Synthesis of Conformationally Restricted Symmetric Macrodiolides via Carbonyl Ylides

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Received: 15.01.2013; Accepted after revision: 18.04.2013

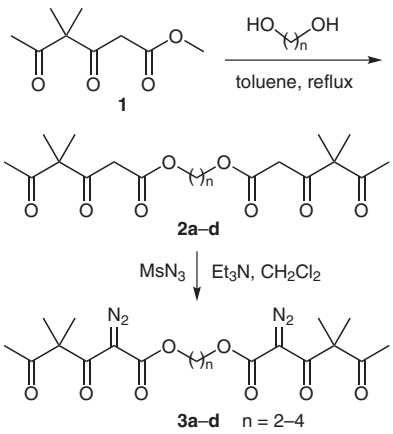
This paper is dedicated with best wishes to Professor Goverdhan Mehta on the occasion of his 70th birthday.

Abstract: Reaction of bis-diazocarbonyl compounds and dicarbaldehyde/divinyl derivatives in the presence of rhodium(II) acetate dimer as the catalyst led to the facile synthesis of conformationally restricted symmetric macrodiolides incorporating oxa/dioxa-bridged bicyclic systems. The structure and configuration of a representative macrodiolide were unequivocally confirmed using single-crystal X-ray analysis.

Key words: cycloaddition, diazo compounds, macrocycles, rhodium, ylides

Diazocarbonyl compounds[1] are excellent precursors for carbenoids and hence they have been employed in cyclopropanation, insertion, and ylide formation. The reaction of metallocarbenoids with carbonyl groups is one of the most effective methods to generate carbonyl ylides, and their use in 1,3-dipolar cycloadditions[2] with π-bonds of C=C or C=O groups to construct carbo/heterocyclic ring systems are well documented. As a result, there has been growing interest in the use of rhodium(II)-generated carbonyl ylides as 1,3-dipoles for the synthesis of many bioactive natural products.[3] In order to synthesize macrocycles via [3+2]-cycloaddition reactions, the selection of dipolarophile and diazocarbonyl compound is of considerable interest. Synthesis[4] and application studies[5] of macrodiolides are valuable in organic synthesis due to their biological as well as ion-selective properties and application in the perfume industry. The synthesis of macrocycles generally results in low yields and requires high dilution techniques. The physicochemical advantages of conformationally restricted macrocycles result from their shape[6] and lower rotatable bond count.[7] However, there is no literature available for the synthesis of macrocycles via carbonyl ylides. As a part of our ongoing research[8] on carbonyl ylides and supramolecular systems,[9] we herein report the reactions of bis-diazo ketones with dicarbaldehyde and divinyl compounds in the presence of rhodium(II) acetate dimer as the catalyst to synthesize conformationally restricted symmetric macrodiolides in a tandem manner.

With an aim to develop new macrocyclic compounds via carbonyl ylide mediated 1,3-dipolar cycloaddition reactions, the synthesis of a series of bis-diazocarbonyl compounds **3a–d** (Scheme 1) was planned. Thus, diazo compounds **3a–d** were synthesized via transesterification[10] of active methylene[11] compound **1** with diols to afford the corresponding diester derivatives **2a–d** (Table 1). Subsequent diazo-transfer[12] reaction of compounds **2a–d** afforded the corresponding bis-diazocarbonyl compounds **3a–d** in very good yields. These compounds have a lower number of carbon signals than expected in their ^{13}C NMR spectra due to their symmetry.



Scheme 1

Table 1 Synthesis of Bis-diazocarbonyl Compounds **3a–d**

Entry	n	Linked diesters		Bis-diazocarbonyl compounds	
		2	Yield[a] (%)	**3**	Yield[a] (%)
1	2	**2a**	41	**3a**	96
2	3	**2b**	51	**3b**	88
3	4	**2c**	39	**3c**	89
4	8	**2d**	38	**3d**	92

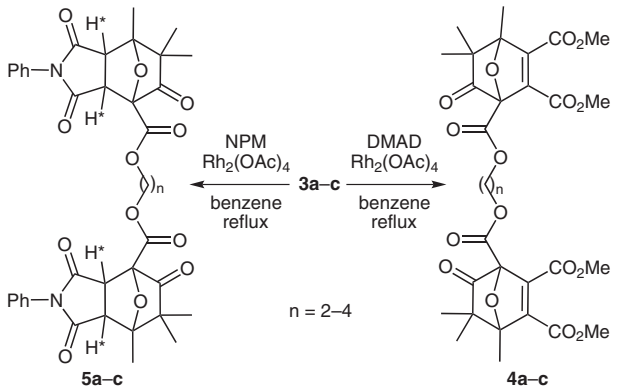
[a] Isolated yields.

Initially, it was planned to study the rhodium(II) acetate dimer catalyzed reaction of bis-diazocarbonyl compounds **3** in the presence of excess alkene or alkyne as a dipolarophile. Thus, for the reaction of **3a**, 2.5 equivalents of dimethyl acetylenedicarboxylate (DMAD) and 1 mol% of

SYNTHESIS 2013, 45, 2034–2042
Advanced online publication: 29.05.2013
DOI: 10.1055/s-0033-1338801; Art ID: SS-2013-T0042-OP

rhodium(II) acetate dimer in dry benzene was refluxed to afford the bis-cycloadduct **4a** in 72% yield (Scheme 2).

Similarly, diazocarbonyl compounds **3b**,**c** were treated with dimethyl acetylenedicarboxylate to furnish the corresponding bis-cycloadducts **4b**,**c** in moderate yields (Scheme 2, Table 2). Treatment of **3a** with 2.5 equivalents of *N*-phenylmaleimide (NPM) in the presence of rhodium(II) acetate catalyst for 60 minutes in benzene under reflux conditions furnished the corresponding bis-cycloadduct **5a** in 86% yield as a mixture of diastereomers (Scheme 2). The ^{1}H NMR spectrum of the crude reaction mixture of compound **5a** exhibited four characteristic signals as a doublet for each C–H* proton. Similarly, the rhodium(II) acetate catalyzed reaction of bis-diazocarbonyl compounds **3b** and **3c** with *N*-phenylmaleimide furnished bis-cycloadducts **5b** and **5c** as white solids in excellent yield, respectively. Based on the NMR of crude reaction mixtures, we observe that products **4** and **5** exist as a mixture of *meso* and *dl* compounds that was inseparable by column chromatography.



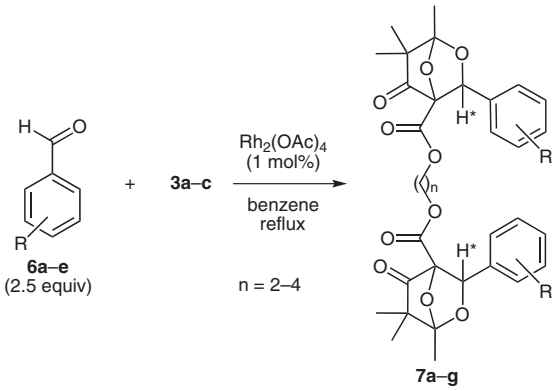
Scheme 2

Table 2 Synthesis of Bis-cycloadducts **4**,**5**

Entry	n	Product	Yield[a] (%)	dr[b]
1	2	**4a**	72	–[c]
2	3	**4b**	62	–[c]
3	4	**4c**	65	–[c]
4	2	**5a**	86	50:50
5	3	**5b**	94	55:45
6	4	**5c**	95	53:47

[a] Isolated yields.
[b] Diastereomeric ratio based on NMR spectra of crude reaction mixture.
[c] Diastereomeric ratio could not be determined.

Optimistic from the above results, we extended the above bis-carbonyl ylide reactions with an excess amount of aromatic aldehydes to furnish the substituted dioxolane[8d,13] ring systems. For this purpose, a mixture of bis-diazocarbonyl compound **3a** and 2.5 equivalents of benzaldehyde (**6a**) in the presence of rhodium(II) acetate dimer was refluxed in benzene to furnish the corresponding bis-cycloadduct **7a** in 76% yield. The ^{1}H NMR spectrum of product **7a** exhibited a characteristic signal at δ = 4.95 and 4.97 as two separate singlets for the H* protons, which clearly indicates the presence of diastereomers in the ratio of 51:49 (Scheme 3, Table 3). Similar reaction of bis-diazocarbonyl compounds **3b**,**c** with substituted benzaldehydes **6b**–**e** afforded bis-cycloadducts **7b**–**g** as mixtures of diastereomers that were inseparable by column chromatography. Although the ^{1}H NMR did not exhibit a mixture of isomers based on H* protons, ^{13}C NMR indicated a mixture isomers for the crude reaction mixture of **7g**.



Scheme 3

Table 3 Synthesis of Bis-cycloadducts **7**

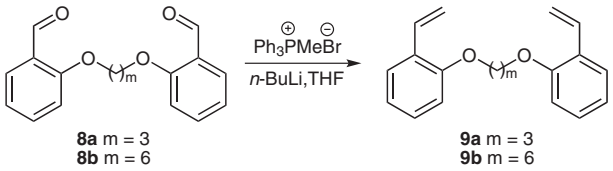
Entry	n	Substrate	R	Product	Yield[a] (%)	dr[b]
1	2	**6a**	H	**7a**	76	51:49
2	4	**6a**	H	**7b**	80	51:49
3	3	**6b**	3-OMe	**7c**	85	50:50
4	4	**6b**	3-OMe	**7d**	88	–[c]
5	4	**6c**	3-F	**7e**	84	–[c]
6	4	**6d**	3-NO_2	**7f**	79	–[c]
7	3	**6e**	2-OH	**7g**	68	–[c]

[a] Isolated yields.
[b] Diastereomeric ratio based on NMR spectra of crude reaction mixture.
[c] Diastereomeric ratio could not be determined.

After the successful intermolecular bis-cycloaddition reaction of carbonyl ylides, generated from compounds **3**, with π-bonds of C=O and C=C functional groups, we were further interested in elaborating the scope and synthetic utility of the tandem cyclization–cycloaddition reaction toward the synthesis of conformationally restricted macrocycles.

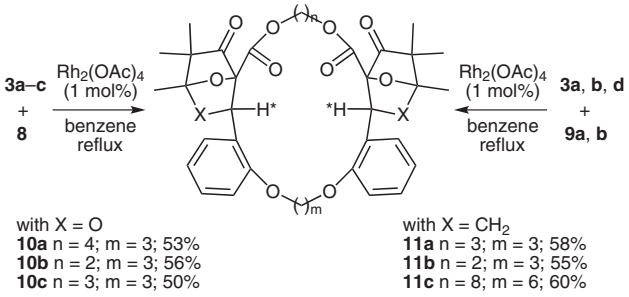
For this purpose, Wittig reaction of dicarbaldehydes **8**, prepared by O-alkylation of salicylaldehyde with dialkyl halides using potassium carbonate as base in dry *N*,*N*-di-

methylformamide, was carried out to afford the corresponding divinyl compound **9** in good yield (Scheme 4).



Scheme 4 Synthesis of divinyl compounds **9**

Next, we planned to investigate the reaction of bis-diazocarbonyl compounds **3** with dicarbaldehyde derivatives **8**. A mixture of bis-diazocarbonyl compound **3c** with dicarbaldehyde **8a** in benzene was refluxed in the presence of rhodium(II) acetate dimer to furnish the conformationally restricted symmetric macrodiolide **10a** (Scheme 5) incorporating the dioxa-bridged units in 53% yield as a single product based on the NMR spectrum of crude reaction mixture. The FT-IR spectrum of compound **10a** exhibited strong bands at 1778 and 1752 cm^{-1}. The presence of a singlet at δ = 5.53 for H* proton and a singlet at δ = 1.67 corresponding to the bridgehead methyl group was recorded by ^1H NMR. An oxygen attached carbon (CH^a) signal appeared at δ = 71.4 in ^{13}C NMR. DEPT spectral analyses of product **10a** showed peaks for three CH_3 carbons, four CH_2 carbons, five CH carbons, and seven quaternary carbons including two carbonyl groups, which clearly confirmed the proposed structure as a bis-cycloadduct having the macrocyclic ring system.



Scheme 5 Synthesis of macrodiolides **10** and **11**

In order to characterize the regio- and stereochemical assignments of the products precisely, we studied the product by single-crystal X-ray analysis. Compound **10a** was recrystallized in chloroform–hexane to provide colorless crystals and these were subjected to low temperature X-ray crystallographic analysis.[14] The X-ray structure of compound **10a** (Figure 1) exhibits two asymmetric units present in a unit cell. No other notable byproducts were observed in the above reaction. Similar reaction of bis-diazocarbonyl compounds **3a**,**b** with dicarbaldehyde derivative **8a** afforded the corresponding macrodiolides **10b**,**c**. From the NMR and X-ray studies one might think that the products **10** might be formed as single stereoisomers. To understand the presence of stereoselectivity issues in **10**, product **10c** was synthesized via dialkylation of **7g** using 1,3-dibromopropane. The ^1H and ^{13}C NMR spectra of the crude reaction mixture of **10c** did not reveal a mixture of isomers. Further, products **10a–c** were tested using analytical HPLC (C18 column) and the results unfortunately did not show the presence of isomers.

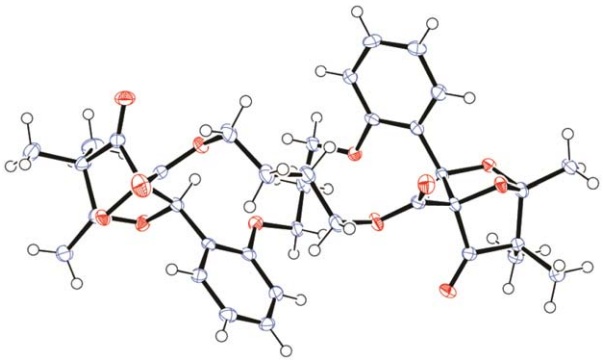


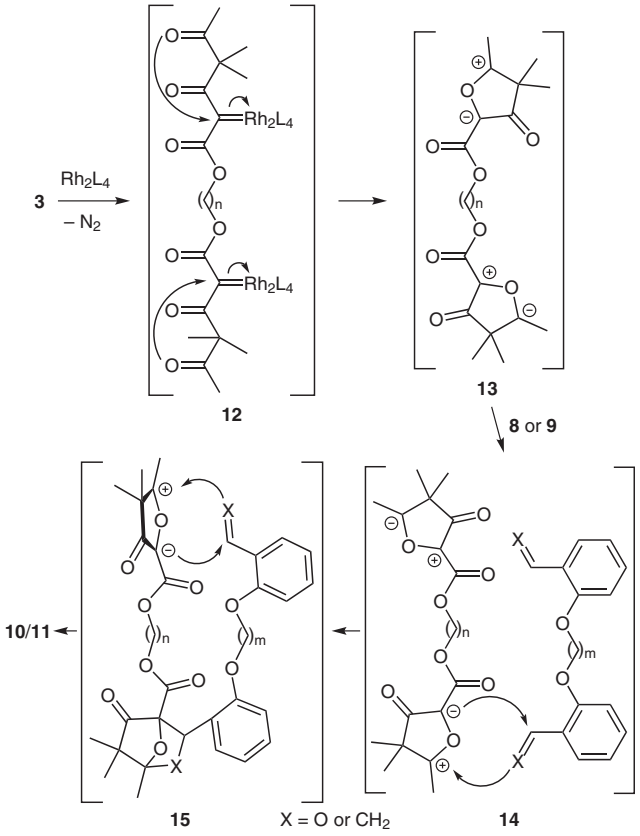
Figure 1 ORTEP diagram for one of the isomers of **10a**; atom numbers are removed for better clarity

Based on these studies, the products **10a–c** might be a mixture of *meso* and *dl* compounds and on crystallization of **10a** might have produced a single isomer.

After obtaining various macrodiolides **10** incorporating dioxa-bridged bicyclic systems, we were further interested in illustrating the scope and synthetic utility of the tandem cyclization–cycloaddition sequence with the π-bond of a C=C group. Towards this, a mixture of bis-diazocarbonyl compound **3b** and divinyl compound **9a** in benzene was refluxed in the presence of rhodium(II) acetate dimer as catalyst to furnish the conformationally restricted symmetric macrodiolide **11a** in 58% yield (Scheme 5). The ^1H NMR spectrum of product **11a** exhibited a characteristic doublet of doublet at δ = 1.70, 2.63, and 3.96. ^{13}C NMR and DEPT-135 spectral analyses of product **11a** showed peaks for three CH_3 carbons, five CH_2 carbons, five CH carbons, and seven quaternary carbons including two carbonyl groups. The product assignment was further supported by using COSY and HSQC experiments. Similar reaction of bis-diazocarbonyl compounds **3a**,**d** and divinyl derivatives **9a**,**b** afforded macrodiolides **11b**,**c** in moderate yields, respectively. In line with products **10**, the compounds **11** might also be a mixture of isomers.

The above results show that the carbonyl ylide dipoles involved in the mechanism while furnishing symmetric macrodiolides **10** and **11**. This process involves rapid cyclization of the transient rhodium carbenoid **12** onto the neighboring ring carbonyl group to give intramolecular five-membered-ring bis-carbonyl ylide **13**. Subsequent intermolecular 1,3-dipolar cycloaddition of ylide **13** with the π-bond of **8**/**9** affording mono-cycloadduct **14** and their successive cyclization–cycloaddition afforded symmetric macrodiolide (Scheme 6) in a tandem manner. This protocol demonstrates the tandem intermolecular 1,3-dipolar cycloaddition of bis-diazocarbonyl compounds with dicarbaldehyde or divinyl compounds affording macrocycles **10** or **11**.

In conclusion, we have demonstrated that the rhodium(II) acetate catalyzed 1,3-dipolar cycloaddition reaction of bis-five-membered-ring carbonyl ylides across π-bonds of vinyl and carbaldehyde functionalities provides novel conformationally restricted symmetric macrodiolides incorporating aryl, oxa/dioxa-bridged units. This tandem intramolecular cyclization–intermolecular cycloaddition sequence is particularly attractive as it forms carbon–carbon and carbon–oxygen bonds concomitantly in a single step under mild experimental conditions. These conformationally restricted macrodiolides were assembled efficiently from simple starting materials without using dilution methods.



Scheme 6 Mechanistic pathway

Melting points were determined on a capillary melting point apparatus and are uncorrected. IR spectra were recorded using ATR technique on a Bruker Alpha FT-IR spectrophotometer. ^{1}H NMR spectra were recorded on a Bruker DPX 200 and Bruker Avance 400 using $CDCl_3$ relative to TMS as an internal standard. ^{13}C NMR spectra were recorded at 100 MHz in $CDCl_3$ relative to the center of the triplet δ = 77.7 for $CDCl_3$. Carbon types were determined using DEPT experiments. HRMS analyses were performed using electrospray ionization technique on a Waters QTof-micromass spectrometer. All solvents were purified by distillation following standard procedures. TLC was performed on silica gel or alumina plates and components visualized by observation under I_2/UV light at 254 nm. Column chromatography was performed on silica gel (100–200, 230–400 mesh). Analytical HPLC was performed on an Agilent 1200 infinity series. All the reactions were conducted in oven-dried glassware under a positive pressure of argon with magnetic stirring. Reagents were added via syringes through septa. The dr was determined using 400 MHz ^{1}H NMR spectrum of the corresponding crude mixture.

Methyl 4,4-Dimethyl-3,5-dioxohexanoate (1)
A soln of *i*-PrMgBr (49.5 mmol) in anhyd THF (50 mL) was added dropwise to a soln of freshly prepared monomethyl malonate (3.2 g, 27.1 mmol) in anhyd CH_2Cl_2 (10 mL) until propane was evolved. To this mixture was added a freshly prepared soln of 2,2-dimethyl-3-oxobutyryl chloride (2.95 g, 19.9 mmol) in anhyd CH_2Cl_2 (10 mL) dropwise with efficient stirring over 1 h. Subsequent workup as described in the literature[11] and purification using column chromatography (hexane–EtOAc, 60:40) afforded **1** (1.57 g, 42%) as a colorless thin oil.

IR (neat): 2989, 2131, 1924, 1701, 1623, 1327 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.38 (s, 6 H, CH_3), 2.17 (s, 3 H, CH_3), 3.52 (s, 2 H, CH_2), 3.72 (s, 3 H, OCH_3).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.8 (CH_3), 25.2 (CH_3), 44.7 (CH_2), 52.1 (OCH_3), 63.2 (C_q), 167.1 (*C*O_2Me), 202.1 (C=O), 206.9 (C=O).

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_9H_{14}O_4$: 209.0790; found: 209.0786.

Ethane-1,2-diyl Bis(4,4-dimethyl-3,5-dioxohexanoate) (2a); Typical Procedure
To a round-bottomed flask attached to a reflux condenser containing a soln of **1** (500 mg, 2.7 mmol) in toluene (10 mL) was added a soln of ethane-1,2-diol (80 mg, 1.3 mmol) in toluene (2 mL) dropwise and the mixture was refluxed for 24 h (TLC monitoring). The reaction was quenched with H_2O (10 mL) and then it was extracted with CH_2Cl_2 (2 × 10 mL). The combined organic layer was washed with H_2O (15 mL), dried over anhyd Na_2SO_4, concentrated and purified by column chromatography (silica gel, 100–200 mesh, hexane–EtOAc, 80:20) to afford **2a** (410 mg, 41%) as a colorless oil.

IR (neat): 2941, 2867, 1720, 1624, 1576, 1472, 1264, 1161, 733 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.32 (s, 12 H, CH_3), 2.10 (s, 6 H, CH_3), 3.46 (s, 4 H, CH_2), 4.27 (s, 4 H, OCH_2).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.1 (CH_3), 26.2 (CH_3), 45.0 (CH_2), 53.7 (C_q), 62.7 (OCH_2), 166.7 (COO), 202.1 (C=O), 207.2 (C=O).

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{18}H_{26}O_8$: 393.1525; found: 393.1522.

Propane-1,3-diyl Bis(4,4-dimethyl-3,5-dioxohexanoate) (2b)
Following the typical procedure for **2a** from **1** gave **2b** as a colorless oil; yield: 526 mg (51%).

IR (neat): 2987, 1746, 1724, 1702, 1265, 1042, 743 cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.29 (s, 12 H, CH_3), 1.94 (q, *J* = 6.2 Hz, 2 H, CH_2), 2.08 (s, 6 H, CH_3), 3.42 (s, 4 H, CH_2), 4.17 (q, *J* = 6.4 Hz, 4 H, OCH_2).

^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 20.9 (CH_3), 25.9 (CH_3), 27.5 (CH_2), 44.9 (OCH_2), 61.7 (OCH_2), 62.5 (C_q), 166.7 (COO), 202.1 (C=O), 206.9 (C=O).

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{19}H_{28}O_8$: 407.1682; found: 407.1689.

Butane-1,4-diyl Bis(4,4-dimethyl-3,5-dioxohexanoate) (2c)
Following the typical procedure for **2a** from **1** gave **2c** as a colorless oil; yield: 100 mg (39%).

IR (neat): 2984, 1744, 1715, 1702, 1618, 1266, 948, 610 cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.25 (s, 12 H, CH_3), 1.60 (t, *J* = 4.6 Hz, 4 H, CH_2), 2.04 (s, 6 H, CH_3), 3.38 (s, 4 H, CH_2), 4.03 (t, *J* = 4.0 Hz, 4 H, OCH_2).

^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 20.8 (CH_3), 24.8 (CH_2), 25.8 (CH_3), 44.9 (CH_2), 62.4 (C_q), 64.8 (OCH_2), 166.7 (COO), 202.2 (C=O), 206.9 (C=O).

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{20}H_{30}O_8$: 421.1838; found: 421.1841.

Octane-1,8-diyl Bis(4,4-dimethyl-3,5-dioxohexanoate) (2d)
Following the typical procedure for **2a** from **1** gave **2d** as a colorless oil; yield: 466 mg (38%).

IR (neat): 2984, 1899, 1744, 1715, 1702, 1618, 1266, 948 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.24 (s, 8 H, CH_2), 1.31 (s, 12 H, CH_3), 1.53–1.59 (m, 4 H, CH_2), 2.09 (s, 6 H, CH_3), 3.41 (s, 4 H, CH_2), 4.04 (t, *J* = 6.8 Hz, 4 H, OCH_2).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.1 (CH_3), 21.1 (CH_2), 24.6 (CH_2), 25.2 (CH_3), 27.4 (CH_2), 28.0 (CH_2), 44.2 (CH_2), 61.8 (C_q), 64.5 (OCH_2), 166.0 (COO), 201.4 (C=O), 206.1 (C=O).

HRMS (ESI):*m*/*z* [M + Na]$^+$ calcd for $C_{24}H_{38}O_8$: 477.2464; found: 477.2461.

Ethane-1,2-diyl Bis(2-diazo-4,4-dimethyl-3,5-dioxohexanoate) (3a); Typical Procedure
To a soln containing **2a** (400 mg, 1.0 mmol) in anhyd CH_2Cl_2 (5 mL) at 0 °C under argon atmosphere was added freshly distilled Et_3N (273 mg, 2.7 mmol), then, methanesulfonyl azide (392 mg, 3.24 mmol) was added dropwise. After completion (TLC monitoring), the mixture was washed with H_2O (2 × 10 mL). The solvent was removed under reduced pressure at r.t. and the residue subjected to column chromatography (alumina, hexane–EtOAc, 70:30) to afford bis-diazo ketone **3a** (438 mg, 96%) as a greenish viscous oil.

IR (neat): 2941, 2124, 1682, 1588, 1526, 1365, 1159, 1086, 746 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.32 (s, 12 H, CH_3), 2.17 (s, 6 H, CH_3), 4.33 (s, 4 H, OCH_2).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 22.3 (CH_3), 25.3 (CH_3), 59.8 (C_q), 62.6 (OCH_2), 75.5 (C_q), 160.8 (C_q), 191.8 (C=O), 208.5 (C=O).

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{18}H_{22}N_4O_8$: 445.1335; found: 445.1332.

Propane-1,3-diyl Bis(2-diazo-4,4-dimethyl-3,5-dioxohexanoate) (3b)
Following the typical procedure for **3a** from **2b** gave **3b** as a yellowish green solid; yield: 400 mg (88%); mp 56–58 °C.

IR (neat): 2931, 2146, 1715, 1653, 1312, 1027, 838 cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.28 (s, 12 H, CH_3), 1.93 (m, 2 H), 2.13 (s, 6 H, CH_3), 4.12 (t, *J* = 6.0 Hz, 4 H, OCH_2).

^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 22.1 (CH_3), 25.0 (CH_3), 27.8 (CH_2), 59.6 (C_q), 61.3 (OCH_2), 75.7 (C_q), 160.7 (COO), 191.7 (C=O), 208.3 (C=O).

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{19}H_{24}N_4O_8$: 459.1492 found: 459.1490.

Butane-1,4-diyl Bis(2-diazo-4,4-dimethyl-3,5-dioxohexanoate) (3c)
Following the typical procedure for **3a** from **2c** gave **3c** as a yellowish green solid; yield: 402 mg (89%); mp 59–61 °C.

IR (neat): 2977, 2138, 1707, 1644, 1392, 1331, 1309, 1162, 1008, 968 cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.40 (s, 12 H, CH_3), 1.73 (s, 4 H, CH_2), 2.26 (s, 6 H, CH_3), 4.20 (s, 4 H, OCH_2).

^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 22.2 (CH_3), 24.9 (CH_2), 25.1 (CH_3), 59.7 (C_q), 64.3 (OCH_2), 75.5 (C_q), 160.9 (COO), 191.9 (C=O), 208.4 (C=O).

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{20}H_{26}N_4O_8$: 473.1648; found: 473.1644.

Octane-1,8-diyl Bis(2-diazo-4,4-dimethyl-3,5-dioxohexanoate) (3d)
Following the typical procedure for **3a** from **2d** gave **3d** as a yellowish green solid; yield: 410 mg (92%); mp 65–67 °C.

IR (neat): 2932, 2858, 2137, 1701, 1653, 1469, 1314, 1122, 1011, 968, 747 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.25 (s, 8 H, CH_2), 1.34 (s, 12 H, CH_3), 1.56–1.59 (m, 4 H, CH_2), 2.19 (s, 6 H, CH_3), 4.08 (t, *J* = 6.8 Hz, 4 H, OCH_2).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 22.5 (CH_3), 25.4 (CH_3), 25.6 (CH_2), 28.5 (CH_2), 29.0 (CH_2), 59.9 (C_q), 65.4 (OCH_2), 75.6 (C_q), 161.2 (COO), 192.3 (C=O), 208.7 (C=O).

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{24}H_{34}N_4O_8$: 529.2274; found: 529.2270.

Ethane-1,2-diyl Bis[5,6-Bis(methoxycarbonyl)-3,3,4-trimethyl-2-oxo-7-oxabicyclo[2.2.1]hept-5-ene-1-carboxylate] (4a); Typical Procedure
To a soln containing DMAD (84 mg, 0.6 mmol) and $Rh_2(OAc)_4$ (1.0 mol%) in anhyd benzene (5 mL) was added dropwise a soln of bis-diazo **3a** (100 mg, 0.2 mmol) in anhyd benzene (5 mL). The mixture was refluxed for 1 h and evaporated to obtain the crude mixture, which was purified by column chromatography (silica gel, 100–200 or 200–400 mesh, hexane–EtOAc, 60:40) to furnish the desired bis-cycloadduct **4a** (150 mg, 72%, mixture of two inseparable diastereomers) as a viscous oil.

IR (neat): 2954, 1749, 1739, 1716, 1657, 1441, 1266, 1202, 739 cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.02 (s, 6 H, CH_3), 1.17 (s, 6 H, CH_3), 1.65 (s, 6 H, CH_3), 3.71 (s, 6 H, OCH_3), 3.77 (s, 6 H, OCH_3), 4.43 (s, 4 H, OCH_2).

^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 13.5 (CH_3), 20.8 (CH_3), 22.4 (CH_3), 43.0 (C_q), 52.5 (OCH_3), 52.8 (OCH_3), 63.1 (OCH_2), 91.7 (C_q), 144.1 (C_q), 161.3 (COO), 162.0 (COO), 203.1 (C=O).

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{30}H_{34}O_{16}$: 673.1745; found: 673.1738.

Propane-1,3-diyl Bis[5,6-bis(methoxycarbonyl)-3,3,4-trimethyl-2-oxo-7-oxabicyclo[2.2.1]hept-5-ene-1-carboxylate] (4b)
Following the typical procedure for **4a** from **3b** gave **4b** as a viscous oil; yield: 94 mg (62%).

IR (neat): 2979, 1715, 1655 1440, 1204, 1026 cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.03 (s, 6 H, CH_3), 1.17 (s, 6 H, CH_3), 1.66 (s, 6 H, CH_3), 1.99–2.04 (m, 2 H, CH_2), 3.72 (s, 6 H, OCH_3), 3.78 (s, 6 H, OCH_3), 4.29 (m, 4 H, OCH_2).

^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 13.7 (CH_3), 20.9 (CH_3), 22.6 (CH_3), 27.8 (CH_2), 43.2 (C_q), 52.6 (OCH_3), 52.9 (OCH_3), 62.6 (OCH_2), 91.7 (C_q), 91.8 (C_q), 142.6 (C_q), 144.1 (C_q), 162.1 (COO), 162.4 (COO), 203.7 (C=O).

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{31}H_{36}O_{16}$: 687.1901; found: 687.1897.

Butane-1,4-diyl Bis[5,6-bis(methoxycarbonyl)-3,3,4-trimethyl-2-oxo-7-oxabicyclo[2.2.1]hept-5-ene-1-carboxylate] (4c)
Following the typical procedure for **4a** from **3c** gave **4c** as a viscous oil; yield: 98 mg (65%).

IR (neat): 2957, 1743, 1712, 1701, 1658, 1441, 1201, 737 cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.02 (s, 6 H, CH_3), 1.17 (s, 6 H, CH_3), 1.66 (s, 6 H, CH_3), 1.71 (s, 4 H, CH_2), 3.72 (s, 6 H, OCH_3), 3.77 (s, 6 H, OCH_3), 4.25 (br s, 4 H, OCH_2).

^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 13.7 (CH_3), 20.9 (CH_3), 22.5 (CH_3), 24.7 (CH_2), 43.2 (C_q), 52.5 (OCH_3), 52.8 (OCH_3), 65.7 (OCH_2), 91.1 (C_q), 91.7 (C_q), 142.8 (C_q), 144.0 (C_q), 161.4 (COO), 162.3 (COO), 162.5 (COO), 203.7 (C=O).

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{32}H_{38}O_{16}$: 701.2058; found: 701.2054.

Ethane-1,2-diyl Bis(6,6,7-trimethyl-1,3,5-trioxo-2-phenyloctahydro-1*H*-4,7-epoxyisoindole-4-carboxylate) (5a)
Following the typical procedure for **4a** from **3a** gave **5a** as a white solid; yield: 145 mg (86%); mp 216–218 °C.

IR (neat): 2985, 1756, 1718, 1598, 1456, 1391 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ (mixture of two diastereomers) = 1.04 (s, 3 H, CH_3), 1.06 (s, 3 H, CH_3), 1.10 (s, 3 H, CH_3), 1.13 (s, 3 H, CH_3), 1.52 (s, 6 H, CH_3), 3.26 (d, *J* = 7.2 Hz, 1 H, CH), 3.29 (d, *J* = 7.6 Hz, 1 H, CH), 3.55 (d, *J* = 7.6 Hz, 1 H, CH), 3.62 (d, *J* = 7.6 Hz, 1 H, CH), 4.43–4.73 (m, 4 H, OCH_2), 7.15–7.19 (m, 4 H, H_{Ar}), 7.31–7.36 (m, 6 H, H_{Ar}).

^{13}C NMR (100 MHz, $CDCl_3$): δ (mixture of two diastereomers) = 13.38 (CH_3), 13.40 (CH_3), 19.2 (CH_3), 20.76 (CH_3), 20.84 (CH_3), 48.1 (CH), 48.2 (CH), 49.2 (CH), 49.3 (CH), 51.15 (C_q), 51.20 (C_q), 63.25 (OCH_2), 63.33 (OCH_2), 88.79 (C_q), 88.85 (C_q), 90.2 (C_q), 90.3 (C_q), 126.4 (CH), 129.05 (CH), 129.08 (C_q), 129.2 (CH), 134.2 (C_q), 162.4 (COO), 162.5 (COO), 171.7 (CON), 171.8 (CON), 173.50 (CON), 173.53 (CON), 206.7 (C=O).

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{38}H_{36}N_2O_{12}$: 735.2166; found: 735.2162.

Propane-1,3-diyl Bis(6,6,7-trimethyl-1,3,5-trioxo-2-phenyloctahydro-1*H*-4,7-epoxyisoindole-4-carboxylate) (5b)
Following the typical procedure for **4a** from **3b** gave **5b** as a white solid; yield: 156 mg (94%); mp 205–207 °C.

IR (neat): 2360, 1773, 1742, 1718, 1387, 1138 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ (mixture of two diastereomers) = 1.06 (s, 3 H, CH_3), 1.08 (s, 3 H, CH_3), 1.10 (s, 3 H, CH_3), 1.15 (s, 3 H, CH_3), 1.53 (s, 3 H, CH_3), 1.54 (s, 3 H, CH_3), 2.16–2.19 (m, 2 H, CH_2), 3.30 (d, *J* = 5.6 Hz, 1 H, CH), 3.32 (d, *J* = 5.6 Hz, 1 H, CH), 3.51 (d, *J* = 7.2 Hz, 1 H, CH), 3.56 (d, *J* = 7.2 Hz, 1 H, CH), 4.47–4.52 (m, 4 H, OCH_2), 7.16–7.18 (m, 4 H, H_{Ar}), 7.31–7.41 (m, 6 H, H_{Ar}).

^{13}C NMR (100 MHz, $CDCl_3$): δ (mixture of two diastereomers) = 13.1 (CH_3), 18.9 (CH_3), 20.5 (CH_3), 27.4 (CH_2), 48.1 (CH), 49.1 (CH), 50.9 (C_q), 62.4 (OCH_2), 88.5 (C_q), 89.8 (C_q), 125.9 (CH), 128.8 (CH), 129.0 (CH), 131.3 (C_q), 162.4 (COO), 171.7 (CON), 173.3 (CON), 206.9 (C=O).

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{39}H_{38}N_2O_{12}$: 749.2322; found: 749.2319.

Butane-1,4-diyl Bis(6,6,7-trimethyl-1,3,5-trioxo-2-phenyloctahydro-1*H*-4,7-epoxyisoindole-4-carboxylate) (5c)
Following the typical procedure for **4a** from **3c** gave **5c** as a white solid; yield: 156 mg (95%); mp 230–232 °C.

IR (neat): 2977, 1774, 1745, 1719, 1500, 1385 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ (mixture of two diastereomers) = 1.06 (s, 3 H, CH_3), 1.08 (s, 3 H, CH_3), 1.15 (s, 6 H, CH_3), 1.54 (s, 3 H, CH_3), 1.55 (s, 3 H, CH_3), 1.90–1.92 (s, 4 H, CH_2), 3.28 (d, *J* = 7.2 Hz, 1 H, CH), 3.32 (d, *J* = 7.2 Hz, 1 H, CH), 3.53 (d, *J* = 7.2 Hz, 1 H, CH), 3.63 (d, *J* = 7.2 Hz, 1 H, CH), 4.37–4.38 (m, 4 H, OCH_2), 7.16–7.18 (m, 4 H, H_{Ar}), 7.31–7.41 (m, 6 H, H_{Ar}).

^{13}C NMR (100 MHz, $CDCl_3$): δ (mixture of two diastereomers) = 13.4 (CH_3), 19.2 (CH_3), 19.3 (CH_3), 20.9 (CH_3), 25.08 (CH_2), 25.12 (CH_2), 48.26 (CH), 48.29 (CH), 49.1 (CH), 51.2 (C_q), 66.0 (OCH_2), 88.9 (C_q), 89.0 (C_q), 90.0 (C_q), 90.1 (C_q), 126.39 (CH), 126.42 (CH), 129.1 (CH), 129.3 (CH), 131.4 (C_q), 162.7 (COO), 171.8 (CON), 173.5 (CON), 207.3 (C=O).

HRMS (ESI):*m*/*z* [M + Na]$^+$ calcd for $C_{40}H_{40}N_2O_{12}$: 763.2479; found: 763.2477.

Ethane-1,2-diyl Bis(1,6,6-trimethyl-5-oxo-3-phenyl-2,7-dioxabicyclo[2.2.1]heptane-4-carboxylate) (7a); Typical Procedure
To a soln containing benzaldehyde **6a** (63 mg, 0.6 mmol) and $Rh_2(OAc)_4$ (1.0 mol%) in anhyd benzene (5 mL) was added dropwise a soln of bis-diazo compound **3a** (100 mg, 0.2 mmol) in anhyd benzene (4 mL). The mixture was refluxed for 1 h and the solvent was removed under reduced pressure. Further chromatographic purification (hexane–EtOAc, 60:40) afforded **7a** (104 mg, 76%) as a white solid; mp 195–197 °C.

IR (neat): 2930, 1786, 1743, 1659, 1400, 1150, 893 cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ (mixture of two diastereomers) = 1.21 (s, 6 H, CH_3), 1.26 (s, 6 H, CH_3), 1.79 (s, 6 H, CH_3), 3.76–3.94 (m, 4 H, OCH_2), 4.95 (s, 1 H, OCH), 4.97 (s, 1 H, OCH), 7.27–7.37 (m, 10 H, H_{Ar}).

^{13}C NMR (50.3 MHz, $CDCl_3$): δ (mixture of two diastereomers) = 14.7 (CH_3), 19.3 (CH_3), 21.0 (CH_3), 53.1 (C_q), 62.3 (OCH_2), 79.3 (OCH), 92.0 (C_q), 113.5 (C_q), 127.6 (=CH), 128.3 (=CH), 129.2 (=CH), 135.8 (C_q), 161.9 (COO), 206.2 (C=O).

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{32}H_{34}O_{10}$:601.2050; found: 601.2047.

Butane-1,4-diyl Bis(1,6,6-trimethyl-5-oxo-3-phenyl-2,7-dioxabicyclo[2.2.1]heptane-4-carboxylate) (7b)
Following the typical procedure for **7a** from **3c** gave **7b** as a yellow solid; yield: 108 mg (80%); mp 198–200 °C.

IR (neat): 2972, 1782, 1751, 1730, 1451, 1404, 1342, 1128, 1061, 699 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ (mixture of two diastereomers) = 1.10–1.14 (m, 4 H, CH_2), 1.13 (s, 6 H, CH_3), 1.17 (s, 6 H, CH_3), 1.70 (s, 6 H, CH_3), 3.68–3.73 (m, 2 H, OCH_2), 3.86–3.92 (m, 2 H, OCH_2), 4.85 (s, 1 H, OCH), 4.86 (s, 1 H, OCH), 7.22–7.25 (m, 6 H, H_{Ar}), 7.29–7.31 (m, 4 H, H_{Ar}).

^{13}C NMR (100 MHz, $CDCl_3$): δ (mixture of two diastereomers) = 14.8 (CH_3), 19.3 (CH_3), 21.0 (CH_3), 24.6 (CH_2), 53.1 (C_q), 64.9 (OCH_2), 79.3 (OCH), 92.3 (C_q), 113.4 (C_q), 127.7 (=CH), 128.3 (=CH), 129.2 (=CH), 136.01 (C_q), 136.03 (C_q), 162.2 (COO), 206.7 (C=O).

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{34}H_{38}O_{10}$: 629.2363; found: 629.2354.

Propane-1,3-diyl Bis[3-(3-methoxyphenyl)-1,6,6-trimethyl-5-oxo-2,7-dioxabicyclo[2.2.1]heptane-4-carboxylate] (7c)
Following the typical procedure for **7a** from **3b** gave **7c** as a white solid; yield: 127 mg (85%); mp 226–228 °C.

IR (neat): 2924, 1749, 1604, 1459, 1336, 1154, 1053, 864, 693 cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ (mixture of two diastereomers) = 1.19 (s, 6 H, CH_3), 1.22 (s, 6 H, CH_3), 1.41–1.47 (m, 2 H, CH_2), 1.76 (s, 6 H, CH_3), 3.77 (s, 6 H, OCH_3), 3.86–3.99 (m, 4 H, OCH_2), 4.88 (s, 1 H, OCH), 4.90 (s, 1 H, OCH), 6.82–6.93 (m, 6 H, H_{Ar}), 7.16–7.29 (m, 2 H, H_{Ar}).

^{13}C NMR (50.3 MHz, $CDCl_3$): δ (mixture of two diastereomers) = 14.6 (CH_3), 19.2 (CH_3), 20.8 (CH_3), 27.5 (CH_2), 52.9 (C_q), 55.1 (OCH_3), 61.7 (OCH_2), 79.0 (OCH), 92.1 (C_q), 113.1 (C_q), 113.2 (=CH), 114.6 (=CH), 119.9 (=CH), 129.2 (=CH), 137.4 (C_q), 159.4 (C_q), 161.9 (COO), 206.4 (C=O).

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{35}H_{40}O_{12}$: 675.2417; found: 675.2411.

Butane-1,4-diyl Bis[3-(3-methoxyphenyl)-1,6,6-trimethyl-5-oxo-2,7-dioxabicyclo[2.2.1]heptane-4-carboxylate] (7d)
Following the typical procedure for **7a** from **3c** gave **7d** as a white solid; yield: 130 mg (88%); mp 233–235 °C.

IR (neat): 2926, 1753, 1603, 1466, 1401, 1336, 1153, 1058, 857, 781 cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ (mixture of two diastereomers) = 1.18 (s, 6 H, CH_3), 1.22 (s, 6 H, CH_3), 1.37–1.46 (m, 4 H, CH_2), 1.76 (s, 6 H, CH_3), 3.76 (s, 6 H, OCH_3), 3.89–4.17 (m, 4 H, OCH_2), 4.90 (s, 2 H, OCH), 6.82–6.96 (m, 6 H, H_{Ar}), 7.17–7.25 (m, 2 H, H_{Ar}).

^{13}C NMR (50.3 MHz, $CDCl_3$): δ (mixture of two diastereomers) = 14.6 (CH_3), 19.2 (CH_3), 20.8 (CH_3), 24.5 (CH_2), 52.9 (C_q), 55.1 (OCH_3), 64.8 (OCH_2), 79.0 (OCH), 92.1 (C_q), 113.2 (=CH), 114.4 (=CH), 119.9 (=CH), 129.2 (=CH), 137.4 (C_q), 159.4 (C_q), 162.0 (COO), 206.5 (C=O).

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{36}H_{42}O_{12}$: 689.2574; found: 689.2567.

Butane-1,4-diyl Bis[3-(3-fluorophenyl)-1,6,6-trimethyl-5-oxo-2,7-dioxabicyclo[2.2.1]heptane-4-carboxylate] (7e)
Following the typical procedure for **7a** using **3c** gave **7e** as a yellow solid; yield: 120 mg (84%); mp 227–229 °C.

IR (neat): 2969, 1787, 1749, 1731, 1606, 1512, 1405, 1343, 1230, 1127, 1062, 892, 840 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ (mixture of two diastereomers) = 1.13 (s, 6 H, CH_3), 1.16 (s, 6 H, CH_3), 1.23–1.26 (m, 4 H, CH_2), 1.69 (s, 6 H, CH_3), 3.73–3.78 (m, 2 H, OCH_2), 3.95–4.00 (m, 2 H, OCH_2), 4.86 (s, 2 H, OCH), 6.95 (t, J = 8.4 Hz, 3 H, H_{Ar}), 7.08 (t, J = 8.8 Hz, 1 H, H_{Ar}), 7.23 (m, 3 H, H_{Ar}), 8.05 (dd, J_1 = 8.8 Hz, J_2 = 5.6 Hz, 1 H, H_{Ar}).

^{13}C NMR (100 MHz, $CDCl_3$): δ (mixture of two diastereomers) = 14.8 (CH_3), 19.3 (CH_3), 21.0 (CH_3), 24.7 (CH_2), 53.1 (C_q), 65.0 (OCH_2), 78.6 (OCH), 92.2 (C_q), 113.5 (C_q), 115.2 (=CH), 115.4 (=CH), 115.6 (=CH), 115.9 (=CH), 129.5 (=CH), 129.6 (=CH), 162.01 (C_q), 162.03 (C_q), 164.5 (COO), 206.5 (C=O).

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{34}H_{36}F_2O_{10}$: 665.2174; found: 665.2166.

Butane-1,4-diyl Bis[1,6,6-trimethyl-3-(3-nitrophenyl)-5-oxo-2,7-dioxabicyclo[2.2.1]heptane-4-carboxylate] (7f)
Following the typical procedure for **7a** from **3c** gave **7f** as a yellow solid; yield: 122 mg (79%); mp 240–242 °C.

IR (neat): 2926, 1784, 1754, 1704, 1605, 1534, 1402, 1352, 1262, 1154, 1061, 891, 735 cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ (mixture of two diastereomers) = 1.22 (s, 6 H, CH_3), 1.26 (s, 6 H, CH_3), 1.45 (s, 4 H, CH_2), 1.83 (s, 6 H, CH_3), 3.84–3.89 (m, 2 H, OCH_2), 4.05–4.09 (m, 2 H, OCH_2), 5.10 (s, 2 H, OCH), 7.50–7.58 (m, 2 H, H_{Ar}), 7.73–7.77 (m, 2 H, H_{Ar}), 8.18–8.26 (m, 4 H, H_{Ar}).

^{13}C NMR (50.3 MHz, $CDCl_3$): δ (mixture of two diastereomers) = 14.5 (CH_3), 19.0 (CH_3), 20.8 (CH_3), 24.5 (CH_2), 53.1 (C_q), 65.1 (OCH_2), 77.8 (OCH), 92.0 (C_q), 114.0 (C_q), 122.5 (=CH), 123.8 (=CH), 129.2 (=CH), 133.5 (=CH), 138.2 (C_q), 148.0 (C_q), 161.7 (COO), 205.3 (C=O).

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{34}H_{36}N_2O_{14}$: 719.2064; found: 719.2060.

Propane-1,3-diyl Bis(3-(2-hydroxyphenyl)-1,6,6-trimethyl-5-oxo-2,7-dioxabicyclo[2.2.1]heptane-4-carboxylate) (7g)
Following the typical procedure for **7a** from **3b** gave **7g** as a brown gel; yield: 98 mg (68%).

IR (neat): 3326, 1786, 1748, 1702, 1608, 1527, 1359, 1260, 1151, 1056, 889, 730 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ (mixture of two diastereomers) = 0.86–0.88 (m, 2 H, CH_2), 1.19 (s, 6 H, CH_3), 1.24 (s, 6 H, CH_3), 1.77 (s, 6 H, CH_3), 3.83–3.95 (m, 2 H, OCH_2), 4.02–4.03 (m, 1 H, OCH_2), 4.11–4.13 (m, 2 H, OCH_2), 5.34 (s, 2 H, OCH), 6.76–6.89 (m, 4 H, H_{Ar}), 7.15–7.20 (m, 2 H, H_{Ar}), 7.30–7.33 (m, 2 H, H_{Ar}).

^{13}C NMR (100 MHz, $CDCl_3$): δ (mixture of two diastereomers) = 14.7 (CH_3), 19.4 (CH_3), 21.0 (CH_3), 52.9 (C_q), 53.0 (C_q), 62.0 (OCH_2), 62.2 (OCH_2), 75.2 (OCH), 75.4 (OCH), 91.6 (C_q), 91.7 (C_q), 113.8 (C_q), 113.9 (C_q), 116.6 (=CH), 117.0 (=CH), 120.7 (=CH), 120.8 (=CH), 129.89 (=CH), 129.93 (=CH), 130.68 (=CH), 130.73 (=CH), 154.0 (C_q), 162.5 (COO), 162.6 (COO), 206.5 (CO), 206.8 (CO).

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{33}H_{36}O_{12}$: 647.2104; found: 647.2097.

1,3-Bis(2-vinylphenoxy)propane (9a); Typical Procedure
To a soln of Wittig salt (1.88 g, 5.2 mmol) in anhyd THF (20 mL) at –10 °C was added a soln of BuLi (15%, 2.5 mL, 5.6 mmol) and the mixture was stirred for 15 min. Then, a soln of dicarbaldehyde **8a** (500 mg, 1.7 mmol) in anhyd THF (10 mL) was added and the mixture was stirred for 1 h. The mixture was quenched with sat. NH_4Cl (20 mL) and extracted with EtOAc (2 × 20 mL). The combined organic layer was washed with H_2O (15 mL), dried over anhyd Na_2SO_4 and concentrated. The residue was purified by column chromatography (silica gel, 100–200 mesh, hexane–EtOAc, 90:10) to afford **9a** (417 mg, 84%) as a white solid; mp 149–151 °C.

IR (neat): 3013, 2944, 2875, 1592, 1450, 1233, 1107, 984, 900, 738 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.22–2.28 (m, 2 H, CH_2), 4.12 (t, J = 6.0 Hz, 4 H, OCH_2), 5.16 (dt, J_1 = 11.2 Hz, J_2 = 1.6 Hz, 2 H, =CH_2), 5.65 (dt, J_1 = 11.2 Hz, J_2 = 1.6 Hz, 2 H, =CH_2), 6.79–6.87 (m, 4 H, H_{Ar}), 6.94–7.02 (m, 2 H, H_{Ar}), 7.13 (td, J_1 = 8.4 Hz, J_2 = 1.6 Hz, 2 H, ArCH), 7.39 (dd, J_1 = 7.6 Hz, J_2 = 1.2 Hz, 2 H, =CH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 29.5 (CH_2), 64.9 (OCH_2), 112.0 (=CH), 114.4 (=CH_2), 120.8 (=CH), 126.5 (=CH), 126.8 (C_q), 128.9 (=CH), 131.6 (=CH), 155.9 (C_q).

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{19}H_{20}O_2$: 303.1361; found: 303.1359.

1,6-Bis(2-vinylphenoxy)hexane (9b)
Following the typical procedure for **9a** from **8b** gave **9b** as a white solid; yield: (357 mg, 72%); mp 157–159 °C.

IR (neat): 3066, 3010, 2942, 2877, 1594, 1450, 1230, 1109, 9823, 740 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.52 (s, 4 H, CH_2), 1.81 (s, 4 H, CH_2), 3.93 (t, J = 6.0 Hz, 4 H, OCH_2), 5.15–5.18 (m, 2 H, =CH_2), 5.65–5.75 (m, 2 H, =CH_2), 6.77–6.86 (m, 4 H, H_{Ar}), 6.95–7.03 (m, 2 H, H_{Ar}), 7.12–7.18 (m, 2 H, H_{Ar}), 7.39–7.41 (m, 2 H, H_{Ar}).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 26.0 (CH_2), 29.3 (CH_2), 68.1 (OCH_2), 111.9 (=CH), 114.2 (=CH_2), 120.5 (=CH), 126.5 (=CH), 126.8 (C_q), 128.8 (=CH), 131.7 (=CH), 156.3 (C_q).

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{22}H_{26}O_2$: 345.1830; found: 345.1828.

(4b*R*,6*S*,8a*S*,16a*S*,19*S*,20a*R*)-6,7,7,18,18,19-Hexamethyl-6,7,11,12,13,14,18,19,27,28-decahydro-4b*H*-6,8a:16a,19-diepoxydibenzo[*f*,*t*]dipyrano[2,3-*h*:3′,2′-*r*][1,5,11,16]tetraoxacyclohenicosine-8,9,16,17(20a*H*,26*H*)-tetraone (10a); Typical Procedure
To a soln of **8a** (63 mg, 0.2 mmol) and $Rh_2(OAc)_4$ (1.0 mol%) in anhyd benzene (5 mL) was added dropwise a soln of bis-diazo compound **3c** (100 mg, 0.2 mmol) in anhyd benzene (5 mL). The mixture was refluxed for 1 h and the solvent was removed under reduced pressure. Further chromatographic purification (hexane–EtOAc, 60:40) afforded **10a** (80 mg, 53%) as a white solid; mp 215–217 °C.

IR (neat): 2931, 1778, 1752, 1683, 1601, 1464, 1399, 1335, 1246, 1147, 1058, 759 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.70–0.74 (m, 4 H, CH_2), 1.14 (s, 6 H, CH_3), 1.20 (s, 6 H, CH_3), 1.67 (s, 6 H, CH_3), 2.18–2.20 (m, 2 H, CH_2), 3.38–3.44 (m, 2 H, OCH_2), 3.90–3.93 (m, 2 H, OCH_2), 4.05–4.09 (m, 2 H, OCH_2), 4.34–4.40 (m, 2 H, OCH_2), 5.53 (s, 2 H, OCH), 6.86–6.93 (m, 4 H, H_{Ar}), 7.22–7.26 (m, 2 H, H_{Ar}), 7.51 (dd, J_1 = 8.0 Hz, J_2 = 2.0 Hz, 2 H, H_{Ar}).

^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 14.8 (CH_3), 19.4 (CH_3), 20.9 (CH_3), 24.9 (CH_2), 29.5 (CH_2), 53.1 (C_q), 63.2 (OCH_2), 64.7 (OCH_2), 71.4 (OCH), 92.0 (C_q), 111.1 (=CH), 112.7 (C_q), 121.1 (=CH), 124.2 (C_q), 128.9 (=CH), 130.3 (=CH), 156.1 (C_q), 162.4 (COO), 206.9 (C=O).

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{37}H_{42}O_{12}$: 701.2574; found: 701.2571.

Crystal data for **10a**: (CCDC 900352) $C_{37}H_{42}O_{12}$, M = 678.71, 0.17 × 0.11 × 0.08 mm triclinic, space group P-1 with a = 9.2900(9) Å, b = 12.2162(11) Å, c = 31.952(3) Å, α = 99.062(2), β = 95.660(2), γ = 99.688(2), V = 3500.5(6) Å^3, T = 100(2) K, R_1 = 0.0579, wR_2 = 0.1393 on observed data, z = 4, D_{calcd} = 1.288 mg cm^{-3}, F(000) = 1440, absorption coefficient = 0.096 mm^{-1}, λ = 0.71073 Å, 12084 reflections were collected on a smart apex CCD single crystal diffractometer 9283 observed reflections [$I \geq 2\sigma$ (I)]. The largest difference peak and hole = 1.024 and –0.319 eÅ^{-3}, respectively. The structure was solved by direct methods and refined by full-matrix least squares on F^2 using SHELXL–97 software.

(3*S*,4a*R*,17b*R*,19*S*,21a*S*,27a*S*)-2,2,3,19,20,20-Hexamethyl-2,3,11,12,19,20,24,25-octahydro-1*H*-3,27a:19,21a-diepoxydibenzo[*h*,*o*]dipyrano[3,2-*f*:2′,3′-*q*][1,4,10,14]tetraoxacyclononadecine-1,21,22,27(4a*H*,10*H*,17b*H*)-tetraone (10b)

Following the typical procedure for **10a** from **3a** and **8a** gave **11b** as a white solid; yield: 86 mg (56%); mp 205–207 °C.

IR (neat): 2972, 1782, 1755, 1689, 1600, 1459, 1288, 1244, 756 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.11 (s, 6 H, CH_3), 1.20 (s, 6 H, CH_3), 1.68 (s, 6 H, CH_3), 2.20–2.30 (m, 4 H, CH_2), 2.32–2.34 (m, 2 H, OCH_2), 3.97–4.01 (m, 2 H, OCH_2), 4.29–4.40 (m, 2 H, OCH_2), 5.55 (s, 2 H, OCH), 6.90 (q, J = 7.6 Hz, 4 H, H_{Ar}), 7.27 (dt, J_1 = 7.6 Hz, J_2 = 1.6 Hz, 2 H, H_{Ar}), 7.45 (dd, J_1 = 7.6 Hz, J_2 = 1.6 Hz, 2 H, H_{Ar}).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.7 (CH_3), 19.5 (CH_3), 21.0 (CH_3), 29.5 (CH_2), 53.2 (C_q), 62.8 (OCH_2), 64.8 (OCH_2), 72.0 (OCH), 91.8 (C_q), 110.6 (=CH), 112.9 (C_q), 121.0 (=CH), 123.4 (C_q), 128.7 (=CH), 130.6 (=CH), 155.8 (C_q), 162.4 (COO), 206.5 (C=O).

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{35}H_{38}O_{12}$: 673.2261; found: 673.2258.

(2*S*,4a*S*,11a*S*,14*S*,15a*R*,28b*R*)-2,3,3,13,13,14-Hexamethyl-2,3,8,9,13,14,22,23-octahydro-2,4a:11a,14-diepoxydibenzo[*f*,*s*]dipyrano[2,3-*h*:3′,2′-*q*][1,5,11,15]tetraoxacycloicosine-4,5,11,12(7*H*,15a*H*,21*H*,28b*H*)-tetraone (10c)

Following the typical procedure for **10a** from **3b** and **8a** gave **10c** as a white solid; yield: 75 mg (50%); mp 210–212 °C.

IR (neat): 2965, 2926, 1780, 1750, 1689, 1601, 1400, 1334, 1262, 1056, 802, 750 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.78–0.83 (m, 2 H, CH_2), 1.13 (s, 6 H, CH_3), 1.20 (s, 6 H, CH_3), 1.67 (s, 6 H, CH_3), 2.21–2.22 (m, 2 H, CH_2), 2.91–2.97 (m, 2 H, OCH_2), 3.74–3.80 (m, 2 H, OCH_2), 3.95–3.98 (m, 2 H, OCH_2), 4.30–4.36 (m, 2 H, OCH_2), 5.50 (s, 2 H, OCH), 6.87 (t, J = 7.6 Hz, 2 H, H_{Ar}), 6.93 (d, J = 8.0 Hz, 2 H, H_{Ar}), 7.26 (dt, J_1 = 8.4 Hz, J_2 = 1.6 Hz, 2 H, H_{Ar}), 7.47 (dd, J_1 = 7.6 Hz, J_2 = 1.6 Hz, 2 H, H_{Ar}).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.8 (CH_3), 19.5 (CH_3), 21.0 (CH_3), 26.6 (CH_2), 29.4 (CH_2), 53.1 (C_q), 61.6 (OCH_2), 63.1 (OCH_2), 71.4 (OCH), 92.2 (C_q), 111.2 (=CH), 112.9 (C_q), 121.1 (=CH), 124.3 (C_q), 128.7 (=CH), 130.5 (=CH), 156.1 (C_q), 162.6 (COO), 207.4 (C=O).

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{36}H_{40}O_{12}$: 687.2417; found: 687.2412.

(2*R*,4a*S*,11a*S*,14*R*,15a*R*,28b*R*)-2,3,3,13,13,14-Hexamethyl-1,2,3,8,9,13,14,15,15a,22,23,28b-dodecahydro-2,4a:11a,14-diepoxytetrabenzo[*f*,*h*,*q*,*s*][1,5,11,15]tetraoxacycloicosine-4,5,11,12(7*H*,21*H*)-tetraone (11a)

Following the typical procedure for **10a** from **3b** and **9a** gave **11a** as a white solid; yield: 88 mg (58%); mp 202–204 °C.

IR (neat): 2973, 1767, 1742, 1495, 1454, 1333, 1243, 1130, 1054, 842, 731 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.88–0.91 (m, 2 H, CH_2), 1.10 (s, 6 H, CH_3), 1.12 (s, 6 H, CH_3), 1.48 (s, 6 H, CH_3), 1.70 (dd, J_1 = 13.1 Hz, J_2 = 6.2 Hz, 2 H, CH_2), 2.17–2.26 (m, 2 H, CH_2), 2.63 (dd, J_1 = 13.1 Hz, J_2 = 9.1 Hz, 2 H, CH_2), 2.73 (dt, J_1 = 13.1 Hz, J_2 = 6.6 Hz, 2 H, OCH_2), 3.70 (dt, J_1 = 13.7 Hz, J_2 = 6.9 Hz, 2 H, OCH_2), 3.96 (dd, J_1 = 9.1 Hz, J_2 = 6.2 Hz, 2 H, CH), 4.01 (dt, J_1 = 8.7 Hz, J_2 = 3.2 Hz, 2 H, OCH_2), 4.21–4.27 (m, 2 H, OCH_2), 6.81 (td, J_1 = 7.6 Hz, J_2= 0.8 Hz, 2 H, H_{Ar}), 6.90 (dd, J_1 = 8.4 Hz, J_2 = 0.8 Hz, 2 H, H_{Ar}), 7.14 (td, J_1 = 8.4 Hz, J_2 = 1.6 Hz, 2 H, H_{Ar}), 7.37 (dd, J_1 = 8.0 Hz, J_2 = 1.6 Hz, 2 H, H_{Ar}).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 16.7 (CH_3), 20.0 (CH_3), 20.7 (CH_3), 26.3 (CH_2), 29.7 (CH_2), 38.7 (CH), 44.0 (CH_2), 50.4 (C_q), 61.2 (OCH_2), 63.3 (OCH_2), 87.2 (C_q), 93.8 (C_q), 111.0 (=CH), 121.3 (=CH), 127.3 (=CH), 128.4 (=CH), 129.9 (C_q), 155.5 (C_q), 164.9 (COO), 210.9 (C=O).

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{38}H_{44}O_{10}$: 683.2832; found: 683.2834.

(3*R*,4a*R*,17b*R*,19*R*,21a*S*,27a*S*)-2,2,3,19,20,20-Hexamethyl-2,3,4,4a,11,12,17b,18,19,20,24,25-dodecahydro-1*H*-3,27a:19,21a-diepoxytetrabenzo[*f*,*h*,*o*,*q*][1,4,10,14]tetraoxacyclononadecine-1,21,22,27(10*H*)-tetraone (11b)

Following the typical procedure for **11a** from **3a** and **9a** gave **11b** as a white solid; yield: 84 mg (55%); mp 191–193 °C.

IR (neat): 2978, 2931, 2361, 1743, 1455, 1377, 1284, 1114, 1052, 863, 733 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.10 (s, 12 H, CH_3), 1.48 (s, 6 H, CH_3), 1.67 (dt, J_1 = 12.2 Hz, J_2 = 2.4 Hz, 2 H, OCH_2), 1.75 (dd, J_1 = 13.0 Hz, J_2 = 6.4 Hz, 2 H, CH_2), 2.20–2.23 (m, 2 H, CH_2), 2.63 (dd, J_1 = 13.0 Hz, J_2 = 9.2 Hz, 2 H, CH_2), 4.01–4.02 (m, 2 H, OCH_2), 4.04 (dd, J_1 = 9.24 Hz, J_2 = 6.4 Hz, 2 H, CH_2), 4.25–4.34 (m, 2 H, OCH_2), 4.32 (dd, J_1 = 10.0 Hz, J_2 = 2.4 Hz, 2 H, OCH_2), 6.81 (td, J_1 = 7.6 Hz, J_2 = 0.8 Hz, 2 H, H_{Ar}), 6.90 (dd, J_1 = 8.4 Hz, J_2 = 0.8 Hz, 2 H, H_{Ar}), 7.17 (td, J_1 = 8.4 Hz, J_2 = 1.6 Hz, 2 H, H_{Ar}), 7.33 (dd, J_1 = 7.6 Hz, J_2 = 1.6 Hz, 2 H, H_{Ar}).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 16.7 (CH_3), 20.1 (CH_3), 20.6 (CH_3), 29.6 (CH_2), 39.3 (CH), 43.6 (CH_2), 50.4 (C_q), 62.7 (OCH_2), 64.2 (OCH_2), 87.1 (C_q), 93.1 (C_q), 110.7 (=CH), 121.0 (=CH), 127.4 (=CH), 128.57 (C_q), 128.64 (=CH), 155.6 (C_q), 164.7 (COO), 210.0 (C=O).

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{37}H_{42}O_{10}$: 669.2676; found: 669.2673.

(4b*R*,6*R*,8a*S*,20a*S*,23*R*,24a*R*)-6,7,7,22,22,23-Hexamethyl-4b,5,6,7,11,12,13,14,15,16,17,18,22,23,24,24a,30,31,32,33,34,35-docosahydro-6,8a:20a,23-diepoxytetrabenzo[*c*,*e*,*o*,*q*][1,7,14,20]tetraoxacyclooctacosine-8,9,20,21-tetraone (11c)

Following the typical procedure for **11a** from **3d** and **9b** gave **11c** as a white solid; yield: 91 mg (60%); mp 215–217 °C.

IR (neat): 2929, 2856, 1769, 1745, 1493, 1454, 1333, 1245, 1110, 1086, 754 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.00–1.20 (m, 24 H), 1.48 (s, 6 H, CH_3), 1.67 (dd, J_1 = 13.2 Hz, J_2 = 6.0 Hz, 4 H, CH_2), 1.79 (s, 6 H, CH_2), 2.63 (dd, J_1 = 12.8 Hz, J_2 = 10.0 Hz, 2 H, CH), 3.63–3.65 (m, 2 H, CH_2), 3.84–3.97 (m, 8 H, OCH_2), 6.81 (dd, J_1 = 16 Hz, J_2 = 7.2 Hz, 4 H, H_{Ar}), 7.07–7.10 (m, 2 H, H_{Ar}), 7.42 (d, J = 7.2 Hz, 2 H, H_{Ar}).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 16.7 (CH_3), 20.0 (CH_3), 20.7 (CH_3), 23.4 (CH_2), 26.0 (CH_2), 26.3 (CH_2), 28.7 (CH_2), 29.7 (CH_2), 38.7 (CH), 44.1 (CH_2), 50.4 (C_q), 61.2 (OCH_2), 63.3 (OCH_2), 87.6 (C_q), 93.8 (C_q), 110.3 (=CH), 120.5 (=CH), 126.3 (=CH), 127.5 (=CH), 128.5 (C_q), 155.0 (C_q), 165.5 (COO), 209.5 (C=O).

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{46}H_{60}O_{10}$: 795.4084; found: 795.4081.

Acknowledgment

This research was supported by Department of Science and Technology (DST), New Delhi. MS thanks CSIR-SRF, for a research fellowship. We thank DST, New Delhi for providing 400 MHz NMR facility under FIST program.

Supporting Information for this article is available online at http://www.thieme-connect.com/ejournals/toc/synthesis.

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(14) CCDC-900352 (for **10a**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

