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3-AZA[5]METACYCLOPHANES: SYNTHESIS AND REACTIONS[‡]

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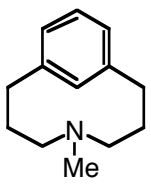
Abstract - The synthesis of the dichloro substituted 3-aza[5]metacyclophane (**6b**) has been achieved starting from the *N*-tosyl derivative (**7**) by a four-step procedure consisting of dichlorocarbene addition, flash vacuum thermolysis, a second dichlorocarbene addition, and base catalyzed elimination; similarly, the monochloro analogue (**6c**) was prepared. Their structure was confirmed by X-Ray crystal structure determination which indicated that the deformation of their benzene rings was only slightly stronger than that of the carbon analogue 8,11-dichloro[5]metacyclophane (**15b**). ^{1}H NMR spectroscopy showed that in solution, like in the crystal, both **6b** and **6c** occurred in the exo conformation exclusively. Contrary to expectation, the reactivity of **6b** and **6c** towards several dienophiles was clearly higher than that of **15b**. Thermally, **6b** was converted to the 1,2,4,5-tetrahydropyrrolo[3,2,1-*hi*]indole (**23b**) by a remarkable intramolecular nucleophilic attack of the tosylamide nitrogen on the benzene ring.

Introduction

Azacyclophanes have been of interest for quite some time. As early as 1919, von Braun reported the synthesis of the aza[7]metacyclophane (**1**).[1] In 1920, the same author claimed the synthesis of a 3-aza[5]metacyclophane (**2**).[2] This latter structure assignment was revised in 1926 by Titley,[3] who identified the product as 2-aminoethyl-3-methylbenzenemethylbenzene (**3**).



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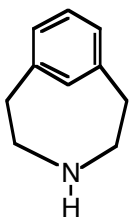

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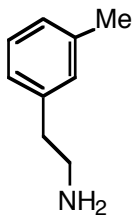

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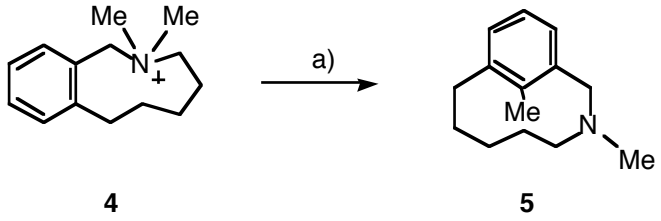
Dedicated to Prof. Dr. Shô Itô, an exceptionally good friend, at the occasion of his 77th birthday.

The most recent report of a small aza[n]metacyclophane (n ≤ 7) was by Barbry and coworkers, who obtained, besides other products, the 2-aza[7]metacyclophane (**5**) *via* a Sommelet-Hauserre arrangement of the benzazoninium salt (**4**) (Scheme 1).[4] So far there have been no reports on the synthesis of aza[6]- or of aza[5]metacyclophanes.

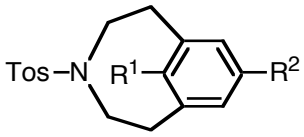


4 **5**

Scheme 1. a) $NaNH_2/NH_3(l)$.

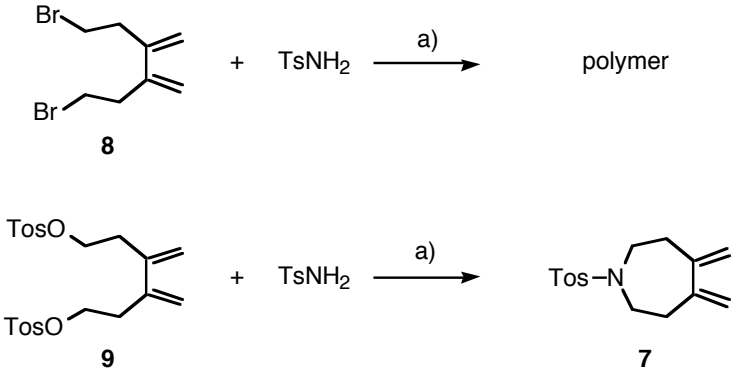
In the context of our interest in small strained metacyclophanes,[5] we investigated strategies to obtain derivatives of 3-aza[5]metacyclophane (**2**). In a short communication, the synthesis and X-Ray crystal structure of 8,11-dichloro-*N*-tosyl-3-aza[5]metacyclophane (**6b**) have been reported.[6] Here we describe the preparation and structure determination of **6b** and of its 11-monochloro derivative (**6c**) as well as results of a preliminary investigation of their reactivity towards dienophiles and of their unexpected behavior on heating.

6a: $R^1 = R^2 = H$
6b: $R^1 = R^2 = Cl$
6c: $R^1 = Cl$, $R^2 = H$



Syntheses

Carbene additions to 1,2-dimethylenecycloalkanes form a crucial aspect of our approach to small metacyclophanes.[5,6] In the present study, a derivative of 3,4-bismethyleneazepane was required in order to subject it to carbene additions. As carbenes tend to attack hetero atoms carrying free electron pairs, it was considered necessary to use a protected derivative such as the *N*-tosyl derivative (**7**). Whereas attempted ring closure of dibromide (**8**)[7] with $TsNH_2$ was not successful as it yielded predominantly elimination products and polymer, the bistosylate (**9**)[7] gave the desired **7** in 49% yield (Scheme 2).



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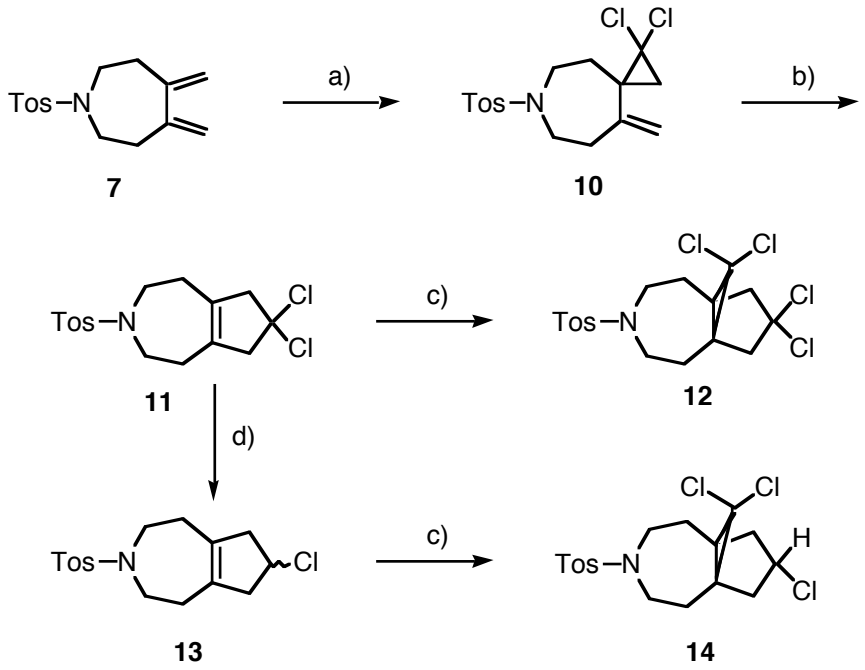
9 **7**

Scheme 2. a) K_2CO_3/DMSO.

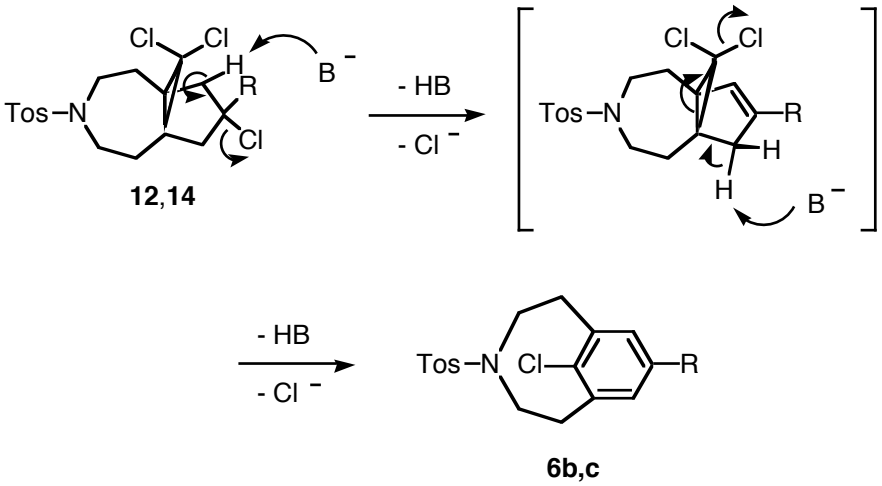
The subsequent synthetic steps are analogous to those applied in the synthesis of 8,11-dichloro[5]metacyclophane.[8,9] Dichlorocarbene addition on **7** by the method of Skattebøl[10] gave **10** which was converted to the cyclopenteno-fused azepane (**11**) by Flash Vacuum Thermolysis[11] (FVT, Scheme 3). The conversion of **11** to the tetrachloropropellane (**12**) required vigorous conditions: addition of a large excess of dichlorocarbene generated by the method of Makosza[12] at 90 °C for 12 h gave **12** in 34% yield after recrystallization. In order to prepare trichloropropellane (**14**), **11** was reduced with Ph_3SnH to furnish **13**, followed by dichlorocarbene addition[12] to give **14**; as **13** contains only one chlorine at the five-membered ring, carbene addition occurred without problems from the unhindered side.



Scheme 3. a) $CHCl_3$/t-BuOK/benzene, RT; b) FVT, 480 °C, 5.10^{-5} mbar; c) 50% NaOH/$CHCl_3$/PTC, 90 °C, 12h; d) Ph_3SnH.

Elimination reactions of the propellanes (**12**) and (**14**) with *t*-BuOK in DMSO gave the cyclophanes (**6b**) and (**6c**), respectively, via the mechanism[5] depicted in Scheme 4.

Unfortunately, all our attempts to prepare the unsubstituted parent compound (**6a**) in an analogous way were unsuccessful; similarly, desirable as it would be, we did not yet succeed in preparing a derivative of **6** with an N-H functionality instead of the *N*-tosyl group.



*Scheme 4. B^- = t-BuO$^-$; **6 b**, **1 2** : R = Cl; **6 c**, **14** : R = H.*

X-Ray crystal structures of 6b and 6c

Compounds (**6b**) and (**6c**) are the smallest and most strained hetera[n]metacyclophanes reported so far. Their crystal structures are shown in Figure 1, selected bond lengths and are listed in Table 1.

From the data in Table 1, it is apparent that analogous to the previously reported carbon analogue 8,11-dichloro[5]metacyclophane (**15b**) (see Figure 2),[13] neither **6b**[6] nor **6c** shows any indication of a cyclohexatriene-like bond alternation in their benzene rings. Despite the severe distortion of these rings, the aromatic delocalization appears to remain intact.

The orientation of the tosyl group in the crystal (which is equal to that in solution, *vide infa*) is consistent with general observations that in the preferred conformation of arylsulfonamides, both the nitrogen lone pair and the aromatic *p*-orbital at the *ipso*-carbon are aligned with the bisector of the O-S-O internuclear angle.[14] Apart from the substituent at C_8, the structural parameters of **6b** and **6c** are very similar. The C-N bond lengths agree well with those reported for several other tosylamides; the C-N-C angle is larger than usual.[15] The nonbonding interactions between two of the four benzylic hydrogens and the chlorine substituent at C_{11} (2.65 – 2.77 Å) are smaller than the sum (3.00 Å) of the van der Waals radii of hydrogen (1.20 Å) and chlorine (1.80 Å).[16] Comparable nonbonding interactions (2.67 Å) between the benzylic hydrogens and the chlorine substituent have been reported for **15b**.[17] Another strong van der Waals interaction exists between C_{11} and the nitrogen atom (2.67 Å versus 1.85 Å (C)+ 1.50 Å (N) = 3.35Å),[16] the possible effect of which will be discussed in connection with the reactivity of **6**. The literature data[15] also indicate that the sulfonamide group is rather flexible with regard to C-N bon lengths and C-N-C bond angles; the geometry at nitrogen is variable, too, ranging from distinctly pyramidal (the sum of angles at nitrogen being 340.2°) to nearly planar.

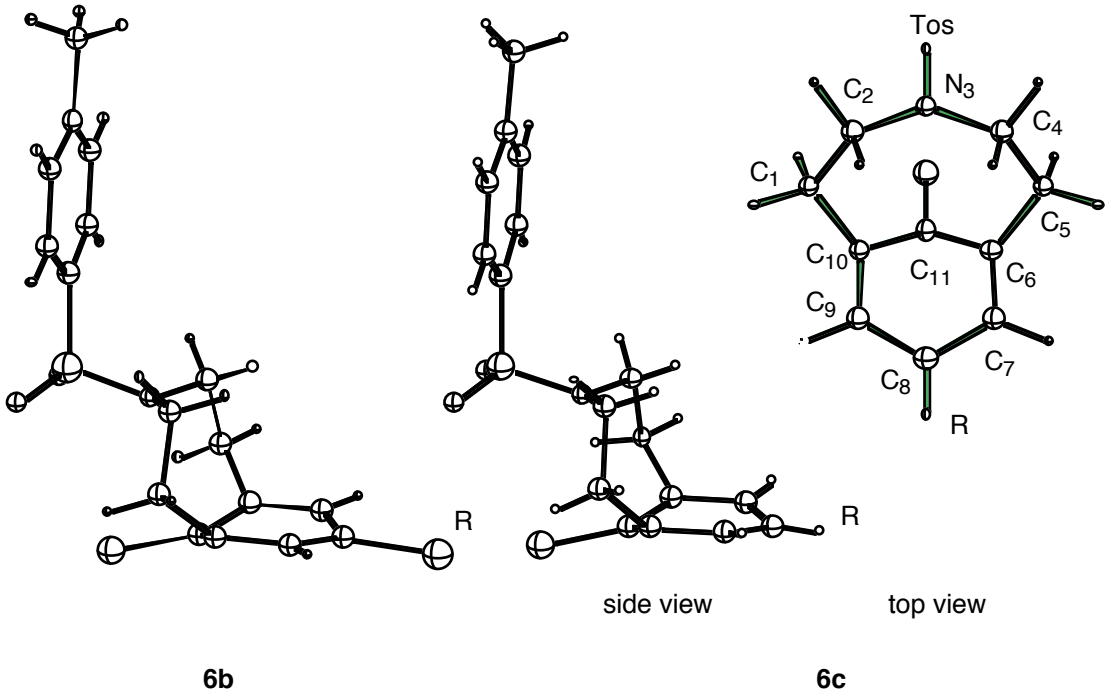


*Figure 1. X-Ray crystal structures of **6 b** and **6 c**; **b** : R = Cl; **c** : R = H*

Bond (a)	**6 b**	**6 c**	Angle (b)	**6 b**	**6 c**
C_1C_2	1.556(4)	1.559(7)	$C_2C_1C_{10}$	104.3(2)	104.3(4)
C_2N_3	1.491(3)	1.485(6)	$C_1C_2N_3$	114.5(2)	114.7(4)
N_3C_4	1.486(4)	1.479(6)	$C_2N_3C_4$	121.9(2)	122.5(4)
C_4C_5	1.560(4)	1.561(7)	$N_3C_4C_5$	114.9(2)	114.4(4)
C_5C_6	1.504(4)	1.507(6)	$C_4C_5C_6$	103.7(2)	104.3(4)
C_6C_7	1.385(4)	1.403(7)	$C_5C_6C_7$	121.5(3)	122.1(4)
C_7C_8	1.371(5)	1.368(8)	$C_7C_8C_9$	120.5(3)	119.4(4)
C_8Cl_2	1.745(3)	-	$C_8C_9C_{10}$	119.2(3)	120.2(5)
C_8C_9	1.375(5)	1.379(8)	$C_9C_{10}C_{11}$	117.2(3)	116.1(4)
C_9C_{10}	1.385(4)	1.403(7)	$C_6C_{11}C_{10}$	117.8(3)	119.0(4)
$C_{10}C_{11}$	1.393(4)	1.396(7)	$O_1S_{12}O_2$	120.31(13)	119.94(19)
C_1C_{10}	1.495(4)	1.501(6)	nb. (c)	**6 b**	**6 c**
$C_{11}Cl_1$	1.739(3)	1.756(5)	Cl_1H_{1A}	2.651(3)	2.77(4)
C_6C_{11}	1.399(4)	1.386(6)	Cl_1H_{5A}	2.712(3)	2.73(5)
N_3S_{12}	1.630(2)	1.636(4)	N_3C_{11}	2.666(4)	2.662(6)

*Table 1. Crystal structure data of **6b** and **6c**; (a) in Å; (b) in degrees; (c) nb.: nonbonding distances in Å (tosyl group not included).*

In Table 2, selected structural data for the cyclophanes (**6b**) and (**6c**) are compared with those of **15b**[13] and 8,11-dichloro-3,3-dimethyl-3sila[5]metacyclophane (**16b**).[18] The definition of the deformation angles α to ε is given in Figure 2.

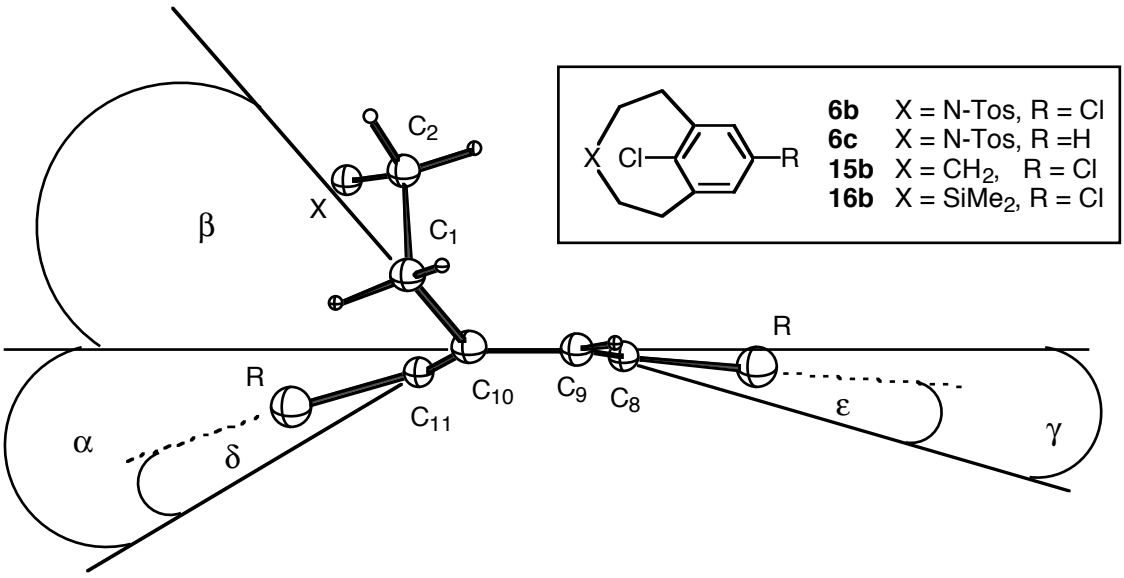


Figure 2. Definition of the deformation angles α, β, γ, δ, and ε

	6b (c)	**6c** (c)	**15b**(d)[13]	**16b**(e,f)[18]
α (a)	27.4	27.3	26.8	21.8/22.3
β	48.7	48.9	48	36.9
γ	12.3	10.4	12	9.2/7.6
δ	12.5	12.1	14	10.4/11.8
ε	7.3	6.5	(g)	6.7/7.6
C_1C_2 (b)	1.556(4)	1.559(7)	1.569(3)	1.574
C_2X_3	1.491(3)	1.485(6)	1.566(3)	1.922
C_1C_{10}	1.495(4)	1.501(6)	1.506(3)	1.505
$C_2C_1C_{10}$ (a)	104.3(2)	104.3(4)	104.7(2)	108.9
$C_1C_2X_3$	114.5(2)	114.7(4)	121.9(3)	124.7
$C_2X_3C_4$	121.9(2)	122.5(4)	122.2(3)	124.6

Table 2. Selected structural data of [5]metacyclophanes. (a) in °; (b) in Å; (c) X = N-Tos; (d) X = CH_2; (e) X =$SiMe_2$; (f) 2 independent molecules in unit cell with distorted C_S symmetry; (g) not given.

Like in Table 1, the differences between **6b** and **6c** are minor. The deformation angles of the benzene rings show a slight increase of the sum of the deformation at the bow and stern of the boat of **6b** (α+γ= 39.7°) compared to **15b** (α + γ = 38.8°). This increase is *less* than was initially expected based on the as sumption that shortening the bridge by incorporation of nitrogen would increase the strain, thus causing a stronger deformation of the benzene ring, while on the other hand, the expected decrease of benzene ring deformation *is* observed in the silacyclophane (**16b**), where the lengthening of the bridge due to the

long C-Si bonds (1.922 Å; $\alpha + \gamma = 31°$) leads to considerable flattening of the boat compared to **15** ($\alpha + \gamma = 38.8°$).

Whereas the benzene rings in **6b**,**c** and **15b** are remarkably similar, this is not the case for their bridges. Apart from the obvious difference in the C_2C_3 or C_2N_3 bond lengths, the most striking feature is the difference in the bond angles $C_1C_2X_3$ of **6b**,**c** and **15b**. In the case of **15b**, the homobenzylic sp^3 carbon atoms experience extreme angular strain at an angle of 122°, while for **6b**,**c**, these angles are much less strained with a value of about 115°. The angle $C_2X_3C_4$ at the 3-position is nearly identical for **6b**,**c** and **15b**. However, in the case of the tosylamides (**6**), an angle of 122° implies less angular strain than in the case of the methylene group in **15b** because of the sp^2 like hybridization at nitrogen. The sum of the angles at nitrogen is 355.3° which is much closer to the value of 360° for sp^2 hybridization than to the value of 328.5° for sp^3 hybridization. Together with the decrease in the angle at carbon atoms C_2 and C_4, this indicates a considerable decrease in strain in the bridge. In addition, torsional strain and non-bonded interaction in the bridge decrease, too, when a methylene group is replaced by a tosylamide group with its flat and tricoordinate nitrogen.

We will later return to the seemingly paradoxical observation that the strain in the bridge of **6** has decreased compared to **15b**, while the distortion of the benzene ring in **6** has increased slightly.

NMR spectra of 6b and 6c

According to the X-Ray crystal structure determination, both **6b** and **6c** possess a slightly distorted C_s symmetry. These distortions are most certainly crystal lattice imposed, as ^1H and ^{13}C NMR measurements in solution show both compounds to be perfectly C_s symmetrical in a temperature range from -60 to +110 °C.

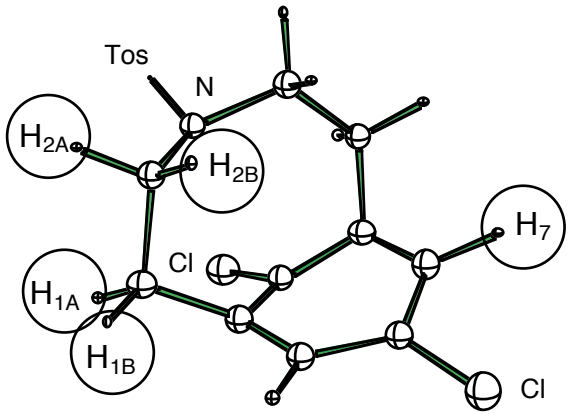


*Figure 3. Designation of the hydrogens of **6 b***
(the tosyl group at nitrogen has been omitted for clarity)

The structural assignments of the ^1H NMR signals of H_{1A}-H_{2B} (Figure 3) are based on HH-COSY, CH-correlation and NOE measurements. NOE experiments also proved that the tosyl group has the same spacial direction in solution as in the crystal, as irradiation of the aromatic tosyl signal at 7.6 ppm (proton in juxtaposition to the sulfone group) revealed an interaction with H_{2A} only.

Comparison of the ^1H NMR data of **6b** and **15b**[13,17] shows that apart from the obvious differences caused by the incorporation of the tosylamide group, the spectra are very similar. The most remarkable difference is the downfield shift of H_{1A} (**6b**: $\delta = 4.24$ ppm; **15b**: $\delta = 3.67$ ppm, while a normal benzylic

value is about δ = 2.50 ppm). This effect is usually attributed to severe steric repulsion, in the present case between H_{1A} and the chlorine substituent at C_{11}.[17] In **6b**, the nonbonded distance between H_{1A} and the chlorine substituent is 2.651(3) Å, which is less than the sum of the van der Waals radii (3.0Å),[16] but still similar to the value reported for **15b** (2.67 Å).[13] This implies that the additional downfield shift of H_{1A} in **6b** by 0.57 ppm must be due to an additional effect, the origin of which is not yet clear. The coupling constants of the bridge protons are similar for both compounds, implying that both cyclophanes have a comparable conformation of the bridge.

A striking difference between **6b** and **15b** is the absence of an *endo*-conformer in the former. The X-Ray crystal structures of **6b**,**c**, and **15b** show all three to possess the *exo*-conformation with the bridge pointing away from the benzene ring (*cf.* Figure 1). In solution at room temperature, **6b** exists exclusively in the same *exo*-conformation; this is supported by a Karplus-analysis of the bridge methylene coupling constants. Lowering the temperature to -60 °C did not result in any change in the NMR spectrum, whereas in **15b**, two conformers could be distinguished at –60°C (85% *exo*, 15% *endo*; in the latter, the bridge is pointing *towards* the benzene ring). Compound (**6c**), like **6b**, is exclusively present in the *exo*-conformation, even at -68 °C.

The conformational rigidity of **6b**,**c** in comparison with **15b**,**c** is surprising. It is probably due to less steric interaction between the chlorine substituent at C_{11} and the substitution around X_3 (flat, trigonal nitrogen in **6b** versus a tetragonal CH_2 group in **15b**) which gives extra stability to the *exo*-conformation of **6b**. However, it should be noted that the *exo*/*endo* ratio of **15b** is not temperature dependent, meaning that the difference in stability is determined by entropy.[5] In order to investigate whether **6b**,**c** would undergo conformational exchange at higher temperatures, solutions in DMSO-d_6 were heated to 120 °C in the NMR spectrometer. When **15a** was heated to 150 °C, the ^{1}H NMR spectrum remained essentially unchanged (100% *exo*-conformer),[19] while the ^{1}H NMR spectrum of **15b** was reversibly temperature dependent, giving a time averaged spectrum at 120 °C; both **15a** and **15b** were recovered intact after their solutions had been cooled down to room temperature. Cyclophanes (**6b**) and (**6c**), like **15a**, displayed a temperature independent spectrum up to 120 °C in DMSO. However, in contrast to their carbon analogues, **6b**,**c** were unstable above 120 °C and underwent an intramolecular ring closure (*vide infra*).

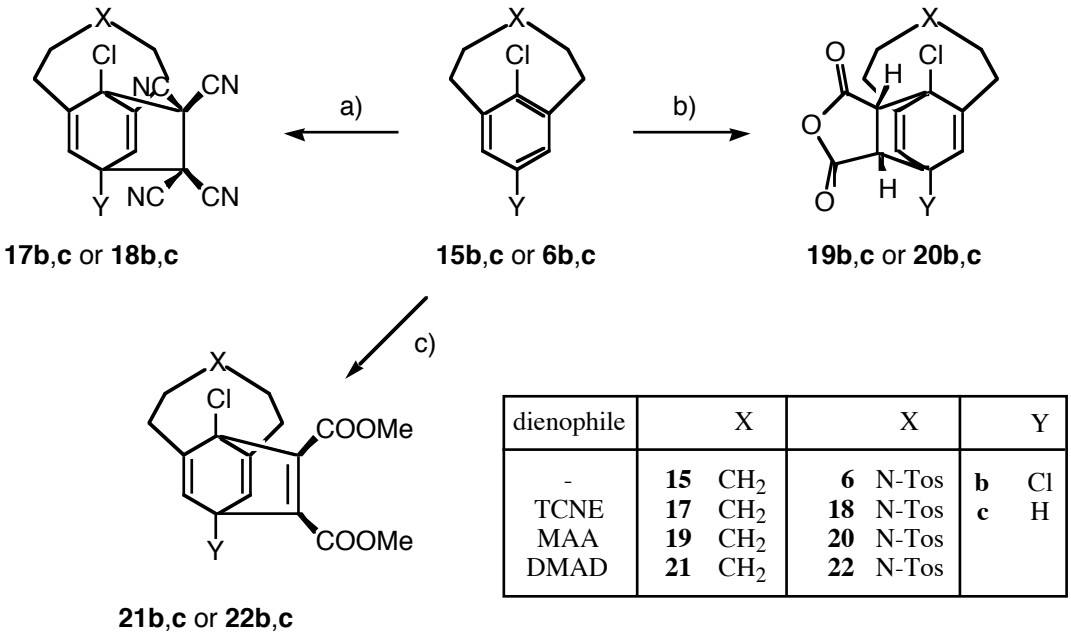
Diels-Alder reactions of 6b and 6c

[5]Metacyclophanes are aromatic, yet highly reactive species. Whereas unstrained benzene derivatives require special conditions to undergo Diels-Alder addition (irradiation, high pressure and/or temperature, or Lewis-acid catalysis), small cyclophanes tend to react with dienophiles under very mild conditions such as room temperature and normal pressure.[5] While generally, cycloaddition to an unstrained benzene derivative is energetically unfavorable due to the loss of the resonance energy, in the case of [5]metacyclophanes, this is compensated by relief of strain in the Diels-Alder adducts as addition of the dienophile at positions 8 and 11 removes the (formal) anti-Bredt double bond.[5,18,20,21]

[5]Metacyclophanes (**15a**-**c**) generally react with dienophiles at room temperature (Scheme 5); the rate depends on the substituents and the type of dienophile. Chlorine substitution tends to retard the reaction due to both steric and electronic factors. The reactivity of the dienophiles decreases in the order tetracyanoethene (TCNE)> maleic acid anhydride (MAA) >> dimethyl acetylenedicarboxylate (DMAD); this reactivity order has also been observed in the reaction of **15a** with these dienophiles.[21]

The *aza*cyclophanes (**6b**) and (**6c**) displayed the expected influence of the substituents on the reactivity towards dienophiles, (Scheme 5): **6c** did react faster than **6b**, and the reactivity order

TCNE>MAA>>DMAD was observed, too. Because of the low reactivity of the dichloro derivative (**6b**), reaction times were not recorded. The results for **6c** suggest that it is less reactive than its carbon analogue (**15c**) (Table 3).



dienophile	X		X		Y	
-	**15**	CH_2	**6**	N-Tos	**b**	Cl
TCNE	**17**	CH_2	**18**	N-Tos	**c**	H
MAA	**19**	CH_2	**20**	N-Tos		
DMAD	**21**	CH_2	**22**	N-Tos		

Scheme 5: Diels-Alder reactions of several cyclophanes; a) TCNE; b) MAA; c) DMAD

	TCNE	MAA	DMAD
15c	< 15 min	2 h	5 days (1.1 eq.)
6c	< 15 min	3.5 h	11 days (3.6 eq.)

*Table 3: Time required for complete reaction of **15c** and **6c** with an excess of several dienophiles (performed in an NMR tube in $CDCl_3$).*

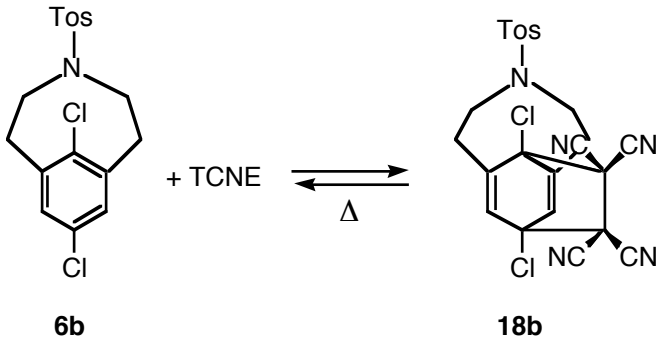
As it was difficult to compare reported cycloaddition reactions on [5]metacyclophanes because of the widely differing reaction conditions, we performed competition experiments between **6** and **15** with several dienophiles. These experiments were performed by adding 1 equivalent of dienophile in small portions to a 1:1 mixture of either **15b**/**6b** or **15c**/**6c** in an NMR tube. In this way the difference in reactivity between both types of cyclophanes could be monitored by comparing the product ratio by ^1H NMR spectroscopy, independent of the reaction conditions. The results were dramatic. Based on the small increase of the total distortion of the benzene ring in **6b** compared to **15b** (0.9°, Table 2), a small increase in reactivity or at least a comparable reactivity was expected. Contrary to these expectations, **15b**,**c** turned out to be more reactive than **6b**,**c** towards all three dienophiles used (Table 4).

	TCNE (1 eq)	TCNE (excess)	MAA (1 eq)	DMAD (1 eq)
15b/**6b** (1:1)	10:1	5:1	1.3:1	-
15c/**6c** (1:1)	10:1	5.9:1	1.2:1	10:1

Table 4: Product ratios of competition reactions.

One may argue that a drawback of this method is that adding small portions of a reagent to a mixture containing two species of different reactivity will yield a distorted product ratio in favor of the more reactive species. Therefore the reaction with TCNE was also performed with an excess of 3 to 5 equivalents of dienophile (Table 4). Although the product ratio expectedly decreased from 10:1 to 5:1, the general trend remained that **15** is more reactive than **6**. Most experiments were repeated several times with a high level of reproducibility.

These results are inconsistent with our previous assumption that the reactivity of a small cyclophane is proportional to the degree of distortion of its benzene ring. Despite the fact that the benzene rings in **6b**,**c** are slightly more distorted than in **15b**,**c**, the reactivity of the former in Diels-Alder reactions is clearly lower. As the reactivity is obviously not (only) related to the distortion of the benzene ring, the cause for the observed differences must reside in differences between the bridges. As discussed above, it is plausible to assume that the bridges of **6b**,**c** are less strained than those of their carbon analogues.



6b **18b**

*Scheme 6: Thermal equilibrium between **6 b** and **1 8 b** (in $CDCl_3$)*

Although the TCNE adducts (**18b**,**c**) were stable at room temperature in $CDCl_3$, at elevated temperatures (50-60 °C) a retro Diels-Alder reaction occurred and an equilibrium between the adduct (**18b**) and the cyclophane (**6b**) was established (Scheme 6). At 120 °C in deuterated toluene, the adduct (**18b**) underwent complete dissociation into **6b** and TCNE; after cooling the reaction mixture to room temperature, **18b** was slowly formed back again. This reversibility was not observed if DMSO-d_6 was used instead of toluene. Heating **18b** in DMSO led to immediate dissociation of the adduct to give **6b**. The reverse reaction was not observed when the solution had been cooled down to room temperature, probably because TCNE either reacts with DMSO, or, more likely, forms very strong donor-acceptor complexes with the solvent. Similarly, **17b** completely dissociated to give **15b** on heating in DSMO.

The enhanced propensity of **18** to undergo a retro-Diels-Alder reaction made it impossible to measure GC-MS or HRMS spectra; the same holds for the Diels-Alder adducts of **15b**. Only the MAA adduct

(**20c**) of **6c** was stable towards heating up to a temperature of 190 °C for 20 min in DMSO, but under GC-MS conditions, it was unstable, too.

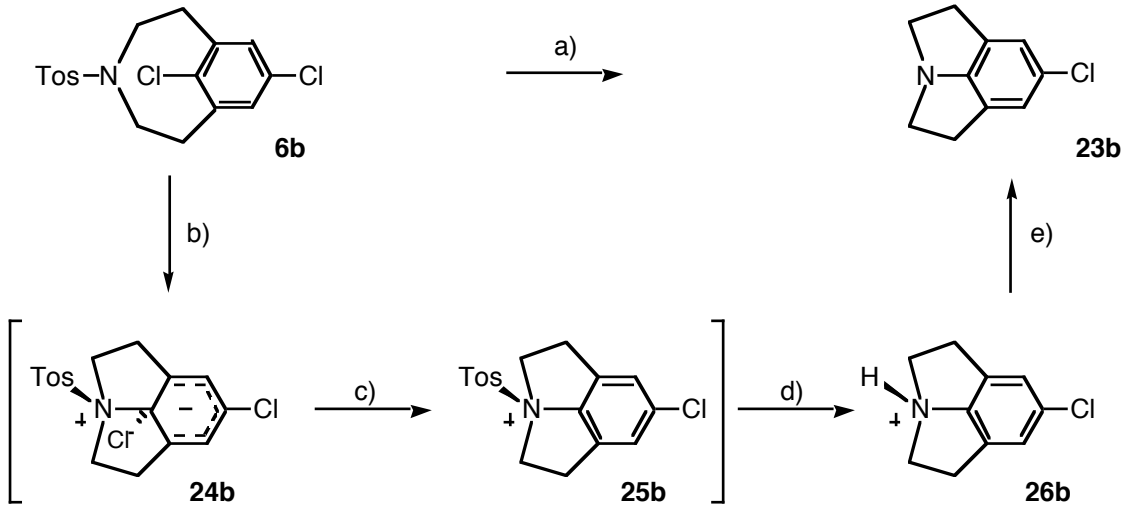
Formation of 1,2,4,5-tetrahydropyrrolo[3,2,1-*hi*]indole derivatives (23b,c) from 6b,c

As mentioned above, during high temperature NMR experiments devised to investigate a possible ring flip in **6b**, it turned out that the cyclophane was unstable at 120 °C in DMSO, in contrast to its carbon analogue (**15b**).[19] On prolonged heating (0.5 h), the signals of **6b** dissappeared at the expense of new ones; further heating resulted in the disappearance of the new signals, leaving broad signals indicative of polymer formation and signals of a tosyl derivative which were shown to be identical with those of free *p*-toluenesulfonic acid in DMSO. Systematic investigation of the thermal reaction of **6b** indicated that an optimal yield of the new product was obtained at 50% conversion of the **6b**. The reaction mixture was worked up by pouring it into dilute aqueous NaOH followed by extraction with $CHCl_3$. NMR analysis of the $CHCl_3$ fraction revealed that the new product gave only 2 signals in the ^1H NMR spectrum: δ 6.90 (s, 2H) and δ 3.25 (br s, 8H). According to ^{13}C NMR spectroscopy, the highly symmetrical new species contained an aromatic CH group (δ 122.4), a methylene group attached to a hetero atom (δ 59.0), and a benzylic methylene group (δ 34.9) in the ratio of 1:1:1. GC-MS analysis revealed its molecular composition to be $C_{10}H_{10}NCl$. These spectroscopic data suggested that the new species was 6-chloro-1,2,4,5-tetrahydropyrrolo[3,2,1-*hi*]indole (**23b**) (Scheme 7), i.e. a 2,3-dihydroindole or indoline derivative. In an analogous reaction, **6c** was converted to **23a** by heating in DMSO; **23a** has been previously obtained by Anet *et al*. *via* a different approach.[22]

In Scheme 7, a mechanism for the formation of **23b** from **6b** is presented. First, the (deactivated!) nitrogen in the bridge performs a trans-annular nucleophilic attack at C11 of the aromatic ring. After formation of the Meisenheimer complex (**24b**), a chloride anion is expelled under re-aromatization of the benzene ring and formation of **25b**. Although the formation of tosylammonium salts such as **24b** and **25b** may seem unlikely, such compounds *are* known and relatively stable, yet highly sensitive towards hydrolysis.[23] As the DMSO-d_6 used unavoidably contains traces of water, it is plausible that **25b** is hydrolyzed under the reaction conditions to form **23b**. However, as hydrolysis of the tosylammonium chloride (**25b**) yields 2 equivalents of acid (1 eq. of HCl and 1 eq. of *p*-TosOH), the latter will be immediately protonated to give **26b**. This assumption was corroborated by comparison of the ^1H NMR spectra in DMSO-d_6 of the reaction mixture as obtained by the thermal rearrangement of **6b** with those of the picrate (**28b**) prepared from **23b** (see Scheme 9): both spectra of the cation part were identical, suggesting that the primary reaction product was indeed **26b**. Workup of the reaction mixture with dilute aqueous NaOH finally gave **23b** with an NMR spectrum slightly different from that of **26b**.

This rationalization may seem highly surprising, because normally, only strong nucleophiles such as hydroxide or methoxide anion lead to nucleophilic aromatic substitution in 11-halo[5]metacylophanes;[5,18,24] indeed, no reaction was observed on heating either 1,4-dichloro-*meta*-xylene or **15b** with unstrained tosylamides in DMSO at 130°C. Nevertheless, the *intramolecular* version of this reaction as proposed for **6b** is not as unlikely as it may seem at first glance.

In the first place, for carba[n]metacyclophanes with a halogen at position 11 such as **15b**, several reactions yielding carbacyclic transannular ring closure products formally analogous to **23b** have been reported; however, they proceed *via* radical intermediates attacking the aromatic ring at position 11.[20,25]



*Scheme 7: Proposed mechanism for the formation of **23b** from **6b**; a) DMSO, 130 °C; b) formation of the Meisenheimer complex; c) - Cl^-; d) + H_2O, -TosOH; e) - H^+*

We feel that the strain and the special steric situation in **6** in combination with particular electronic features make this unique intramolecular $S_N2(Ar)$ reaction feasible. Figure 4a is a schematic representation of the LUMO of **15b**.[20,24,26] According to these calculations, the LUMO has the highest coefficient at C_{11}, making a nucleophilic attack at this position plausible, as has been confirmed by several reports of nucleophilic attack on 11-halo[5]metacyclophanes.[18,20,24] Extending this analysis to **6b**, the lone-pair orbital at nitrogen[14] is directed towards the orbital at C11 (Figure 4b), and in the X-Ray crystal structure, the non-bonded distance between C11 and N3 is 2.666(4) Å, considerably less than the sum of the van der Waals radii of carbon and nitrogen (3.35 Å[16]). The relief of strain going along with the replacement of this repulsive constellation in **6b** by formation of a bond between N3 and C11 in **24b** will aid in making this unusual reaction occur.

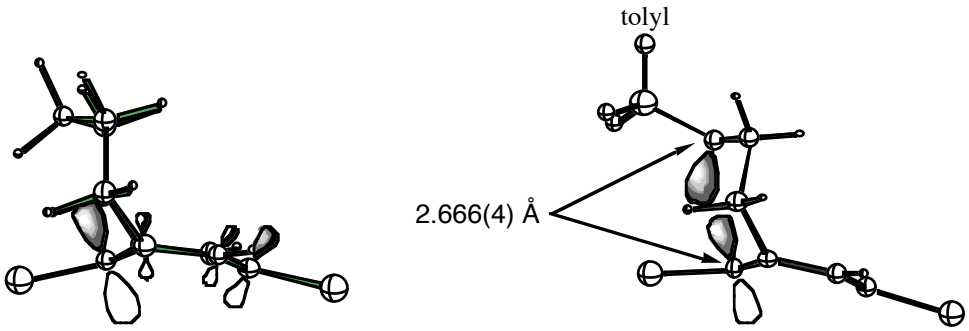


*Figure 4: a) LUMO of **15b**; b) extrapolation of the LUMO of **15b** to that of **6b** (side views)*

Our assumption that the trans-annular reaction of **6** proceeds *via* an ionic pathway, rather than the radical pathway operative in the case of **15**, is further supported by the following experiment. When **6b** was heated to 120 °C in toluene-d_8 instead of DMSO-d_6, the formation of **23b** did not occur; prolonged heating led to the polymerization of **6b** only. As reactions proceeding by a radical pathway are in general

independent of the polarity of the solvent, it is more likely that an ionic mechanism applies in the case of **23b**.

Thus, although the proposed mechanism for the formation of **23b** from **6b** remains speculative, all available evidence points to an intramolecular nucleophilic attack of the *deactivated* tosylamide nitrogen at C11 of the strained aromatic system; while such $S_N2(Ar)$ reactions normally do not occur, they are facilitated in this very special case by the proximity of the two reaction centers and by the relief of strain accompanying the formation of the tricyclic system of the primary intermediate (**24b**) (Scheme 7).

The ^{1}H NMR spectrum of **23b** (Figure 5) was independent both of the temperature (-68 to 25 °C) and of the solvent ($CDCl_3$, DMSO-d_6). Density functional calculations (ADF program, version 2.2.2[27]) indicate that the minimum energy geometry of **23b** is not planar; however, the planar transition state was calculated to be only 5.4 kcal/mol higher in energy, so that one can assume that **23b** adopts a time averaged planar geometry. Even so, the benzylic and homobenzylic methylene groups are expected to form an AA'BB'-system. The simplicity of the proton spectrum, which shows a singlet of 8 H at δ 3.25, suggests that in this specific case, the 8 methylene protons are magnetically equivalent, so that the J_{HH} coupling constants are not expressed in the ^{1}H NMR spectrum.[28] Substitution of the chlorine in **23b** by hydrogen, as in the case of **23a**, causes a subtle change in the chemical shifts of the protons of the benzylic and the homobenzylic methylene groups, resulting in an AA'BB' system (multiplet at δ 3.22 instead of the singlet for **23b**). While the instability of **23** (vide infra) prevented their isolation in pure form, the ^{1}H NMR spectra of both **23b** (Figure 5) and **23a**[22] document the purity of both compounds in solution.

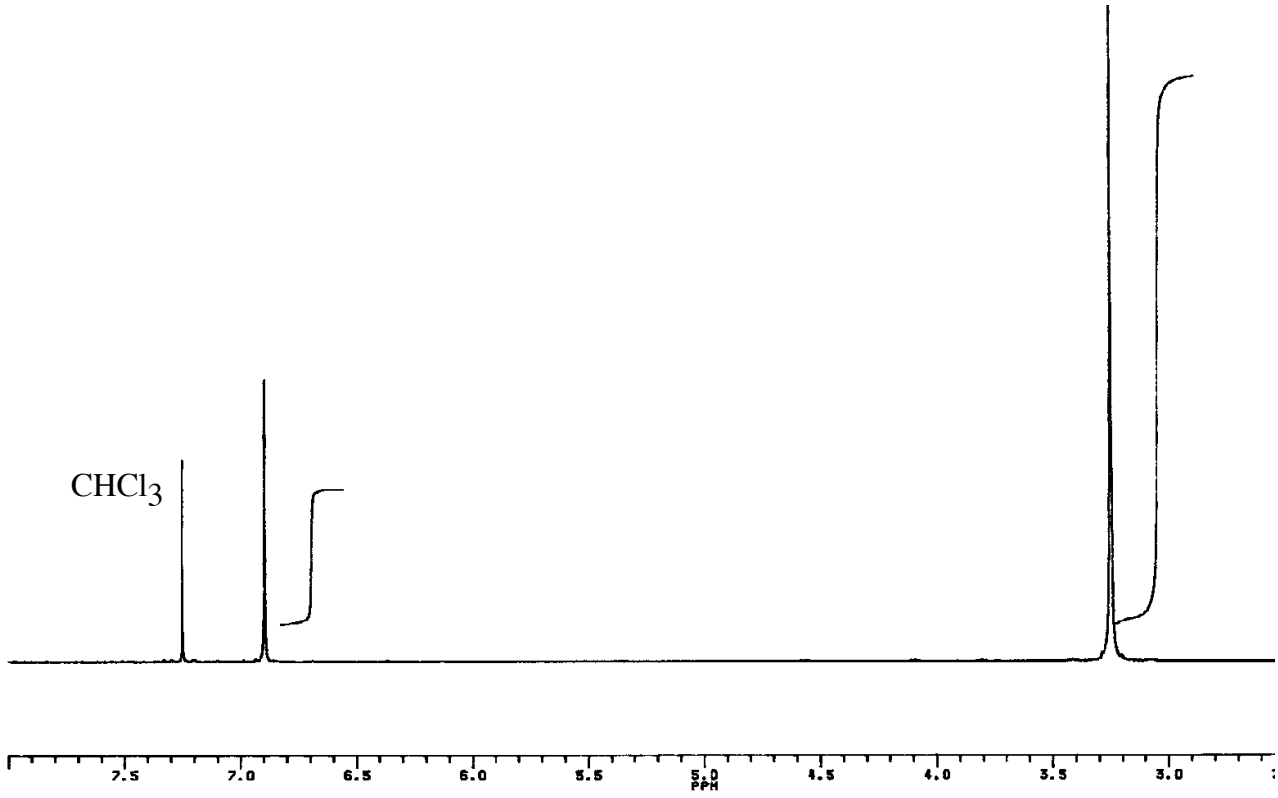
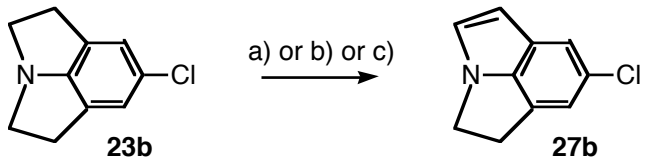


*Figure 5. ^{1}H NMR spectrum of **23b** ($CDCl_3$, rt)*

Reactivity of the 1,2,4,5-tetrahydropyrrolo[3,2,1-*hi*]indole derivatives (23)

In a preliminary investigation aimed primarily at purification of the unstable compounds (**23a**,**b**), some interesting reactions were discovered. Thus, the spontaneous oxidation of indoline (**23b**) to the corresponding indole (**27b**) by atmospheric oxygen (Scheme 8) prevented the isolation of **23b** in pure form. A colorless solution of **23b** in $CDCl_3$ turned blue after exposure to air for several days at room temperature; ^1H NMR analysis revealed the presence of **27b** and (presumably) polymer. Therefore, it was decided to purposely oxidize **23b** in order to obtain the aromatic heterocycle (**27b**) which was expected to be more stable. The oxidation was performed with DDQ[29,30] (dichlorodicyanoquinone, Scheme 8) and proceeded smoothly at room temperature in $CDCl_3$, whereas Walton *et al.* reported oxidations of indolines to indoles with DDQ to require refluxing in xylene for several hours.[30]

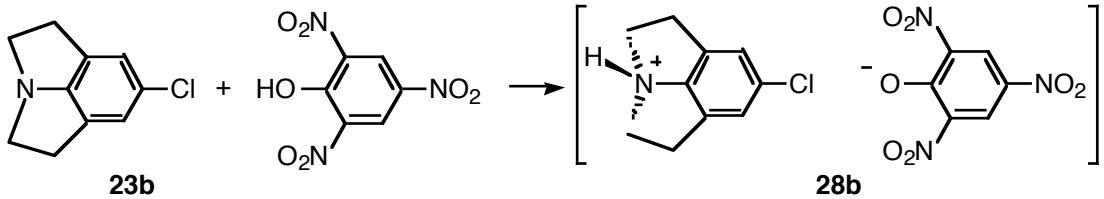


23b **27b**

Scheme 8: a) atmospheric oxygen; b) DDQ (1 eq.); c) TCNE (excess)

When TCNE was reacted with **23b** in an attempt to isolate a donor-acceptor complex or possibly a Diels-Alder adduct, the product surprisingly turned out to be **27b**, too. Dehydrogenations by TCNE are well-known; thus, Longone and Smith reported that TCNE was capable of aromatizing cyclohexa-1,4-diene under mild conditions.[31] The unsubstituted parent compound of **27b**, 1,2-dihydropyrrolo[3,2,1-*hi*]indole (**27a**)[32] and some alkyl derivatives thereof[33] have been obtained by different approaches.

Another attempt to purify **23b** by derivatization was based on the reaction with picric acid, which was expected to yield a crystalline ammonium picrate (**28b**) (Scheme 9). The reaction was performed by adding small portions of a solution of picric acid in $CDCl_3$ to a $CDCl_3$ solution of **23b**. It was instantaneous, as monitored by ^1H NMR spectroscopy, and **28b** precipitated from the solution as a yellow/green solid. Unfortunately, attempted recrystallization of **28b** was unsuccessful due to its extremely low solubility in most solvents.

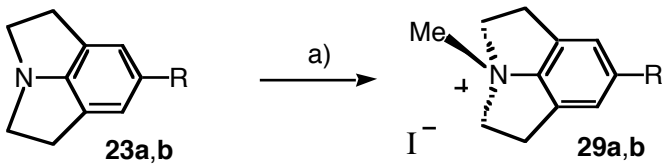


23b **28b**

Scheme 9. $CDCl_3$, rt

However, the cation (**26**b) formed by protonation of the nitrogen (Scheme 7; also part of **28b**, Scheme 9) was found to be much more stable than the free base (**23b**). This inspired us to attempt the quaternization of **23a**,**b** with methyl iodide (1-2 eq.) in $CDCl_3$. The reaction proceeded smoothly within 24 h at room temperature under formation of a greenish precipitate of **29a**,**b** (Scheme 10). Attempted

recrystallization from chloroform or acetone was unsuccessful; purification was finally achieved by extraction of **29a**,**b** from the chloroform phase with water, followed by evaporation of the water layer at low temperature as otherwise, degradation of the ammonium salt occurred as indicated by the solution turning yellow and the appearance of new signals in the ^{1}H NMR spectrum.



Scheme 10. a) MeI (1-2 eq.), rt

Derivatization of **23** removes the C_{2v} symmetry as well as the magnetic equivalence of the methylene groups. As a result of the oxidation of **23b** to **27b**, the singlet at δ 3.25 in **23b** was replaced by two triplets (J = 7.0 Hz) at δ 4.54 and δ 3.80 in **27b**. According to ADF calculations, **27a** has a practically planar minimum energy geometry, so that the inversion barrier for **27b** will be essentially zero. Not surprisingly, the ^{1}H NMR spectrum of **27b** was temperature independent from -68 to 25 °C. The two doublets at δ 7.16 and δ 6.38 with a small $^3J_{HH}$ coupling constant of 2.7 Hz are very indicative of an indole derivative. The triplet nature of the signals at δ 4.54 and δ 3.80 is not straightforward considering the structure of **27b**; one would again, as in the case of **23b**, expect an AA'BB'-system.
In the ^{1}H NMR spectrum of the protonated derivative (**28b**) (with formal C_s symmetry), the methylene groups appear as two triplet-like multiplets indicating a rapid exchange of the hydrogen at nitrogen. This is further supported by comparison with the spectra of the methylated derivatives (**29a**) and (**29b**); due to their rigid C_s symmetrical structure, **29a**,**b** display the expected ABKL-systems.

Conclusions

The incorporation of a tosylamide group into the bridge of a [5]metacyclophane has led to several interesting results. Not only have we been able to synthesize two new 3-aza[5]metacyclophanes (**6b**) and (**6c**) with the most higly distorted benzene rings reported, but by investigating their reactivity, we have opened new aspects of cyclophane chemistry. Furthermore, we had to reconsider some of our previous hypotheses on the interplay of strain, reactivity, and structure of [5]metacyclophanes.
Thus, we had previously assumed that the degree of bending of the benzene ring of a cyclophane would give an indication of the total amount of strain and hence of the reactivity,[5] e.g. in Diels-Alder reactions. As the distortion of the benzene rings of **6b** and **6c** is comparable to those of their carba analogues (**15b**) and (**15c**), the differences in reactivity must be attributed to the strain in the bridges of the aza- and carbacyclophanes. It is plausible that the bridge in **6b** and **6c** is less strained as a consequence of the incorporation of the tosylamide group which causes a reduction of both angular and torsional strain in the bridge. This reduction of strain in the bridge apparently leads to a dramatic change in reactivity; presumably changes occurring in the bridge *en route* to the transition state play an important role, too. Clearly, this hypothesis needs further investigation.
The incorporation of the tosyamide functionality in the bridge not only increased the stability of the [5]metacyclophane system, but also gave rise to unexpected reactivity. The thermal transannular reaction

of **6b** and **6c** leading to the indoline derivatives (**23b**) and (**23a**), respectively, was remarkable. Although the reaction may have appeared unlikely at first glance, the structurally imposed close proximity of the reaction centers together with a decrease in strain energy in the products make this unprecedented reactivity understandable.

ACKNOWLEDGEMENTS
We thank Dr. B. L. M. van Baar for the mass spectrometric measurements. This work was financially supported by SON/NWO (M.J.v.E., A.L.S.).

EXPERIMENTAL
^{1}H NMR spectra were recorded at 200.13 MHz (Bruker AC 200) or at 400.13 MHz (Bruker MSL 400). ^{13}C NMR spectra were recorded at 50.32 MHz (Bruker AC 200) or at 100.32 MHz (Bruker MSL 400). The assignment of NMR signals is based on HH-COSY, CH-correlation, and NOE experiments. HRMS spectra were recorded on a Finnigan MAT-90 mass spectrometer operating at an ionization potential of 70 eV. GC-MS spectra were recorded on a Hewlett Packard 5971 series mass selective detector. Sample separation for GC-MS was performed on a Hewlett Packard 5890 series II gas chromatograph fitted with a a HP-1 column (50m, 0.2 mm i.d., 0.33μm film thickness). Aluminum oxide used: Merck, Aluminum oxide 90, standardized (activity II-III), 0.063-0.200 mm. Silica gel used: Riedel-de Haën, Silicagel S, 0.2-0.5mm. All chemicals were commercially available from either Acros or Aldrich Chemicals.

8,11-Dichloro-*N*-tosyl-3-aza[5]metacyclophane (**6b**).
To a stirred solution of **12** (0.13 g, 0.29 mmol) in dry DMSO, *t*-BuOK (0.069 g, 0.62 mmol) was added during a period of 1 h at rt under nitrogen. Afterwards, the dark brown solution was stirred for another 1.5 h. The reaction mixture was then poured into ice water and extracted with ether (3x). The combined ether layers were washed with water (4x), brine (1x), and dried over $MgSO_4$. The solvent was evaporated under reduced pressure. The resulting light brown solid residue was purified by column chromatography (alumina, ether/pentane 3:2). ^{1}H NMR analysis showed the presence of a mixture of 78 % **6b** and 22 % **12**. After recrystallization from $CHCl_3$/pentane, the yield was 0.040 g (40%) of transparent crystals of **6b**; mp 180 °C; ^{1}H NMR ($CDCl_3$): δ 7.56 (d, J = 8.3 Hz, 2 H), δ 7.17 (d, J = 8.3 Hz, 2 H), δ 6.67 (s, 2 H), δ 4.24 (A part of AB-system, J_{AB} = 13.0 Hz, J = 11.2 Hz, 3.1 Hz, 2 H), δ 3.73 (A part of AB-system, J_{AB} = 14.5 Hz, J = 2.7 Hz, 2.6 Hz, 2 H), δ 2.51 (B part of AB-system, J_{AB} = 13.0 Hz, J = 2.1 Hz, 1.9 Hz, 2 H), δ 2.32 (s, 3 H), δ 2.12 (B part of AB-system, J_{AB} = 14.5 Hz, J = 11.2 Hz, 2.2 Hz, 2 H); ^{13}C NMR ($CDCl_3$): δ 143.8 (s), δ 143.2 (s), δ 142.0 (s), δ 136.5 (s), δ 134.0 (s), δ 129.6 (d, J = 138 Hz), δ 126.6 (d, J = 127.0 Hz), δ 123.6 (d, J =168 Hz), δ 62.2 (t, J = 138 Hz), δδ 45.0 (dd, J = 140 Hz, 132 Hz), δ 21.3 (q, J = 125 Hz), HRMS ($C_{17}H_{17}{}^{14}N^{32}O_2{}^{35}Cl^{37}ClS$), calcd 371.0327, observed: 371.0332 ± 0.0006; Anal. Calcd for $C_{17}H_{17}NO_2Cl_2S$: C, 55.14; H, 4.63; N, 3.78; Cl, 19.15. Found: C, 55.38; H, 4.43; N, 3.43; Cl, 19.10.

11-Chloro-*N*-tosyl-3-aza[5]metacyclophane (**6c**).
To a stirred solution of **14** (0.28 g, 0.69 mmol) in DMSO (50 mL, dry), *t*-BuOK (0.24 g, 2.14 mmol) was added during 2 h at rt under nitrogen. Afterwards, the reaction mixture was poured into ice water and extracted with $CHCl_3$ (3x). The combined organic layers were washed with water (4x), brine (1x),

and dried over $MgSO_4$. The solvent was evaporated under reduced pressure. The resulting light brown solid residue was purified by column chromatography (alumina, ether/pentane 3:2) yielding **6c** (0.15 g, 65%) as a colorless solid. Further purification was achieved by recrystallization from ethyl acetate; mp 171 °C; ^{1}H NMR ($CDCl_3$): δ 7.62 (d, J = 8.3 Hz, 2 H), δ 7.22 (d, J = 8.3 Hz, 2 H), δ 7.08 (t, J = 7.1 Hz, 1 H), δ 6.72 (d, J = 7.1 Hz, 2 H), δ 4.32 (A part of AB-system, J_{AB} = 12.8 Hz, J = 11.5 Hz, 2.0 Hz, 2 H), δ 3.75 (A part of AB-system, J_{AB} = 14.4 Hz, J = 2.8 Hz, 2.1 Hz, 2 H), δ 2.57 (B part of AB-system, J_{AB} = 12.8 Hz, J = 2.1 Hz, 2.0 Hz, 2 H), δ 2.36 (s, 3 H), δ 2.12 (B part of AB-system, J_{AB} = 14.4 Hz, J = 11.5 Hz, 2.1 Hz, 2 H); ^{13}C NMR ($CDCl_3$): δ 144.6 (s, C11), δ 143.1 (s, C12), δ 141.1 (s, C6), δ 136.7 (s, C15), δ 129.5 (d, J = 154 Hz, C13), δ 129.0 (d, J = 164 Hz), δ 126.6 (d, J = 167.0 Hz), δ 124.3 (d, J =164 Hz), δ 62.1 (t, J = 138 Hz), δ 44.8 (dd, J = 139 Hz, 130 Hz), δ 21.3 (q, J = 127 Hz); Anal. Calcd for $C_{17}H_{18}NO_2ClS$: C, 60.79; H, 5.41; N, 4.17; Cl, 10.56. Found: C, 60.75; H, 5.32; N, 4.21; Cl, 10.6.

4,5-Dimethylene-2,3,6,7-tetrahydro-azep-1-yl-*p*-tolylsulfone (**7**).
A suspension of **9**[8] (3.03 g, 6.73 mmol), *p*-toluenesulphonamide (1.15 g, 6.70 mmol), and K_2CO_3 (0.25 g) in DMSO (100 mL) was stirred for 20 h at 100 °C. The resulting brown mixture was cooled, poured into ice water (500 mL) and extracted with ether (3x, 150 mL). The combined organic layers were thoroughly washed with water to remove the DMSO, washed with brine and dried ($MgSO_4$). The solvent was evaporated under reduced pressure. The resulting yellow solid residue was recrystallized from ether/pentane to yield 0.90 g (3.25 mmol, 48.4%) of **7** (colorless crystals): mp 65 °C; ^{1}H NMR ($CDCl_3$): δ 7.64 (d, J = 8.0 Hz, 2 H), δ 7.33 (d, J = 8.0 Hz, 2 H), δ 5.13 (d, J = 1.7 Hz, 2 H), δ 4.73 (d, J = 1.7 Hz, 2 H), δ 3.23 (m, J unres., 4 H), δ 2.54 (m, J unres., 4 H), δ 2.41 (s, 3 H); ^{13}C NMR ($CDCl_3$): δ 148.1 (s), δ 143.1 (s), δ 135.3 (s), δ 129.5 (d, J = 162 Hz), δ 126.9 (d, J = 166 Hz), δ 112.3 (t, J = 157 Hz), δ 49.4 (t, J = 138 Hz), δ 36.1 (t, J = 128 Hz), δ 21.3 (q, J = 127 Hz); HRMS ($C_{15}H_{19}{}^{14}N^{32}O_2S$), calcd 277.1136, observed: 277.1134 ± 0.0008; Anal. Calcd for $C_{15}H_{19}NO_2S$: C, 64.95; H, 6.91. Found: C, 64.92; H, 6.96.

1,1-Dichloro-9-methylene-6-azaspiro[2,6]non-6-yl-*p*-tolylsulfone (**10**)
To a solution of **7** (1.40 g, 5.05 mmol) and $CHCl_3$ (8.45 g, 70.7 mmol) in benzene (50 mL) in a round bottom flask fitted with a solid reagent addition tube, was added under nitrogen *t*-BuOK (6.80 g, 60.60 mmol) during 4 h. After the addition, the mixture was stirred for another 1.5 h at rt. The resulting brown reaction mixture was poured into ice water (200 mL), 2N HCl was added to obtain a neutral pH, and than the water layer was extracted with ether (3x). The combined organic layers were washed with water (1x) and brine (1x), and dried over $MgSO_4$. NMR-analysis showed a 35 % conversion to **10** with 65% **7** remaining. Therefore, the procedure described above was repeated twice. The total conversion was more than 97 %, with a total recovery of 81 %. The crude product was recrystallized from ether/pentane, yielding 1.24 g (69 %) of **10** : mp 66-68 °C; ^{1}H NMR ($CDCl_3$): δ 7.71 (d, J = 8.2 Hz, 2 H), δ 7.32 (d, J = 8.2 Hz, 2 H), δ 5.10 (d, J = 0.6 Hz, 1 H), δ 5.01 (s, 1 H), δ 3.69 (ABKL-system, δ_A = 3.69, δ_B = 3.70, J_{AB} = 10.2 Hz, J = 8.8 Hz, 5.5 Hz, 5.0 Hz, 4.1 Hz, 2 H), δ 3.15 (ABKL-system, δ_A = 3.15, δ_B = 3.14, J_{AB} = 13.6 Hz, J = 11.1 Hz, 4.2 Hz, 4.1 Hz, 2.8 Hz, 2 H), δ 2.68 (ABKL-system, δ_A = 2.74, δ_B = 2.63, J_{AB} = 15.5 Hz, J = 8.8 Hz, 5.5 Hz, 5.0 Hz, 4.1 Hz, J = 0.6 Hz, 2 H), δ 2.44 (s, 3 H), δ 2.02 (ABKL-system, δ_A = 2.17, δ_B = 1.87, J_{AB} = 14.6 Hz, J = 11.1 Hz, 4.2 Hz, 4.1 Hz, 2.8 Hz, 2 H), δ 1.60 (AB-system, δ_A = 1.74, δ_B = 1.46, J_{AB} = 7.1 Hz, 2 H); ^{13}C NMR ($CDCl_3$): δ 145.8

(s), δ 143.1 (s), δ 136.2 (s), δ 129.6 (d, J = 156 Hz), δ 126.9 (d, J = 166 Hz), δ 117.7 (t, J = 157 Hz), δ 65.0 (s), δ 61.0 (s), δ 47.9 (t, J = 138 Hz), δ 46.8 (t, J = 138 Hz), δ 38.9 (t, J = 130 Hz), δ 34.8 (t, J = 136 Hz), δ 33.4 (t, J = 164 Hz), δ 21.3 (q, J = 127 Hz); HRMS ($C_{16}H_{19}{}^{14}N^{32}O_2{}^{35}Cl_2S$), calcd 359.0514, observed 359.0515 ± 0.0008; Anal. Calcd for $C_{16}H_{19}NO_2Cl_2S$: C, 53.34; H, 5.32; Cl, 19.68. Found: C, 53.39; H, 5.41; Cl, 19.40.

7,7-Dichloro-1,2,4,5,6,8-hexahydrocyclopenta[d]azepin-3-yl-*p*-tolylsulfone (**11**).
Compound (**10**) was pyrolyzed under Flash Vacuum Thermolysis conditions: pressure: 2.10^{-5} mbar; preheating temperature: 150 °C; oven temperature: 480 °C. The mass recovery was about 90 %. The yield after crystallization from ether/pentane (1:2) was about 60%. Because of the nature of the experimental technique and the formation of polymers during thermolysis, absolute yields have not been determined. **11**: transparent crystals: mp 140 °C; ^{1}H NMR ($CDCl_3$): δ 7.68 (d, J = 8.2 Hz, 2 H), δ 7.31 (d, J = 8.2 Hz, 2 H), δ 3.37 (m, J unres., 4 H), δ 3.28 (br s, 4 H), δ 2.43 (s, 3 H), δ 2.33 (m, J unres., 4 H); ^{13}C NMR ($CDCl_3$): δ 143.1 (s), δ 136.3 (s), δ 133.1 (s), δ 129.6 (d), δ 126.9 (d), δ 87.8 (s), δ 61.0 (t), δ 48.3 (t), δ 30.7 (t), δ 21.3 (q); HRMS ($C_{16}H_{19}{}^{14}N^{32}O_2{}^{35}Cl_2S$), calcd 359.0514, observed: 359.0516 ± 0.0011.

9,9,11,11-Tetrachloro-4-azatricyclo[5.3.1.0]undec-4-yl-*p*-tolylsulfone (**12**).
To a solution containing $CHCl_3$ (1.2 g, 3.36 mmol), a drop of ethanol, *N*,*N*,*N*,*N*-cetyltrimethylammoniumbromide (0.01 g), and **11** (0.10 g, 0.28 mmol) in CH_2Cl_2 (10 mL) was added under cooling (0 °C) 50%aqueous NaOH (3.36 mmol, 0.13 g NaOH). The resulting brown two-phase system was vigorously stirred at 90 °C for 18 h. The reaction mixture was then poured into ice water and extracted with ether (3x). The combined organic layers were washed with water (3x) and brine (1x), and dried over $MgSO_4$. After evaporation of the solvent under reduced pressure, a brown solid residue remained. ^{1}H NMR analysis showed that only 30% conversion had occurred. After repeating the above described procedure three times, a total conversion of 85% was achieved with a recovery of 80%. The resulting brown solid residue was purified by column chromatography (silica, ether). Yield after recrystallization from $CHCl_3$/pentane; 0.041 g **12** (34.2 %): colorless crystals, mp 202 °C; ^{1}H NMR ($CDCl_3$): δ 7.65 (δ, J =8.4 Hz, 2 H), δ 7.32 (d, J = 8.4 Hz, 2 H), δ 3.21 (ABKL-system, δ_A = 3.31, δ_B = 3.10, J_{AB} = 13.1 Hz, J_{AL}=J_{AK} unres., J_{BK} = 3.05 Hz, J_{BL} = 9.1 Hz, 4 H), δ 3.19 (AB-system, δ_A = 3.37, δ_B = 2.98, J_{AB} = 15.2 Hz, 4 H), δ 2.42 (s, 3 H), δ 2.22 (ABKL-system, δ_A = 2.26, δ_B = 2.16, J_{AB} = 13.0 Hz, J_{AK} = 15.5, J_{AL} = 2.5 Hz, J_{BK} = 12.8 Hz, J_{BL} = 4.7 Hz, 4 H);^{13}C NMR ($CDCl_3$): δ 134.1 (s), δ 136.8 (s), δ 129.6 (d, J = 136 Hz), δ 126.7 (d, J = 151 Hz), δ 91.5 (s), δ 78.2 (s), δ 59.6 (t, J = 142Hz), δ 46.9 (t, J = 139 Hz), δ 43.8 (s), δ 33.3 (t, J = 129 Hz), δ 21.3 (q, J = 127 Hz); HRMS($C_{17}H_{19}{}^{14}N^{32}O_2{}^{35}Cl_4S$), calcd 440.9891, observed: 440.9890 ± 0.0009; Anal. Calcd for $C_{17}H_{19}NO_2Cl_4S$: C, 46.07; H, 4.23; Cl, 31.99. Found: C, 46.38; H, 4.30; Cl, 32.20.

7-Chloro-1,2,4,5,6,8-hexahydrocylopenta[*d*]azepin-3-yl-*p*-tolylsulfone (**13**)
A mixture of **11** (1.00 g, 2.78 mmol) and Ph_3SnH (1.08 g, 3.08 mmol, 1.1 eq.) was stirred at 120 °C for 3 h under nitrogen. Afterwards the (brown) mixture was allowed to cool to rt and transferred with some ether onto an alumina column. Eluting with ether gave 0.87 g of **13** (2.68 mmol, 96%) as a colorless solid: mp 110 °C; ^{1}H NMR ($CDCl_3$): δ 7.66 (d, J = 8.3 Hz, 2 H), δ 7.28 (d, J = 8.3 Hz, 2H), δ 4.41 (XAA'BB'-system, J = 6.9 Hz, J = 3.3 Hz, 1 H), δ 2.90 (ABKL-system, δ_A = 3.39, δ_B = 3.28,

J_{AB} = 13.9 Hz, J_{AK} = 5.4, J_{BK} = 5.8 Hz, 4 H), δ 2.74 (AA'BB'X-system, δ_A = 2.90, δ_B = 2.57 J = unres., 4 H), δ 2.41 (s, 3 H), δ 2.30 (m, 4 H); ^{13}C NMR ($CDCl_3$): δ 143.0 (s), δ 136.3 (s), δ 132.9 (s), δ 129.6 (d, J = 155 Hz), δ 126.8 (d, J = 166 Hz), δ 56.8 (d, J = 155 Hz), δ 50.0 (t, J = 132 Hz), δ 48.4 (t, J = 136 Hz), δ 30.6 (t, J = 128 Hz), δ 21.4 (q, J = 128 Hz); Anal. Calcd for $C_{16}H_{20}{}^{14}N^{32}O_2{}^{35}ClS$: C, 58.97; H, 6.19; Cl, 10.88. Found: C, 58.82; H, 5.97; Cl, 10.7.

9,11,11-Trichloro-4-azatricyclo[5.3.1.0]undec-4-yl-*p*-tolylsulfone (**14**).
To a solution containing $CHCl_3$ (7.09 g, 59.3 mmol), a drop of ethanol, *N*,*N*,*N*,*N*-cetyltrimethylammonium bromide (0.05 g), and **13** (0.88 g, 2.7 mmol) in CH_2Cl_2 (10 mL) was added under cooling (0 °C) 50% aqueous NaOH (63.4 mmol, 5.07 g). The resulting brown two-phase system was vigorously stirred at 90 °C for 18 h. The reaction mixture was then poured into ice water and extracted with ether (3x). The combined organic layers were washed with water (3x) and brine (1x), and dried over $MgSO_4$. After evaporation of the solvent under reduced pressure, a brown solid residue remained. ^{1}H NMR analysis showed that 88% conversion had occurred. After repeating the above described procedure, total conversion was achieved with a recovery of 63%. The resulting brown solid residue was purified by column chromatography (alumina, ether). Yield after recrystallization from ethyl acetate/pentane: 0.42 g of **14** (38 %): white crystals, mp 166 °C; ^{1}H NMR ($CDCl_3$): δ 7.65 (d, J = 8.3 Hz, 2 H), δ 7.27 (d, J =8.3 Hz, 2 H), δ 4.15 (XA_2B_2-system, J_{XA} = 7.7 Hz, J_{XB} = 3.9 Hz, 1 H), δ 3.55 (ABKL-system, , δ_A = 3.98, δ_B = 3.12, J_{AB} = 14.1 Hz, , J_{AK} = J_{AL} = unres., J_{BK} = 8.7 Hz, J_{BL} = 4.1 Hz, 4 H), δ 2.61 (A_2B_2X-system, , δ_A = 2.98, δ_B = 2.32, J_{AB} = 16.3 Hz, J_{AX} = 7.7 Hz, J_{BX}= 4.0 Hz, 4 H), δ 2.40 (s, 3 H), δ 2.12 (m, 4 H); ^{13}C NMR ($CDCl_3$): δ 143.2 (s, C12), δ 136.8 (s, C15), δ 129.7 (d, C13), δ 126.7 (d, C14), δ 76.9 (s, C11), δ 58.6 (d, C9), δ 47.7 (t, C2, C3), δ 43.6 (s, C1), δ 32.5 (t, C8), δ 21.4 (q, C16); HRMS ($C_{17}H_{20}{}^{14}N^{32}O_2{}^{35}Cl_3S$), calcd 407.0280, observed: 407.0281 ± 0.0009; Anal. Calcd for $C_{17}H_{20}NO_2Cl_3S$: C, 49.95; H, 4.94; Cl, 26.02. Found: C, 49.94; H, 4.95; Cl, 26.2.

1,10-Dichloro-*N*-tosyl-11,11,12,12-tetracycano-6-azatricyclo[7.3.1.0^{3,10}]trideca-2,9(13)-diene (**18b**).
To an NMR solution of **6b** (*ca.* 10 mg) in $CDCl_3$ (0.5 mL), TCNE (excess) was added. The resulting dispersion turned slightly yellow. After 12 h the ^{1}H NMR signals of **6b** had disappeared, leaving only the signals of **18b**. In contrast to **6b**, **18b** is present in two conformations at rt, so two different sets of bridge conformers can be distinguished in a ratio of 0.45 (*endo*) : 0.55 (*exo*). The dispersion was filtered to remove the excess (solid) TCNE. After removal of the solvent from the filtrate, the resulting brownish solid residue was washed with pentane and ether to remove impurities, leaving a slightly pink solid residue. Elemental analysis was too low in carbon, which means that despite repeated attempts to remove the excess of TCNE, this purification was not entirely successful on this scale. **18b**: Anal. Calcd for $C_{23}H_{17}N_5O_2Cl_2S$: C, 55.43; H, 3.44. Found: C, 53.89; H, 3.35. HRMS measurements were also unsuccessful, as at the source temperature needed to evaporate **18b**, only **6b** was observed (as a result of a retro Diels-Alder reaction). ^{1}H NMR ($CDCl_3$) two conformations; *exo* and *endo;* δ 7.68 (d, J = 8.3 Hz, 2 H, tosyl, *exo* or *endo*-conformer), δ 7.64 (d, J = 8.3 Hz, 2 H, tosyl, *exo* or *endo*-conformer), δ 7.32 (d, J = 8.0 Hz, 4 H, tosyl, *exo* and *endo*-conformers) δ 6.71 (s, 2 H, *endo*-conformer), δ 6.38 (s, 2 H, *exo*-conformer), δ 4.19 (A part of AB-sytem, J_{AB} = 14.8 Hz, J = 3.3 Hz, 3.1 Hz, 2 H, CH_2-N, *exo*-conformer), δ 3.80 (A part of AB-sytem, J_{AB} = 15.6 Hz, J = 8.8 Hz, 1.5 Hz, 2 H, CH_2-N, *endo*-conformer), δ 3.53 (A part of AB-sytem, J_{AB} = 13.6 Hz, J = 11.7 Hz, 3.5 Hz, 2 H, allylic, *exo*-

conformer), δ 3.36 (B part of AB-sytem, J_{AB} = 15.6 Hz, J = 8.5 Hz, 8.6 Hz, 2 H, CH_2-N, *endo*-conformer), δ 3.15-2.85 (ABKL-system, J_{AB} = 13.5 Hz, J = unresolved, 4 H, allylic, *endo*-conformer), δ 2.63 (B part of AB-sytem, J_{AB} = 13.8 Hz, J = 2.5 Hz, 2.3 Hz, 2 H, allylic, *exo*-conformer), δ 2.42 (s, 6H, tosyl-CH_3, *exo* and *endo*-conformers), δ 2.08 (B part of AB-sytem, J_{AB} = 14.6 Hz, J = 11.6 Hz, 2.3 Hz, 2 H, CH_2-N, *exo*-conformer); ^{13}C NMR ($CDCl_3$): δ 156.2 (s, bridgehead, *exo or endo*-conformer), δ 150.0 (s, bridgehead, *exo or endo*-conformer), δ 144.3 (s, tosyl, *exo or endo*-conformer), δ 144.2 (s, tosyl, *exo or endo*-conformer), δ 137.8 (d, olefinic-CH, *endo*-conformer), δ 135.8 (s, tosyl, *exo or endo*-conformer), δ 135.8 (s, tosyl, *exo or endo*-conformer), δ 131.0 (d, olefinic-CH, *exo*-conformer), δ 130.0 (d, tosyl, *exo* and *endo*-conformer), δ 110.2 (s, -CN, *exo* or *endo*-conformer), δ 110.1 (s, -CN, *exo* or *endo*-conformer), δ 110.1(s, -CN, *exo* or *endo*-conformer), δ 110.0(s, -CN, *exo* or *endo* conformer), δ 67.6 (s, CH-C-Cl, *exo* or *endo*-conformer), δ 66.8 (s, CH-C-Cl, *exo* or *endo*-conformer), δ 58.8 (t, CH_2-N, *exo*-conformer), δ 51.0 (t, CH_2-N, *endo*-conformer), δ 36.5 (t, allylic, *exo*-conformer), δ 34.9 (t, allylic, *endo*-conformer), δ 21.5 (q, tosyl, *exo* and *endo*-conformer). The second quaternary C-Cl as well as both quaternary $C(CN)_2$ atoms could not be detected.

10-Chloro-*N*-tosyl-11,11,12,12-tetracycano-6-azatricyclo[7.3.1.0^{3,10}]trideca-2,9(13)-diene (**18c**).
To an NMR solution of **6c** (*ca.* 10 mg) in $CDCl_3$ (0.5 mL), TCNE (excess) was added. The resulting dispersion turned slightly yellow. After 45 min the ^{1}H NMR signals of **6c** had disappeared, leaving only the signals of **18c**, which was present in 2 conformations (*exo* and *endo*) in a ratio of 0.44 (*exo*) : 0.56 (*endo*). GC-MS or HRMS measurement attempts failed because of the thermal lability of the adduct, only **6c** was observed. Because of the earlier problems with **18b**, elemental analysis has not been attempted.
18c: ^{1}H NMR ($CDCl_3$) two conformations; *exo* and *endo*: δ 7.69 (d, J = 8.3 Hz, 2 H, tosyl, *exo* or *endo*-conformer), δ 7.63 (d, J = 8.3 Hz, 2 H, tosyl, *exo* or *endo*-conformer), δ 7.31 (d, J = 8.0 Hz, 4 H, tosyl, *exo* or *endo*-conformer) δ 6.71 (dd, J = 6.1, 0.4 Hz, 2 H, *endo*-conformer), δ 6.39 (d, J =6.0 Hz, 2 H, *exo*-conformer), δ 4.57 (t, J = 5.9 Hz, 1 H, *exo*-conformer), δ 4.54 (t, J =6.1 Hz, 1 H, *endo*-conformer), δ 4.17 (A part of AB-sytem, J_{AB} = 14.4 Hz, J = 3.0 Hz, J =unresolved, 2 H, CH_2-N, *exo*-conformer), δ 3.77 (A part of AB-sytem, J_{AB} = 15.6 Hz, J = 9.0 Hz, 1.2 Hz, 2 H, CH_2-N, *endo*-conformer), δ 3.52 (A part of AB-sytem, J_{AB} = 13.6 Hz, J = 11.7 Hz, 3.5 Hz, 2 H, allylic, *exo*-conformer), δ 3.36 (B part of AB-sytem, J_{AB} = 15.6 Hz, J = 8.5 Hz, 8.4 Hz, 2 H, CH_2-N, *endo*-conformer), δ 3.07-2.92 (ABKL-system, J = unresolved, 4 H, allylic, *endo*-conformer), δ 2.63 (B part of AB-sytem, J_{AB} = 13.8 Hz, J = unresolved, 2 H, allylic, *exo*-conformer), δ 2.42 (s, 6H, tosyl-CH_3, *exo* and *endo*-conformer), δ 2.01 (B part of AB-sytem, J_{AB} = 13.1 Hz, J = unresolved, 2 H, CH_2-N, *exo*-conformer); ^{13}C NMR ($CDCl_3$): δ 157.5 (s, bridgehead, *exo* or *endo*-conformer), δ 151.1 (s, bridgehead, *exo* or *endo*-conformer), δ 144.1 (s, tosyl, *exo* or *endo*-conformer), δ 143.9 (s, tosyl, *exo* or *endo*-conformer), δ 136.0 (s, tosyl, *exo* or *endo*-conformer), δ 135.9 (s, tosyl, *exo* or *endo*-conformer), δ 133.5 (d, J = 181.2 Hz, olefinic-CH, *endo*-conformer), δ 130.0 (d, J = 161 Hz, tosyl, *exo* and *endo*-conformer), δ 126.9 (d, J = unresolved, tosyl, *exo* or *endo*-conformer), δ 126.7 (d, J = unresolved, tosyl, *exo* or *endo*-conformer), δ 126.6 (d, J = unresolved, olefinic-CH, *exo*-conformer), δ 111.9 (s, -CN, *exo* or *endo*-conformer), δ 111.7 (s, -CN, *exo* or *endo*-conformer), δ 110.7 (s, -CN, *exo* or *endo*-conformer), δ 110.5 (s, -CN, *exo* or *endo*-conformer), δ 107.8 (s, >CCl, *exo* or *endo*-conformer), δ 59.0 (t, J = 140 Hz, CH_2-N, *exo*-conformer), δ 51.1 (t, J = 141 Hz, CH_2-N, *endo*-conformer), δ 45.7 (d, J = 156 Hz, >CH, *exo*-

conformer), δ 44.9 (d, J = 151 Hz, >CH, *endo*-conformer), δ 36.5 (t, J = 125 Hz, allylic, *exo*-conformer), δ 35.1 (t, J = 133 Hz, allylic, *endo*-conformer), δ 21.5 (q, tosyl, *exo* and *endo*-conformer). Both quaternary $C(CN)_2$ atoms could not be detected.

2-Chloro-*N*-tosyl-6-aza-14-oxatetracyclo[$10.3.1^{3,11}.0.0^{2,9}$]pentadeca-3(16),9-dien-13,15-dione (**20c**)
To an NMR solution of **6c** (*ca.* 10 mg) in $CDCl_3$ (0.5 mL), a dilute solution in $CDCl_3$ of MAA was added. Addition was terminated when **6c** had been consumed (checked by ^{1}H NMR). The ^{1}H NMR spectrum of **20c** at 205 K revealed the presence of 2 conformers in a ratio of 0.69 (*exo*) to 0.31 (*endo*); at rt, **20c** gave broad signals only. Because **20c** was present in 2 non-symmetrical conformations in low concentration, it was impossible to assign all the ^{1}H NMR signals of the methylene groups in the bridge. For the same reason it was impossible to obtain a meaningful ^{13}C NMR spectrum at low temperature. **20c**: ^{1}H NMR ($CDCl_3$, 205 K) two conformations; *exo* and *endo*: δ 7.6 (d, J = 8.1 Hz, 2 H, tosyl, *exo* -conformer), δ 7.63 (d, J = 8.1 Hz, 2 H, tosyl, *endo*-conformer), δ 7.29 (d, J = 8.1 Hz, 2 H, tosyl, *exo* and *endo*-conformer), δ 7.68 (d, J = 8.1 Hz, 2 H, tosyl, *exo*-conformer), δ 6.58 (d, J = 6.2 Hz, 1 H, *endo*-conformer), δ 6.41 (d, J = 5.7 Hz, 1 H, *endo*-conformer), δ 6.31 (d, J = 5.9 Hz, 1 H, *exo*-conformer), δ 6.12 (d, J = 5.5 Hz, 1 H, *exo*-conformer), δ 4.18 (m, 1 H, *exo*-conformer), δ 4.13 (m, 1 H, *endo*-conformer), δ 4.02 (m), δ 3.65 (m, 2 H, *exo*-conformer), δ 3.59 (m, 2 H, *endo*-conformer), δ 3.43-3.25 (m), δ 2.84-2.76 (m), δ 2.42 (s, 3 H, *endo*-conformer), δ 2.40 (s, 3 H, *exo*-conformer), δ 1.93 (m, 2 H, *exo*-conformer).

10-Chloro-*N*-tosyl-11,12-bis(methoxycarbonyl)-6-azatricyclo[$7.3.1.0^{3,10}$]trideca-2,9(13)-diene (**22c**).
To an NMR solution of **6c** (*ca.* 10 mg) in $CDCl_3$ (0.5 mL), DMAD (*ca.* 4 eq) was added. The resulting NMR solution was kept at rt for 12 d, at which point the ^{1}H NMR signals of **6c** had disappeared. The ^{1}H NMR spectrum of **22c** gave broad lines at rt. At 230 K, the signals sharpened showing **22c** to be present in 2 conformations in a ratio of 0.96 (*exo*) : 0.04 (*endo*). NMR data of the second conformer are not given because of low intensity. **22c**: ^{1}H NMR ($CDCl_3$): δ 7.70 (d, J = 8.2 Hz, 2 H), δ 7.31 (d, J = 8.2 Hz, 2 H), δ 6.48 (d, J = 5.8 Hz, 2 H) δ 5.10 (t, J = 5.8 Hz, 1 H), δ 4.00 (A part of AB-sytem, J_{AB} = 14.4 Hz, J = unresolved, 2 H), δ 3.88 (s, 3H), δ 3.76 (s, 3H), δ 3.38 (B part of AB-sytem, J_{AB} = 14.4 Hz, J = unresolved, 2 H), δ 2.45 (A part of AB-sytem, J_{AB} = 12.6 Hz, J = unresolved, 2 H), δ 2.40 (s, 3H), δ 1.97 (B part of AB-sytem, J_{AB} = 12.6 Hz, J = unresolved, 2 H); ^{13}C NMR ($CDCl_3$): δ 166.8, δ 163.0, δ 155.6, δ 153.6, δ 143.5, δ 138.5, δ 136.2, δ 133.9, δ 133.0, δ 126.8, δ 58.8, δ 53.8, δ 45.4, δ 33.4, δ 30.0, δ 21.9.

General procedure for Diels-Alder competition experiments.
To a 1:1 mixture (*ca.* 15 mg) of **15** and **6** in $CDCl_3$ (0.5 mL), small portions of a $CDCl_3$ solution of the dienophile were added using a microsyringe. The progress of the reaction was monitored by ^{1}H NMR spectroscopy. Addition of dienophile was terminated when one of the two cyclophanes had undergone complete conversion. With an excess of the dienophile, the product ratio was determined from the ^{1}H NMR spectrum before total conversion of the most reactive cyclophane had occurred.

Diels-Alder adducts of **15b**,**c**.

The TCNE, MAA and DMAD Diels-Alder adducts (**17b**,**c**, **19b**,**c**, and **21b**,**c**) of **15b** and **15c**, respectively, were obtained by the same procedures as described for the Diels-Alder reactions of **6b** and **6c**. Their NMR spectra were in accordance with those reported.[18,20,21]

General procedure for the formation of 1,2,4,5-tetrahydropyrrolo[3,2,1-*hi*]indoles (**23**) from **6**.

A colorless solution of **6b** or **6c**, respectively, (20-40 mg) in DMSO-d_6 (0.5 mL) in an NMR tube was heated in an oil bath at 130 °C for 15 to 30 min. The progress of the reaction was monitored by ^{1}H NMR spectroscopy at intervals of 5-10 min. At 50 % conversion, the brown-purple reaction mixture was poured into water (pH > 7.0) in a test tube. The water layer was extracted with $CHCl_3$ (3x), which turned red-purple. The combined $CHCl_3$ layers were then extracted with aqueous 1N HCl (3x). After separation of the slightly yellow acidic water layers, the test tube was cooled with ice and NaOH (s) was added until the solution became slightly basic (pH >8). The water layer turned milky and was extracted with $CHCl_3$ (3x). The combined $CHCl_3$ layers were dried (Na_2SO_4) and the solvent was removed under reduced pressure, leaving **23b** or **23a**, respectively, as a slightly yellow oil in about 40% yield. Compounds (**23**) are sensitive towards oxidation and should be kept under inert atmosphere at low temperature (-75 °C). For that reason, not all signals in the ^{13}C NMR spectrum could be observed and/or assigned; generally, the spectra in DMSO-d_6 showed a better resolution.

1,2,4,5-tetrahydropyrrolo[3,2,1-*hi*]indole (**23a**). ^{1}H NMR ($CDCl_3$): δ 6.90 (d, *J*= 7.3 Hz, 2 H), δ 6.60 (t, *J*= 7.3 Hz, 1 H), δ 3.22 (m, 8 H); ^{13}C NMR ($CDCl_3$): δ 122.0, δ 120.0 (d, *J* = 159 Hz), δ 58.6 (t, *J* = 137 Hz), δ 34.9 (t, *J* = 134 Hz); MS *m/z* (rel. intens.) 145 ($M^{+\bullet}$, 79), 144 (100, 130 (8), 117 (13), 115 (11).

6-Chloro-1,2,4,5-tetrahydropyrrolo[3,2,1-*hi*]indole (**23b**). ^{1}H NMR ($CDCl_3$): δ 6.90 (s, 2 H), δ 3.25 (br s, 8 H); ^{1}H NMR (DMSO-d_6): δ 6.90 (s, 2 H), δ 3.17 (br s, 8 H);^{13}C NMR ($CDCl_3$): δ 124.3, δ 122.4, δ 59.0, δ 34.9; ^{13}C NMR (DMSO-d_6): δ 163.1 (s), δ 123.8 (s), δ 122.1 (dd, *J* = 165 Hz, 5 Hz), δ 57.9 (t, *J* = 142 Hz), δ 34.2 (t, *J* = 134 Hz); MS *m/z* (rel. intens.) 179 ($M^{+\bullet}$, ^{35}Cl, 100), 178 (83), 143 (60), 142 (12); HRMS ($C_{10}H_{10}{}^{14}N^{35}Cl$), calcd 179.0502; observed: 179.0502 ± 0.0005.

Formation of 6-chloro-1,2-dihydropyrrolo[3,2,1-*hi*]indole (**27b**) from **23b**.

a) *Reaction with O_2*:

When a solution of **23b** in $CDCl_3$ was kept at rt for several days, **23b** was slowly oxidized to **27b** by atmospheric oxygen (^{1}H NMR spectroscopy).

b) *Reaction with DDQ*:

To an NMR tube containing a (slightly yellow) $CDCl_3$ solution of **23b**, small portions of a solution of DDQ in $CDCl_3$ were added. After the first addition, the solution turned bright blue. The progress of the reaction was monitored by ^{1}H NMR spectroscopy. After quantitative conversion had been achieved and the solution had turned deep purple, it was transferred to a column. Column chromatography (alumina, pentane/ ether, 50:50) gave **27b** as a colorless solid.

c) *Reaction with TCNE:*

To an NMR tube containing a (slightly yellow) $CDCl_3$ solution of **23b,** solid TCNE was added. After vigorously shaking the tube for several hours, **23b** had been quantitatively converted to **27b**, according to ^{1}H NMR spectroscopy.

27b. ^{1}H NMR ($CDCl_3$) : δ 7.31 (s, 2 H), δ 7.16 (d, *J*= 2.7 Hz, 1 H), δ 6.38 (d, *J*= 2.6 Hz, 1 H), δ 4.54 (t, *J*= 7.0 Hz, 2 H), δ 3.80 (t, *J*= 7.0 Hz, 2 H); MS *m/z* (rel. intens.) 177 ($M^{+\bullet}$, ^{35}Cl, 100), 176 (19), 142 (41), 141 (26), 115 (18).

6-Chloro-1,2,4,5-tetrahydropyrrolo[3,2,1-*hi*]indolinium picrate (**28b**).
To an NMR tube containing a $CDCl_3$ solution of **23b**, small portions of a dilute solution of picric acid in $CDCl_3$ were added. The progress of the reaction was monitored by ^{1}H NMR spectroscopy. During the reaction a green precipitate formed. Recrystallization attempts from several solvents failed due to insolubility of the precipitate. **28b**. ^{1}H NMR (DMSO-d_6): δ 8.95 (s, 2 H, picrate), δ 7.15 (s, 2 H), δ 3.60 (m, 4 H), δ 3.31 (m, 4 H);^{13}C NMR ($CDCl_3$): δ 124.3 (s), δ 122.4 (d), δ 59.0 (t), δ 34.9 (t); ^{13}C NMR (DMSO-d_6): δ 160.5 (s), δ 155.4 (s), δ 141.6 (s), δ 128.4 (s), δ 125.0 (d, *J* = 168 Hz, picrate), δ 124.1 (s), δ 123.0 (d, *J* = 168 Hz), δ 40.5 (t, *J* = 145 Hz), δ 34.1 (t, *J* = 134 Hz)

N-Methyl-1,2,4,5-tetrahydropyrrolo[3,2,1-*hi*]indolinium iodides (**29**).
A mixture of the **23a** or **23b** and MeI (> 4eq.) in $CDCl_3$ solution was stirred for 24 h at rt. Reaction progress was monitored by ^{1}H NMR spectroscopy. After completion, the solvent and the excess of MeI were removed under reduced pressure. The yellow/white solid residue was dissolved in $CHCl_3$ and extracted with water. Evaporation of the aqueous layer at rt gave a white solid residue of **29**.
N-Methyl-1,2,4,5-tetrahydropyrrolo[3,2,1-*hi*]indolinium iodide (**29a**). ^{1}H NMR (D_2O): δ 7.41 (B part of A_2B system, dd, 2x *J* = 7.0 Hz, 1 H), δ 7.28 (A part of A_2B system, d, *J* = 7.0 Hz, 2 H), ABKL system: δ_A = 4.31, δ_B = 4.04, δ_K = 3.90, δ_L = 3.37, (J_{AB} = 11.0 Hz, J_{AK} = 6.3 Hz, J_{AL} 0.2 Hz, J_{BK}= 11.2 Hz, J_{BL} = 7.4 Hz, J_{KL} = 16.5 Hz 8 H), δ 3.36 (s, 3H). ^{13}C NMR (D_2O): δ 133.8 (d), δ 131.2 (s), δ 71.0 (t), δ 50.0 (q), δ 34.0 (t).
6-Chloro-*N*-methyl-1,2,4,5-tetrahydropyrrolo[3,2,1-*hi*]indolinium iodide (**29b**). ^{1}H NMR ($CDCl_3$): δ 7.30 (s, 2 H), ABKL system: δ_A = 5.12, δ_B = 4.31, δ_K = 3.98, δ_L = 3.44, J_{AB} = 11.7 Hz, J_{AK} = 6.0 Hz, J_{BK} = 11.4 Hz, J_{BL} = 7.3 Hz, J_{KL} = 16.8 Hz, 8 H), δ 2.85 (s, 3H).

Crystal structure determination of 6c.
Numerical data on the structure determination of **6c** have been collected in Table 5; selected structural data have been presented in Tables1 and 2. X-Ray data were collected on an Enraf-Nonius CAD4T diffractometer (on rotating anode) for a transparent colorless crystal. The structure was solved by Direct Methods using the program SIR97[34] and refined of F^2 using the program SHELXL97.[35] Hydrogen atoms were located from a difference map and their position and isotropic displacement parameters refined except for the methyl moiety that was refined as a rigid rotator. All other calculations were done with functions from the PLATON package.[36] The crystallographic data have been deposited with the Cambridge Crystallographic Database (CCDC 145094).

Supplementary material.
Tables of atomic coordinates, thermal parameters, bond lengths, and bond angles (11 pages).

Table 5. Crystal data and details of the structure determination of **6c**.

Crystal Data

Empirical Formula	C17 H18 Cl N O2 S
Formula Weight	335.84
Crystal System	Orthorhombic
Space Group	P212121 (No. 19)
a, b, c [Å]	6.8558(5) 10.7102(7) 21.567(2)
V [$Å^3$]	1583.6(2)
Z	4
D(calc) [g/cm^3]	1.409
F(000)	704
μ(MoKα) [mm^{-1}]	0.379
Crystal Size [mm]	0.13 x 0.38 x 0.62

Data Collection

Temperature [K]	150
Radiation [Å]	MoKα 0.71073
Theta Min-Max [°]	1.9 27.5
Dataset	0: 8 ; 0: 13 ; -27: 27
Tot., Uniq. Data, R(int)	4190, 3621, 0.40
Observed Data [I > 2.0 sigma(I)]	2766

Refinement

Nref, Npar	3621, 260
R1, wR2, S	0.0627, 0.1405, 1.13
$w^{-1} = \sigma^2(FO^2) + (0.0530P)^2 + 0.696P$	WHERE $P = (F_O^2 + 2F_C^2)/3$'
Max. and Av. Shift/Error	0.00, 0.00
Flack Parameter	-0.17(0.12)
Min. and Max. resd. dens. [e/A^3]	-0.43, 0.23

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