Pergamon

Tetrahedron Vol. 50, No. 29, pp. 8665-8672, 1994
Elsevier Science Ltd
Printed in Great Britain
0040-4020/94 $7.00+0.00

0040-4020(94)00485-4

Synthesis of [10]Heterophanes Using a Ring Enlargement Reaction

Ferrid Hadj-Abo,[1] Stefan Bienz, and Manfred Hesse*

Organisch-chemisches Institut der Universität Zürich, Winterthurerstrasse 190, CH-8057 Zürich

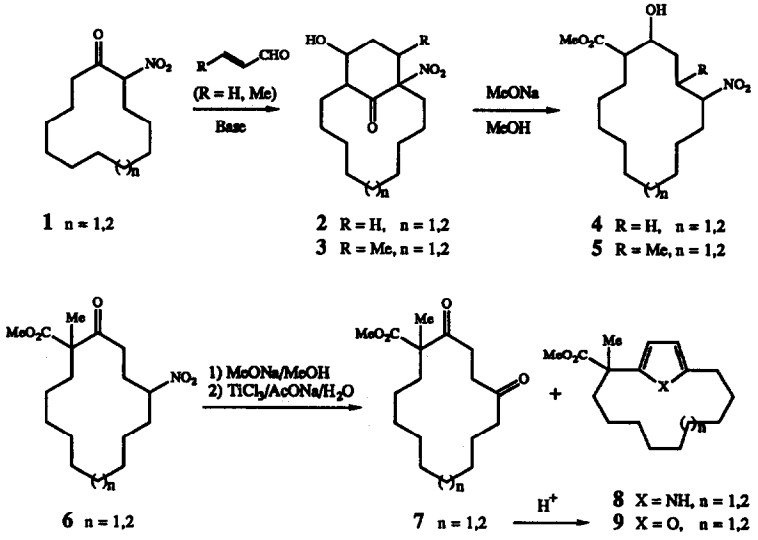
Abstract: The ring enlargement of 2-nitrocyclododecanone (1, n = 1) to methyl 2-hydroxy-5-nitrocyclotetradecane-carboxylate (4, n = 1) *via* 12-hydroxy-1-nitrobicyclo[9.3.1]pentadecane-12-one (2, n = 1) delivered after further transformations in good yield cyclotetradecane-1,4-dione (12). Treatment of this compound with *para*-toluene sulfonic acid at a Dean-Stark water trap afforded [10](2,5)furanophane (20). In presence of ammonia or of a primary amine, the respective [10](2,5)pyrrolophanes 15–19 were obtained. The corresponding preparation of [10](2,5)thiophenophane (21) by action of several sulfuring reagents on 12, however, was less successful. Only small amounts of impure 21 were obtained.

INTRODUCTION

In our preceding investigations towards the syntheses of (±)-muscone[2] and macrocyclic lactone antibiotic A26771B[3] we utilized a novel ring enlargement reaction introduced by Lorenzi-Riatsch *et al.*[4,5](*Scheme 1*). Michael addition of the 2-nitrocycloalkanones 1 to acrylic aldehyde or crotonic aldehyde, respectively, followed by base catalyzed intramolecular aldol reaction afforded the bicyclic compounds 2 or 3, the treatment of which with sodium methoxide in methanol delivered in good to excellent yields the [n+2] ring-enlarged macrocyclic β-hydroxy-ε-nitro carboxylic acid derivatives 4 and 5. These compounds gave after further modification rise to γ-nitroketones: For instance, from the macrocyclic substrates 4 the compounds 6 were obtained by an oxidation/methylation sequence. In the course of our attempts to transfer the $CHNO_2$ unit of 6 into a carbonyl group using a reductive variation of the Nef reaction (MeONa followed by $TiCl_3$[6]), we found that considerable amounts of the pyrrolophanes 8 (up to 16%) were formed in addition to the desired 1,4-diketones 7. The former arose probably from imine intermediates by dehydration. Analogously, the furanophanes 7 (13%) were found as dehydration side products in the acid-catalyzed mono-acetalization of 6 performed as a subsequent step towards the lactone antibiotic A26771B[7].

The synthesis of some heterophanes *via* cycloalkane-1,4-diones is already described in literature: Nozaki and his coworkers have successfully prepared [8](2,5)pyrrolo-, [8](2,5)furano-, and [8](2,5)thiophenophane[8,9] as well as [8](3,6)pyridazinophane[10] using cyclododecane-1,4-dione as the starting material (for reviews on heterophanes see[11-13], for more recent syntheses of functionalized and strained heterophanes[14-18], and for phannomenclature[19-21]). The latter arose from cyclododecanone on a rather tedious synthetic path[22], which is furthermore not flexible concerning the variation of substitution patterns on the cycloalkane-1,4-dione framework.

We would like to show with the example of the synthesis of cyclotetradecane-1,4-dione **12** and with the subsequent conversion of this compound to the [10]heterophanes **15–21** (cf. *Scheme 2*) that the [n+2]-ring enlargement reaction described above provides a more efficient and flexible entry into cycloalkane-1,4-diones and finally into cyclophanes.



1 n = 1,2

2 R = H, n = 1,2
3 R = Me, n = 1,2

4 R = H, n = 1,2
5 R = Me, n = 1,2

6 n = 1,2

7 n = 1,2

8 X = NH, n = 1,2
9 X = O, n = 1,2

Scheme 1

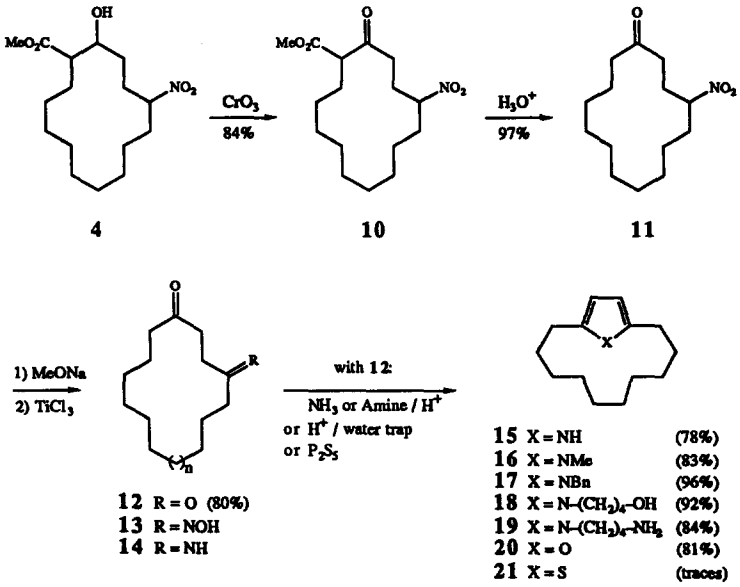
RESULTS

The synthesis of the cyclolkane-1,4-dione **12** starts with the easily accessible cyclotetradecane carboxylic acid derivative **4** already described earlier[4] (*Scheme 2*). Oxidation of the alcoholic moiety of this compound with Jones reagent[23] delivered in 84% yield the β-ketoester **10**, which gave rise to the demethoxycarbonylated γ-nitrocycloalkanone **11** in almost quantitative yield (97%) upon acid catalyzed hydrolysis in water/methanol solution. Earlier attempts to obtain **11** by a base catalyzed hydrolysis/decarboxylation sequence were unsuccessful: For example, treatment of **11** with potassium hydroxide in ethanol at reflux for several hours resulted in a complex mixture of products which contained in addition to diketone **12** and oxime **13** only a number of further compounds lacking the nitro group (IR evidence).

The directed conversion of the nitro compound **11** to the diketone **12** was performed by the well approved Nef type reaction already mentioned above: Deprotonation of **11** by action of sodium methoxide and subsequent reduction of the nitro-aci form of the starting compound with titanium trichloride afforded the desired diketone in 80% yield. A small amount of oxime **13** and, as in the case of the analogous reaction with **6** (see above), a small quantity of the corresponding pyrrolophane **15** were formed together with some further minor side products. Whereas the oxime **13** is proposed as an intermediate in the reductive Nef type reaction[6] and originates most probably from incomplete reduction of the aci-nitro group, the pyrrol derivative **15** was

presumably formed by cyclization and dehydration of γ-iminoketone **14**, which is suggested as an intermediary structure arising in reductive Nef type reactions, too.

With the 1,4-diketone **12** at hand, a number of [10]heterophanes were synthesized. The Paal-Knorr reaction of **12** with ammonia and some selected primary amines was bringing forth the corresponding [10](2,5)pyrrolophanes **15–19** in good to excellent yields (78–96%). The reactions proceeded even smoothly with 4-aminobutanol or butane-1,4-diamine as the amine components, delivering functionalized *N*-substituted pyrrolophanes that are interesting for us in connection with the planned construction of some heterophane-based host molecules and for further ring enlargement reactions.



Scheme 2

Equally simple as the production of [10](2,5)pyrrolophanes was the preparation of [10](2,5)furanophane **20**. Heating a mixture of diketone **12** and *para*-toluene sulfonic acid in toluene at a Dean-Stark water trap delivered the aromatic condensation product **20** in satisfactory 81% yield.

In contrast to the furano- and pyrrolophanes **15–20**, the synthesis of thiophenophane **21** turned out to be more problematic than anticipated. Sulfuration of the starting diketone **12** by its treatment with P_2S_5 – analogously to the procedure published by Nozaki *et al.*[8] to form [8](2,5)thiophenophane (51%) from cyclododecane-1,4-dione – gave with low yields rise to inseparable mixtures of thiophenophane **21**, furanophane **20**, and other side products only. Likewise, the use of other sulfuring reagents than P_2S_5 proved to be not superior. Remarkable is the reaction of **12** with the Lawesson reagent (2,4-bis(4-methoxyphenyl)-1,3,2,4-dithiadiphosphetane-2,4-disulfide) in toluene affording no thiophenophane **21** at all but only furanophane **20** in a yield as high as 91%. Apparently, the Lawesson reagent acts in this case not as a sulfuring reagent but as a Lewis acid and simultaneously as a water trap assisting efficiently the condensation of diketone **12** to furane derivative **20**. The

different behavior of cyclotetradecane-1,4-dione (**12**) compared to cyclododecane-1,4-dione in respect of the thiophenophane formation is unclear. We do not recognize unfavorable steric or electronic factors preventing sulfuration of our 1,4-diketone.

The [10]heterophanes exhibit characteristic spectral behavior. Their ^1H and ^{13}C NMR spectra are, due to the symmetry of the molecules, not too complex: They exhibit for the heterophane frameworks half the number of signals in respect to the responsive groups. Characteristic absorptions for the aromatic protons are found in the ^1H NMR spectra for both the pyrrolo- and furanophanes in the region of 5.8 ppm, whereas the corresponding signal for the thiophenophane is detected at 6.64 ppm. The ^{13}C NMR spectra of the several heterophanes are very similar, too. The chemical shifts of the signals deriving from the aromatic tertiary carbon nuclei are detected at 104.9 ppm for the *N*-unsubstituted pyrrol derivative, at characteristically lower field as compared with the corresponding signals at 106.4–107.6 ppm arising from the *N*-substituted pyrrolophanes. The corresponding signal of the furanophane is recorded at 105.8 ppm and the one of the thiophenophane diagnostically at 124.4 ppm. The signals for the quarternary aromatic carbons appear at 132.8–130.4 ppm for the pyrrolophanes, at 154.7 ppm for the furanophane, and at 142.9 ppm for the thiophenophane.

Of special diagnostic value is the mass spectral behavior of the heterophanes upon electron impact ionization. The spectra of all three types of heterophanes, the pyrrolo-, furano-, as well as the thiophenophanes, exhibit a series of signals corresponding by mass to fragments of the composition $[C_7H_7X + (CH_2)_n)]^+$ with X = NR, O, or S for the respective heterophanes and n = 0, 1, 2, etc. up to 6. The exact structures of these fragments as well as the mechanism of their formation is not known yet.

CONCLUSION

We have shown with the synthesis of the diketone **12** and with its transformation into the compounds **15**–**21** that 2-nitrocycloalkanones of the type **1** are versatile starting materials for the preparation of a variety of heterophane derivatives. With the potential to bring about heterophanes specifically substituted on the carbon skeleton of the aromatic moiety or of the polymethylene bridge – either by using appropriately substituted α,β-unsaturated aldehydes for the construction of the bicylic ring enlargement precursors or by derivatization of the 2-nitroketone precursors or the ring enlarged β-ketoester derivatives – the presented method to prepare heterophanes is more flexible than former published synthetic paths. This newly gained flexibility is important in respect to the design of heterophane derivatives potentially acting as host molecules in supramolecular chemistry.

EXPERIMENTAL

General Procedures. Where not remarked differently: all reactions were carried out under a blanket of inert gas. During the workup, all extracts are dried over disodium sulfate prior to evaporation of the solvents *in vacuo*. Chromatography was performed on Merck Kieselgel 60 (230–400 mesh). Infrared spectra (IR) were taken on a Perkin-Elmer 297 or 781 (frequencies given in cm^{-1}), ^1H (200 or 300 MHz) and ^{13}C NMR (50.4 MHz) on a Bruker AM-300 or a Varian XL-200 in $CDCl_3$ as the solvent (δ in ppm relative to the solvent: δ_H ($CHCl_3$) = 7.26, δ_C ($CDCl_3$) = 77.0; coupling constants (J) in Hertz, multiplicities of the ^{13}C NMR signals

from DEPT experiments), mass spectra in *m/z* (rel.%) on a Varian MAT 112S (chemical ionization (CI-MS) with 2-methylpropane as the reactant gase and electron impact ionization (EI-MS) at 70 eV).

Methyl 5-Nitro-2-oxocyclotetradecanecarboxylate (10): To a soln. of 6.56 g (20.8 mmol) of methyl 2-hydroxy-5-nitrocyclotetradecanecarboxylate (**4**) in 100 ml of acetone were added at 23°C dropwise 11.0 ml of Jones reagent[23] (2.3 M CrO_3 in conc. H_2SO_4, corresponds to 25.3 mmol of CrO_3). After 4 h, the excess CrO_3 was destroyed by treatment of the mixture with 10.0 ml of isopropanol for 30 min. The solvents were evaporated, the residue admixed with H_2O and extracted with CH_2Cl_2. The combined organic layers were washed with H_2O and brine and gave after crystallization of the crude product (hexane/Et_2O) 5.48 g (17.5 mmol, 84%) of **10** as colorless needles (mixture of diastereomers in a ratio of apprx. 2:1). The major isomer was obtained in pure form by crystallization from ethanol: m.p. (hexane/Et_2O, mixture): 47–49°C and 77–85°C, (MeOH, major isomer, pure): 86–88°C; IR (KBr): 2930, 2870, 1740, 1715, 1545, 1460, 1435, 1405, 1380, 1365, 1305, 1275, 1260, 1255, 1230, 1210, 1200, 1170, 1160, 1145, 1090, 1030, 990, 970, 895, 810, 795, 760, 735, 705, 685; ^{1}H NMR (pure isomer): 4.58–4.50 (*m*, H–C(5)), 3.71 (*s*, OCH_3), 3.46 (*dd*, *J* = 10.8, 4.9, H–C(1)), 2.85–1.07 (*m*, 22 H); (Mixture of isomers, relevant signals): 4.46–4.48 (*m*, H–C(5)), 3.71, 3.70 (2*s*, OCH_3), 3.65, 3.45 (2*dd*, *J* = 10.8, 4.9 and 11.4, 3.8, H–C(1)); ^{13}C NMR (pure isomer): 204.4 (*s*, C=O), 169.9 (*s*, *C*OOMe), 85.8 (*d*, C–NO_2), 59.2 (*d*, *C*–COOMe), 52.4 (*q*, MeO), 34.6, 28.8, 28.5, 26.1, 25.6, 25.5, 25.2, 24.5, 23.7, 23.5, 21.9 (11*t*); (Mixture of isomers, relevant signals): 204.4, 203.9 (2*s*, C=O), 169.9, 169.7 (2*s*, *C*OOMe), 85.8, 84.6 (2*d*, C–NO_2), 59.6, 59.2 (2*d*, *C*-COOMe), 56.6 (*q*, MeO); CI-MS: 314 [*M* + 1]$^+$, 267 [*M* – NO_2]$^+$; Anal. Calcd. for $C_{16}H_{27}NO_5$ (313.40): C 61.32, H 8.68, N 4.47. Found: C 61.29, H 8.69, N 4.51.

4-Nitrocyclotetradecanone (11): A soln. of 10.0 g (31.9 mmol) of **10** in a mixture of 200 ml of ethanol and 100 ml of a 10% aqueous HCl soln. was heated at reflux for 5 h. It was allowed to cool slowly to room temperature, and after standing at –5°C overnight, the precipitate was collected by filtration and was washed with a small portion of cold ethanol to give 7.95 g (30.7 mmol, 96%) of **11** as colorless needles: m.p. (MeOH/H_2O): 68–69°C; IR ($CHCl_3$): 2930, 2860, 1715, 1550, 1460, 1440, 1415, 1380, 1360, 1300, 1150, 1120, 1090, 990, 860; ^{1}H NMR: 4.61–4.54 (*m*, H–C(4)), 2.72–1.18 (*m*, 24 H); ^{13}C NMR: 209.5 (*s*, C=O), 85.2 (*d*, C-NO_2), 41.5, 37.0, 28.7, 26.3, 25.9, 25.7, 25.4, 25.1, 24.6, 24.0, 23.5, 22.4 (12*t*). CI-MS: 256 [*M* + 1]$^+$. Anal. Calcd. for $C_{14}H_{25}NO_3$ (255.36): C 65.85, H 9.87, N 5.49. Found: C 65.73, H 9.90, N 5.49.

Cyclotetradecane-1,4-dione (12): To a soln. of 2.04 g (8.00 mmol) of **11** in 50.0 ml of methanol were added at 23°C 21.0 mmol of sodium methoxide (10.5 ml of a 0.5 M soln. in methanol). After 15 min, a soln. of 5.37 g (36.4 mmol) of $TiCl_3$ and 19.65 g (254.1 mmol) of sodium acetate in 20 ml of H_2O was added in one batch and the resulting mixture was stirred for 4 h. It was acidified with 3 N aqueous HCl soln. and extracted with ether. The combined organic layers were washed with H_2O and brine and gave after chromatography (CH_2Cl_2) of the crude product 1.43 g (6.37 mmol, 80%) of **12** as a colorless crystallizing oil, 172 mg (0.72 mmol) of **13** as a colorless amorphous solid, and 80 mg (0.39 mmol) of **15** as colorless crystals. Data for **12**: m.p. (from oil): 52–54°C; IR (KBr): 2930, 2900, 2860, 2840, 1705, 1415, 1440, 1430, 1410, 1400, 1375, 1350, 1330, 1320, 1285, 1260, 1235, 1220, 1210, 1165, 1150, 1115, 1100, 1085, 1060, 1030, 1010, 975, 955, 900, 775, 765, 740, 715; ^{1}H NMR: 2.71 (*s*, 2 H–C(2), 2 H–C(3)), 2.47 (*t*, *J* = 6.1, 2 H–C(5), 2 H–C(14)), 1.69–1.60 (*m*, 4 H), 1.30–1.08 (*m*, 12 H); ^{13}C NMR: 210.7 (*s*, 2 C=O), 41.5, 36.7, 26.8, 25.9,

25.4, 21.7 (6*t*, 12 CH_2); EI-MS: 224 (12, $M^{+\cdot}$), 206 (4), 181 (10), 153 (12), 139 (10), 127 (30), 111 (91), 98 (46), 83 (46), 71 (89), 55 (100), 41(99); Anal. Calcd. for $C_{14}H_{24}O_2$ (224.35): C 74.95, H 10.78. Found: C 74.90, H 10.80. Data for **13**: m.p. (amorphous): 143–148°C; IR ($CHCl_3$): 3590, 3010, 2930, 2860, 1710, 1615, 1465, 1450, 1410, 1370, 1345, 1325, 1300, 1270, 1240, 1190, 1175, 1150, 1130, 1090, 1050, 1010, 960, 940, 710, 660; ^1H NMR: 8.07 (*s*, NOH, exchanged with D_2O), 2.78–2.72 (*m*, 2 H), 2.65–2.59 (*m*, 2 H), 2.44–2.39 (*m*, 2 H), 2.20 (*t*, J = 7.1, 2 H), 1.74–1.64 (*m*, 2 H), 1.53–1.46 (*m*, 2 H), 1.36–1.22 (*m*, 12 H); ^{13}C NMR: 210.6 (*s*, C=O), 161.0 (*s*, C=NOH), 42.5, 37.3, 33.7, 26.4, 26.3, 26.1, 26.0, 25.7, 24.8, 23.8, 21.1 (11*t*, 12 CH_2); CI-MS: 240 $[M + 1]^+$, 222 $[M - OH]^+$; Anal. Calcd. for $C_{14}H_{25}NO_2$ (239.36): C 70.25, H 10.53, N 5.85. Found: C 70.18, H 10.32, N 5.62. Data for **15** see below.

[10](2,5)Pyrrolophane[24] (15-azabicyclo[10.2.1]pentadecane-12,14(1)-diene, **15**): Into a soln. of 135.0 mg (0.6 mmol) of **12** in 15.0 ml of ethanol and 10 ml of conc. aqueous NH_3 soln. was introduced a small quantity of CO_2 (gas) and the resulting mixture was heated at reflux for 6 h. It was allowed to cool slowly to 23°C, and after standing at –5°C for 3–4 d, the precipitated solid was collected by filtration and was recrystallized to give 7.95 g (30.7 mmol, 96%) of **15** as colorless needles: m.p. ($MeOH/NH_4OH$): 132–133°C; IR ($CHCl_3$): 3470, 3000, 2930, 2860, 1585, 1510, 1460, 1445, 1420, 1350, 1330, 1290, 1230, 1200, 1175, 1085, 1040, 1020, 975, 710, 680, 670, 660; ^1H NMR: 7.65 (*s*, NH), 5.78 (*d*, J = 2.7, H–C(13), H–C(14)), 2.62–2.58 (*m*, 4 H), 1.64–1.55 (*m*, 4 H), 1.36–1.27 (*m*, 4 H), 1.17–1.10 (*m*, 4 H), 1.06–0.98 (*m*, 4 H); ^{13}C NMR (d_6-DMSO): 130.4 (*s*, C(1), C(12)), 104.9 (*d*, C(13), C(14)), 27.7, 27.9, 27.2, 26.9, 26.4 (5*t*, 10 CH_2); EI-MS: 205 (78, $M^{+\cdot}$), 204 (24), 176 (29), 162 (24), 148 (24), 134 (35), 120 (18), 107 (18), 106 (100), 94 (29), 93 (51), 84 (25), 80 (30), 65 (26); Anal. Calcd. for $C_{14}H_{23}N$ (205.35): C 81.89, H 11.29, N 6.82 Found: C 82.13, H 11.11, N 6.62.

N-Methyl[10](2,5)pyrrolophane[24] (N-methyl-15-azabicyclo[10.2.1]pentadecane-12,14(1)-diene, **16**): Into a soln. of 225.0 mg (1.00 mmol) of **12** in 20 ml of ethanol was introduced at 23°C methylamine (gas) until the color of the mixture turned to deep yellow. It was stirred at 23°C for 3 h, the solvent was evaporated, and the residue chromatographed (CH_2Cl_2) to give 182.0 mg (0.83 mmol, 83%) of **16** as a colorless oil: IR ($CHCl_3$): 3090, 2990, 2930, 2860, 1505, 1460, 1445, 1435, 1410, 1350, 1325, 1300, 1230, 1200, 1075, 1025, 1010, 910, 880, 720, 710, 675, 665; ^1H NMR: 5.82 (*s*, H–C(13), H–C(14)), 3.49 (*s*, NCH_3), 2.65–2.61 (*m*, 4 H), 1.73–1.60 (*m*, 2 H), 1.57–1.44 (*m*, 2 H), 1.35–1.14 (*m*, 4 H), 1.09–0.98 (*m*, 2 H), 0.96–0.83 (*m*, 6 H); ^{13}C NMR: 132.8 (*s*, C(1), C(12)), 106.4 (*d*, C(13), C(14)), 31.1 (*q*, NCH_3), 27.8, 27.3, 26.5, 26.4, 25.9 (5*t*, 10 CH_2); EI-MS: 219 (45, $M^{+\cdot}$), 204 (5), 190 (30), 176 (8), 162 (19), 148 (38), 134 (10), 120 (100), 107 (51), 94 (35), 41 (18); Anal. Calcd. for $C_{15}H_{25}N$ (219.37): C 82.13, H 11.49, N 6.38. Found: C 81.92, H 11.26, N 6.29.

N-Benzyl[10](2,5)pyrrolophane[24] (N-benzyl-15-azabicyclo[10.2.1]pentadecane-12,14(1)-diene, **17**): A soln. of 113.0 mg (0.50 mmol) of **12**, 64.3 mg (0.60 mmol) of benzylamine, and 0.5 ml of acetic acid in 4.0 ml of ethanol was heated at reflux for 7 h. The solvent was evaporated and the residue chromatographed (CH_2Cl_2) to give 144.0 mg (0.48 mmol, 96%) of **17** as colorless crystals: m.p. (CH_2Cl_2): 59–61°C; IR (KBr): 3090, 3070, 3030, 2930, 2860, 1700, 1605, 1500, 1455, 1440, 1420, 1390, 1350, 1330, 1300, 1250, 1210, 1180, 1080, 1030, 930, 885, 800, 765, 745, 735, 695, 680, 650; ^1H NMR: 7.20–7.08 (*m*, 3 arom. H), 6.70 (*d*, J = 6.9, 2 arom. H), 5.84 (*s*, H–C(13), H–C(14)), 5.07 (*s*, NCH_2), 2.55–2.34 (*m*, 4 H), 1.68–1.55 (*m*, 2 H), 1.47–1.34 (*m*, 2 H), 1.31–1.12 (*m*, 4 H), 1.09–1.06 (*m*, 2 H), 0.96–0.87 (*m*, 6 H); ^{13}C NMR: 139.3 (*s*,

arom. C), 132.7 (*s*, C(1), C(12)), 128.5 (*d*, 2 arom. C), 126.8 (*d*, arom. C), 125.3 (*d*, 2 arom. C), 107.6 (*d*, C(13), C(14)), 47.3 (*t*, NCH_2), 28.2, 27.3, 26.5, 26.2, 25.8 (5*t*, 10 CH_2); CI-MS: 296 [*M* + 1]$^+$, 295 [*M*]$^+$; Anal. Calcd. for $C_{21}H_{29}N$ (295.47): C 85.37, H 9.89, N 4.74. Found: C 85.47, H 9.65, N 4.71.

N-(4-Hydroxybutyl)[10](2,5)pyrrolophane[24] (4-(15-azabicyclo[10.2.1]pentadecane-12,14(1)-diene-15-yl)butanol, **18**): A soln. of 113.0 mg (0.50 mmol) of **12**, 50.0 mg (0.56 mmol) of 4-aminobutanol, and 1.0 ml of acetic acid in 3.0 ml of ethanol was heated at reflux for 6 h. The solvent was evaporated, the residue chromatographed (CH_2Cl_2/EtOH 4:1), and the fractions containing **18** were distilled bulb-to-bulb (140–150°C (air bath)/0.06 torr) to give 127.2 mg (0.46 mmol, 92%) of **18** as a colorless hygroscopic oil: IR ($CHCl_3$): 3620, 3090, 2930, 2860, 1500, 1475, 1455, 1435, 1420, 1390, 1370, 1350, 1290, 1235, 1200, 1055, 1025, 910, 710, 680, 665; ^{1}H NMR: 5.74 (*s*, H–C(13), H–C(14)), 3.85 (*t*, *J* = 7.0, NCH_2), 3.50 (*t*, *J* = 6.1, OCH_2), 2.61–2.46 (*m*, 4 H), 1.66–1.50 (*m*, 4 H), 1.46–1.34 (*m*, 4 H), 1.28–0.93 (*m*, 7 H, therein OH exchanged with D_2O), 0.90–0.74 (*m*, 6 H); ^{13}C NMR: 132.0 (*s*, C(1), C(12)), 107.1 (*d*, C(13), C(14)), 62.2 (*t*, OCH_2), 43.6 (*t*, NCH_2), 29.6 (*t*), 28.3 (*t*, 2 CH_2), 28.2 (*t*), 27.1, 26.5, 26.3, 25.7 (4*t*, 8 CH_2); EI-MS: 277 (50, *M* $^{+\cdot}$), 248 (23), 218 (100), 206 (27), 178 (24), 164 (67), 134 (27), 108 (24), 97 (45), 83 (44), 69 (63), 55 (62), 43 (38); Anal. Calcd. for $C_{18}H_{31}NO$ (277.45): C 77.92, H 11.26, N 5.05. Found: C 77.86, H 11.09, N 5.03.

N-(4-Aminobutyl)[10](2,5)pyrrolophane[24] (4-(15-azabicyclo[10.2.1]pentadecane-12,14(1)-diene-15-yl)butylamine, **19**): To a soln. of 882.0 mg (10.0 mmol) of 1,4-butanediamine and 0.5 ml of acetic acid in 1.0 ml of ethanol was added at 23°C slowly a soln. of 225.0 mg (1.00 mmol) of **12** in 1 ml of ethanol. After 1 h, the solvent was evaporated, the residue chromatographed (CH_2Cl_2/EtOH/conc. NH_4OH 75:19:3), and the fractions containing **19** were distilled bulb-to-bulb (190–200°C (air bath)/0.06 torr) to give 231.0 mg (0.84 mmol, 84%) of **19** as a colorless oil: IR ($CHCl_3$): 3440, 3400, 3090, 2930, 2860, 1720, 1680, 1575, 1550, 1450, 1415, 1385, 1365, 1345, 1320, 1285, 1230, 1295, 1110, 1070, 1015, 870, 850; ^{1}H NMR: 5.82 (*s*, H–C(13), H–C(14)), 3.90 (*t*, *J* = 7.2, NCH_2), 2.68–2.51 (*m*, 6 H), 1.73–0.81 (*m*, 22 H); ^{13}C NMR: 131.9 (*s*, C(1), C(12)), 107.1 (*d*, C(13), C(14)), 43.6 (*t*, NCH_2), 41.6 (*t*, H_2NCH_2), 30.4, 29.2 (2*t*), 28.3, 27.1, 26.4, 26.2, 25.7 (5*t*, 10 CH_2); CI-MS: 277 [*M* + 1]$^+$, 276 [*M*]$^+$; Anal. Calcd. for $C_{18}H_{32}N_2$ (276.47): C 78.20, H 11.67, N 10.13. Found: C 75 32, H 11.45, N 9.83.

[10](2,5)Furanophane[24] (15-oxabicyclo[10.2.1]pentadecane-12,14(1)-diene, **20**): A soln. of 250.0 mg (1.11 mmol) of **12** and a catalytic amount of *para*-toluene sulfonic acid in 20 ml of dry toluene was heated at a Dean-Stark water trap to reflux for 30 min. The solvent was evaporated, the residue chromatographed (CH_2Cl_2), and the fractions containing **20** were distilled bulb-to-bulb (70–75°C (air bath)/0.06 torr) to give 186.0 mg (0.90 mmol, 81%) of **20** as a slightly yellow oil: IR ($CHCl_3$): 3080, 3000, 2930, 2860, 1605, 1560, 1460, 1445, 1435, 1375, 1350, 1330, 1230, 1200, 1140, 1070, 1030, 1010, 975, 960, 910; ^{1}H NMR: 5.86 (*s*, H–C(13), H–C(14)), 2.64–2.60 (*m*, 4 H), 1.69–1.60 (*m*, 4 H), 1.36–1.29 (*m*, 4 H), 1.24–1.22 (*m*, 8 H); ^{13}C NMR: 154.7 (*s*, C(1), C(12)), 105.8 (*d*, C(13), C(14)), 27.4, 27.1, 26.4, 26.2, 25.8 (5*t*, 10 CH_2); EI-MS: 206 (46, *M* $^{+\cdot}$), 177 (4), 163 (9), 149 (10), 135 (13), 121 (19), 107 (94), 94 (100), 81 (31), 67 (16), 55 (29), 41 (43); Anal. Calcd. for $C_{14}H_{22}O$ (206.33): C 80.50, H 10.75. Found: C 80.61, H 10.71.

10](2,5)Thiophenophane[24] (15-thiabicyclo[10.2.1]pentadecane-12,14(1)-diene, **21**): A mixture of 225.0 mg (1.0 mmol) of **12** and approximately 2.0 g (9.0 mmol) of P_2S_5 was kept at 100°C for 3 h. After cooling to 23°C, it was extracted with ether, reduced *in vacuo* and filtered through silica gel. Chromatography

(CH_2Cl_2) provided 121.0 mg of a mixture of products and a small fraction of pure **21**: ^1H NMR: 6.63 (*s*, H–(C12), H–C(13)), 2.79–2.75 (*m*, 4 H), 1.65–1.57 (*m*, 4 H), 1.44–1.26 (*m*, 4 H), 1.10–1.06 (*m*, 4 H), 0.84–0.79 (*m*, 4 H); ^{13}C NMR (relevant data from impure fraction): 142.9 (*s*, C(11), C(14)), 124.4 (*d*, C(12), C(13)), 30.2, 30.0, 27.9, 26.7, 26.6 (5*t*, 10 CH_2); EI-MS: 222 (68, $M^{+\cdot}$), 193 (11), 165 (10), 151 (29), 123 (73), 112 (24), 111 (39), 110 (100), 97 (37), 91 (10), 77 (10), 55 (12), 45 (12), 41 (29), 39 (14).

Acknowledgment. We wish to thank the analytical departments of our institute for their help, particularly Mr. M. Vöhler for ^1H and ^{13}C NMR spectra, Mrs. Dr. A. Lorenzi-Riatsch and Mr. N. Bild for mass spectra, and Mr. H. Frohofer for microanalyses. The financial support of this project by the Swiss National Science Foundation is greatfully acknowledged, too.

REFERENCES AND NOTES

1. Part of the Ph.D. thesis of F. Hadj-Abo, University of Zurich 1994.
2. Bienz, S.; Hesse, M., *Helv. Chim. Acta* **1987**, *70*, 2146.
3. Bienz, S.; Hesse, M., *Helv. Chim. Acta* **1987**, *70*, 1333.
4. Lorenzi-Riatsch, A.; Nakashita, Y.; Hesse, M., *Helv. Chim. Acta* **1984**, *67*, 249.
5. Lorenzi-Riatsch, A.; Wälchli, R.; Hesse, M., *Helv. Chim. Acta* **1985**, *68*, 2177.
6. McMurry, J. E.; Melton, L., *J. Org. Chem.* **1973**, *38*, 4367.
7. Bienz, S., Ph.D. thesis, University of Zurich 1987.
8. Nozaki, H.; Koyoma, T.; Mori, T.; Noyori, R., *Tetrahedron Lett.* **1968**, 2181.
9. Nozaki, H.; Koyama, T.; Mori, T., *Tetrahedron* **1969**, *25*, 5357.
10. Hiyama, T.; Hiramo, S.; Nozaki, H., *J. Am. Chem. Soc.* **1974**, *96*, 5287.
11. Keehn, P. M.; Rosenfeld, S. M., Eds.; *Cyclophanes*; Vol. I and II; Academic Press: New York, 1983.
12. Newkome, G. R.; Traynham, J. G.; Baker, G. R., in *Comprehensive Heterocyclic Chemistry*, Vol. 7; Katritzky, A. R.; Rees, C. W., Eds.; Pergamon Press: Oxford, 1984; p. 763.
13. Marshall, J. A.; Wang, X., *J. Org. Chem.* **1991**, *56*, 6264.
14. Tochtermann, W.; Luttmann, K., *Tetrahedron Lett.* **1987**, *28*, 2521.
15. Tochtermann, W.; Luttmann, K.; Sdunnus, N.; Peters, E.-A.; Peters, K.; von Schnering, H. G., *Chem. Ber.* **1992**, *125*, 1485.
16. Eberbach, W.; Laber, N., *Tetrahedron Lett.* **1992**, *33*, 57.
17. Müller, F.; Mattay, J., *Angew. Chem. Int. Ed. Engl.* **1992**, *31*, 209.
18. Müller, F.; Mattay, J., *Chem. Ber.* **1993**, *126*, 543.
19. Vögtle, F., *Tetrahedron Lett.* **1969**, 3193.
20. Vögtle, F.; Neumann, P., *Tetrahedron Lett.* **1969**, 5329.
21. Vögtle, F.; Neumann, P., *Tetrahedron* **1970**, *26*, 5847.
22. Camerino, B.; Patelli, B., *Experientia* **1964**, *20*, 260.
23. Bowder, K.; Heilbron, J. M.; Jones, E. R. H.; Weedon, B. C. L., *J. Chem. Soc.* **1946**, 39.
24. The numbering according to the IUPAC name (in brackets) is used in the description of the spectra.

(*Received in Germany* 11 *April* 1994; *accepted* 31 *May* 1994)