ON THE REACTION OF DIPIVALOYLKETENE DIMER WITH OXIMES AND HYDRAZINES - SYNTHESIS OF TETRAOXAADAMANTANES

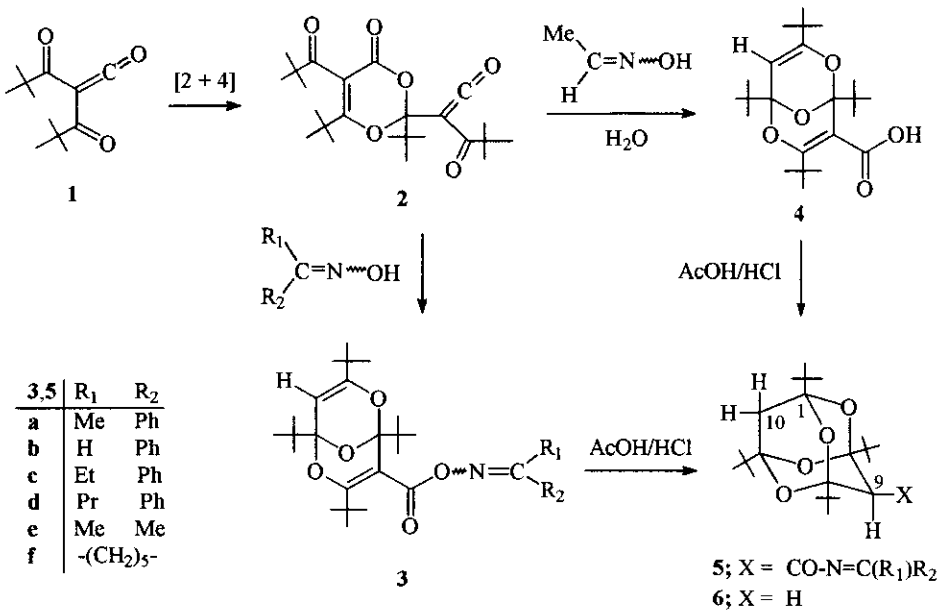
Turkaram S. Dalvi,[a] C. Oliver Kappe,[a] Curt Wentrup,[b] and Gert Kollenz[a,*]

[a] Institute of Organic Chemistry, KF-University of Graz, A-8010 Graz, Austria
[b] Chemistry Department, University of Queensland, Brisbane, Q-4072, Australia

Abstract - Synthesis of mono-functionalized trioxabicyclo[3.3.1]nona-3,7-dienes („bridged bisdioxines") (**3**) as well as (**7**), and their transformation into the corresponding 2,4,6,8-tetraoxadamantanes (**5**) and (**8**), respectively, by proton-catalyzed hydrolysis, is described.

Dipivaloylketene (**1**), generated in excellent yield by preparative flash vacuum pyrolysis (FVP) of the corresponding furandione,[1] and its dimer (**2**), obtained in quantitative yield from an unusual [4+2] - dimerization of **1** ,[1] represent extraordinarily stable α-oxo ketenes.[2] Their chemical behaviour towards nucleophiles (amines and alcohols) as well as dienophiles has already been reported.[1,3,4] In particular, an unusual chiral and concave trioxabicyclo[3.3.1]nona-3,7-diene ring system ("bridged bisdioxine")[5] is formed by addition of primary aromatic amines to the dimeric ketene (**2**) during a one-step process,[2] which, furthermore, as described in a preliminary communication,[6] can be converted into the uncommon 2,4,6,8-tetraoxaadamantane core. In clear contrast to these findings, more basic aliphatic amines afford the corresponding dipivaloylacetamides, *via* a cycloreversion of the dioxinone ring of **2**.[3] On the other hand, in case of simple OH-nucleophiles like alcohols or water, the primary addition products onto the ketene moiety of **2** were isolated and subsequently, by treatment with *p*-TsOH in acetonitrile, transfered into bi-functionalized bridged bisdioxines having still one (or two) carboxylic acid functionalities within the molecule.[3] These divergent results prompted us to extend our investigations on several further nucleophiles and their behaviour towards the dimeric oxo ketene (**2**).

Thus, when various oximes as formal OH-nucleophiles have been employed under the usual reaction conditions (room temperature, dichloromethane, 24 h) to our surprise the reaction did not follow the pathway observed with alcohols, but instead spontaneous evolution of carbon dioxide occurred and the bridged bisdioxines (**3**) were obtained in moderate yields (40–75%). This is analogous to the experimental result observed from reactions of **2** with primary aromatic amines.[3]



3,5	R_1	R_2
a	Me	Ph
b	H	Ph
c	Et	Ph
d	Pr	Ph
e	Me	Me
f	$-(CH_2)_5-$	

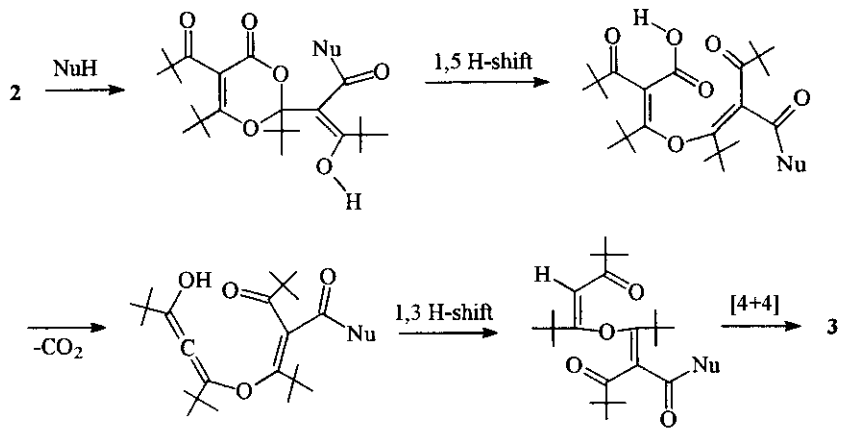
Scheme 1

Apart from the results of elemental analyses and IR absorptions (e.g. 1765-1730 cm^{-1} for the ester moiety), structural elucidation of the bridged bisdioxines (**3**) is mainly based upon the very characteristical singlets due to the CH=C protons of the heterocyclic ring in the ^{1}H-NMR spectra (4.70-4.85 ppm), as found for several analogues where the structures were confirmed by an X-Ray study.[3] As an example, the ^{13}C-NMR spectrum of **3a** exhibits structure determinant signals at 167.4 (C=O), 163.6, 165.7 (C-3, C-7), 162.0 (C=N), 101.3, 90.5 (C-4, C-8), 99.2, 98.1 (C-1, C-5) ppm. The assignment of these signals is again based upon comparison with close analogues representing identical heterocyclic systems (see ref. 3; for further analytical and spectroscopic data of **3** see the Experimental Part).

The product obtained from reaction of **2** with acetaldoxime in rather low yield (20%) was identified as the corresponding mono-carboxylic acid (**4**), obviously the result of a hydrolytic cleavage of the acylated oxime side chain. It is interesting to note that this mono acid (**4**) was not obtainable by any other route so far, since addition of water to the dimeric ketene (**2**) affords a bis acid [3] and all attempts to decarboxylate this compound failed.[3]

A reasonable mechanistic pathway regarding the transformation of the dimeric oxo ketene (**2**) into the trioxabicyclo[3.3.1]nonadiene skeleton (e.g. **3**), supported by semiempirical AM1 calculations,[3] is detailed in Scheme 2. Addition of the nucleophile to the ketene moiety in **2** produces the expected addition product which undergoes a 1,5 H-shift followed by decarboxylation. The resulting intermediate can

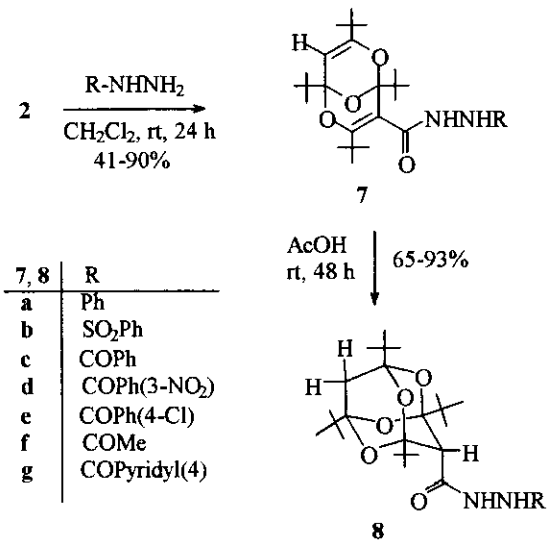
tautomerize to an oxygen-bridged double 1,3-oxadiene which can cyclize to the final bisdioxine system *via* a pseudopericyclic [4+4] tandem cyclization. The mechanism outlined in Scheme 2 is analogous to the reaction of dimeric oxo ketene (**2**) with aromatic amines that we have reported earlier.[3]



Scheme 2

Following the procedure recently published in preliminary form,[6] bridged bisdioxines (**3**) and (**4**) can easily be converted into the corresponding 2,4,6,8-tetraoxaadamantanes (**5**) and (**6**), respectively, in high yields (60-90%) under acidic hydrolytic conditions (AcOH/aqueous HCl). In the case of the transformation **4** → **6** adamantane formation is accompanied by spontaneous decarboxylation to yield the known[6] unsubstituted tetraoxadamantane (**6**). It seems remarkable, that neither the ester group nor the C=N-moiety is hydrolized under these conditions. A more general discussion of this unusual transformation will be reported in due course. The tetraoxaadamantanes (**5**) and (**6**) are achiral (no splitting of signals in the ^{1}H-NMR spectrum after adding the chiral shift reagent Eu(hfc)$_3$) and exhibit C_s symmetry, the acylated oxime substituent at C-9 should occupy a position nearly perpendicular to the plane bisecting the adamantane moiety as revealed by the X-Ray data of a close analogue.[5] Thus, the axial/equatorial positions at C-9 are equivalent, as verified by the ^{1}H-NMR spectra of **5a–e** and **6**, where only one singlet is observed for the protons at C-9 (δ = 2.9-3.0 ppm), respectively. The corresponding signals for the CH_2-group at C-10 are found between δ = 1.68 and 1.77 ppm. In the ^{13}C-NMR spectrum of **5a** as an example, the carbon atoms of the adamantyl nucleus appear at δ = 99.6, 100.7, 100.9, 101.2 (quarternary carbons C-1, C-3, C-5, C-7), 42.9 (CH, C-9), 26.5 (CH_2, C-10). The IR absorption bands for the ester carbonyls are found at 1745-1790 cm^{-1}. All spectroscopic data are in excellent agreement with those found for structural analogues.[5]

Reaction of the dimeric α-oxo ketene (**2**) with phenylhydrazine and several hydrazides [7] under reaction conditions similar to those described above for oximes again resulted in the formation of the corresponding bridged bisdioxines (**7**) in moderate to good yields (60-90%). No break-up of the trioxabicyclo-[3.3.1]nonadiene ring system was observed as found from interaction of aliphatic amines with **2**.[3] Structural confirmation was successfully made following the criteria employed for the closely related analogues **3**. In particular, the CH=C protons of the bisdioxine skeleton in **7** are again located at δ = 4.80-4.87 ppm, and the vicinal NH-groups in **7c-g** exhibit doublets at 8.38-8.67 as well as 9.22-9.57 ppm, respectively; for further analytical and spectroscopic details see the Experimental Part.



7, 8	R
a	Ph
b	SO_2Ph
c	COPh
d	$COPh(3\text{-}NO_2)$
e	COPh(4-Cl)
f	COMe
g	COPyridyl(4)

Scheme 3

The conversion of the bridged bisdioxines (**7**) into the corresponding tetraoxaadamantanes (**8**) in moderate to good yields (65-93%) was again easily achieved under the usual acidic hydrolysis conditions. In the ^{1}H-NMR spectra of **8** the singlets at δ = 1.77-2.08 ppm are assigned to the two protons at C-10; the signals at δ = 2.78-3.08 ppm correspond to the proton at C-9. Both agree well with chemical shift values of close analogues e.g. **5** and literature data (see discussion above and ref. 5).

EXPERIMENTAL

Melting points were determined on a Tottoli Apparatus and are uncorrected. Elemental Analyses were performed with a Carlo Erba Elemental Analyzer. IR spectra were recorded on a Perkin Elmer 421. ^{1}H and

^{13}C NMR spectra were obtained on a Varian 200 Gemini spectrometer and a Bruker AM360 spectrometer with TMS as internal standard.

Synthesis of Functionalized Bridged Bisdioxines (**3**). - General Procedure

To a solution of the oxime (0.5 mmol in 2 mL of dichloromethane), equimolar amounts of the dimeric oxo ketene (**2**) were added and the reaction mixture was stirred at 20°C for 24 h. After evaporating the solvent, a colourless solid product was obtained and recrystallized from acetonitrile.

*Methylphenylmethyleneamino 1,3,5,7-Tetra-t-butyl-2,6,9-trioxabicyclo[3.3.1]nona-3,7-diene-4-carboxylate (**3a**)*

2 (210 mg) and acetophenone oxime (70 mg); yield 180 mg (74%); mp 145-146°C. IR(KBr): 3020-2810 (CH), 1760 (C=O), 1660 (C=N), 1610 (C=C) cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ = 1.04, 1.15, 1.16, 1.18 (4s, 36H, *t*-Bu), 2.40 (s, 3H, Me), 4.75 (s, 1H, H-8), 7.35-7.85 (m, 5H, Ar-H) ppm; ^{13}C-NMR ($CDCl_3$): δ = 14.8 (CH_3); 24.3, 24.8, 27.9, 28.9 ($C(\underline{C}H_3)_3$); 34.5, 37.5, 39.6, 41.9 ($\underline{C}(CH_3)_3$); 90.5 (C-8), 98.1, 99.2 (C-1, C-5); 101.3 (C-4), 126.7, 127.2, 128.7, 130.5, 135.1 (Ar-C); 162.0 (C=N), 163.7, 165.7 (C-3, C-7), 167.4 (C=O) ppm; Anal. Calcd for $C_{31}H_{45}NO_5$: C 72.77, H 8.87, N 2.73; Found: C 72.81, H 8.80, N 2.70.

*Phenylmethyleneamino 1,3,5,7-Tetra-t-butyl-2,6,9-trioxabicyclo[3.3.1]nona-3,7-diene-4-carboxylate (**3b**)*

2 (110 mg) and benzaldehyde oxime (30 mg); yield 70 mg (60%); mp 113-114°C. IR(KBr): 3010-2810 (CH), 1760 (C=O), 1660 (C=N), 1610 (C=C) cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ = 1.04, 1.10, 1.12, 1.15 (4s, 36H, *t*-Bu), 4.75 (s, 1H, H-8), 7.35-7.80 (m, 5H, Ar-H), 8.35 (s, 1H, CH=) ppm; Anal. Calcd for $C_{30}H_{43}NO_5$: C 72.43, H 8.65, N 2.81; Found: C 72.25, H 8.68, N 2.81.

*Ethylphenylmethyleneamino 1,3,5,7-Tetra-t-butyl-2,6,9-trioxabicyclo[3.3.1]nona-3,7-diene-4-carboxylate (**3c**)*

2 (210 mg) and propiophenone oxime (75 mg); yield: 160 mg (61%); mp 125-126°C. IR(KBr): 3040-2810 (CH), 1765 (C=O), 1665 (C=N), 1620 (C=C); ^{1}H-NMR ($CDCl_3$): δ = 1.04, 1.14, 1.15, 1.17 (4s, 36H, *t*-Bu), 1.20 (t, *J* = 6.0 Hz, 3H, CH_3), 2.90 (q, *J* = 6.0 Hz, 2H, CH_2), 4.73 (s, 1H, H-8), 7.38-7.80 (m, 5H, Ar-H) ppm; Anal. Calcd for $C_{32}H_{47}NO_5$: C 73.14, H 8.95, N 2,66; Found: C 73.37, H 9.07, N 2.63.

*Phenylpropylmethyleneamino 1,3,5,7-Tetra-t-butyl-2,5,9-trioxabicyclo[3.3.1]nona-3,7-diene-4-carboxylate (**3d**)*

2 (210 mg) and butyrophenone oxime (85 mg); yield: 180 mg (74%); mp 115-116°C. IR(KBr): 3020-2820 (CH), 1750 (C=O), 1660 (C=N), 1620 (C=C) cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ = 0.95 (t, *J* = 7.5 Hz, 3H, CH_3), 1.04, 1.11, 1.14, 1.16 (s, 36H, *t*-Bu), 1.40-1.60 (m, 2H, CH_2), 2.95 (t, *J* = 7.5 Hz, 2H, CH_2), 4.85 (s, 1H,

H-8), 7.45-7.85 (m, 5H, Ar-H) ppm; Anal. Calcd for $C_{33}H_{49}NO_5$: C 73.43, H 9.19, N 2.59; Found: C 73.39, H 9.10, N 2.54.

Dimethylmethylenamino 1,3,5,7-Tetra-t-butyl-2,6,9-trioxabicyclo[3.3.1]nona-3,7-diene-4-carboxylate (3e)

2 (150 mg) and acetone oxime (30 mg); yield: 90 mg (42%); mp 69-70°C (n-hexane). IR(KBr): 3050-2800 (CH), 1755 (C=O), 1655 (C=N), 1610 (C=C); ^{1}H-NMR ($CDCl_3$): δ = 1.00, 1.08, 1.10, 1.14 (s, 36H, *t*-Bu), 2.00, 2.08 (s, 6H, CH_3), 4.70 (s, 1H, H-8) ppm; Anal. Calcd for $C_{26}H_{43}NO_5$: C 69.48, H 9.57, N 3.11; Found: C 69.22, H 9.46, N 2,98.

Cyclohexylideneamino 1,3,5,7-Tetra-t-butyl-2,6,9-trioxabicyclo[3.3.1]nona-3,7-diene-4-carboxylate (3f)

2 (210 mg) and cyclohexanone oxime (60 mg); yield: 140 mg (60%); mp 93-94°C. IR(KBr): 3020-2810 (CH), 1730 (C=O), 1660 (C=N), 1610 (C=C); ^{1}H-NMR ($CDCl_3$): δ = 1.02, 1.08, 1.10, 1.12 (s, 36H, *t*-Bu), 1.55-1.70 (m, 6H, 3 CH_2), 2.45-2.66 (m, 4H, 2CH_2), 4.70 (s, 1H, H-8); Anal. Calcd for $C_{29}H_{47}NO_5$: C 71.16, H 9.61, N 2.86; Found: C 70.76, H 9.76, N 2.77.

1,3,5,7-Tetra-t-butyl-2,6,9-trioxabicyclo[3.3.1]nona-3,7-diene-4-carboxylic acid (4)

150 mg of **2** and 25 mg of acetaldehyde oxime react under conditions described in the General Procedure. After recrystallization from acetonitrile 50 mg (20%) of **4** are obtained, mp 138-139°C. IR(KBr): 3300-3020 (br, OH), 3000-2800 (CH), 1685, 1655 (C=O), 1610 (C=C) cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ = 1.02, 1.09, 1.11, 1.15 (s, 36H, *t*-Bu), 4.70 (s, 1H, H-8); Anal. Calcd for $C_{23}H_{38}O_5$: C 70.05, H 9.64; Found: C 70.02, H 9.61.

Synthesis of Functionalized 2,4,6,8-Tetraoxaadamantanes (5). - General Procedure

0.5 mL of acetic acid and 100 mg of concentrated hydrochloric acid were added to a solution of 0.2 mmol of the corresponding bisdioxine (**3**) in 1.5 mL of dichloromethane. This mixture was stirred at 20°C for 48 h. After evaporation of the solvent a colourless crude product precipitates, which was washed with cold acetonitrile and further purified by recrystallization from acetonitrile.

Methylphenylmethylenamino 1,3,5,7-Tetra-t-butyl-2,4,6,8-tetraoxaadamantane-9-carboxylate (5a)

100 mg of **3a**; yield: 60 mg (58%); mp 159-161°C. IR(KBr): 3040-2820 (CH), 1785 (C=O) cm^{-1}; ^{1}H-NMR($CDCl_3$): δ = 0.98, 1.02, 1.08 (s, 36H, *t*-Bu), 1.68 (s, 2H, CH_2), 2.45 (s, 3H, CH_3), 2.98 (s, 1H; CH), 7.34-7.85 (m, 5H, Ar-H) ppm; ^{13}C-NMR ($CDCl_3$): δ = 14.6 (CH_3), 23.5, 24.1, 24.5, 24.8 (C($\underline{C}H_3$)$_3$), 26.6 (t, C-10), 38.2, 38.5, 40.7 ($\underline{C}(CH_3)_3$, 42.4 (d, C-9), 99.6, 100.7, 101.5 (C-1, C-3, C-5, C-7), 127.2, 128.5, 130.6, 135.1 (Ar-C), 162.0 (C=N), 165,2 (C=O) ppm; Anal. Calcd for $C_{31}H_{47}NO_6$: C 70.32, H 8.88, N 2.65; Found: C 70.06, H 8.78, N 2.69.

*Phenylmethylenamino 1,3,5,7-Tetra-t-butyl-2,4,6,8-tetraoxaadamantane-9-carboxylate (**5b**)*

140 mg of **3b**; yield: 100 mg (81%); mp 196-197°C. IR(KBr): 3050-2800 (CH), 1745 (C=O) cm^{-1}; ^{1}H-NMR($CDCl_3$): δ = 0.91, 0.95, 1.00, 1.06 (s, 36H, *t*-Bu), 1.77 (s, 2H, CH_2), 2.98 (s, 1H, CH), 7.35-7.83 (*m*, 5H, Ar-H), 8.38 (s, 1H, CH=) ppm; Anal. Calcd for $C_{30}H_{45}NO_6$: C 69.87, H 8.79, N 2.71; Found: C 69.86, H 8.80, N 2.65.

*Ethylphenylmethylenamino 1,3,5,7-Tetra-t-butyl-2,4,6,8-tetraoxaadamantane-9-carboxylate (**5c**)*

100 mg of **3c**; Yield: 90 mg (87%); mp 148-150°C. IR(KBr): 3080-2900 (CH), 1785 (CO) cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ = 0.97, 1.02, 1.04, 1.09 (s, 36H, *t*-Bu), 1.25 (t, *J* = 7.4 Hz, 3H, CH_3), 1.70 (s, 2H, CH_2), 2.93 (q, *J* = 7.4 Hz, 2H, CH_2), 3.00 (s, 1H, CH), 7.35-7.85 (m, Ar-H) ppm; Anal. Calcd for $C_{32}H_{49}NO_6$: C 70.74, H 9.02, N 2.57; Found: C 70.58, H 9.12, N 2.29.

*Phenylpropylmethyleneamino 1,3,5,7-Tetra-t-butyl-2,4,6,8-tetraoxaadamantane-9-carboxylate (**5d**)*

100 mg of **3d**; yield: 70 mg (68%); mp 145-147°C. IR(KBr): 3080-2800 (CH), 1790 (C=O) cm^{-1}; ^{1}H-NMR($CDCl_3$): δ = 0.97, 1.00, 1.03, 1.09 (36H, *t*-Bu, 3H, CH_3), 1.62 (m, 2H, CH_2), 1.69 (s, 2H, CH_2), 2.87 (t, *J* = 7.0 Hz, 2H, CH_2), 2.97 (s, 1H, CH), 7.35-7.82 (m, 5H, Ar-H) ppm; Anal. Calcd for $C_{33}H_{51}NO_6$: C 71.06, H 9.22, N 2.51; Found: C 70.89, H 9.43, N 2.44.

*Dimethylmethyleneamino 1,3,5,7-Tetra-t-butyl-2,4,6,8-tetraoxaadamantane-9-carboxylate (**5e**)*

100 mg of **3e**; Yield : 70 mg (68%); mp 106-108°C. IR(KBr): 3060-2780 (CH), 1780 (C=O) cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ = 0.98, 1.01, 1.07, 1.10 (s, 36H, *t*-Bu), 1.70 (s, 2H, CH_2), 2.07 (s, 3H, CH_3), 2.09 (s, 3H, CH_3), 2.91 (s, 1H, CH) ppm; Anal. Calcd for $C_{26}H_{45}NO_6$: C 66.81, H 9.63, N 2.99; Found: C 67.00, H 9.88, N 2.78.

Conversion of Dimer (**2**) into Functionalized Bridged Bisdioxines (**7**). - General Procedure

Equimolar amounts of dimeric oxo ketene (**2**) were added to a solution of the corresponding acid hydrazide (0.35–0.5 mmol in 2 mL of dichloromethane or acetonitrile) and the mixture was stirred at 20°C (**7b** at 40-45°C) for 24 h. After evaporation of the solvents, the crude product was further purified either by recrystallization from acetonitrile or with aid of chromatographic methods (column or preparative thin layer chromatography).

*N'-Phenyl-1,3,5,7-tetra-t-butyl-2,6,9-trioxabicyclo[3.3.1]nona-3,7-diene-4-carbohydrazide (**7a**)*

40 mg of phenylhydrazine and 150 mg of **2**; Yield: 70 mg (41%, acetonitrile); mp 84-85°C. IR(KBr): 3420, 3280 (NH), 3060-2800 (CH), 1670 (C=O), 1600 (C=C) cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ = 0.19, 1.10, 1.14, 1.24 (s, 36H, *t*-Bu), 4.87 (s, 1H,H-8), 6.83-7.34 (m, 5H, Ar-H) ppm; Anal. Calcd for $C_{29}H_{44}N_2O_4$: C 71.90, H 9.09, N 5.78; Found: C 71.51, H 8.90, N 5.69.

N'-Benzenesulfonyl-1,3,5,7-tetra-t-butyl-2,6,9-trioxabicyclo[3.3.1]nona-3,7-diene-4-carbohydrazide (7b)
60 mg of benzenesulfonic acid hydrazide and 150 mg of **2** in 2 mL of acetonitrile; Yield: 60 mg (30 %), mp 135-136°C (preparative TLC, eluent $CHCl_3$, R_f-value: 0.35). IR(KBr): 3400, 3180 (NH), 3020-2800 (CH), 1655, 1620 (C=O), 1600 (C=C); ^{1}H-NMR ($CDCl_3$): δ = 0.80, 0.83, 0.98, 1.17 (s, 36H, 4 *t*-Bu), 4.80 (s, 1H, H-8), 7.35-8.00 (m, 6H, Ar-H, NH) ppm; Anal. Calcd for $C_{29}H_{44}N_2O_6S$: C 63.48, H 8.08, N 5.10; Found: C 63.49, H 8.12, N 5.06.

N'-Benzoyl-1,3,5,7-tetra-t-butyl-2,6,9-trioxabicyclo[3.3.1]nona-3,7-diene-4-carbohydrazide (7c)
70 mg of benzhydrazide and 210 mg of **2**; Yield: 210 mg (acetonitrile), mp 158-159°C. IR(KBr): 3380, 3300-3150 (NH), 3020-2800 (CH), 1655 (C=O), 1610 (C=C) cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ = 1.04, 1.10, 1.18, 1.25 (s, 36H, *t*-Bu), 4.84 (s, 1H, H-8), 7.38-7.88 (m, 5H, Ar-H), 8.67 (d, *J* = 9.0 Hz, 1H, NH), 9.22 (d, *J* = 9.0 Hz, 1H, NH) ppm; Anal. Calcd for $C_{30}H_{44}N_2O_5$: C 70.28, H 8.65, N 5.46; Found: C 70.30, H 8.68, N 5.50.

N'-(3-Nitrobenzoyl)-1,3,5,7-tetra-t-butyl-2,6,9-trioxabicyclo[3.3.1]nona-3,7-diene-4-carbohydrazide (7d)
60 mg of 3-nitrobenzhydrazide and 140 mg of **2**; Yield: 120 mg (65%); mp 80-82°C (column chromatography: silicagel 60 (70-230 mesh), eluent dichloromethane). IR(KBr): 3380, 3240 (NH), 3010-2760 (CH), 1660, 1640 (C=O) cm^{-1}; ^{1}H-NMR($CDCl_3$): δ = 1.02, 1.09, 1.14, 1.23 (s, 36H, *t*-Bu), 4.85 (s, 1H, H-8), 7.60-7.85 (m, 4H, Ar-H), 8.40 (d, *J* = 9.0 Hz, 1H, NH), 9.57 (d, *J* = 9.0 Hz, 1H, NH) ppm; Anal. Calcd for $C_{30}H_{43}N_3O_7$: C 64.61, H 7.77, N 7,53; Found: C 64.70, H 7.91, N 7,36.

N'-(4-Chlorobenzoyl)-1,3,5,7-tetra-t-butyl-2,6,9-trioxabicyclo[3.3.1]nona-3,7-diene-4-carbohydrazide (7e)
60 mg of 4-chlorobenzhydrazide and 150 mg of **2**; Yield: 140 mg (73%); mp 188-190°C (petrolether/ethylacetate 10:1). IR(KBr): 3380, 3300-3140 (NH), 1660 (C=O), 1610 cm^{-1}: ^{1}H-NMR ($CDCl_3$): δ = 1.05, 1.10, 1.18, 1.25 (s, 36H, *t*-Bu), 4.85 (s, 1H, H-8), 7.38-7.86 (m, 4H, Ar-H), 8.76 (d, *J* = 9.0 Hz, 1H, NH), 9.25 (d, *J* = 9.0 Hz, 1H, NH) ppm; Anal. Calcd for $C_{30}H_{43}N_2O_5Cl$: C 65.86, H 7.92, N 5.12; Found: C 65.90, H 8.18, N 5.10.

N'-Acetyl-1,3,5,7-tetra-t-butyl-2,6,9-trioxabicyclo[3.3.1]nona-3,7-diene-4-carbohydrazide (7f)
35 mg of acethydrazide and 190 mg of **2**; Yield: 160 mg (79%); mp 234-236°C (acetonitrile). IR(KBr): 3425, 3200 (NH), 3120-2700 (CH), 1690, 1655 (C=O), 1620 cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ = 1.02, 1.08, 1.15, 1.20 (s, 36H, *t*-Bu), 2.05 (s, 3H, Me), 4.80 (s, 1H, H-8), 8.38 (d, *J* = 9.0 Hz, 1H, NH), 9.48 (s, 1H, NH) ppm; Anal.Calcd for $C_{25}H_{42}N_2O_5$: C 66.63, H 9.39, N 6.21; Found: C 66.63, H 9.58, N 6.17.

N'-(4-Pyridylcarbonyl)-1,3,5,7-tetra-t-butyl-2,6,9-trioxabicyclo[3.3.1]nona-3,7-diene-4-carbohydrazide (7g)

50 mg of isonicotinic acid hydrazide and 160 mg of **2**; Yield: 170 mg (91%), mp 228-229°C (ethyl acetate). IR(KBr): 3395, 3320-3140 (NH), 3020-2700 (CH), 1660 (C=O), 1620 cm^{-1}; ^{1}H-NMR($CDCl_3$): δ = 1.02, 1.08, 1.18, 1.23 (s, 36H, *t*-Bu), 4.85 (s, 1H, H-8), 7.69 and 8.77 (2d, *J* = 4.5 Hz, 4H, Pyr-H), 8.67 (d, *J* = 9.0 Hz. 1H, NH), 9.55 (d, *J* = 9.0 Hz, 1H, NH) ppm; Anal. Calcd for $C_{29}H_{43}N_3O_5$: C 67.81, H 6.44, N 8.18; Found: 67.98, H 6.64, N 8.32.

Transformation of the Bisdioxines (7) into the 2,4,6,8-Tetraoxaadamantanes (**8**). - General Procedure

0.5 mL of glacial acetic acid and 150 mg of conc. HCl were added to a solution of **7c-g** (approx. 0.2 mmol) in 1.5 mL of dichloromethane. This mixture was stirred at 20°C for 24 h. After removing the solvent *in vacuo*, a colourless crude product was obtained, which could be further purified by crystallization from acetonitrile.

*N'-Benzoyl-1,3,5,7-tetra-t-butyl-2,4,6,8-tetraoxaadamantane-9-carbohydrazide (**8c**)*

150 mg of **7c**; Yield: 140 mg (93%), mp 232-233°C. IR(KBr): 3410, 3220 (NH), 3040-2800 (CH), 1695, 1640 (C=O) cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ = 0.98, 1.02, 1.19 (s, 36H, *t*-Bu), 1.76 (s, 2H, CH_2), 3.00 (s, 1H, CH), 7.37-7.86 (m, 5H, Ar-H), 9.25 (d, *J* = 7.4 Hz, 1H, NH), 9.54 (d, *J* = 7.4 Hz, 1H, NH); Anal. Calcd for $C_{30}H_{46}N_2O_6$: C 67.90, H 8.74, N 5.28; Found: C 68.16, H 8.84, N 5.25.

*N'-(3-Nitrobenzoyl)-1,3,5,7-tetra-t-butyl-2,4,6,8-tetraoxaadamantane-9-carbohydrazide (**8d**)*

120 mg of **7d**; Yield: 80 mg (65%), mp 258-260°C (the crude product was purified by column chromatography (silicagel 60, 70-230 mesh) with $CHCl_3$/MeOH 100:1 as eluent). IR(KBr): 3395, 3200 (NH), 3010-2800 (CH), 1650, 1620 (C=O) cm^{-1}; ^{1}H-NMR (DMSO-d_6): δ = 0.92, 0.95, 1.04, 1.14 (s, 36H, *t*-Bu), 1.80 (s, 2H, CH_2), 2.93 (s, 1H, CH), 7.73-8.48 (m, 4H, Ar-H), 9.0 (d, *J* = 7.0 Hz, 1H, NH), 10.60 (d, *J* = 7.0 Hz, 1H, NH) ppm; Anal.Calcd for $C_{30}H_{45}N_3O_8$: C 62.59, H 7.88, N 7.29; Found: C 62.75, H 8.08, N 7.07.

*N'-(4-Chlorobenzoyl)-1,3,5,7-tetra-t-butyl-2,4,6,8-tetraoxaadamantane-9-carbohydrazide (**8e**)*

130 mg of **7e**; Yield: 120 mg (76%), mp 258-259°C (acetonitrile). IR(KBr): 3380, 3220 (NH), 3030-2780 (CH), 1690, 1640 (C=O) cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ = 0.93, 1.00, 1.17, (s, 38H, *t*-Bu), 1.77 (s, 2H, CH_2), 3.07 (s, 1H, CH), 7.40 and 7.75 (2d, *J* = 8.5 Hz, 4H, Ar-H), 9.38 (d, *J* = 8.2 Hz, 1H, NH), 9.5 (d, *J* = 8.2 Hz, 1H, NH) ppm; Anal. Calcd for $C_{30}H_{45}N_2O_6Cl$: C 63.76, H 8.03, N 4.96; Found: C 63.83, H 8.08, N 4.86.

*N'-Acetyl-1,3,5,7-tetra-t-butyl-2,4,6,8-tetraoxaadamantane-9-carbohydrazide (**8f**)*

110 mg of **7f**; Yield: 90 mg (79%), mp 223-224°C (acetonitrile). IR(KBr): 3390, 3210 (NH), 3040-2760 (CH), 1710, 1640 (C=O) cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ = 0.92, 0.95, 1.00, 1.05 (s, 36H, *t*-Bu), 2.02 (s, 3H,

Me), 2.08 (s, 2H, CH_2), 2.88 (s, 1H, CH), 9.70 (d, J = 6.5 Hz, 1H, NH), 10.45 (d, J = 6.5 Hz, 1H, NH) ppm; Anal. Calcd for $C_{25}H_{44}N_2O_6$: C 64.07, H 9.46, N 5.98; Found: C 64.47, H 9.66, N 5.94.

*N'-(Pyridylcarbonyl)-1,3,5,7-tetra-t-butyl-2,4,6,8-tetraoxaadamantane-9-carbohydrazide (**8g**)*

100 mg of **7g**; Yield: 80 mg (77%), mp 255-257°C (ethyl acetate). IR(KBr): 3540-3400 (br, NH), 3220-3100 (br, NH), 3050-2700 (CH), 1705, 1645 (C=O), 1610 cm^{-1}; ^{1}H-NMR (DMSO-d_6): δ = 0.95, 0.98, 1.15, (s, 36H, *t*-Bu), 2.65 (s, 2H, CH_2), 2.78 (s, 1H, CH), 8.15 and 8.95 (2d, J = 4.5 Hz, 4H, Ar-H), 10.60 (s, 1H, NH), 10.90 (s, 1H, NH) ppm ; Anal. Calcd for $C_{29}H_{45}N_3O_6$: C 65.51, H 8.53, N 7.90; Found: C 65.75, H 8.43, N 7.73.

REFERENCES

1. C. O. Kappe, R. A. Evans, C. H. L. Kennard, and C. Wentrup, *J. Am. Chem. Soc.*, 1991, **116**, 4234; C. O. Kappe, G. Färber, C. Wentrup, and G. Kollenz, *J. Org. Chem.*, 1992, **57**, 7078.
2. C. Wentrup, W. Heilmayer, and G. Kollenz, *Synthesis*, **1994**, 1219.
3. C. O. Kappe, G. Färber, C. Wentrup, and G. Kollenz, *Tetrahedron Lett.*, 1992, **33**, 4553; C. O. Kappe, G. Kollenz, W. M. F. Fabian, C. Wentrup, and G. Färber, *J. Org. Chem.*, 1993, **58**, 3361.
4. C. O. Kappe, C. Wentrup, and G. Kollenz, *Monatsh. Chem.*, 1993, **124**, 1133.
5. A. DeRenzi, A. Panunzi, L. Paolillo, and A. Vitagliano, *J. Organomet. Chem.*, 1977, **124**, 221; R. Mason, and G. B. Robertson, *J. Chem. Soc., A* **1969**, 492; Z. Arnold, and M. Budesinsky, *J. Org. Chem.*, 1988, **53**, 5352; M. Hauteville, R. Stomberg, P. Gaillard, and M. C. Duclos, *Liebigs Ann.*, **1995**, 1707.
6. W. Heilmayer, T. S. Dalvi, C. O. Kappe, C. Wentrup, K. Gruber, H. Sterk, and G. Kollenz, *J. Chem. Soc., Chem. Comm.*, **1995**, 797.
7. Preparation of oximes and hydrazides: A. I. Vogel, "A Text Book of Practical Organc Chemistry", 3rd Edition 1957, p. 345, 395 and 721.

Received, 6th May, 1998