis(*o*-formylphenoxy)-2-butene **11** and the corresponding *E* isomer **12**, respectively. Reduction of **11** and **12** with sodium borohydride in methanol gave the corresponding diols **13** and **14**, respectively. Reaction of compounds **13** and **14** with thionyl chloride in chloroform gave the corresponding bischloro compounds **8** and **9**, respectively, in 95% yield.

The second synthetic method (Scheme 2) attempted was the CM of *o*-allyloxybenzaldehyde (**15**), *o*-allyloxybenzyl alcohol (**16**) and *o*-allyloxybenzyl chloride (**17**) using Grubbs' catalysts **I** and **II**. Results of CM are shown in Table 2. From Table 2 it is clear that the CM reactions can convert **15**, **16** and **17** to the required product; however, as a mixture of *E* and *Z* isomers. It is also clear that Grubbs' catalyst **II** gave better yield with better *E* selectivity compared to the same percent of catalyst **I**. Also, compound **11** was isomerized to the *E* isomer **12** with 89% conversion. Compounds **11** and **12** were also obtained as byproducts from the reaction of allylbenzene with *o*-allyloxybenzaldehyde using Grubbs' catalyst **I**.[12]

Table 2 Catalysts, Yields and *Z*/*E* Ratios of CM Products

Entry	Substrate	Catalyst (conditions)[a]	Yield (%)	Products (*Z*:*E* ratio)
1	**11**	**II**	89	**11**, **12** (1:7.8)
2	**15**	**I**	13	**11**, **12** (1:2)
3	**15**	**II**	61	**11**, **12** (1:14)
4	**16**	**I**	32	**13**, **14** (1:2)
5	**16**	**II**	34	**13**, **14** (1:5)
6	**17**	**I**	30	**8**, **9** (1:1.6)
7	**17**	**II**	70	**8**, **9** (1:7)

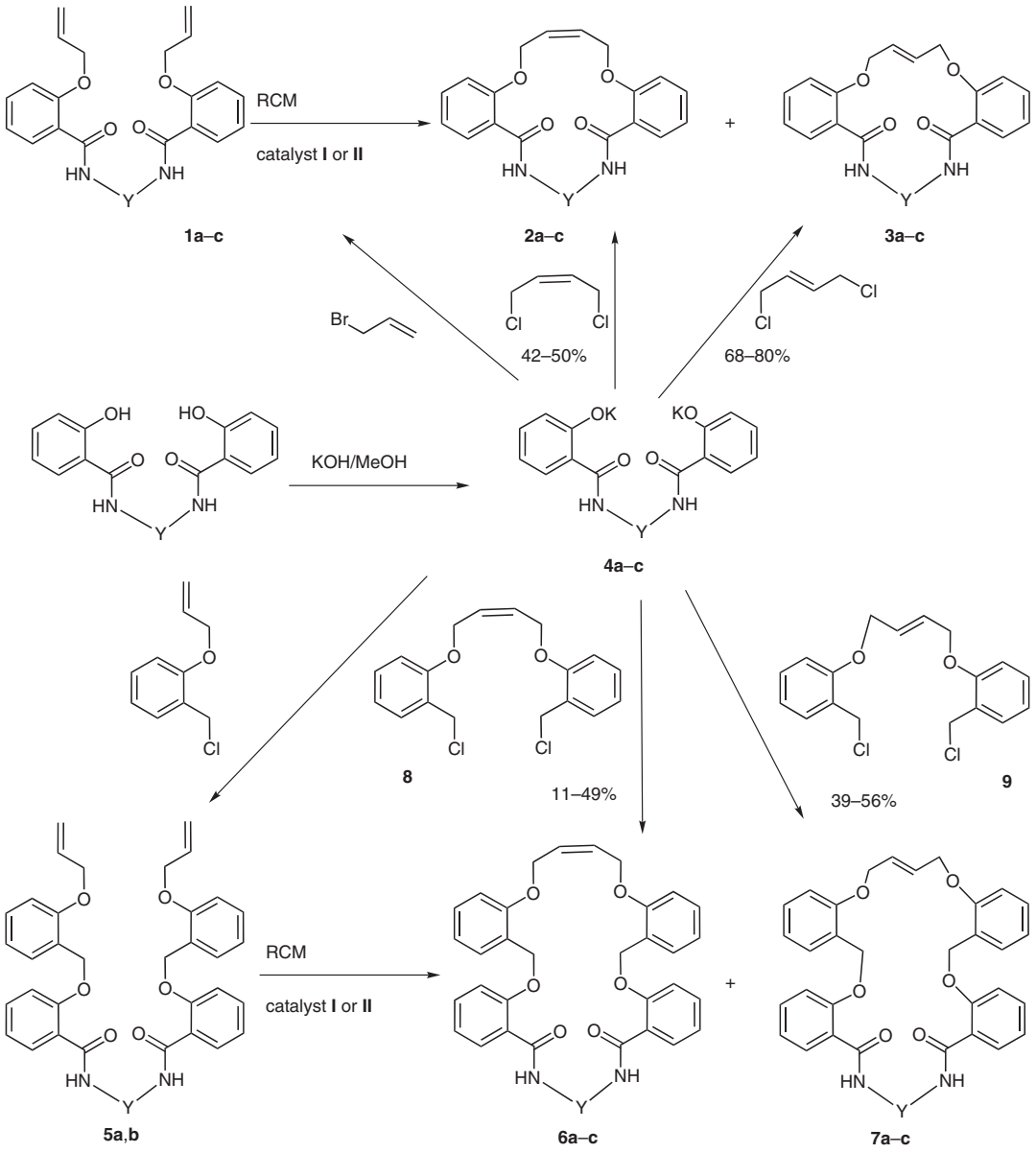
[a] Substrate (1 mM), catalysts **I** or **II** (1%), CH_2Cl_2 (10 mL), reflux, 2 h.

The *E*/*Z* selectivity and isomerization in RCM reactions and practical solutions to this problem have been addressed in many reviews; e.g., the Prunet review[13a] as well as other papers.[13b–d] The problem has also been discussed in Blechert's review on cross-metathesis[13e] and in Schmidt's review on olefin metathesis.[13f]

Cycloaddition of the olefinic crown diamides **2a**,**b** and **3a**,**b** with diphenylnitrileimine gave the corresponding condensed pyrazolino macrocycles **18a**,**b** and **19a**,**b**, respectively (Scheme 3). The latter exhibited absorption and interesting emission spectra in the UV−Vis region. Compounds **18**, **19** showed absorption bands at λ_{max} = 284–360 nm and emission bands at λ_{max} = 436–463 nm.

In conclusion, RCM and CM techniques have shown to give efficient access to macrocycles and the required precursor bisolefinic compounds. The application of Grubbs' catalysts of 1st and 2nd generation showed different behavior towards their efficiency and *E*:*Z* ratios. Comparison with other synthetic methods illustrates the synthetic potentialities of these novel catalytic techniques. The conversion of these olefinic macrocycles to photoluminescent pyrazolino derivatives paves the path for future applications.

Melting points are uncorrected. IR spectra were recorded in KBr disks on a Perkin–Elmer System 2000 FT-IR spectrophotometer. ^1H and ^{13}C NMR spectra were recorded on a Bruker DPX 400, 400 MHz super-conducting NMR spectrometer at 400 MHz and 100 MHz, respectively. Mass spectra were measured on VG Auto-spec-Q (high resolution, high performance, tri-sector GC/MS/MS) and with LCMS using Agilent 1100 series LC/MSD with an API-ES/



a: Y = $(CH_2)_2$; **b**: Y = 1,2-C_6H_4; **c**: Y = 1,2-C_6H_{10}

Scheme 1

APCI ionization mode. The UV–Vis spectra were recorded on a Cary-5/Varian spectrophotometer and the emission spectra were recorded using a SIM AMINCO.BOWMAN series Luminescence spectrometer. Microanalyses were performed on a LECO CHNS-932 Elemental Analyzer. The UV-Vis absorption spectra of compounds **18a**,**b**, **19a**,**b** were scanned in chloroform at concentrations 1.0×10^{-4} M, 9.4×10^{-5} M, 1.4×10^{-4} M, 3.7×10^{-5} M, respectively, in the wavelength range 250–450 nm using a dry, clean, quartz cuvette of 1.0 cm path length. From the spectra obtained, absorbance values at λ_{max} were used to calculate the extinction coefficient. The emission spectra of compounds **18a**,**b**, **19a**,**b** in chloroform at the above-mentioned concentrations were obtained after excitation at λ = 294, 285, 360, 284 nm, respectively.

The starting compounds **1a**,[14] 1,2-bis(2-hydroxybenzamido)ethane[15] and 1,2-bis(2-hydroxybenzamido)benzene[15] were prepared as reported.

1,2-Bis(2-hydroxybenzamido)cyclohexane

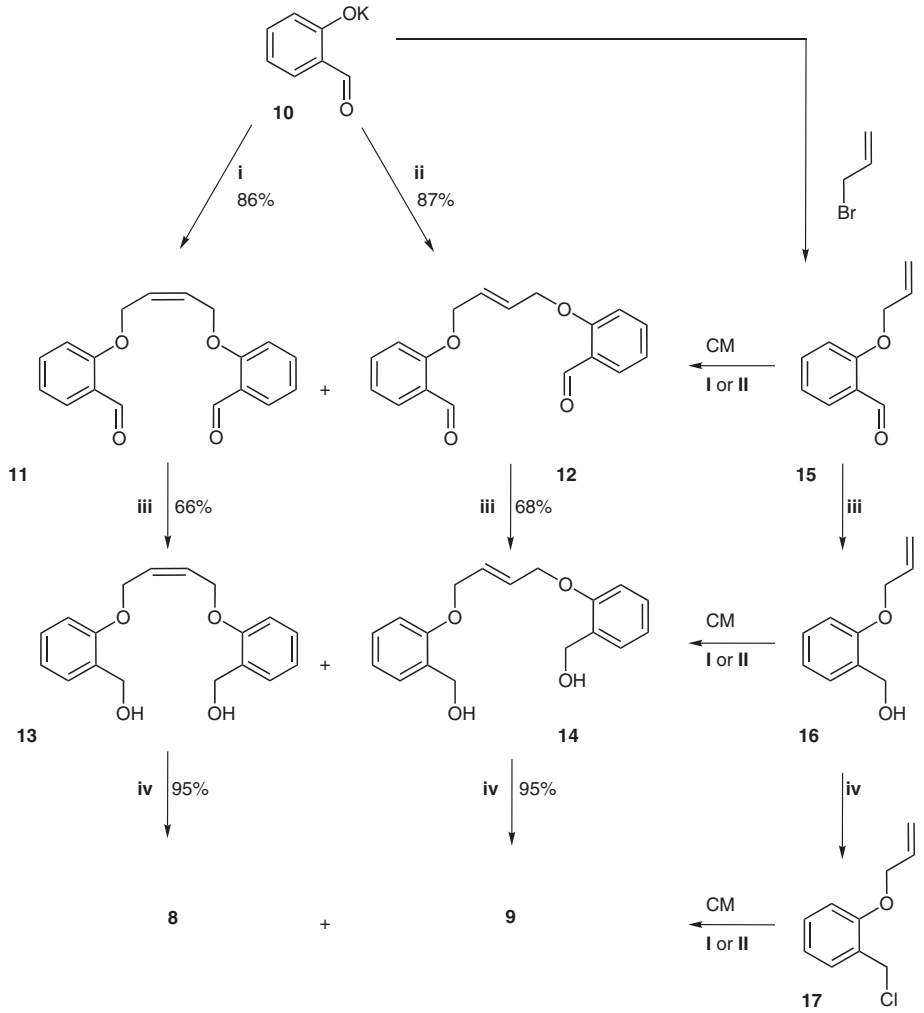
A mixture of 1,2-cyclohexanediamine (*cis* and *trans* isomers; 5.0 g, 43.8 mmol) and methyl salicylate (11.3 g, 87.4 mmol) was heated on a steam bath for 5 h. After cooling, the mixture was recrystallized from EtOH to give colorless crystals; yield: 8.4 g (54%); mp 238–239 °C.

IR: 3380, 3319, 3077, 2943, 2856, 2772, 1635, 1595, 1547, 1488, 1444, 1344, 1250, 1220, 1145, 815, 756 cm^{-1}.

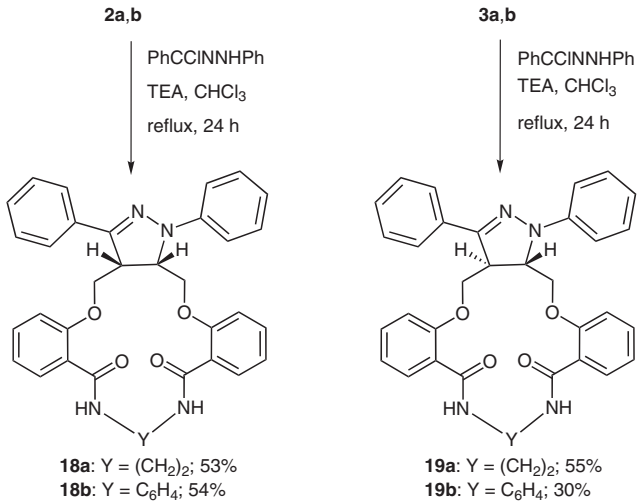
^1H NMR (DMSO): δ = 1.33 (d, *J* = 9.7 Hz, 2 H), 1.51 (d, *J* = 9.7 Hz, 2 H), 1.74 (d, *J* = 7.9 Hz, 2 H), 1.94 (d, *J* = 12.0 Hz, 2 H), 4.02 (br, 2 H), 6.82 (m, 4 H), 7.33 (t, *J* = 7.6 Hz, 2 H), 7.76 (d, *J* = 7.5 Hz, 2 H), 8.71 (br, 2 H, NH), 12.21 (br, 2 H, OH).

^{13}C NMR ($CDCl_3$): δ = 22.6, 29.6, 50.2, 113.3, 115.3, 116.3, 125.9, 131.4, 158.1, 166.6.

MS: *m*/*z* = 354 [M^+].



Scheme 2 *Reagents and conditions*: i) (*Z*)-1,4-dichloro-2-butene, DMF, 15 min reflux; ii) (*E*)-1,4-dichloro-2-butene, DMF, 15 min reflux; iii) $NaBH_4$, MeOH, stirring, 0–5 °C; iv) $SOCl_2$, $CHCl_3$, stirring, 2 h.



Scheme 3

Anal. Calcd for $C_{20}H_{22}N_2O_4$ (354.41): C, 67.78; H, 6.26; N, 7.95. Found: C, 67.52; H, 6.48; N, 8.22.

1,2-Bis(2-allyloxybenzamido)benzene (1b)

A solution of 1,2-bis(2-hydroxybenzamido)benzene[15] (0.35 g, 1 mmol) and KOH (0.12 g, 2 mmol) in MeOH (5 mL) was stirred for 5 min and the solvent was then removed in vacuo to give the corresponding potassium salt. To the latter were added DMF (10 mL) and allyl bromide (2 mmol). The reaction mixture was then heated under reflux for 15 min. The mixture was diluted with ice-water (20 mL). The precipitate was collected, washed with cold H_2O and finally crystallized from EtOH to give colorless crystals; yield: 0.28 g (66%); mp 120–122 °C.[4a]

^{1}H NMR ($CDCl_3$): δ = 4.64 (d, *J* = 5.4 Hz, 4 H, OCH_2), 5.15 (d, *J* = 10.5 Hz, 2 H, CH_2=), 5.22 (d, *J* = 17.2 Hz, 2 H, CH_2=), 5.88 (m, 2 H, CH=), 6.78 (d, *J* = 8.3 Hz, 2 H), 7.14 (t, *J* = 7.5 Hz, 2 H), 7.29 (m, 2 H), 7.46 (dt, *J* = 1.5, 8.5 Hz, 2 H), 7.81 (m, 2 H), 8.30 (dd, *J* = 1.5, 7.8 Hz, 2 H), 9.91 (br, 2 H, NH).

^{13}C NMR ($CDCl_3$): δ = 69.1 (CH_2), 112.9, 119.1, 121.5, 121.7, 125.6, 126.0, 131.0, 131.8, 132.7, 133.2, 156.7, 164.1.

MS: *m*/*z* = 428 [M^+].

Anal. Calcd for $C_{26}H_{24}N_2O_4$ (428.49): C, 72.88; H, 5.65; N, 6.54. Found: C, 72.58; H, 5.61; N, 6.48.

1,2-Bis(2-allyloxybenzoylamino)cyclohexane (1c)

A solution of 1,2-bis(2-hydroxybenzamido)cyclohexane (0.35 g, 1 mmol) and KOH (0.12 g, 2 mmol) in MeOH (5 mL) was stirred for 5 min and the solvent was then removed in vacuo to give **4c**. To the latter, DMF (10 mL) and the allyl bromide (2 mmol) were added. The reaction mixture was then heated under reflux for 15 min. The mixture was diluted with ice-water (20 mL) and the precipitate was collected, washed with cold H_2O and crystallized from EtOH to give colorless crystals; yield: 0.34 g (79%); mp 118–119 °C.

IR: 3377, 3074, 2933, 2858, 1642, 1600, 1531, 1482, 1449, 1300, 1230, 995, 755 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 1.43–1.46 (m, 4 H), 1.81 (m, 2 H), 2.28 (d, *J* = 12.9 Hz, 2 H), 4.06 (m, 2 H), 4.62–4.73 (m, 4 H), 5.29 (d, *J* = 10.7 Hz, 2 H), 5.37 (dd, *J* = 1.0, 17.2 Hz, 2 H), 6.03 (m, 2 H), 6.90 (d, *J* = 8.3 Hz, 2 H), 7.00 (t, *J* = 7.6 Hz, 2 H), 7.34–7.38 (dt, *J* = 1.7, 8.5 Hz, 2 H), 8.07–8.10 (dd, *J* = 1.7, 7.6 Hz, 2 H), 8.13 (br, 2 H, NH).

^{13}C NMR ($CDCl_3$): δ = 24.8, 32.8, 53.3, 69.8, 112.8, 118.8, 121.1 (2 overlapped signals), 132.0, 132.4, 132.42, 156.6, 165.3.

MS: *m*/*z* = 434 [M^+].

Anal. Calcd for $C_{34}H_{32}N_2O_6$ (434.54): C, 71.87; H, 6.96; N, 6.45. Found: C, 71.71; H, 7.22; N, 6.72.

Synthesis of Macrocycles 2a–c, 3a–c, 6a–c, 7a–c via Bisalkylation; General procedure

A solution of each of the appropriate 1,2-bis(2-hydroxybenzoylamino) derivatives (1 mmol) and KOH (0.12 g, 2 mmol) in MeOH (5 mL) was stirred for 5 min and the solvent was then removed in vacuo to give the corresponding dipotassium salts **4a**–**c**. To the latter were added DMF (10 mL) and the appropriate dihalo derivatives (1 mmol). The reaction mixture was then heated under reflux for 15 min (during this time the potassium halide precipitated). The mixture was diluted with ice-water (30 mL) and kept for 24 h in the fridge. The precipitate was collected, washed with cold H_2O and crystallized from the proper solvent to give the corresponding macrocycles **2a**–**c**, **3a**–**c**, **6a**–**c**, **7a**–**c**.

(*Z*)-1,12-Dioxa-5,8-diazadibenzo[*b*,*j*]cyclohexadec-14-ene-4,9-dione (2a)

Prepared from **4a** and *cis*-1,4-dichloro-2-butene; colorless crystals (EtOH); yield: 0.18 g (50%); mp 189–190 °C.

IR: 3404, 3064, 2941, 2887, 1651, 1639, 1599, 1533, 1482, 1299, 1219, 995, 759 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 3.72 (br, 4 H, NCH_2), 4.80 (d, *J* = 4.6 Hz, 4 H, OCH_2), 6.19 (t, *J* = 4.6 Hz, 2 H, CH=), 7.05 (d, *J* = 8.3 Hz, 2 H), 7.14 (t, *J* = 7.5 Hz, 2 H), 7.47 (t, *J* = 7.6 Hz, 2 H), 8.14 (br, 2 H, NH), 8.22 (d, *J* = 7.6 Hz, 2 H).

^{13}C NMR ($CDCl_3$): δ = 39.5, 63.1, 112.9, 122.1, 122.5, 129.7, 132.4, 132.7, 156.1, 165.3.

MS: *m*/*z* = 352 [M^+].

Anal. Calcd for $C_{20}H_{20}N_2O_4$ (352.4): C, 68.17; H, 5.72; N, 7.95. Found: C, 67.93; H, 5.47; N, 7.81.

(*E*)-1,12-Dioxa-5,8-diazadibenzo[*b*,*j*]cyclohexadec-14-ene-4,9-dione (3a)

Prepared from **4a** and *trans*-1,4-dichloro-2-butene; colorless crystals (EtOH); yield: 0.25 g (70%); mp 210–212 °C.

IR: 3399, 3104, 3072, 3038, 2933, 2875, 1638, 1599, 1520, 1484, 1295, 1232, 990, 752 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 3.77 (br, 4 H, NCH_2), 4.69 (m, 4 H, OCH_2), 6.32 (m, 2 H, CH=), 7.00 (d, *J* = 8.3 Hz, 2 H), 7.13 (t, *J* = 7.6 Hz, 2 H), 7.46 (dt, *J* = 1.5, 7.8 Hz, 2 H), 8.17 (br, 2 H, NH), 8.24 (dd, *J* = 1.5, 7.8 Hz, 2 H).

^{13}C NMR ($CDCl_3$): δ = 40.6, 68.5, 113.0, 122.1, 122.2, 130.3, 132.4, 132.9, 156.5, 165.8.

MS: *m*/*z* = 352 [M^+].

Anal. Calcd for $C_{20}H_{20}N_2O_4$ (352.4): C, 68.17; H, 5.72; N, 7.95. Found: C, 68.01; H, 5.64; N. 8.05.

(*Z*)-1,12-Dioxa-5,8-diazatribenzo[*b*,*f*,*j*]cyclohexadec-14-ene-4,9-dione (2b)

Prepared from **4b** and *cis*-1,4-dichloro-2-butene; colorless crystals (EtOH); yield: 0.16 g (42%); mp 210–212 °C.

IR: 3387, 3312, 3072, 2957, 2890, 1664, 1598, 1537, 1478, 1455, 1294, 1230, 995, 951, 755 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 4.77 (br, 4 H, OCH_2), 6.19 (br, 2 H, CH=), 6.94 (d, *J* = 8.2 Hz, 2 H), 7.17 (t, *J* = 7.4 Hz, 2 H), 7.27 (m, 2 H), 7.48 (m, 2 H), 8.12 (m, 2 H), 8.34 (m, 2 H), 9.79 (br, 2 H, NH).

^{13}C NMR ($CDCl_3$): δ = 63.8, 112.4, 121.5, 121.9, 124.4, 125.4, 129.4, 129.6, 133.1, 133.2, 155.4, 163.7.

MS: *m*/*z* = 400 [M^+].

Anal. Calcd for $C_{24}H_{20}N_2O_4$ (400.4): C, 71.99; H, 5.03; N, 7.00. Found: C, 71.71; H, 5.04; N, 7.10.

(*E*)-1,12-Dioxa-5,8-diazatribenzo[*b*,*f*,*j*]cyclohexadec-14-ene-4,9-dione (3b)

Prepared from **4b** and *trans*-1,4-dichloro-2-butene; colorless crystals (EtOH); yield: 0.28 g (68%); mp 280–282 °C.

IR: 3333, 3069, 2958, 2878, 1662, 1597, 1532, 1470, 1453, 1309, 1287, 1233, 1089, 994, 974, 759 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 4.58 (s, 4 H, OCH_2), 5.98 (s, 2 H, CH=), 7.04 (d, *J* = 8.2 Hz, 2 H), 7.19 (t, *J* = 7.5 Hz, 2 H), 7.29 (m, 2 H), 7.49 (dt, *J* = 1.8, 7.4 Hz, 2 H), 7.85 (m, 2 H), 8.04 (dd, *J* = 1.7, 7.8 Hz, 2 H), 9.36 (br, 2 H, NH).

^{13}C NMR ($CDCl_3$): δ = 70.9, 116.9, 123.1, 125.4, 126.1, 126.3, 128.3, 130.7, 131.6, 133.0, 155.1, 165.3.

MS: *m*/*z* = 400 [M^+].

Anal. Calcd for $C_{24}H_{20}N_2O_4$ (400.4): C, 71.99; H, 5.03; N, 7.00. Found: C, 71.77; H, 5.18; N, 7.11.

(*Z*)-1,12-Dioxa-5,8-diazadibenzo[*b*,*j*]cyclohexano[*f*]cyclohexadec-14-ene-4,9-dione (2c)

Prepared from **4c** and *cis*-1,4-dichloro-2-butene; colorless crystals (EtOH); yield: 0.19 g (46%); mp 104–106 °C.

IR: 3377, 2991, 2935, 2861, 1641, 1533, 1483, 1300, 1227, 1004, 753 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 1.31–1.40 (m, 4 H), 1.77 (br, 2 H), 2.25 (m, 2 H), 4.02 (s, 2 H), 4.73–4.81 (m, 4 H), 5.95 (s, 2 H, CH=), 6.84–6.89 (m, 2 H), 6.93–7.04 (m, 2 H), 7.31 (s, 2 H, NH), 7.99–8.07 (m, 4 H).

^{13}C NMR ($CDCl_3$): δ = 24.9, 32.8, 53.1 65.7, 112.6, 122.0, 128.5, 128.6, 131.9, 132.0, 156.3, 165.1.

LCMS: *m*/*z* = 407 [M + 1].

Anal. Calcd for $C_{24}H_{26}N_2O_4$ (406.5): C, 70.92; H, 6.45; N, 6.89. Found: C, 70.74; H, 6.15; N, 6.75.

(*E*)-1,12-Dioxa-5,8-diazadibenzo[*b*,*j*]cyclohexano[*f*]cyclohexadec-14-ene-4,9-dione (3c)

Prepared from **4c** and *trans*-1,4-dichloro-2-butene; colorless crystals (EtOH–$CHCl_3$); yield: 0.32 g (80%); mp > 330 °C (charred).

IR: 3426, 3362, 3071, 2998, 2961, 2936, 1643, 1598, 1495, 1301, 1231, 1036, 752 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 1.39 (m, 2 H), 1.81 (m, 2 H), 1.44 (m, 2 H), 2.40 (m, 2 H), 3.99 (m, 2 H), 4.41 (dt, *J* = 1.8, 12.2 Hz, 2 H, OCH_2), 4.63 (d, *J* = 12.3 Hz, 2 H, OCH_2), 5.80 (t, *J* = 1.9 Hz, 2 H, CH=), 6.94 (dd, *J* = 1.0, 8.2 Hz, 2 H), 7.07 (t, *J* = 7.7 Hz, 2 H), 7.38 (dt, *J* = 1.2, 8.2 Hz, 2 H), 7.48 (br, 2 H, NH), 7.72 (dd, *J* = 1.6, 7.7 Hz, 2 H).

^{13}C NMR ($CDCl_3$): δ = 24.7, 32.8, 54.3, 71.2, 117.2, 122.6, 127.2, 127.6, 129.7, 131.8, 155.2, 167.4.

MS: *m*/*z* = 406 [M^+].

Anal. Calcd for $C_{24}H_{26}N_2O_4$ (406.5): C, 70.92; H, 6.45; N, 6.89. Found: C, 70.64; H, 6.23; N, 6.81.

(*Z*)-1,12,16,21-Tetraoxa-5,8-diazatetrabenzo[*b*,*j*,*n*,*v*]cyclotetracos-18-ene-4,9-dione (6a)

Prepared from **4a** and **8**; colorless crystals (EtOH); yield: 0.10 g (11%); mp 158–160 °C.

IR: 3475, 3522, 3364, 3070, 3035, 2941, 2864, 1649, 1599, 1531, 1484, 1452, 1298, 1245, 1159, 1013, 987, 754 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 3.52 (m, 4 H, NCH_2), 4.66 (d, *J* = 3.6 Hz, 4 H, OCH_2CH=), 4.99 (s, 4 H, OCH_2Ar), 5.95 (t, *J* = 3.6 Hz, 2 H, CH=), 6.68 (d, *J* = 8.2 Hz, 2 H), 6.79 (t, *J* = 7.4 Hz, 2 H), 7.01 (m, 4 H), 7.10 (t, *J* = 7.6 Hz, 2 H), 7.25 (d, *J* = 7.5 Hz, 2 H), 7.42 (dt, *J* = 1.8, 8.4 Hz, 2 H), 8.07 (br, 2 H, NH), 8.21 (dd, *J* = 1.7, 7.9 Hz, 2 H).

^{13}C NMR ($CDCl_3$): δ = 39.8, 64.8, 66.8, 112.0, 113.1, 121.2, 121.3, 121.8, 124.0, 128.8, 129.3, 129.9, 132.2, 130.5, 155.8, 156.9, 165.5.

MS: *m*/*z* = 564 [M^+].

LCMS: *m*/*z* = 565 [M + 1].

Anal. Calcd for $C_{34}H_{32}N_2O_6$ (564.6): C, 72.33; H, 5.71; N, 4.96. Found: C, 72.12; H, 5.56; N, 4.82.

(*E*)-1,12,16,21-Tetraoxa-5,8-diazatetrabenzo[*b*,*j*,*n*,*v*]cyclotetracos-18-ene-4,9-dione (7a)

Prepared from **4a** and **9**; colorless crystals (EtOH); yield: 0.53 g (56%); mp 158–160 °C.

IR: 3375, 3314, 3066, 2936, 1651, 1600, 1529, 1490, 1451, 1297, 1239, 978, 753 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 3.44 (m, 4 H, NCH_2), 4.50 (s, 4 H, OCH_2CH=), 5.21 (s, 4 H, OCH_2), 5.93 (s, 2 H, CH=), 6.89 (d, *J* = 8.2 Hz, 2 H), 6.96 (t, *J* = 7.3 Hz, 2 H), 7.06 (t, *J* = 7.6 Hz, 2 H), 7.11 (d, *J* = 8.2 Hz, 2 H), 7.29 (t, *J* = 8.0 Hz, 2 H), 7.37 (dd, *J* = 1.2, 7.7 Hz, 2 H), 7.43 (m, 2 H), 8.15 (dd, *J* = 1.7, 7.8 Hz, 2 H), 8.24 (br, 2 H, NH).

^{13}C NMR ($CDCl_3$): δ = 40.0, 67.6, 67.9, 112.1, 112.8, 112.9, 120.9, 121.1, 121.2, 127.4, 130.0, 132.0, 132.1, 132.6, 156.8, 157.3, 166.0.

MS: *m*/*z* = 564 [M^+].

Anal. Calcd for $C_{34}H_{32}N_2O_6$ (564.6): C, 72.33; H, 5.71; N, 4.96. Found: C, 72.12; H, 5.63; N, 4.85.

(*Z*)-1,12,16,21-Tetraoxa-5,8-diazapentabenzo[*b*,*f*,*j*,*n*,*v*]cyclotetracos-18-ene-4,9-dione (6b)

Prepared from **4b** and **8**; colorless crystals ($CHCl_3$); yield: 0.43 g (49%); mp 248–250 °C.

IR: 3329, 3068, 3036, 2936, 2881, 1699, 1660, 1599, 1535, 1493, 1476, 1455, 1294, 1243, 1123, 999, 753 cm^{-1}.

^{1}H NMR (acetone-d_6): δ = 4.67 (m, 4 H, OCH_2CH=), 5.18 (s, 4 H, OCH_2), 5.63 (m, 2 H, CH=), 6.89 (t, *J* = 7.8 Hz, 2 H), 7.04 (m, 4 H), 7.15–7.20 (m, 4 H), 7.28 (t, *J* = 7.6 Hz, 2 H), 7.42 (m, 4 H), 7.65 (m, 2 H), 8.06 (dd, *J* = 1.3, 7.7 Hz, 2 H), 9.99 (br, 2 H, NH).

^{13}C NMR (acetone-d_6): δ = 64.0, 68.3, 113.0, 115.0, 121.8, 122.0, 123.9, 125.2, 126.1, 129.9 (overlapped, 2 × C), 131.2, 131.8, 132.9, 133.2, 133.8, 157.5, 158.0, 164.6.

MS: *m*/*z* = 612 [M^+].

Anal. Calcd for $C_{38}H_{32}N_2O_6$ (612.7): C, 74.50; H, 5.26; N, 4.57. Found: C, 74.12; H, 5.16; N, 4.45.

(*E*)-1,12,16,21-Tetraoxa-5,8-diazapentabenzo[*b*,*f*,*j*,*n*,*v*]cyclotetracos-18-ene-4,9-dione (7b)

Prepared from **4b** and **9**; colorless crystals ($CHCl_3$); yield: 0.46 g (53%); mp 248–250 °C.

IR: 3321, 3068, 3028, 2917, 1650, 1597, 1514, 1477, 1450, 1288, 1243, 1251, 1002, 914, 752 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 4.24 (s, 4 H, OCH_2CH=), 5.10 (s, 4 H, OCH_2), 5.84 (s, 2 H, CH=), 6.81 (d, *J* = 8.1 Hz, 2 H), 6.96 (t, *J* = 7.4 Hz, 2 H), 7.05 (t, *J* = 7.5 Hz, 2 H), 7.11 (m, 2 H), 7.14 (d, *J* = 8.3 Hz, 2 H), 7.32–7.37 (m, 4 H), 7.43 (dt, *J* = 1.7, 7.8 Hz, 2 H), 7.50 (m, 2 H), 8.10 (dd, *J* = 1.6, 7.9 Hz, 2 H), 9.99 (br, 2 H, NH).

^{13}C NMR ($CDCl_3$): δ = 67.6, 67.8, 111.8, 113.3, 120.5, 121.0, 123.5, 123.7, 124.5, 125.3, 128.1, 130.6, 131.2, 131.8, 132.25, 132.28, 155.7, 157.4, 164.6.

MS: *m*/*z* = 612 [M^+].

Anal. Calcd for $C_{38}H_{32}N_2O_6$ (612.7): C, 74.50; H, 5.26; N, 4.57. Found: C, 74.32; H, 5.18; N, 4.55.

(*Z*)-1,12,16,21-Tetraoxa-5,8-diazatetrabenzo[*b*,*j*,*n*,*v*]cyclohexano[*f*]cyclotetracos-18-ene-4,9-dione (6c)

Prepared from **4c** and **8**; colorless crystals (EtOH); yield: 0.28 g (32%); mp 120–122 °C.

IR: 3325, 3064, 2930, 2872, 1659, 1598, 1532, 1482, 1456, 1298, 1233, 1005, 753 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 1.05 (br, 2 H), 1.25 (m, 3 H), 2.01 (m, 2 H), 3.88 (br, 2 H), 4.67–4.74 (m, 5 H), 5.23–5.33 (m, 4 H), 5.87 (m, 2 H), 6.87–6.95 (m, 8 H), 7.25 (m, 4 H), 7.36 (d, *J* = 7.2 Hz, 2 H), 8.01 (dd, *J* = 1.4, 7.6 Hz, 2 H), 8.18 (d, *J* = 6.3 Hz, 2 H, NH).

LCMS: *m*/*z* = 619 [M + 1].

Anal. Calcd for $C_{38}H_{38}N_2O_6$ (618.7): C, 73.77; H, 6.19; N, 4.53. Found: C, 73.55; H, 6.17; N, 4.43.

(*E*)-1,12,16,21-Tetraoxa-5,8-diazatetrabenzo[*b*,*j*,*n*,*v*]cyclohexano[*f*]cyclotetracos-18-ene-4,9-dione (7c)

Prepared from **4c** and **9**; colorless crystals (EtOH); yield: 0.34 g (39%); mp 120–122 °C.

IR: 3366, 3064, 2932, 2860, 1639, 1599, 1534, 1489, 1451, 1243, 999, 755 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 1.03 (s, 2 H), 1.27 (m, 4 H), 2.00 (d, *J* = 9.6 Hz, 2 H), 3.86 (s, 2 H), 4.51 (d, *J* = 13.2 Hz, 4 H), 5.23–5.33 (m, 4 H), 5.94 (s, 2 H), 6.84–6.92 (m, 8 H), 7.23–7.40 (m, 6 H), 7.99 (d, *J* = 7.2 Hz, 2 H), 8.17 (d, *J* = 6.1 Hz, 2 H, NH).

^{13}C NMR ($CDCl_3$): δ = 24.6, 32.1, 53.0, 66.0, 67.4, 111.5, 112.8, 120.8, 120.9, 121.6, 124.5, 127.8, 129.1, 129.3, 131.9, 132.3, 155.7, 156.9, 165.3.

MS: *m*/*z* = 618 [M^+].

Anal. Calcd for $C_{38}H_{38}N_2O_6$ (618.7): C, 73.77; H, 6.19; N, 4.53. Found: C, 73.55; H, 6.17; N, 4.43.

2-Allyloxybenzaldehyde (15)

To a solution of salicylaldehyde (20 g, 0.16 mol) and KOH (12.5 g) in EtOH (50 mL) was added allyl bromide (18 mL, 0.24 mol). The reaction mixture was heated under reflux for 4 h. The solvent was then removed in vacuo and the remaining oily product was extracted with CH_2Cl_2 (50 mL) and washed with a KOH solution (50 mL, 10%). The organic layer was separated and dried over Na_2SO_4 and the solvent was then removed in vacuo to give **15** (25 g, 94%; Lit.[16] bp 85–88 °C, 0.25 mmHg) as a yellow oil which was found to be

pure enough by ^{1}H NMR to be used without further purification in the next step.

IR: 3351, 3080, 3020, 2989, 2865, 2762, 1687, 1598, 1481, 1457, 1395, 1290, 1240, 1192, 1162, 1104, 998, 931, 841, 760, 658 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 4.68 (m, 2 H, OCH_2), 5.36 (dd, *J* = 1.3, 10.4 Hz, 1 H, CH_2=), 5.47 (dd, *J* = 1.3, 17.2 Hz, 1 H, CH_2=), 6.06 (m, 1 H, CH=), 6.99–7.05 (m, 2 H), 7.55 (m, 1 H), 7.86 (dd, *J* = 2.0, 8.0 Hz, 1 H), 10.56 (s, 1 H, CHO).

MS: *m*/*z* = 162 [M$^+$].

2-Allyloxybenzyl Alcohol (16)
To a solution of **15** (3.24 g, 20 mmol) in boiling MeOH (25 mL) was added $NaBH_4$ (1.2 g, 30 mmol) portionwise with stirring over 15 min. The mixture was refluxed for 1 h and then poured over ice-water mixture (100 mL). The separated oil was extracted with $CHCl_3$ (50 mL), dried over Na_2SO_4 and the solvent was removed in vacuo to give **16** as a yellow oil (3.25 g, almost 100%; Lit.[17] bp 83–85 °C, 0.02 mm Hg) which was used without further purification in the next step.

IR: 3369, 3079, 3041, 2984, 2920, 2871, 1649, 1603, 1590, 1492, 1454, 1423, 1365, 1288, 1239, 1098, 1043, 1020, 999, 929, 754 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 2.40 (s, 1 H, OH), 4.62 (d, *J* = 5.1 Hz, 2 H, OCH_2CH=), 4.74 (s, 2 H, CH_2OH), 5.34 (dd, *J* = 1.0, 10.7 Hz, 1 H, CH_2=), 5.44 (dd, *J* = 1.3, 17.2 Hz, 1 H, CH_2=), 6.05 (m, 1 H, CH=), 6.90 (d, 1 H, *J* = 8.2 Hz), 6.98 (t, *J* = 7.4 Hz, 1 H), 7.29 (m, 2 H).

MS: *m*/*z* = 164 [M$^+$].

2-Allyloxybenzyl Chloride (17)
To the alcohol **16** (3.25 g, 20 mmol) in $CHCl_3$ (20 mL) was added $SOCl_2$ (2.5 mL) dropwise with stirring at r.t.. The mixture was stirred in anhydrous atmosphere at r.t. for 1 h and the solvent was then removed in vacuo to leave a dark oil in 95% yield (Lit.[18]) which was used without further purification in the next step.

IR: 3078, 3024, 2970, 2921, 2867, 1648, 1599, 1494, 1455, 1293, 1251, 1112, 1018, 998, 929, 842, 753, 671 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 4.64 (m, 2 H, OCH_2CH=), 4.72 (s, 2 H, CH_2Cl), 5.33 (dd, *J* = 1.3, 10.6 Hz, 1 H, CH_2=), 5.52 (dd, *J* = 1.3, 17.3 Hz, 1 H, CH_2=), 6.09 (m, 1 H, CH=), 6.91 (d, *J* = 8.3 Hz, 1 H), 6.99 (t, *J* = 8.1 Hz, 1 H), 7.30 (m, 1 H), 7.39 (dd, *J* = 1.6, 7.5 Hz, 1 H).

MS: *m*/*z* = 182 [M$^+$], 184 [M + 2].

1,4-Bis(*o*-formylphenoxy)-2-butenes 11 and 12; General Procedure
A solution of salicylaldehyde (7.94 g, 65 mmol) and KOH (3.67 g, 65 mmol) in MeOH (25 mL) was stirred for 5 min and the solvent was then removed in vacuo to give the corresponding potassium salt to which DMF (10 mL) and *cis*-1,4-dichloro-2-butene or *trans*-1,4-dichloro-2-butene (31 mmol) was added. The reaction mixture was then heated under reflux for 15 min (during this time the potassium halide precipitated). The mixture was then diluted with ice-water (50 mL) and the precipitate was collected, washed with cold H_2O and finally crystallized from EtOH to give the corresponding derivative **11** or **12**.

(*Z*)-1,4-Bis(*o*-formylphenoxy)-2-butene (11)
Colorless crystals; yield: 8.3 g (86%); mp 97–99 °C.

IR: 3424, 3108, 3074, 3040, 2969, 2925, 2875, 2765, 1682, 1598, 1485, 1455, 1393, 1288, 1235, 1163, 1005, 841, 758, 697 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 4.84 (d, *J* = 3.4 Hz, 4 H, OCH_2), 6.07 (t, *J* = 3.4 Hz, 2 H, CH=), 6.99 (d, *J* = 8.4 Hz, 2 H), 7.08 (t, *J* = 7.5 Hz, 2 H), 7.57 (t, *J* = 8.2 Hz, 2 H), 7.87 (d, *J* = 7.6 Hz, 2 H), 10.51 (s, 2 H, CHO).

^{13}C NMR ($CDCl_3$): δ = 64.5, 112.5, 121.2, 125.0, 128.5, 128.8, 135.9, 160.5, 189.6.

MS: *m*/*z* = 296 [M$^+$].

Anal. Calcd for $C_{18}H_{16}O_4$ (296.3): C, 72.96; H, 5.44. Found: C, 72.69; H, 5.67.

(*E*)-1,4-Bis(*o*-formylphenoxy)-2-butene (12)
Colorless crystals; yield: 8.4 g (87%); mp 150–152 °C.

IR: 3323, 3101, 3079, 2925, 2867, 2767, 1674, 1599, 1487, 1459, 1391, 1290, 1237, 1167, 1009, 990, 816, 759 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 4.75 (d, *J* = 2.0 Hz, 4 H, OCH_2), 6.18 (t, *J* = 2.0 Hz, 2 H, CH=), 7.00 (d, *J* = 8.4 Hz, 2 H), 7.08 (t, *J* = 7.6 Hz, 2 H), 7.56 (dt, *J* = 1.8, 7.8 Hz, 2 H), 7.88 (dd, *J* = 1.8, 7.7 Hz, 2 H), 10.55 (s, 2 H, CHO).

^{13}C NMR ($CDCl_3$): δ = 68.0, 112.7, 121.1, 125.1, 127.8, 128.7, 135.9, 160.6, 189.6.

MS: *m*/*z* = 296 [M$^+$].

Anal. Calcd for $C_{18}H_{16}O_4$ (296.3): C, 72.96; H, 5.44. Found: C, 72.72; H, 5.44.

1,4-Bis(*o*-hydroxymethylphenoxy)-2-butenes 13, 14; General Procedure
To a cold (0–5 °C) and stirred solution of bis(carbonyl)ethers **11** or **12** (10 mmol) in MeOH (100 mL) was added dropwise a solution of $NaBH_4$ (2.57 g, 67 mmol) dissolved in H_2O (4.28 mL) and aq NaOH solution (4.28 mL, 2 N). The reaction mixture was stirred for 2 h (0–5 °C) and kept in the refrigerator overnight. The insoluble material was filtered off and the solvent was removed in vacuo. The remaining material was crystallized from EtOH to give the corresponding diols **13** or **14**.

(*Z*)-1,4-Bis(*o*-hydroxymethylphenoxy)-2-butene (13)
Colorless crystals; yield: 2.0 g (66%); mp 66–68 °C.

IR: 3366, 3066, 3038, 2924, 2872, 1601, 1491, 1454, 1289, 1233, 1116, 1015, 839, 754 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 2.72 (s, 2 H, OH), 4.69 (s, 4 H, CH_2OH), 4.73 (d, *J* = 4.0 Hz, 4 H, OCH_2), 5.99 (t, *J* = 4.0 Hz, 2 H, CH=), 6.89 (d, *J* = 8.2 Hz, 2 H), 6.99 (t, *J* = 7.4 Hz, 2 H), 7.28 (dt, *J* = 1.6, 7.8 Hz, 2 H), 7.33 (dd, *J* = 1.2, 7.4 Hz, 2 H).

^{13}C NMR ($CDCl_3$): δ = 61.6, 64.1, 111.3, 121.1, 128.7, 128.8, 128.9, 129.4, 156.1.

MS: *m*/*z* =300 [M$^+$].

Anal. Calcd for $C_{18}H_{20}O_4$ (300.4): C, 71.98; H, 6.71. Found: C, 72.07; H, 6.93.

(*E*)-1,4-Bis(*o*-hydroxymethylphenoxy)-2-butene (14)
Colorless crystals; yield: 1.9 g (62%); mp 94–95 °C.

IR: 3326, 3242, 3065, 3025, 2925, 2888, 2849, 1600, 1489, 1453, 1373, 1281, 1227, 1044, 1027, 988, 837, 748 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 2.32 (s, 2 H, OH), 4.67 (d, *J* = 2.0 Hz, 4 H, OCH_2), 4.74 (s, 4 H, CH_2OH), 6.12 (t, *J* = 2.0 Hz, 2 H, CH=), 6.89 (d, *J* = 8.2 Hz, 2 H), 6.99 (t, *J* = 7.4 Hz, 2 H), 7.26–7.31 (m, 2 H), 7.33 (dd, *J* = 1.2, 7.3 Hz, 2 H).

^{13}C NMR ($CDCl_3$): δ = 62.1, 67.6, 111.5, 121.0, 128.2, 128.9, 128.9, 129.3, 156.2.

MS: *m*/*z* = 300 [M$^+$].

Anal. Calcd for $C_{18}H_{20}O_4$ (300.4): C, 71.98; H, 6.71. Found: C, 72.10; H, 6.96.

1,4-Bis(*o*-chloromethylphenoxy)-2-butenes 8, 9; General Procedure

To a cold stirred solution (–10 °C) of diols **13** or **14** (10.9 mmol) in $CHCl_3$ (100 mL) was added dropwise a solution of $SOCl_2$ (5 mL) in $CHCl_3$ (5 mL). Stirring was continued for 2 h. The solvent was then removed in vacuo and the remaining solid was crystallized from EtOH to give **8** or **9**.

(*Z*)-1,4-Bis(*o*-chloromethylphenoxy)-2-butene (8)

Colorless crystals; yield: 3.2 g (95%); mp 40–42 °C.

IR: 3067, 3035, 2968, 2927, 1688, 1601, 1492, 1456, 1293, 1246, 1108, 1048, 1022, 842, 753, 670, 561 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 4.69 (s, 4 H, CH_2Cl), 4.79 (d, *J* = 2.3 Hz, 4 H, OCH_2), 6.02 (t, *J* = 2.3 Hz, 2 H, CH=), 6.92 (d, *J* = 8.3 Hz, 2 H), 6.99 (t, *J* = 7.5 Hz, 2 H), 7.28–7.32 (m, 2 H), 7.39 (d, *J* = 7.5 Hz, 2 H).

^{13}C NMR ($CDCl_3$): δ = 41.6, 64.6, 111.9, 121.0, 126.1, 128.5, 130.0, 130.7, 156.1.

MS: *m*/z = 336 [M^+], 338 [M + 2], 340 [M + 4].

Anal. Calcd for $C_{18}H_{18}Cl_2O_2$ (337.3): C, 64.11; H, 5.38. Found: C, 64.09; H, 5.44.

(*E*)-1,4-Bis(*o*-chloromethylphenoxy)-2-butene (9)

Colorless crystals (EtOH); yield: 3.2 g (95%); mp 96–98 °C.

IR: 3073, 3036, 2971, 2898, 2858, 1778, 1686, 1599, 1498, 1443, 1370, 1302, 1256, 1199, 1159, 1113, 994, 972, 848, 792, 751, 662 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 4.70 (br, 4 H, OCH_2), 4.72 (s, 4 H, CH_2Cl), 6.16 (br, 2 H, CH=), 6.90 (d, *J* = 8.2 Hz, 2 H), 6.98 (t, *J* = 7.3 Hz, 2 H), 7.29–7.34 (m, 2 H), 7.39 (d, *J* = 7.5 Hz, 2 H).

^{13}C NMR ($CDCl_3$): δ = 41.7, 67.8, 112.1, 120.9, 126.1, 127.7, 130.0, 130.6, 156.2.

MS: *m*/*z* = 336 [M^+], 338 [M + 2], 340 [M + 4].

Anal. Calcd for $C_{18}H_{18}Cl_2O_2$ (337.3): C, 64.11; H, 5.38. Found: C, 63.98; H, 5.66.

Ring-Closing Metathesis (RCM) of 1a–c: Synthesis of 2a–c and 3a–c; General Procedure

A solution of the substrates **1a–c** (1 mmol) in CH_2Cl_2 (10 mL) and Grubbs' catalyst **I** (1–5 mol% of the substrate as indicated in Table 1) or **II** (1 mol% or 5 mol% of the substrate) was heated under reflux for the time indicated in Table 1. The solvent was then removed in vacuo and the resulting products were analyzed by ^1H NMR. The yields and *Z*/*E* ratios were then determined by ^1H NMR (Table 1) and by comparing their signals with pure-*Z* and pure-*E* NMR signals prepared by bisalkylation method.

Isomerization Experiments of 2a and 6a,b, 11; General Procedure

A solution of **2a** or **6a**,**b** (1 mol) in CH_2Cl_2 (10 mL) and Grubbs' catalyst **I** or **II** (1 mol% of the substrate) was heated under reflux for 2 h. The solvent was then evaporated in vacuo and the resulting reaction products, yields and *Z*/*E* ratios were then determined by ^1H NMR.

Cross-Metathesis (CM) of 15–17: Synthesis of 8, 9 and 11–14; General Procedure

A solution of the substrates **15**, **16** or **17** (1 mol) in CH_2Cl_2 (10 mL) and Grubbs' catalyst **I** or **II** (1 mol% of the substrate) was heated under reflux for 2 h. The solvent was then evaporated in vacuo and the resulting reaction products were analyzed by ^1H NMR. The yield and *Z*/*E* ratios were then determined by ^1H NMR and compared with the pure *Z* and pure *E* NMR signals prepared by the other methods.

Cycloaddition Reactions of 2a,b, 3a,b; General Procedure

To a solution of **2a**,**b**, **3a**,**b** (0.31 mmol) and *N*-phenylbenzohydrazonoyl chloride[19] (1.26 mmol) in $CHCl_3$ (15 mL) was added Et_3N (0.5 mL). The reaction mixture was then heated under reflux for 24 h. The solvent was removed in vacuo and the resulting solid was washed with water and crystallized to give the corresponding derivatives **18a**,**b**, **19a**,**b**.

(*Z*)-1,3-Diphenyl-1,12-dioxa-5,8-diazadibenzo[*b*,*j*]pyrazolino[3,4-*n*]cyclohexadecane-4,9-dione (18a)

Prepared from **2a**; colorless crystals (dilute EtOH); yield: 0.36 g (53%); mp 152–153 °C.

IR: 3408, 3016, 2926, 2855, 1650, 1600, 1531, 1482, 1455, 1368, 1301, 1216, 993, 758 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 3.57 (m, 2 H, NCH_2), 4.00 (m, 2 H, NCH_2), 4.17 (m, 2 H), 4.27 (t, *J* = 8.2 Hz, 1 H), 4.73 (m, 3 H), 6.27 (d, *J* = 8.3 Hz, 1 H), 6.94 (d, *J* = 8.3 Hz, 1 H), 7.03 (t, *J* = 7.4 Hz, 1 H), 7.12 (m, 2 H), 7.28–7.48 (m, 9 H), 7.77 (dd, *J* = 1.1, 7.2 Hz, 2 H), 7.87 (t, *J* = 6.1 Hz, 1 H, NH), 7.98 (t, *J* = 5.4 Hz, 1 H, NH), 8.07 (dd, *J* = 1.6, 7.6 Hz, 1 H), 8.18 (dd, *J* = 1.6, 7.7 Hz, 1 H).

^{13}C NMR ($CDCl_3$): δ = 38.8, 39.6, 47.9, 63.7, 64.1, 67.4, 112.6, 122.1, 122.2, 122.24, 123.2, 124.9, 125.6, 126.3, 128.1, 129.0, 129.6, 129.9, 130.5, 132.2, 132.22, 132.4, 132.8, 146.2, 152.1, 155.1, 156.1, 165.4, 165.5.

MS: *m*/*z* = 546 [M^+].

UV–Vis (abs): λ_{max} (ε) = 294 (10680) nm.

UV–Vis (em): λ_{max} (ε) = 463 (61890) nm.

Anal. Calcd for $C_{33}H_{30}N_4O_4$ (546.6): C, 72.51; H, 5.53; N, 10.25. Found: C, 72.21; H, 5.41; N, 10.19.

(*Z*)-1,3-Diphenyl-1,12-dioxa-5,8-diazatribenzo[*b*,*f*,*j*]pyrazolino[3,4-*n*]cyclohexadecane-4,9-dione (18b)

Prepared from **2b**; yellowish crystals [CH_2Cl_2–PE (40–60)]; yield: 0.34 g (45%); mp 274–276 °C.

IR: 3455, 3361, 3062, 2928, 2880, 1663, 1598, 1534, 1479, 1294, 1228, 1009, 753, 694 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 4.64–4.73 (m, 4 H), 4.84 (d, *J* = 10.8 Hz, 1 H), 4.90 (dd, *J* = 6.5, 12.2 Hz, 1 H), 6.86 (t, *J* = 7.3 Hz, 1 H), 6.98–7.01 (m, 3 H), 7.07 (t, *J* = 7.6 Hz, 1 H), 7.11 (d, *J* = 8.3 Hz, 1 H), 7.18 (t, *J* = 8.0 Hz, 2 H), 7.27 (d, *J* = 8.3 Hz, 1 H), 7.30–7.44 (m, 6 H), 7.48–7.55 (m, 2 H), 7.65–7.68 (m, 3 H), 7.76 (dd, *J* = 1.7, 7.7 Hz, 1 H), 7.85 (dd, *J* = 1.7, 7.7 Hz, 1 H), 9.54 (s, 1 H, NH), 9.61 (s, 1 H, NH).

^{13}C NMR (DMSO): δ = 48.0, 61.7, 65.2, 66.1, 113.8, 114.5, 115.5, 121.2, 121.8, 122.1, 122.7, 125.2, 125.8, 126.4, 126.5, 126.8, 129.1, 129.4, 129.5, 131.26, 131.32, 131.5, 131.8, 132.4, 133.5, 133.8, 134.5, 145.2, 150.3, 156.8, 156.9, 163.6, 163.8.

MS: *m*/*z* = 594 [M^+].

UV–Vis (abs): λ_{max} (ε) = 285 (26626), 330 (shoulder, 13910) nm.

UV–Vis (em): λ_{max} (ε) = 459 (172514) nm.

Anal. Calcd for $C_{37}H_{30}N_4O_4$ (594.7): C, 74.73; H, 5.08; N, 9.42. Found: C, 74.53; H, 4.99; N, 9.32.

(*E*)-1,3-Diphenyl-1,12-dioxa-5,8-diazadibenzo[*b*,*j*]pyrazolino[3,4-*n*]cyclohexadecane-4,9-dione (19a)

Prepared from **3a**; pale yellow crystals ($CHCl_3$); yield: 0.38 g (55%); mp 298–300 °C.

IR: 3426, 3361, 3068, 2998, 2964, 2938, 1643, 1598, 1532, 1494, 1302, 1231, 1036, 752, 690 cm^{-1}.

^{1}H NMR (DMSO-d_6): δ = 3.41 (m, 2 H, NCH_2), 3.70 (m, 2 H, NCH_2), 3.88 (t, *J* = 9.6 Hz, 1 H), 4.00 (m, 3 H), 4.55 (dd, *J* = 5.2, 8.8 Hz, 1 H), 5.40 (dd, *J* = 3.4, 10.3 Hz, 1 H), 6.85 (t, *J* = 7.6 Hz, 1 H), 7.00–7.08 (m, 3 H), 7.15 (d, *J* = 8.5 Hz, 1 H), 7.29–7.42 (m, 7 H), 7.47 (t, *J* = 7.5 Hz, 2 H), 7.79 (dt, *J* = 1.6, 7.7 Hz, 2 H), 7.95 (d, *J* = 8.1 Hz, 2 H), 8.48 (t, *J* = 5.6 Hz, 1 H, NH), 8.52 (t, *J* = 4.8 Hz, 1 H, NH).

^{13}C NMR (DMSO): δ = 47.7 (2 × C), 61.1 (2 × C), 63.1, 65.1, 113.2, 113.9 (2 × C), 120.0, 121.4, 121.5, 123.6, 123.7, 126.6 (2 × C), 129.4, 129.6, 129.9, 131.3, 131.9, 132.8 (2 × C), 143.8, 148.4, 156.3, 156.4, 165.9, 165.92.

MS: *m*/*z* = 546 [M$^+$].

UV–Vis (abs): λ_{max} (ε) = 290 (shoulder, 20000), 360 (37143) nm.

UV–Vis (em): λ_{max} (ε) = 450 (41909) nm.

Anal. Calcd for $C_{33}H_{30}N_4O_4$ (546.6): C, 72.51; H, 5.53; N, 10.25. Found: C, 72.31; H, 5.35; N, 10.21.

(*E*)-1,3-Diphenyl-1,12-dioxa-5,8-diazatribenzo[*b*,*f*,*j*]pyrazolino[3,4-*n*]cyclohexadecane-4,9-dione (19b)

Prepared from **3b**; colorless crystals ($CHCl_3$); yield: 0.23 g (30%); mp 274–276 °C.

IR: 3385, 3053, 3005, 2933, 2880, 1652, 1597, 1494, 1453, 1384, 1317, 1237, 1136, 1028, 758 cm^{-1}.

^{1}H NMR (DMSO): δ = 3.78 (m, 2 H), 4.10–4.50 (m, 3 H), 5.14 (m, 1 H), 6.67–6.82 (m, 3 H), 7.07–7.26 (m, 9 H), 7.36–7.87 (m, 10 H), 10.47 (s, 1 H), 10.50 (s, 1 H).

LCMS: *m*/*z* = 595 [M + 1].

UV–Vis (abs): λ_{max} (ε) = 284 (4478) nm.

UV–Vis (em): λ_{max} (ε) = 436 (169784) nm.

Anal. Calcd for $C_{37}H_{30}N_4O_4$ (594.7): C, 74.73; H, 5.08; N, 9.42. Found: C, 74.47; H, 5.33; N, 9.31.

Acknowledgment

The support of the University of Kuwait received through research grant no. SC10/02 and the facilities of ANALAB and SAF (grant nos. GS01/01, GS02/01, GS03/01) are gratefully acknowledged. Also, the support of College of Graduate Studies, Kuwait University to the Ph.D. student Rana N. Malhas is highly appreciated.

References

(1) Atwood, J.; Davis, J.; Machicol, D.; Vogtle, F. *Comprehensive Supramolecular Chemistry*; Lehn, J.; Gokel, G., Eds.; Pergamon: New York, **1996**, 1–11.

(2) (a) Fu, G. C.; Grubbs, R. H. *J. Am. Chem. Soc.* **1992**, *114*, 5426. (b) Fu, G. C.; Nguyen, S.; Grubbs, R. H. *J. Am. Chem. Soc.* **1993**, *115*, 9856. (c) Grubbs, R. H. *Tetrahedron* **2004**, *60*, 7117. (d) Deiters, A.; Martin, S. *Chem. Rev.* **2004**, *104*, 2199. (e) Nakamura, I.; Ymamoto, Y. *Chem. Rev.* **2004**, *104*, 2127. (f) Konig, B.; Horn, C. *Synlett* **1996**, 1013. (g) Weck, M.; Mohr, B.; Sauvage, J. P.; Grubbs, R. H. *J. Org. Chem.* **1999**, *64*, 5463. (h) Dietrich-Buchecker, C.; Sauvage, J. P. *Chem. Commun.* **1999**, 615. (i) Kidd, J. T.; Leigh, A. O.; Wilson, A. J. *J. Am. Chem. Soc.* **1999**, *121*, 1599. (j) Grubbs, R. H.; Miller, S. J.; Fu, G. C. *Acc. Chem. Res.* **1995**, *28*, 446. (k) Grubbs, R. H.; Chang, S. *Tetrahedron* **1998**, *54*, 4413. (l) Kingsbury, J. S.; Harrity, J. P.; Bonitatebus, P. J.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1999**, *121*, 791. (m) Wakamatsu, H.; Blechert, S. *Angew. Chem. Int. Ed.* **2002**, *41*, 2403. (n) Akiyama, R.; Kobayashi, S. *Angew. Chem. Int. Ed.* **2002**, *41*, 2602. (o) Connon, S. J.; Blechert, S. *Top. Organomet. Chem.* **2004**, *11*, 93.

(3) Ibrahim, Y. A.; El Wahy, A. H.; Elkareish, G. *J. Chem. Res., Synop.* **1994**, 414.

(4) (a) Behbehani, H.; Ibrahim, M. R.; Ibrahim, Y. A. *Tetrahedron Lett.* **2002**, *43*, 6421. (b) Ibrahim, Y. A.; Behbehani, H.; Ibrahim, M. R.; Malhas, R. N. *Tetrahedron* **2003**, *59*, 7273.

(5) Ibrahim, Y. A.; Behbehani, H.; Abrar, N. M. *Tetrahedron* **2004**, *60*, 8429.

(6) Ibrahim, Y. A.; Behbehani, H.; Ibrahim, M. R.; Abrar, N. M. *Tetrahedron Lett.* **2002**, *43*, 6971.

(7) Ibrahim, Y. A.; Behbehani, H.; Ibrahim, M. R. *Tetrahedron Lett.* **2002**, *43*, 4207.

(8) (a) Grubbs, R. H.; Chang, S. *Tetrahedron* **1998**, *54*, 4413. (b) Furstner, A. *Angew. Chem. Int. Ed.* **2000**, *39*, 3012.

(9) Schrock, R. R.; Murdzed, J. S.; Bazan, G. C.; Robbins, J.; Dimare, M.; Regan, M. O. *J. Am. Chem. Soc.* **1990**, *112*, 3875.

(10) Fu, G. C.; Nguyen, S. T.; Grubbs, R. H. *J. Am. Chem. Soc.* **1993**, *115*, 9856.

(11) Sanford, M. S.; Love, J. A.; Grubbs, R. H. *J. Am. Chem. Soc.* **2001**, *123*, 6543.

(12) Giger, T.; Wigger, M.; Audétat, S.; Benner, S. A. *Synlett* **1998**, 688.

(13) (a) Prunet, J. *Angew. Chem. Int. Ed.* **2003**, *42*, 2826. (b) Kalesse, M.; Quitschalle, M.; Claus, E.; Gerlach, K.; Pahl, A.; Meyer, H. H. *Eur. J. Org. Chem.* **1999**, 2817. (c) Fürstner, A.; Mathes, C.; Grela, K. *Chem. Commun.* **2001**, 1057. (d) Murga, J.; Falomir, E.; Garcia-Fortanet, J.; Carda, M.; Marco, J. A. *Org. Lett.* **2002**, *4*, 3447. (e) Connon, S. J.; Blechert, S. *Angew. Chem. Int. Ed.* **2003**, *42*, 1900. (f) Schmidt, B.; Hermanns, J. *Top. Organomet. Chem.* **2004**, *13*, 223.

(14) Ibrahim, Y. A.; Elwahy, A. H. M.; Abbas, A. A.; Kassab, R. M. *J. Chem. Res., Synop.* **1999**, 522.

(15) Ibrahim, Y. A.; Elwahy, A. H. M. *Synthesis* **1993**, 504.

(16) Abiko, A.; Davis, W.; Masamune, S. *Tetrahedron: Asymmetry* **1995**, *6*, 1295.

(17) Lachapelle, A.; Jacques, M. *Tetrahedron* **1988**, *44*, 5033.

(18) Orlek, B.; Sammers, P.; Weller, D. *Tetrahedron* **1993**, *49*, 8179.

(19) Patel, H. V.; Vyas, K. A.; Pandy, S. P.; Fernandes, P. S. *Tetrahedron* **1996**, *52*, 661.