Transannular Reactions of Two Parallel 1,3-Butadiynes: Syntheses, Structures, and Reactions of 1-Azacyclotetradeca-3,5,10,12-tetrayne Derivatives

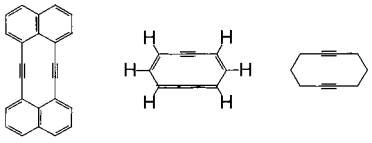
Erik M. Schmidt, Rolf Gleiter,* and Frank Rominger[a]

Abstract: The synthesis of 1-alkyl and 1-aryl-1-azacyclotetradeca-3,5,10,12-tetraynes was achieved in a stepwise approach. The key intermediate was 1,13-dibromotrideca-2,4,9,11-tetrayne (**18**). Reaction with methyl- (**19a**), ethyl- (**19b**), isopropyl- (**19c**), *n*-butyl- (**19d**), and *tert*-butylamine (**19e**) as well as aniline (**19f**) and *p*-methoxyaniline (**19g**) gave the corresponding 14-membered tetraynes **20a**–**20g**. The ring inversion process of **20b** was studied by variable temperature ^{1}H NMR spectroscopy. From these measurements a value of 10.6 kcal mol^{-1} was calculated for $\Delta G^{\neq}$. X-ray investigations on single crystals of **20b**, **20c**, and **20f** revealed the axial position for the substituent at each nitrogen atom. For **20b** we encountered the chair conformation, for **20c** both chair and boat conformations, and for **20f** the boat conformation in the solid state. The reaction of **20c** with concentrated HCl in ethanol yielded 2,10-dichloro-6-isopropyl-6-azatricyclo-[9.3.0.0^{4,8}]tetradeca-1(11),2,4(8),9-tetraene (**25c**). Compound **25c** was oxidized by 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) to **27c**. The structure of the latter was confirmed by X-ray investigations. The reaction of **20c** in aqueous HCl lead to the formation of 10-chloro-2-isopropyl-1,3,4,6,7,8-hexahydro-*2H*-benzo[*g*]isoquinolin-9-one (**37c**). The structure of **37c** was verified by X-ray studies on single crystals.

Keywords: butadiynes · medium-ring compounds · structure elucidation · transannular reactions

Introduction

The close proximity of two triple bonds results in bond formation between them. Examples for this reaction are the dinaphthalene derivative **1**,[1] 1,6-didehydro[10]annulene (**2**),[2] and 1,6-cyclodecadiyne (**3**).[3] The parallel alignment of



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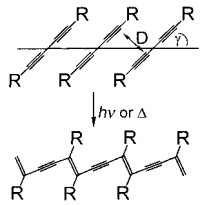
1,3-butadiyne units in the solid state (Scheme 1) causes a 1,4-addition in a topochemical reaction if the angle γ is close to 45° and the distance d is below 4.3 Å.[4, 5] This polymerization creates single crystals of organic polymers with a conjugated back bone. It is proposed that the polymerization propagates through a biradical species.[5]



Scheme 1. Polymerization of 1,3-butadiyne in the solid state.

When the two 1,3-butadiyne units are oriented in a parallel arrangement and are incorporated in a ring system we expect transannular ring closure to a polycyclic system. Indeed, when 1,2:7,8-dibenzocyclododeca-1,7-dien-3,5,7,11-tetrayne (**4a**) was reduced with sodium in liquid ammonia, the pentacyclic system **5** resulted as the main product and **7** and **8** as side products (Scheme 2). The catalytic hydrogenation with palladium on charcoal yielded **6** as main product together with **7** and **8**.[6]

Analogous results were obtained when 5,6:11,12-bis(tetramethylene)-1,3,7,9-tetradehydro[12]annulene was used instead of **4a**.[7]

Treatment of a tetraalkyl-substituted derivative (**4b**) with iodine in benzene as solvent at room temperature yielded the fully conjugated pentacyclus **9** (Scheme 3).[8] It consists of the same 6-5-6-5-6 fused ring architecture as encountered in **5** and **7** (Scheme 2).

[a] Prof. Dr. R. Gleiter, Dipl.-Chem. E. M. Schmidt, Dr. F. Rominger
Organisch-Chemisches Institut der Universität Heidelberg
Im Neuenheimer Feld 270, 69120 Heidelberg (Germany)
Fax: (+49) 6221-544205
E-mail: rolf.gleiter@urz.uni-heidelberg.de

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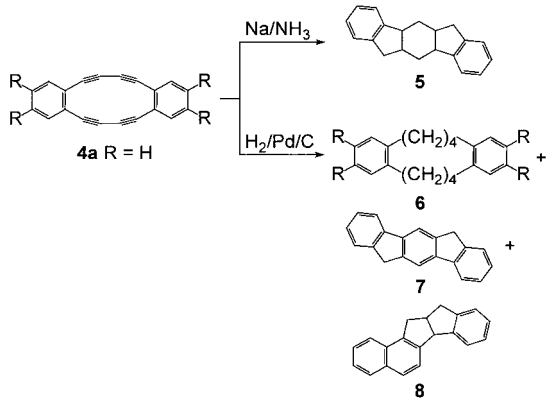
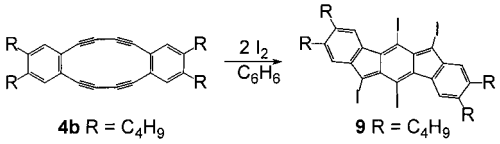
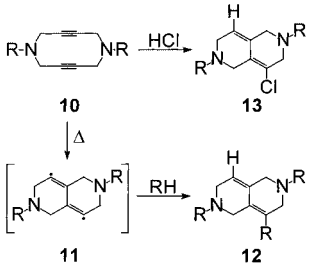


Scheme 2. Reduction of **4a**.



Scheme 3. Reaction of **4b** with iodine.

In connection with our investigations on transannular ring closures of **3**[3] and 1,6-disubstituted 1,6-diazacyclodeca-3,8-diynes[9] (**10**) (Scheme 4) we were interested in the transannular interactions of two 1,3-butadiyne units incorporated

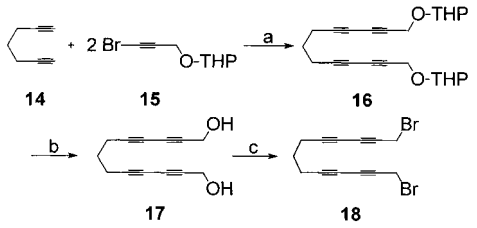


Scheme 4. Ring closure modes of **10** induced by heat or HCl.

in a 14-membered ring system. We chose a system in which both 1,3-butadiyne units are tethered with a three-membered bridge. This guarantees a parallel alignment of both 1,3-butadiyne units in sufficient close proximity. Furthermore, the 14-membered ring allows more flexibility than the 12-membered ring system of **4a**. It makes ring closure modes other than a *n*-6-*n* one likely.[6, 7] In this paper we report the syntheses, structures, and reactivities of azacyclotetradeca-3,5,10,12-tetraynes.

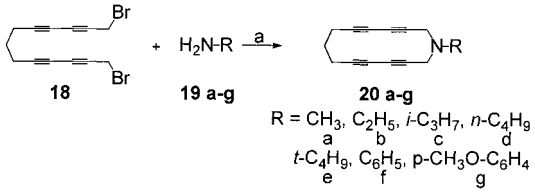
Results and Discussion

Syntheses: Our synthesis of the 1-azacyclotetradeca-3,5,10,12-tetraynes commenced by constructing the trideca-2,4,9,11-tetrayne unit from 1,6-heptadiyne (**14**)[10] and the THP-protected 1-bromo-prop-1-yne-3-ol (**15**)[11] (Scheme 5) by a Cadiot–Chodkiewicz coupling[12] with copper(I) iodide and pyrrolidine.[13] The free diol **17**[14] was obtained from **16** by hydrolization with sulfuric acid. The diol **17** was converted



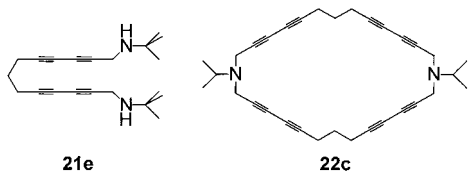
Scheme 5. Synthesis of **18**. a) CuI, pyrrolidine; b) H_2SO_4, H_2O/MeOH; c) PBr_3, pyridine/Et_2O.

into the dibromide **18** with PBr_3 and pyridine. Reactions of **18** with various primary amines in presence of potassium carbonate as base afforded, in small yields, the 1-substituted azacyclotetradeca-3,5,10,12-tetraynes **20a–g** as shown in Scheme 6.

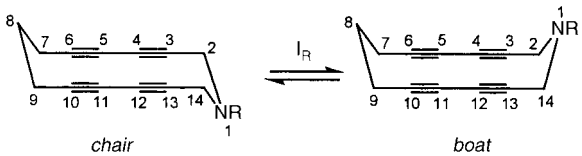


Scheme 6. Synthesis of **20a–g**. a) K_2CO_3, acetonitrile.

As further products we identified in the case of *tert*-butylamine (**19e**) the α,ω-diamine **21** in 44% yield. By using isopropylamine (**19c**) we were able to isolate the corresponding dimer **22c**. The yield of the cyclization product **20** was highest for **20b** (32%), **20c** (31%), and **20d** (35%). For the others it varied between 5% and 15%.



Structural investigations: The assigned structures of **20** follow from their analytical properties, especially their NMR and mass spectra. By using dynamic NMR spectroscopy[15] we were also able to investigate the half ring inversion (I_R) process of **20b**. Analogous to our studies on 1,6-diazacyclodeca-3,8-diyne (**10**),[16] we expect a half ring inversion process (Scheme 7) and inversion at the nitrogen atom. From these investigations we figured that the energy for the ring inversion might be estimated by means of ^{1}H NMR spectroscopy, whereas the activation barrier for inversion at the nitrogen center should be too low for this technique.



Scheme 7. Chair and boat conformation of **20**.

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At room temperature the ^{1}H NMR spectrum of the diethyl derivative **20b** exhibits a singlet for the diastereotopic protons at C2 and C14 at $\delta = 3.57$ ppm (for the numbering of the atoms see Scheme 7). Lowering the temperature leads to a broadened signal, which eventually splits into an AA′ signal. The coalescence temperature for the half ring inversion process is $T_c = 210$ K. From this we estimate $\Delta G^{\neq} = 10.6$ kcal mol^{-1}. This value is close to that found for **10** (R = CH_3; $\Delta G^{\neq} = 11.0$ kcal mol^{-1}).[16]

Calculations: Having obtained a value of $\Delta G^{\neq}$ for the ring inversion process, we were interested in both the energetic differences ΔG of chair and boat conformations and the influence of the arrangement (axial/equatorial position) of the substituent at the nitrogen atom on the stability of the azacyclotetradeca-3,5,10,12-tetraynes. As a result of AM1 - calculations[17] of the unsubstituted 1-azacyclotetradeca-3,5,10,12-tetrayne, we found that both conformers with the hydrogen in axial position are 7.5 kcal mol^{-1} more stable than the equatorially substituted ones. The energetic difference between the two chair and boat conformations is below 0.25 kcal mol^{-1}, the boat-shaped one being the more stable molecule. For 1-methyl-1-azacyclotetradeca-3,5,10,12-tetrayne we determined 6.2 kcal mol^{-1} as the difference in energy between the axially and the equatorially substituted conformers. The energetic difference between boat and chair conformation is minute. The predicted preference of the axial position for the substituents at the nitrogen atoms as well as the small energy difference between boat and chair conformation is corroborated by the results of the X-ray investigations (see below).

X-ray investigations: Single crystals of the azacyclotetradeca-3,5,10,12-tetraynes were obtained by crystallization of **20b**, **20c**, and **20f** from ethyl acetate. As an example we show the molecular arrangement of **20b** in the solid state in Figure 1 and the molecular structure of **20c** in Figure 2. It is seen from Figure 1 that the ethyl group adopts the axial position and the chairlike rings utilize a herring bone motif in the solid state. The substituents in **20c** and **20f** adopt also the axial position. In the solid state of **20c** both the boat and chair conformations are present (Figure 2). For **20f** we encountered only the boat conformation in the solid state.

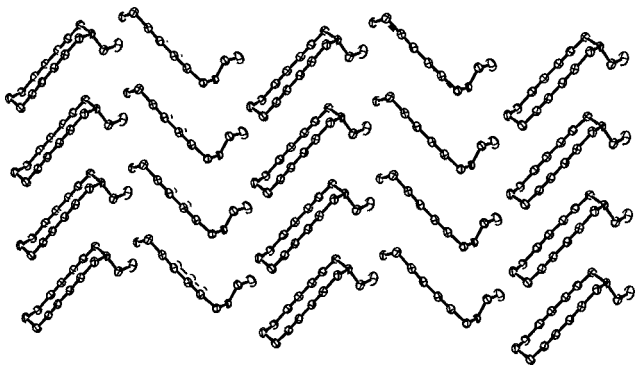


Figure 1. Arrangement of **20b** in the crystal (50% ellipsoid probability, H atoms have been omitted for the sake of clarity).

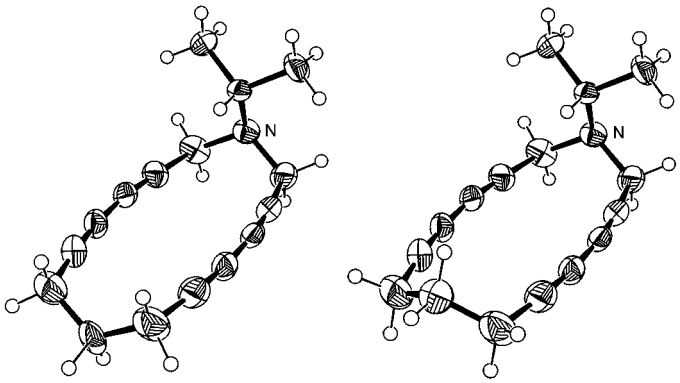
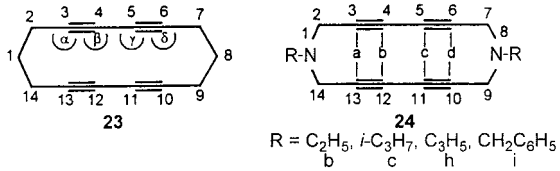


Figure 2. Molecular structures (chair and boat conformations) of **20c** (50% ellipsoid probability).

The most relevant bond lengths of **20b**, **20c**, and **20f** are compared with those of cyclotetradeca-1,3,8,10-tetrayne (**23**)[18] and the 1,8-diazacyclotetradeca-3,5,10,12-tetrayne derivatives **24b**,**c**,**h**,**i**[19] in Table 1.



The bond lengths for the triple bonds in **20b**, **20c**, and **20f** are close to those of the other four species (see Table 1). In all cases the angles at the peripheral sp centers (α, δ) have bigger values than those (β, γ) at the central sp centers. As a result the transannular distances between the peripheral C(sp) centers (**a**, **d**) are shorter (3.06–3.11 Å) than the distances between the inner C(sp) centers (**b**, **c**) (3.35–3.41 Å).

Reactions with HCl: The treatment of **20c** with concentrated HCl in ethanol under argon atmosphere yielded a new product whose analytical properties (MS) revealed that two equivalents of HCl were added. Based on the ^{13}C NMR data it was evident that the sp carbons of **20c** were changed into sp^2 carbons. We observed four different sp^2 carbons at $\delta = 141.8$, 136.4, 131.2, and 125.5 ppm. Three of them (141.8, 136.4, 131.2) were assigned to quaternary carbons, and one (125.5) to a tertiary carbon. The NMR data also revealed that the original C_s symmetry of **20c** was retained. The ^{1}H NMR spectrum showed only two equivalent hydrogen atoms in the olefinic region ($\delta = 5.85$ ppm). These data indicated four possible structures (**25c**, **25c′**, **26c**, and **26c′**), two of which contain a 5-8-5 and two a 7-4-7 tricyclic ring system. Systems with three six-membered rings (e.g., **9**) can be ruled out for reasons of symmetry.

For the structures **25** and **25′** we propose a central cyclooctatetraene ring. The valence isomers of **25c** and **25c′** (not shown) are unfavorable for steric reasons since the five-membered rings were more strained. For **26** and **26′** the center is formed by a [4]radialene system. In the latter case we expect

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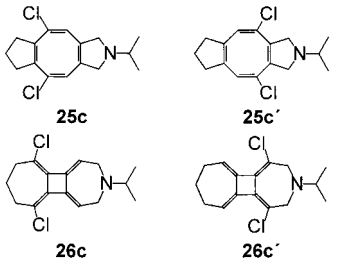
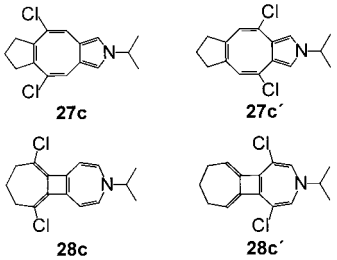
Table 1. Comparison between selected bond lengths [Å] and bond angles [°] of **20b**, **c**, **f**, **23**, and **24b**, **c**, **h**, **i**. For the definition of *a*, *b*, *c*, *d*, α, β, γ and δ as well as the numbering see structural formulae.

	20b	**20c**	**20f**	**23**[18]	**24b**[19]	**24c**[19]	**24h**[19]	**24i**[19]
α	174.5(2)	174.9(4)	170.4(2)	177.9(1)	173.6(1)	175.6(1)	174.3(1)	175.7(1)
α'	175.0(2)		170.0(4)					
β	173.2(2)	171.9(4)	174.6(6)	172.9(1)	173.1(1)	172.8(1)	173.3(1)	173.1(1)
β'	172.8(2)		174.9(5)					
γ	171.9(2)	173.7(4)	173.0(4)	173.0(2)	172.5(1)	173.3(1)	172.2(1)	172.6(1)
γ'	173.2(2)		173.1(2)					
δ	176.4(2)	175.7(4)	176.0(4)	175.6(2)	176.0(2)	172.1(1)	175.9(1)	174.3(1)
δ'	176.4(2)		175.7(7)					
a	3.078(2)	3.103(6)	3.193(3)	3.098(2)	3.074(2)	3.081(2)	3.058(2)	3.067(2)
b	3.375(2)	3.413(6)	3.394(3)	3.390(2)	3.361(2)	3.365(2)	3.351(2)	3.356(2)
c	3.393(2)	3.392(6)	3.382(3)	3.390(2)	3.361(2)	3.365(2)	3.351(2)	3.356(2)
d	3.110(2)	3.113(6)	3.096(3)	3.098(2)	3.074(2)	3.081(2)	3.058(2)	3.067(2)
C3–C4	1.196(2)	1.202(6)	1.195(2)	1.194(2)	1.202(1)	1.197(2)	1.189(4)	1.199(2)
C12–C13	1.198(2)		1.196(2)					
C4–C5	1.384(3)	1.384(5)	1.384(3)	1.385(2)	1.380(1)	1.382(2)	1.378(4)	1.378(2)
C11–C12	1.379(3)		1.380(2)					
C5–C6	1.198(2)	1.201(6)	1.195(2)	1.195(2)	1.200(1)	1.198(2)	1.186(4)	1.199(2)
C10–C11	1.192(2)		1.195(3)					



for the ^{13}C NMR spectrum a chemical shift in the order of $\delta =$ 148 ppm for the central carbons and $\delta = 100$ ppm for the peripheral carbons.[20] For the cyclooctatetraene nuclei in **25** and **25′** we expect δ values between 120 and 150 ppm.[21] The values observed for our product fit somewhat better to **25** and **25′**.

The oxidation of the tricyclic product by DDQ at room temperature led to a new product, for which signals for two further equivalent aromatic hydrogen atoms at $\delta = 6.5$ ppm and five carbon signals between $\delta = 118.2$ and 139.8 ppm were observed. These new data fit better with either of the pyrrol derivatives[22] **27** and **27′** than with the azepine[23] derivatives **28** and **28′**.



The new compound was stable at room temperature, which was not expected if it were an azepine derivative.[23] Fortunately, we were able to isolate single crystals of the oxidation product which proved to be structure **27c** (Figure 3). As anticipated the central ring shows the boat conformation. In

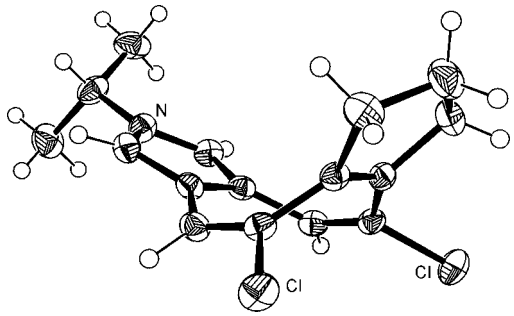
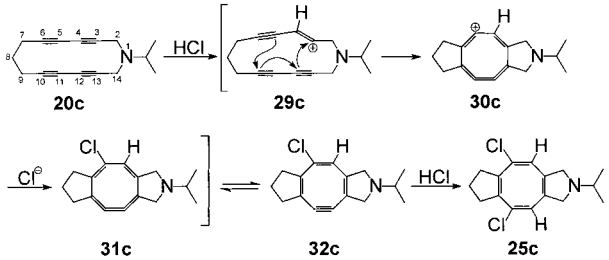


Figure 3. Molecular structure of **27c** (50% ellipsoid probability). The hetero atoms are indicated.

Scheme 8 a mechanism for the HCl addition to **20c** is suggested. We assume as a first step the protonation at C4 to yield the highly energetic vinyl cation **29c**, which reverts to the bicyclic buta-1,2,3-triene **31c**, probably via the cation **30c**.



Scheme 8. Proposed reaction mechanism to generate **25c** from **20c**.

The highly strained buta-1,2,3-triene isomerizes to cyclooctatrienyne **32c**. B3LYP 6-31G* calculations[24] of **31c** revealed structure **32c** as a minimum in energy.[28]. The latter adds a second molecule of HCl giving rise to the bicyclic cyclooctatetraene derivative **25c**. Our assumption for the highly strained 1,2,3-triene **31c** as an intermediate is corroborated by the observation of 1,2,3-cyclooctatriene.[29] When we used DCl instead of HCl we obtained [D_2]**25c** deuterated in the α-position to the chlorine atoms. This result supports the proposed mechanism as shown in Scheme 8.

By treating **20c** with concentrated HCl without the presence of ethanol we isolated a further product (**37c**) in low yield. The analytical properties of **37c** revealed that one equivalent of water and HCl were added to **20c**. Its structure was elucidated by NMR spectroscopy (HMBC).

The investigation of single crystals of **37c** also revealed a tricyclic structure. In contrast to the 5-8-5 ring system of **25c** we encountered for **37c** three annelated six-membered rings (Figure 4). The generation of **36c** from **20c** can be rationalized by assuming a different mode of ring closure as indicated

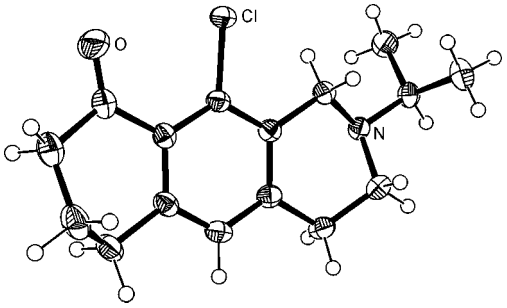
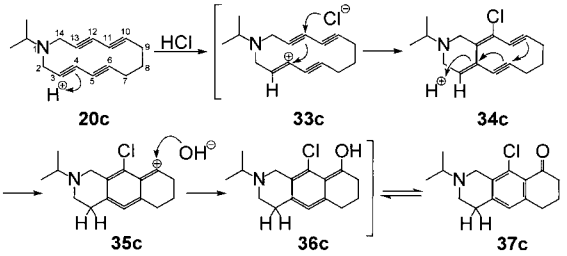


Figure 4. Molecular structure of **37c** (50% ellipsoid probability). The hetero atoms are indicated.

in Scheme 9. We assume that protonation at C3 of **20c** generates the highly energetic vinyl cation **33c**, which reverts to the bicyclic system **34c** by adding a Cl anion. Further protonation creates the highly energetic tricyclic cation **35c**. This species contains in its center a cyclohexa-1,2,4-triene unit



Scheme 9. Proposed reaction mechanism to generate **37c** from **20c**.

and a vinyl cation. We assume that the vinyl cation is trapped by OH^- (or H_2O with loss of H^+) to yield **36c**. This derivative of isobenzene[30] tautomerizes to **37c**. By carrying out the experiment with DCl instead of HCl we found [D_3]**37c** with two deuterium atoms at the 4-position and one at the 5-position. This supports the proposed mechanism of HCl addition to **20c** as shown in Scheme 9.

Conclusion

We were able to elaborate a synthetic protocol to synthesize a series of N-substituted 1-azacyclotetradeca-3,5,10,12-tetraynes **20a–g**. We found little energy difference between the chair and boat conformations, both of which were present in the solid state of **20c**. The most interesting results were obtained by treating **20c** with concentrated HCl in the absence and presence of ethanol as solvent. In the presence of ethanol the two parallel 1,3-butadiyne units in **20c** underwent ring closure and HCl addition to give a 5-8-5 tricyclic system. Such a ring-closing mode has never been observed in this type of chemistry. We ascribe this to our concept of allowing the two parallel 1,3-butadiyne units in the 14-membered ring system of **20** more flexibility than in the 12-membered system **4**. By adding concentrated HCl in the absence of ethanol a 6-6-6 tricyclic system was built up. This is reminiscent to the reactions shown in Schemes 2 and 3.

Experimental Section

General: Starting compounds and solvents used in the syntheses were reagent grade. Diethyl ether and chloroform were dried following standard drying techniques and degassed by distillation under argon atmosphere. Reactions were performed under argon in standard glassware. For column chromatography, neutral aluminium oxide was deactivated with 6% (weight) of water prior to use. ^1H and ^{13}C NMR spectra were recorded on Bruker Avance 300 (300 and 75 MHz, respectively) or Bruker Avance 500 spectrometers (500 and 125 MHz, respectively). For the variable temperature experiments the latter was equipped with a Bruker BVT 3000 Digital variable temperature unit. Chemical shifts are quoted in ppm on the δ scale, with the residual protonated solvent as the internal standard. IR spectra were measured with a Bruker Vector 22 FT-IR spectrometer, UV/Vis spectra were obtained from a Hewlett–Packard HP 8452A spectrometer with CH_2Cl_2 as solvent. Absorption maxima of IR spectra are quoted in cm^{-1} and those of UV/Vis spectra in nm, with log ε quoted in 1000 $cm^2\,mol^{-1}$. Elemental analyses were carried out by the Mikroanalytisches Labor der Chemischen Institute der Universität Heidelberg. Mass spectroscopy was performed with a JEOL JMS-700 spectrometer. Melting points were obtained from a melting point determination apparatus as described by Dr. Tottoli (Büchi) and are uncorrected.

1,13-Bis(tetrahydro-2-pyranyloxy)trideca-2,4,9,11-tetrayne (16): Copper(i) iodide (0.76 g, 4 mmol) was dissolved in pyrrolidine (50 mL) with magnetic stirring. At 0 °C compound **14**[10] (1.84 g, 20 mmol) was added to the solution and compound **15**[11] (8.60 g, 40 mmol) was added dropwise through a syringe into the reaction mixture over a period of 2 h. After stirring for 30 minutes at 0 °C, the resulting solution was poured into a stirred mixture of ice (200 g) and diethyl ether (100 mL). Concentrated hydrochloric acid was added slowly until the the green color of the resulting mixture turned slightly red. The ether layer was seperated quickly, and the acidic aqueous solution was extracted with diethyl ether (2 × 50 mL). The combined organic layers were washed twice with a saturated aqueous solution of sodium hydrogencarbonate and brine, and dried over anhydrous sodium sulfate. After filtration the solvent was evaporated, and the crude product was purified by column chromatography (Alox III, petrol ether/diethyl ether 5:1, $R_f = 0.25$) to yield **16** (2.88 g, 7.8 mmol, 39%) as a pale yellow oil. ^1H NMR (300 MHz, $CDCl_3$): $\delta = 4.80$ (t, $^3J_{H\text{-}14,H\text{-}15/H\text{-}19,H\text{-}20} = 3.1$ Hz, 2H; H-14/19), 4.31, 4.28 (2d, $^2J_{HH} = 18.7$ Hz, 4H; H-1^a/13^a, H-1^b/13^b), 3.82–3.77 (m, 2H; H-18^a/23^a), 3.55–3.51 (m, 2H; H-18^b/23^b), 2.41 (t, $^3J_{H\text{-}6/8,H\text{-}7} = 6.9$ Hz, 4H; H-6/8), 1.79–1.51 ppm (m, 14H; H-7, 15/20, 16/21, 17/22); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 97.5$ (C-14/19), 79.9 (C-5/9), 73.0 (C-2/12), 71.3 (C-3/11), 66.2 (C-4/10), 62.7 (C-18/23), 55.1 (C-1/13), 30.9 (C-15/20), 27.4 (C-7), 26.0 (C-16/21), 19.7 (C-17/22), 19.0 (C-6/8); IR (film): $\tilde{\nu} = 2942$ (s), 2869 (m), 2257 (w), 1120 (s), 1026 cm^{-1} (vs); UV/Vis: λ_{max} (log ε) = 244 (3.01), 258 (2.78), 276 nm (1.93); HRMS (FAB+) *m/z* calcd: 369.2066 [M^++H]; found: 369.2078; elemental analysis calcd (%) for $C_{23}H_{28}O_4$ (368.47): C 74.97, H 7.66; found: C 74.91, H 7.71.

Trideca-2,4,9,11-tetrayne-1,13-diol (17): A solution of concentrated H_2SO_4 (0.1 mL) in water (2.5 mL) was added dropwise to a magnetically stirred solution of **16** (2.88 g, 7.8 mmol) in methanol (50 mL). Stirring was continued at room temperature over night. The solvent was evaporated and the residue dissolved in ethyl acetate. The organic solution was washed with a saturated aqueous solution of sodium hydrogencarbonate (2 × 50 mL) and brine (1 × 50 mL), and dried over anhydrous sodium sulfate. After filtration the ethyl acetate was partly removed, leaving approx-

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imately 10 mL. Petroleum ether (100 mL) was added dropwise to the resulting solution and the beginning crystallization was completed at −30 °C over night. The crystals were filtered off and dried in vacuo yielding **17** (1.31 g, 6.5 mmol, 84 %) as colorless solid, which turns readily red on expose to light (m.p. 88–89 °C, R_f (Al_2O_3, Et_2O) = 0.5). ^{1}H NMR (CD_3OD, 500 MHz): δ = 4.21 (s, 4H; H-1/13), 2.41 (t, $^3J_{H6,H7/H8,H7}$ = 6.9 Hz, 4H; H-6/8), 1.74 ppm (quin, $^3J_{H7,H6/H7,H8}$ = 6.9 Hz, 2H; H-7); ^{13}C NMR (CD_3OD, 125 MHz): δ = 80.1 (C-5/9), 75.8 (C-2/12), 70.2 (C-3/11), 66.3 (C-4/10), 51.0 (C-1/13), 28.1 (C-7), 18.9 ppm (C-6/8); IR (KBr): $\tilde{\nu}$ = 2928 (s), 2858 (m), 2252 (w), 1630 (m), 1426 (m), 1353 (s), 1229 (m), 1120 (w), 1022 cm^{-1} (vs); UV/Vis: λ_{max} (log ε) = 244 (2.94), 258 (2.75), 274 (2.10), 286 nm (1.93); HRMS (EI+) *m*/*z* calcd: 200.0837 [M^+]; found: 200.0845.

1,13-Dibromotrideca-2,4,9,11-tetrayne (18): Diol **17** (1.31 g, 6.5 mmol) was dissolved in diethyl ether (150 mL). Pyridine (0.5 mL) was added, and the reaction mixture was cooled to 0 °C. Under magnetic stirring a solution of phosphorus(III) bromide (0.94 mL, 9.8 mmol) in diethyl ether (20 mL) was added dropwise within 1.5 h. Then the reaction mixture was stirred at room temperature for 2 days. The polyphosphorus acid was neutralized by addition of a saturated aqueous solution of sodium hydrogencarbonate (30 mL). The ether layer was separated, and the aqueous layer was extracted twice with diethyl ether. The combined organic layers were washed with a saturated aqueous solution of sodium hydrogencarbonate and water, and dried over anhydrous sodium sulfate. After filtration the solvent was removed and the crude product was purified by column chromatography (Alox III, petrol ether/diethyl ether 5:1, R_f = 0.5) to yield **18** (1.31 g, 4.0 mmol, 62 %) as a pale yellow oil. By freezing the oil becomes a colorless solid (m.p. 36–37 °C) that turns pink on exposure to light. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 3.95 (s, 4H; H-1/13), 2.44 (t, $^3J_{H-6/8,H-7}$ = 6.9 Hz, 4H; H-6/8), 1.77 ppm (quin, $^3J_{H-7,H-6/8}$ = 6.9 Hz, 2H; H-7); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 82.0 (C-5/9), 72.2 (C-2/12), 71.2 (C-3/11), 66.1 (C-4/10), 27.2 (C-7), 19.1 (C-6/8), 15.2 ppm (C-1/13); IR (KBr): $\tilde{\nu}$ = 2938 (w), 2252 (s), 1422 (m), 1259 (s), 1198 (vs), 607 ppm (s); UV/Vis: λ_{max} (log ε) = 242 (3.74), 256 (3.83), 268 nm (3.71); HRMS (EI+) *m*/*z* calcd: 246.9945 [$C_{13}H_{10}{}^{81}Br^+$], 244.9966 [$C_{13}H_{10}{}^{79}Br^+$]; found: 246.9927, 244.9968; elemental analysis calcd (%) for $C_{13}H_{10}Br_2$ (326.03): C 47.89, H 3.09, Br 49.02; found: C 48.00, H 3.16, Br 48.81.

General procedure for the preparation of 1-alkyl/aryl-substituted 1-azacyclotetradeca-3,5,10,12-tetraynes (20a–20g): Freshly ground potassium carbonate and the relevant amine were added to a solution of **18** in acetonitrile. The mixture was heated to slight reflux, and the reaction monitored by TLC. After the starting material had disappeared, the reaction mixture was allowed to cool to room temperature. The solvent was evaporated, and the residue was dissolved in a mixture of diethyl ether and water. The ether layer was separated and the aqueous layer was extracted twice with diethyl ether. The combined organic layers were dried over anhydrous sodium sulfate and filtered. After evaporation of the solvent, the crude product was purified by column chromatography, by using Alox III and mixtures of petrol ether and diethyl ether. Ratios and further data are given below.

1-Methyl-1-azacyclotetradeca-3,5,10,12-tetrayne (20a): Compound **18** (326 mg, 1.0 mmol) was heated together with methylamine (0.1 mL, 1.5 mmol) and potassium carbonate (1.39 g) in acetonitrile (135 mL), yielding **20a** (12 mg, 0.06 mmol, 6 %) as a light brown, light-sensitive solid after column chromatography (R_f = 0.2; 5:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.52 (s, 4H; H-2/14), 2.55 (s, 3H; H-15), 2.40 (t, $^3J_{H-7/9,H-8}$ = 5.7 Hz, 2H; H-7/9), 1.78 ppm (quin, $^3J_{H-8,H-7/9}$ = 5.7 Hz, 2H; H-8); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 80.3 (C-6/10), 73.3 (C-3/13), 72.4 (C-4/12), 68.3 (C-5/11), 47.0 (C-2/14), 39.4 (C-15), 24.3 (C-8), 20.3 ppm (C-7/9); HRMS (EI+) *m*/*z* calcd: 195.1048 [M^+]; found: 195.1031.

1-Ethyl-1-azacyclotetradeca-3,5,10,12-tetrayne (20b): Compound **18** (0.49 g, 1.5 mmol), ethylamine (0.15 mL, 2.25 mmol), and potassium carbonate (2.07 g) were refluxed in acetonitrile (200 mL). Column chromatography (R_f = 0.35; 5:1) yielded **20b** (100 mg, 0.48 mmol, 32 %) as a colorless, felted, slightly light-sensitive solid (m.p. >90 °C decomp). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 3.57 (s, 4H; H-2/14), 2.89 (quart, $^3J_{H-15,H-16}$ = 7.2 Hz, 2H; H-15), 2.41 (t, $^3J_{H-7/9,H-8}$ = 5.7 Hz, 2H; H-7/9), 1.78 (quin, $^3J_{H-8,H-7/9}$ = 5.7 Hz, 2H; H-8), 1.09 ppm (t, $^3J_{H-16,H-15}$ = 7.2 Hz, 3H; H-16); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 80.3 (C-6/10), 73.6 (C-3/13), 72.1 (C-4/12), 68.4 (C-5/11), 45.0 (C-15), 44.8 (C-2/14), 24.3 (C-8), 20.4 (C-7/9), 13.0 ppm (C-16); IR (KBr): $\tilde{\nu}$ = 2968 (m), 2931 (m), 2853 (w), 2248 (w), 1631 (m), 1424 (m), 1327 cm^{-1} (m); UV/Vis: λ_{max} (log ε) = 252 (4.23), 264 nm (3.92); HRMS (EI+) *m*/*z* calcd: 209.1205 [M^+]; found: 209.1187; elemental analysis calcd (%) for $C_{15}H_{15}N$ (209.29): C 86.08, H 7.22, N 6.69; found: C 85.96, H 7.19, N 6.73.

1-Isopropyl-1-azacyclotetradeca-3,5,10,12-tetrayne (20c): Compound **18** (2.99 g, 9.2 mmol) and isopropylamine (0.80 mL, 9.2 mmol) were refluxed toghether with potassium carbonate (12.7 g) in acetonitrile (1.2 L). After column chromatography (R_f = 0.21; 10:1) **20c** (657 mg, 2.3 mmol, 32 %) was obtained as light brown, felted, light-sensitive solid (m.p. >115 °C decomp). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 3.61 (s, 4H; H-2/14), 3.42 (sept, $^3J_{H-15,H-16/17}$ = 6.2 Hz, 1H; H-15), 2.41 (t, $^3J_{H-7/9,H-8}$ = 5.8 Hz, 4H; H-7/9), 1.78 (quin, $^3J_{H-8,H-7/9}$ = 5.8 Hz, 2H; H-8), 1.14 ppm (d, $^3J_{H-16/17,H-15}$ = 6.2 Hz, 6H; H-16/17); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 80.4 (C-6/10), 74.0 (C-3/13), 72.2 (C-4/12), 68.3 (C-5/11), 47.7 (C-15), 43.9 (C-2/14), 24.3 (C-8), 21.5 (C-16/17), 20.4 ppm (C-7/9); IR (KBr): $\tilde{\nu}$ = 2970 (m), 2931 (m), 2247 (w), 1630 (m), 1429 (m), 1331 (m), 1158 cm^{-1} (w); UV/Vis: λ_{max} (log ε) = 252 (3.06), 264 nm (2.79); HRMS (EI+) *m*/*z* calcd: 223.1361 [M^+]; found: 223.1356; elemental analysis calcd (%) for $C_{16}H_{17}N$ (223.31): C 86.05, H 7.67, N 6.27; found :C 85.78, H 7.61, N 6.26.

1-*n*-Butyl-1-azacyclotetradeca-3,5,10,12-tetrayne (20d): Compound **18** (326 mg, 1.0 mmol) was heated together with *n*-butylamine (0.07 mL, 1.0 mmol) and potassium carbonate (1.39 g) in acetonitrile (125 mL). Column chromatography (R_f = 0.29; 10:1) yielded **20d** (83 mg, 0.4 mmol, 35 %) as a colorless, slightly light-sensitive solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.54 (s, 4H; H-2/14), 2.81 (t, $^3J_{H-15,H-16}$ = 7.0 Hz, 2H; H-15), 2.41 (t, $^3J_{H-7/9,H-8}$ = 6.0 Hz, 4H; H-7/9), 1.78 (quin, $^3J_{H-8,H-7/9}$ = 6.0 Hz, 2H; H-8), 1.45–1.31 (m, 4H; H-16,17), 0.92 (t, $^3J_{H-18,H-17}$ = 7.0 Hz, 3H; H-18); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 80.2 (C-6/10), 73.7 (C-3/13), 72.1 (C-4/12), 68.4 (C-5/11), 50.5 (C-15), 45.1 (C-2/14), 29.8 (C-16), 24.3 (C-8), 20.6 (C-17), 20.4 (C-7/9), 14.2 cm^{-1} (C-19); IR (Kbr): ν = 2953 (m), 2930 (m), 2860 (m), 2246 (w), 1722 (w), 1628 (m), 1424 (m), 1331 (m), 1162 (w), 958 (w), 670 (w), 558 cm^{-1} (w); UV/Vis: λ_{max} (log ε) = 250 (3.11), 264 nm (2.76); HRMS (EI+) *m*/*z* calcd: 237.1517 [M^+]; found: 237.1506.

1-*tert*-Butyl-1-azacyclotetradeca-3,5,10,12-tetrayne (20e): Compound **18** (0.50 g, 1.5 mmol) and *tert*-butylamine (0.16 mL, 1.5 mmol) were refluxed together with potassium carbonate (2.12 g) in acetonitrile (200 mL). After column chromatography (R_f = 0.42; 5:1) **20e** (47 mg, 0.2 mmol, 13 %) was obtained as colorless, needle-shaped, slightly light-sensitive crystals (m.p. 88 °C decomp). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 3.62 (s, 4H; H-2/14), 2.40 (t, $^3J_{H-7/9,H-8}$ = 5.8 Hz, 4H; H-7/9), 1.77 (quin, $^3J_{H-8,H-7/9}$ = 5.8 Hz, 2H; H-8), 1.29 ppm (s, 9H; H-16,17,18); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 80.6 (C-6/10), 77.6 (C-3/13), 71.6 (C-4/12), 68.6 (C-5/11), 55.6 (C-15), 40.8 (C-2/14), 28.6 (C-16,17,18), 24.5 (C-8), 20.5 ppm (C-7/9); IR (Kbr): $\tilde{\nu}$ = 2963 (vs), 2243 (w), 1604 (w), 1421 (m), 1386 (s), 1260 (vs), 1207 (s), 1084 (vs), 1022 (vs), 933 (m), 802 cm^{-1} (vs); UV/Vis: λ_{max} (log ε) = 242 (3.40), 252 (3.37), 264 (3.28), 282 (2.87), 296 (2.60), 344 nm (2.27); HRMS (EI+) *m*/*z* calcd: 237.1518 [M^+]; found: 237.1525.

1-Phenyl-1-azacyclotetradeca-3,5,10,12-tetrayne (20f): Compound **18** (500 mg, 1.5 mmol) and freshly destilled aniline (0.14 mL, 1.5 mmol) were refluxed with potassium carbonate (2.11 g) in acetonitrile (200 mL). Column chromatography (R_f = 0.25; 5:1) yielded **20f** (9 mg, 0.04 mmol, 2 %) as a colorless solid. ^{1}H NMR (500 MHz, CD_2Cl_2): δ = 7.33 (dd, $^3J_{H-17,H-16/H-19,H-20}$ = 8.4 Hz, $^3J_{H-17/19,H-18}$ = 7.4 Hz, 2H; H-17/19), 6.94 (d, $^3J_{H-16,H-17/H-20,H-19}$ = 8.4 Hz, 2H; H-16/20), 6.92 (t, $^3J_{H-18,H-17/19}$ = 7.4 Hz, 1H; H-18), 4.20 (s, 4H; H-2/14), 2.33 (t, $^3J_{H-7/9,H-8}$ = 5.8 Hz, 4H; H-7/9), 1.70 ppm (quin, $^3J_{H-8,H-7/9}$ = 5.8 Hz, 2H; H-8); ^{13}C NMR (125 MHz, CD_2Cl_2): δ = 146.5 (C-15), 129.6 (C-17/19), 119.6 (C-18), 115.4 (C-16/20), 81.3 (C-6/10), 74.0 (C-3/13), 70.7 (C-4/12), 67.9 (C-5/11), 42.6 (C-2/14), 24.6 (C-8), 20.3 ppm (C-7/9); HRMS (EI+) *m*/*z* calcd: 257.1205 [M^+]; found: 257.1189.

1-(*p*-Methoxyphenyl)-1-azacyclotetradeca-3,5,10,12-tetrayne (20g): Compound **18** (0.90 g, 2.8 mmol), *p*-anisidine (0.34 g, 2.8 mmol), and potassium carbonate (3.81 g) were heated in acetonitrile (360 mL). After column chromatography (R_f = 0.23; 5:1) **20g** (52 mg, 0.2 mmol, 7 %) was obtained as slightly yellow crystals (m.p. > 105 °C decomp). ^{1}H NMR (500 MHz, C_6D_6): δ = 6.84 (d, $^3J_{H-17,H-16/H-19,H-20}$ = 9.4 Hz, 2H; H-17/19), 6.75 (d, $^3J_{H-16,H-17/H-20,H-19}$ = 9.4 Hz, 2H; H-16/20), 3.62 (s, 4H; H-2/14), 3.32 (s, 3H; H-21), 1.66 (t, $^3J_{H-7/9,H-8}$ = 6.0 Hz, 4H; H-7/9), 0.93 ppm (quin, $^3J_{H-8,H-7/9}$ = 6.0 Hz, 2H; H-8); ^{13}C NMR (75 MHz, C_6D_6): δ = 154.1 (C-18), 140.8 (C-15), 117.8 (C-17/19), 115.1 (C-16/20), 80.8 (C-6/10), 74.4 (C-3/13), 72.1 (C-4/12), 69.3 (C-5/11), 55.0 (C-21), 43.1 (C-2/14), 24.3 (C-8), 20.0 ppm (C-7/9); IR (KBr): $\tilde{\nu}$ = 2962 (w), 1512 (vs), 1444 (m), 1259 (s), 1029 (s), 818 cm^{-1} (s);

UV/Vis: λ_{max} ($\log\varepsilon$) = 244 (3.87), 280 nm (3.52); HRMS (EI+) *m*/*z* calcd: 287.1310 [M^+]; found: 287.1303.

***N,N'*-Di-*tert*-butyltrideca-2,4,9,11-tetrayne-1,13-diamine (21e)**: From the synthetic procedure described for compound **20e**, compound **21e** (209 mg, 0.7 mmol, 44%) was formed in a side reaction. A yellow, viscous liquid was obtained from column chromatography (R_f = 0.18; 1:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.43 (s, 4H; H-1/13), 2.37 (t, $^3J_{H\text{-}6/8,H\text{-}7}$ = 7.0 Hz, 4H; H-6/8), 1.69 (quin, $^3J_{H\text{-}7,H\text{-}6/8}$ = 7.0 Hz, 2H; H-7), 1.10 ppm (s, 18H; H-15/16/17/19/20/21); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 77.8 (C-5/9), 76.3 (C-2/12), 67.7 (C-3/11), 66.0 (C-4/10), 51.0 (C-14/18), 32.9 (C-1/13), 29.1 (C-15/16/17/19/20/21), 27.0 (C-7), 18.4 ppm (C-6/8); IR (film): $\tilde{\nu}$ = 2962 (vs), 2258 (w), 1479 (m), 1364 (s), 1228 (s), 1086 (m), 1032 (w), 744 cm^{-1} (m); UV/Vis: λ_{max} ($\log\varepsilon$) = 242 (3.36), 254 (3.07) 286 nm (2.91); HRMS (EI+) *m*/*z* calcd: 310.2409 [M^+]; found: 310.2401.

1,15-Diisopropyl-1,15-diazacyclooctaeicosa-3,5,10,12,17,19,24,26-octayne (22c): We were able to isolate 159 mg (0.4 mmol, 4%) of **22c**, a side product of the synthesis of **20c**, after column chromatography (R_f = 0.43; 1:1) as light brown solid (m.p. >90 °C decomp). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 3.61 (s, 8H; H-2/14/16/28), 3.04 (sept, $^3J_{H\text{-}29,H\text{-}30/31/H\text{-}32,H\text{-}33/34}$ = 6.3 Hz, 2H; H-29/32), 2.43 (t, $^3J_{H\text{-}7/9,H\text{-}8/H\text{-}21/23,H\text{-}22}$ = 6.8 Hz, 8H; H-7/9/21/23), 1.77 (quin, $^3J_{H\text{-}8,H\text{-}7/9/H\text{-}22,H\text{-}21/23}$ = 6.8 Hz, 4H; H-8/22), 1.10 ppm (d, $^3J_{H\text{-}30/31,H\text{-}29/H\text{-}33/34,H\text{-}32}$ = 6.3 Hz, 12H; H-30/31/33/34); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 77.9 (C-6/10/20/24), 72.9 (C-3/13/17/27), 70.4 (C-4/12/18/26), 66.3 (C-5/11/19/25), 50.3 (C-29/32), 41.9 (C-2/14/16/28), 27.2 (C-8/22), 20.9 (C-30/31/33/34), 18.5 ppm (C-7/9/21/23); HRMS (FAB+) *m*/*z* calcd: 447.2800 [M^++H]; found: 447.2773.

2,10-Dichloro-6-isopropyl-6-azatricyclo[9.3.0.0^{4,8}]tetradeca-1(11),2,4(8),9-tetraene (25c): A suspension of tetrayne **20c** (200 mg, 0.9 mmol) in ethanol (5 mL) and concentrated hydrochloric acid (10 mL) was heated to 80 °C with magnetic stirring. To monitor the reaction, small quantities were withdrawn from the reaction mixture periodically, treated with sodium hydroxide solution, extracted with diethyl ether and subjected to TLC. To avoid oxidation of the product, the workup was carried out in an argon atmosphere: the reaction mixture was added slowly to a magnetically stirred and cooled mixture of a solution of sodium hydroxide (10 g) in water (20 mL) and diethyl ether (50 mL). The organic layer was separated, and the aqueous layer was extracted three times with diethyl ether. The ether layers were combined and the solvent was distilled off at room temperature by using a cryo trap cooled with liquid nitrogen. The crude product was purified by column chromatography under protective gas (Alox III, petrol ether/diethyl ether 20:1, R_f = 0.27), yielding **25c** (0.2 g, 0.7 mmol, 74%) as a slightly yellow solid (m.p. 91–93 °C). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 5.85 (s, 2H; H-3/9), 3.52–3.44 (m, 2H; H-5/7^a), 3.33–3.27 (m, 2H; H-5/7^b), 2.76–2.65 (m, 2H; H-12/14^a), 2.57 (sept, $^3J_{H\text{-}15,H\text{-}16/17}$ = 6.3 Hz, 1H; H-15,), 2.35–2.25 (m, 2H; H-12/14^b), 2.11–1.90 (m, 2H; H-13), 1.05 ppm (d, $^3J_{H\text{-}16/17,H\text{-}15}$ = 6.3 Hz, 6H; H-16/17); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 141.8 (C-1/11), 136.4 (C-4/8), 131.2 (C-2/10), 125.5 (C-3/9), 60.9 (C-5/7), 54.3 (C-15), 36.2 (C-12/14), 22.1 (C-13), 2.8 ppm (C-16/17); IR (Kbr): $\tilde{\nu}$ = 2963 (s), 2874 (s), 2783 (s), 2607 (w), 1610 (s), 1447 (m), 1379 (m), 1323 (s), 1233 (m), 1190 (m), 889 (m), 851 (m), 829 (m), 770 (m), 693 cm^{-1} (m); UV/Vis: λ_{max} ($\log\varepsilon$) = 296 (2.88), 350 nm (2.52); HRMS (EI+) *m*/*z* calcd: 299.0837 [$C_{16}H_{19}{}^{37}Cl_2N^+$], 297.0865 [$C_{16}H_{19}{}^{37}Cl^{35}ClN^+$], 295.0895 [$C_{16}H_{19}{}^{35}Cl_2N^+$]; found: 299.0886, 297.0852, 295.0889; elemental analysis calcd (%) for $C_{16}H_{19}Cl_2N$ (296.23): C 64.87, H 6.46, N 4.73, Cl 23.94; found: C 64.92, H 6.49, N 4.76, Cl 23.94.

[3,9-D$_2$]-2,10-Dichloro-6-isopropyl-6-azatricyclo[9.3.0.0^{4,8}]tetradeca-1(11),2,4(8),9-tetraene ([D$_2$]25c): The reaction was carried out according to the synthesis of **25c** but with [D$_1$]ethanol (5 mL) and DCl (10 mL) in D_2O yielding [D$_2$]**25c** (7 mg, 0.02 mmol, 3%) as yellow crystals. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 3.56–3.44 (m, 2H; H-5/7^a), 3.35–3.27 (m, 2H; H-5/7^b), 2.76–2.65 (m, 2H; H-12/14^a), 2.59 (sept, $^3J_{H\text{-}15,H\text{-}16/17}$ = 6.3 Hz, 1H; H-15), 2.33–2.24 (m, 2H; H-12/14^b), 2.13–1.85 (m, 2H; H-13), 1.05 ppm (d, $^3J_{H\text{-}16/17,H\text{-}15}$ = 6.3 Hz, 6H; H-16/17); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 141.8 (C-1/11), 136.4 (C-4/8), 132.0 (C-2/10), 60.8 (C-5/7), 54.3 (C-15), 36.2 (C-12/14), 22.1 (C-13), 21.8 ppm (C-16/17); HRMS (EI+) *m*/*z* calcd: 301.0961 [$C_{16}H_{17}{}^{37}Cl_2D_2N^+$], 299.0990 [$C_{16}H_{17}{}^{37}Cl^{35}ClD_2N^+$], 297.1200 [$C_{16}H_{17}{}^{35}Cl_2D_2N^+$]; found: 301.0974, 299.0965, 297.0952.

2,10-Dichloro-6-isopropyl-6-azatricyclo[9.3.0.0^{4,8}]tetradeca-1(11),2,4,7,9-pentaene (27c): 2,3-Dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) (224 mg, 1.0 mmol) was added to a solution of **25c** (257 mg, 0.9 mmol) in chloroform (25 mL). After 5 minutes the resulting residue was filtered off. Purification of the crude product was done by column chromatography (Alox III, petrol ether, R_f = 0.35). Compound **27c** (117 mg, 0.4 mmol, 46%) was obtained as colorless crystals (m.p. 125–127 °C). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 6.50 (s, 2H; H-5/7), 6.38 (s, 2H; H-3/9), 4.09 (sept, $^3J_{H\text{-}15,H\text{-}16/17}$ = 6.7 Hz, 1H; H-15), 2.59 (br, 4H; H-12/14), 1.94 (quin, $^3J_{H\text{-}13,H\text{-}12/14}$ = 7.6 Hz, 2H; H-13), 1.40 ppm (d, $^3J_{H\text{-}16/17,H\text{-}15}$ = 6.7 Hz, 6H; H-16/17); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 139.8 (C-1/11), 129.1 (C-2/10), 124.5 (C-3/9), 119.4 (C-5/7), 118.2 (C-4/8), 51.2 (C-15), 36.9 (C-12/14), 23.8 (C-16/17), 22.3 ppm (C-13); IR (KBr): $\tilde{\nu}$ = 2967 (s), 2851 (m), 1629 (m), 1527 (s), 1442 (m), 1367 (m), 1297 (m), 1199 (m), 1176 (s), 1139 (s), 1031 (m), 899 (s), 839 (s), 784 (vs), 709 (s), 629 cm^{-1} (m); UV/Vis: λ_{max} ($\log\varepsilon$) = 236 (4.35), 306 nm (3.67); HRMS (EI+) *m*/*z* calcd: 297.0679 [$C_{16}H_{17}{}^{37}Cl_2N^+$], 295.0708 [$C_{16}H_{17}{}^{37}Cl^{35}ClN^+$], 293.0738 [$C_{16}H_{17}{}^{35}Cl_2N^+$]; found: 297.0671, 295.0705, 293.0741; elemental analysis calcd (%) for $C_{16}H_{17}Cl_2N$ (294.22): C 65.32, H 5.82, N 4.76; found: C 65.23, H 5.88, N 4.73.

10-Chloro-2-isopropyl-1,3,4,6,7,8-hexahydro-2*H*-benzo[*g*]isoquinolin-9-one (37c): Compound **20c** (300 mg, 1.3 mmol) was suspended in concentrated hydrochloric acid (20 mL). The reaction mixture was heated to 80 °C for 3 h, until there was no more starting material detectable by TLC (a small quantity was taken from the reaction mixture, treated with sodium hydroxide solution, and extracted with diethyl ether). The reaction mixture was allowed to cool to room temperature and was added to a stirred and cooled mixture of a solution of sodium hydroxide (15 g) in water (20 mL) and diethyl ether (20 mL). The ether layer was separated, and the aqueous layer extracted with three portions of ether. The combined organic layers were dried over anhydrous sodium sulfate and filtered. After removal of the solvent the crude product was purified by column chromatography (Alox III, petrol ether/diethyl ether 2:1, R_f = 0.16) yielding **37c** (19 mg, 0.1 mmol, 5%) as yellow solid (m.p. 63–66 °C). **WARNING**: Although the reaction was carried out safely several times, in one case spontaneous deflagration occured leaving a black, powdery, graphite-like solid! ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 6.92 (s, 1H; H-5), 3.75 (s, 2H; H-1), 2.98 (sept, $^3J_{H\text{-}11,H\text{-}12/13}$ = 6.5 Hz, 1H; H-11), 2.88 (t, $^3J_{H\text{-}4,H\text{-}3}$ = 5.8 Hz, , 2H; H-4), 2.86 (t, $^3J_{H\text{-}6,H\text{-}7}$ = 6.5 Hz, 2H; H-6), 2.70 (t, $^3J_{H\text{-}3,H\text{-}4}$ = 5.8 Hz, 2H; H-3), 2.64 (t, $^3J_{H\text{-}8,H\text{-}7}$ = 6.6 Hz, 2H; H-8), 2.04 (m, 2H; H-7), 1.14 ppm (d, $^3J_{H\text{-}12/13,H\text{-}11}$ = 6.5 Hz, 6H; H-12/13); ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 197.0 (C-9), 144.0 (C-5a), 141.9 (C-4a), 134.2 (C-10a), 132.7 (C-10), 127.9 (C-9a), 127.5 (C-5), 54.3 (C-11), 50.2 (C-1), 44.8 (C-3), 40.8 (C-8), 30.7, 30.6 (C-4,6), 22.8 (C-7), 18.5 ppm (C-12/13); IR (KBr): $\tilde{\nu}$ = 2920 (s), 2851 (m), 1686 (s), 1598 cm^{-1} (s); UV/Vis: λ_{max} ($\log\varepsilon$) = 262 (4.06), 302 nm (3.31); HRMS (EI+): *m*/*z*: calcd: 279.1204 [$C_{16}H_{20}{}^{37}ClNO^+$], 277.1233 [$C_{16}H_{20}{}^{35}ClNO^+$]; found: 279.1195, 277.1190.

[4,4,5-D$_3$]-10-Chloro-2-isopropyl-1,3,4,6,7,8-hexahydro-2*H*-benzo[*g*]isoquinolin-9-one ([D$_3$]37c): The reaction was carried out according to the synthesis of **37c**. Compound **20c** (300 mg, 1.33 mmol) was suspended in DCl (20 mL) in D_2O yielding **[D$_3$]37c** (21 mg, 0.07 mmol, 5%) as a yellow solid. ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 3.75 (s, 2H; H-1), 2.98 (sept, $^3J_{H\text{-}11,H\text{-}12/13}$ = 6.5 Hz, 1H; H-11), 2.87 (t, $^3J_{H\text{-}6,H\text{-}7}$ = 6.5 Hz, 2H; H-6), 2.69 (s, 2H; H-3), 2.64 (t, $^3J_{H\text{-}8,H\text{-}7}$ = 6.6 Hz, 2H; H-8), 2.04 (m, 2H; H-7), 1.14 ppm (d, $^3J_{H\text{-}12/13,H\text{-}11}$ = 6.5 Hz, 6H; H-12/13); ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 197.0 (C-9), 143.9 (C-5a), 141.7 (C-4a), 134.2 (C-10a), 132.7 (C-10), 128.0 (C-9a), 54.3 (C-11), 50.1 (C-1), 44.6 (C-3), 40.8 (C-8), 30.6 (C-6), 22.9 (C-7), 18.4 ppm (C-12/13); HRMS (EI+) *m*/*z* calcd: 282.1392 [$C_{16}H_{17}{}^{37}ClD_3NO^+$], 280.1421 [$C_{16}H_{17}{}^{35}ClD_3NO^+$]; found: 282.1390, 280.1432.

X-ray diffraction analyses: All measurements were carried out on a Brucker SMART diffractometer with graphite monochromated $Mo_{K\alpha}$ radiation using a CCD detector. Frames corresponding to a sphere of data were collected using the ω-scan technique; in each case 20 s exposures of 0.3° in ω were taken. The reflections were integrated and equivalent reflections were merged and an absorption correction was applied to all structures, except for **20b** and **20c** by using SADABS.[31] The data were corrected for Lorentz and polarization effects. The structures were solved by direct methods and expanded using Fourier techniques (SHELXTL 5.10).[31]. The structural parameters of the non-hydrogen atoms were refined anisotropically; hydrogen atoms were included in calculated positions except for the structures of **20b** and **27c**. The single crystals of **20c** were disordered: we found about 28% chair, 53% boat, and 19% "inverted" boat conformation, in which N and C8 (of the chair conformation) had changed places. The final cycle of full-matrix least-squares

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Table 2. Selected crystallographic data for **20b**, **20c**, **20f**, **27c**, and **37c**.

	20b	**20c**	**20f**	**27c**	**37c**
empirical formula	$C_{15}H_{15}N$	$C_{16}H_{17}N$	$C_{19}H_{15}N$	$C_{16}H_{17}Cl_2N$	$C_{16}H_{20}ClNO$
M_r	209.28	223.31	257.32	294.21	277.78
crystal size [mm^3]	$0.44 \times 0.21 \times 0.08$	$0.60 \times 0.10 \times 0.10$	$0.38 \times 0.32 \times 0.22$	$0.42 \times 0.22 \times 0.16$	$0.44 \times 0.20 \times 0.16$
crystal system	monoclinic	orthorhombic	triclinic	monoclinic	triclinic
space group	$P2_1/c$	$Pmn2_1$	$P\bar{1}$	$P2_1/c$	$P\bar{1}$
a [Å]	12.8262(8)	12.0906(3)	8.9469(3)	12.8798(3)	8.6299(4)
b [Å]	5.2560(3)	10.5958(3)	13.9246(4)	7.6161(2)	9.2301(4)
c [Å]	18.2412(11)	5.1624(2)	17.0568(5)	15.9958(4)	9.6701(4)
α [°]	90	90	92.332(1)	90	101.597(1)
β [°]	101.389(2)	90	99.508(1)	111.387(1)	98.863(1)
γ [°]	90	90	92.017(1)	90	108.105(1)
V [Å^3]	1205.51(13)	661.35(4)	2092.15(11)	1461.04(6)	697.52(5)
ρ_{calcd} [g cm^{-3}]	1.15	1.12	1.23	1.34	1.32
θ range [°]	1.6 to 24.1	1.9 to 23.3	1.2 to 27.5	1.7 to 27.5	2.2 to 27.5
Z	4	2	6	4	2
$F(000)$	448	240	816	616	344
h_{min}/h_{max}	−14/14	−13/13	−11/11	−16/16	−10/11
k_{min}/k_{max}	−6/6	−11/11	−18/18	−9/9	−11/11
l_{min}/l_{max}	−20/20	−5/5	−22/22	−20/20	−12/12
μ [mm^{-1}]	0.07	0.06	0.07	0.43	0.27
reflns collected	8867	4768	21819	14515	7224
unique reflns	1906	1004	9531	3336	3165
observed reflns	1295	870	6166	2855	2678
variables	205	96	541	240	174
$R(F^2)$	0.040	0.056	0.041	0.029	0.033
$R_w(F^2)$	0.083	0.137	0.093	0.075	0.086
S (Gof) on F^2	1.02	1.18	0.99	1.06	1.03
$[\Delta\rho]_{max}$ [e Å^{-3}]	0.13	0.21	0.17	0.29	0.30
$[\Delta\rho]_{min}$ [e Å^{-3}]	−0.16	−0.19	−0.21	−0.23	−0.25

refinement converged. The function minimized was $\Sigma w[(F_o)^2 - (F_c)^2]^2$. All calculations were performed with the SHELXTL crystallographic software package of Bruker.[31] Table 2 contains the crystallographic data and details of the refinement procedure for componds **20b**, **20c**, **20f**, **27c**, and **37c**. The X-ray studies were performed at 200(2) K. CCDC-197950 (**20b**), CCDC-197951 (**20c**), CCDC-197952 (**20f**), CCDC-197953 (**27c**) and CCDC-197954 (**37c**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: (+44) 1223–336–033; or email: deposit@ccdc.cam.ac.uk).

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[1] R. H. Mitchell, F. Sondheimer, *Tetrahedron* **1970**, *26*, 2140–2150; H. A. Staab, J. Ipaktschi, A. Nissen, *Chem. Ber.* **1971**, *109*, 1182–1190.
[2] A. G. Myers, N. S. Finney, *J. Am. Chem. Soc.* **1992**, *114*, 10986–10987 and references therein.
[3] W. R. Roth, T. Wasser, R. Gleiter, H. Weigl, *Liebigs Ann./Recueil* **1997**, 1329–1331; G. Haberhauer, R. Gleiter, *J. Am. Chem. Soc.* **1999**, *121*, 4664–4668.
[4] G. Wegner, *Z. Naturforsch. Teil B* **1969**, *24*, 824–832; G. Wegner, *Mater. Chem.* **1971**, *45*, 85–94
[5] H. Sixl, *Adv. Polym. Sci.* **1984**, *43*, 49–90.
[6] O. M. Behr, G. Eglinton, A. R. Galbraith, R. A. Raphael, *J. Chem. Soc.* **1960**, 3614–3625.
[7] G. M. Pilling, F. Sondheimer, *J. Am. Chem. Soc.* **1971**, *93*, 1970–1977.
[8] Q. Zhou, P. J. Carroll, T. M. Swager, *J. Org. Chem.* **1994**, *51*, 1294–1301.
[9] J. Ritter, R. Gleiter, *Eur. J. Org. Chem.* **1997**, 1179–1188; R. Gleiter, H. Weigl. G. Haberhauer, *Eur. J. Org. Chem.* **1998**, 1447–1453.
[10] A. L. Henne, K. W. Greenlee, *J. Am. Chem. Soc.* **1945**, *67*, 484–485.
[11] A. Commercon, J. F. Normant, J. V. Villieras, *Tetrahedron* **1980**, *36*, 1215–1221; P.-Y. Kwok, F. W. Muellner, C.-K. Chen, J. Fried, *J. Am. Chem. Soc.* **1987**, *109*, 3684–3692.
[12] W. Chodkiewicz, P. Cadiot, *C. R. Hebd. Seances Acad. Sci.* **1955**, *241*, 1055–1057; W. Chodkiewicz, *Ann. Chim. (Paris)* **1957**, *2*, 819–869; P. Cadiot, W. Chodkiewicz in *Chemistry of Acetylenes* (Ed.: H. G. Viehe), Marcel Dekker, New York, **1969**, 597–647; F. Bohlmann, P. Herbst, H. Gleinig, *Chem. Ber.* **1961**, *94*, 948–957; G. Eglinton, W. McCrae, *Adv. Org. Chem.* **1963**, *4*, 225–2328.
[13] M. Alami, F. Ferri, *Tetrahedron Lett.* **1996**, *37*, 2763–2766
[14] J. J. Langer, G. P. Moss, *Mol. Cryst. Liq. Cryst.* **1993**, *237*, 459–461.
[15] J. J. Delpuech in *Cyclic Organonitrogen Stereodynamics* (Eds.: J. B. Lambert, Y. Takeuchi), VCH, Weinheim (Germany), **1992**, 169–252; H. Friebolin, *One- and Two-Dimensional NMR spectroscopy*, VCH, Weinheim (Germany), **1992**.
[16] J. Ritter, R. Gleiter, H. Irngartinger, T. Oeser, *J. Am. Chem. Soc.* **1997**, *119*, 10599–10607.
[17] M. J. S. Dewar, E. G. Zoebisch, E. F. Healy, J. J. P. Stewart, *J. Am. Chem. Soc.* **1985**, *107*, 3902–3909.
[18] R. Gleiter, R. Merger, J. Chavez, T. Oeser, H. Irngartinger, H. Pritzkow, B. Nuber, *Eur. J. Org. Chem.* **1999**, 2841–2843.
[19] K. Hövermann, J. Ritter, F. Rominger, B. Nuber, R. Gleiter, *Eur. J. Org. Chem.* **2000**, 2291–2294.
[20] H. Hopf, G. Maas, *Angew. Chem.* **1992**, *104*, 953–977: *Angew. Chem. Int. Ed. Engl.* **1992**, *31*, 1068–1092 and references therein.
[21] S. W. Staley, R. A. Grimm, R. A. Sablosky, *J. Am. Chem. Soc.* **1998**, *120*, 3671–3674
[22] R. Kreher, J. Seubert, *Angew. Chem.* **1964**, *76*, 682–683; *Angew. Chem. Int. Ed. Engl.* **1964**, *3*, 639–640; R. P. Kreher, J. Seubert, D. Schmitt, G. Use, N. Kohl, *Chemiker-Ztg.* **1988**, *112*, 85–92.
[23] E. Vogel, H.-J. Altenbach, J.-M. Drossard, H. Schmickler, H. Stegelmeier, *Angew. Chem.* **1980**, *92*, 1053–1054; *Angew. Chem. Int. Ed. Engl.* **1980**, *19*, 1016–1017.

  0947-6539/03/0908-1821 $ 20.00+.50/0

[24] Structures were fully optimized at the B3LYP 6–31G* density functional theory level. The combination of Beckes three-parameter exchange functional (B3)[25] together with the correlation functional of Lee, Young, and Parr (LYP),[26] as implemented in Gaussian 98,[27] was employed.
[25] A. D. Becke, *J. Chem. Phys.* **1993**, *98*, 5648–5652.
[26] C. Lee, W. Yang, R. G. Parr, *Phys. Rev. B* **1988**, *37*, 785–789.
[27] Gaussian 98, Revision A.9, M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, V. G. Zakrzewski, J. A. Montgomery, Jr., R. E. Stratmann, J. C. Burant, S. Dapprich, J. M. Millam, A. D. Daniels, K. N. Kudin, M. C. Strain, O. Farkas, J. Tomasi, V. Barone, M. Cossi, R. Cammi, B. Mennucci, C. Pomelli, C. Adamo, S. Clifford, J. Ochterski, G. A. Petersson, P. Y. Ayala, Q. Cui, K. Morokuma, D. K. Malick, A. D. Rabuck, K. Raghavachari, J. B. Foresman, J. Cioslowski, J. V. Oritz, A. G. Baboul, B. B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R. Gomperts, R. L. Martin, D. J. Fox, T. Keith, M. A. Al-Laham, C. Y. Peng, A. Nanayakkara, M. Challacombe, P. M. W. Gill, B. Johnson, W. Chen, M. W. Wong, J. L. Andres, C. Gonzalez, M. Head-Gordon, E. S. Replogle, J. A. Pople, Gaussian, Inc., Pittsburgh PA, **1998**.
[28] E. M. Schmidt, S. K. Goll, unpublished results.
[29] S. Hernandez, M. M. Kirchhoff, S. G. Swartz, Jr., R. P. Johnson, *Tetrahedron Lett.* **1996**, *37*, 4907–4910.
[30] B. Engels, J. C. Schöneboom. A. F. Münster, S. Groetsch, M. Christl, *J. Am. Chem. Soc.* **2002**, *124*, 287–297; R. P. Johnson, *Chem. Rev.* **1989**, *89*, 1111–1124.
[31] G. M. Sheldrick, Bruker Analytical X-ray Division, Madison, WI, **1997**.

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  0947-6539/03/0908-1822 $ 20.00+.50/0