

11-t-Butyl-8-chloro[5]metacyclophane

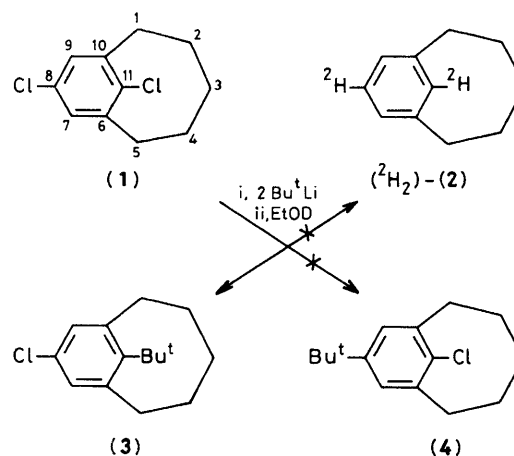
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The reaction of 8,11-dichloro[5]metacyclophane with t-butyl-lithium gave the very crowded title compound in an unusual substitution reaction at the most hindered position of the molecule, C-11.

We have recently synthesized 8,11-dichloro[5]metacyclophane (**1**)¹ with the dual goal of opening a better preparative access to the intriguing parent compound [5]metacyclophane (**2**) and obtaining a crystalline derivative suitable for X-ray crystal structure determination. While the latter goal has been achieved,² we have not yet been able to reduce the two chlorine atoms. Instead, in an attempt to do so by reaction of (**1**) with t-butyl-lithium followed by protonation or deuteration (Scheme 1), (**1**) was converted in an unusual and efficient substitution reaction into the highly crowded 11-t-butyl-8-chloro[5]metacyclophane (**3**).

A solution of (**1**) in tetrahydrofuran was cooled to -70°C and treated with two equivalents of Bu^tLi in hexane. After 5 h, EtOD was added and the temperature raised to room temperature. The usual workup and preparative g.l.c. gave no indication of the formation of deuteriated products such as the desired dideuterio-derivative ($^2\text{H}_2$)-(**2**) of (**2**). Instead, (**3**) was isolated in 70% yield; its structure assignment is based on its spectral properties.[†] Both the exact mass and a ^1H n.m.r. singlet at δ 1.38 proved the substitution of one chlorine by the t-butyl group; the great similarity of the ^1H n.m.r. spectrum with those of (**1**) and (**2**)³ revealed its [5]metacyclophane nature, and, because of the C_s symmetry observed, excluded *cine*-substitution. Only the two regioisomers (**3**) and (**4**) can be made by the rapid and clean rearrangement at room temperature to (**5**) under the catalytic influence of $\text{CF}_3\text{CO}_2\text{D}$ in CDCl_3 ; (**5**) was the only product observed and was characterized by its spectral properties.[‡] The mechanistic considera-



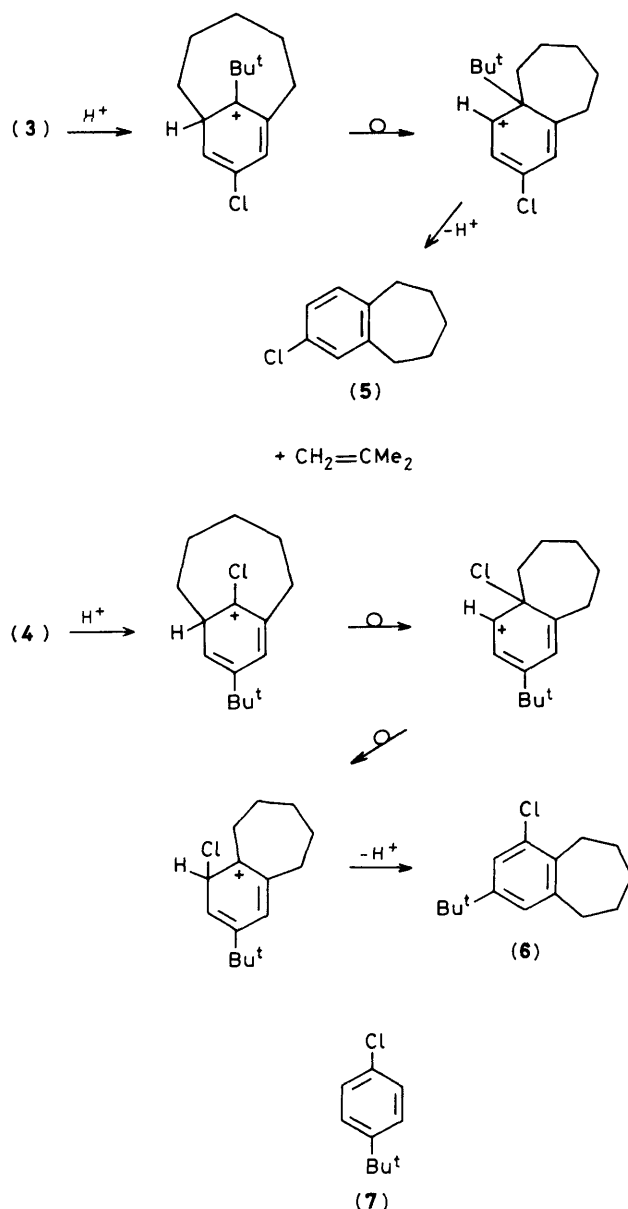
Scheme 1

tions reflected in Scheme 2 explain the formation of (**5**) from (**3**); in particular, the ready loss of the t-butyl group and formation of isobutene (^1H n.m.r.) can only be reconciled with structure (**3**), while (**4**) would be expected^{1,4} to yield (**6**); the stability of the t-butyl group of 4-chloro-t-butylbenzene (**7**) under the reaction conditions was checked experimentally.

The structure assignment of (**3**) is corroborated by the ^{13}C n.m.r. spectra.[†] Most diagnostic is the low field shift of C-11 ($\Delta\delta +15.4$ compared to the value calculated by additivity rules⁵); similar deviations from additivity are also observed for C-11 of other [5]metacyclophanes.⁶

The mechanism of formation of (**3**) is not clear at the moment, but the following remarkable features of this reaction should be pointed out. Formally, the reaction is a nucleophilic substitution of Cl by Bu^t . It is unexpected that this reaction takes place at the highly hindered position C-11 and not at the readily accessible C-8. However, low reactivity of aryl chlorides towards organolithium reagents is in fact the normal behaviour;⁷ this is further illustrated by the retainment of 8-Cl in the presence of an excess of Bu^tLi , and by the stability of (**7**) under the same conditions. Therefore, the unexpected reactivity must clearly be caused by the exceptional structural situation at C-11:² 26.8° bending of the 'bow'

[†] (**3**): Mass spectrum $m/z(\%)$ 238(3.9), 236(13), (**3**)⁺; 57(100); calcd. for $\text{C}_{15}\text{H}_{21}^{35}\text{Cl}$: 236.1332, found: 236.1325. ^1H N.m.r. (250 MHz, CDCl_3 , δ) 6.56 (s, 2H), 3.14 (ddd, 2J , 3J 12.1, 3J 3.3 Hz, 2H), 2.60 (ddd, 2J 12.3 Hz, 3J , 3J 3.3 Hz, 2H), 1.83 (m, 2H), 1.50 (m, 1H), 1.38 (s, 9H), 1.30 (m, 1H), 0.17 (m, 2H). ^{13}C N.m.r. (62.89 MHz, CDCl_3 , δ) 156.8 (s, C-11), 147.0 (s, C-6, C-10), 131.1 (s, C-8), 121.9 (d, J 165 Hz, C-7, C-9), 42.8 (t, J 129.4 Hz, C-1, C-5), 40.8 (t, J 129.1 Hz, C-2, C-4), 38.2 (s, 11- CMe_3), 35.6 (q, J 129.0 Hz, 11- CMe_3), 23.5 (t, J 121.8 Hz, C-3). U.v. [cyclohexane, λ_{max} in nm (log ϵ)] 270(3.45), 280(3.40), 320(3.15). (**5**): Mass spectrum $m/z(\%)$ 182(12), 180(42), (**5**)⁺; 145(100); calcd. for $\text{C}_{11}\text{H}_{13}^{35}\text{Cl}$ 180.0706, found: 180.0691. ^1H N.m.r. (90 MHz, CDCl_3 , δ) 7.07 (s, 1H), 7.03 (m, 2H), 2.85–2.69 (m, 4H), 1.93–1.53 (m, 6H).

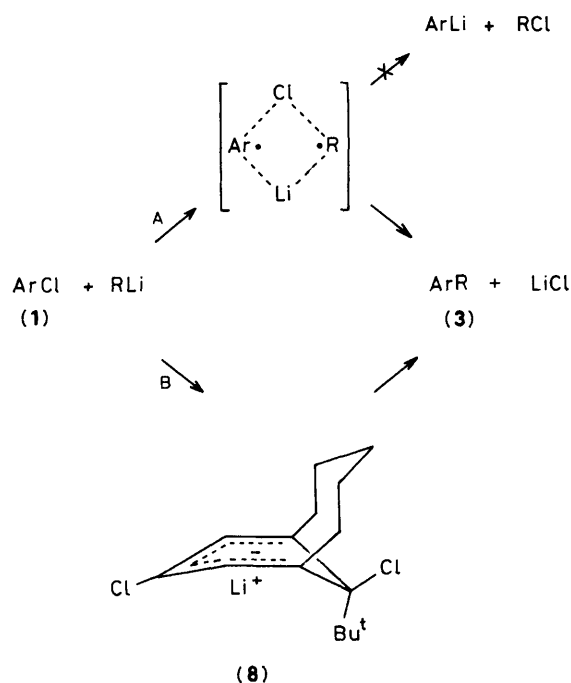


Scheme 2

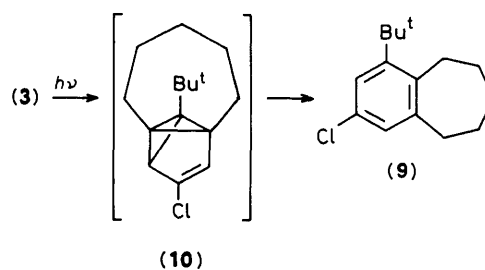
out of the aromatic plane and the opposite tilt of 11-Cl towards the pentamethylene bridge, leading to a slight pyramidalization at C-11. An $S_{RN}1$ mechanism⁸ can be excluded; it would imply the intermediacy of the 11-aryl radical of (1) which is expected to attack the oligomethylene bridge quite efficiently under transannular ring closure,^{6,9} but such products were not observed. A radical cage mechanism¹⁰ (Scheme 3, pathway A) might prevent the transannular hydrogen abstraction and cannot be fully excluded.

At present, however, we consider a reaction by addition-elimination with (8) as an intermediate (Scheme 3, pathway B) to be the most attractive alternative. Normally, such reactions do not occur with unactivated benzene derivatives, but the high strain of (1) and the abnormal bonding situation at C-11 may facilitate the process in this particular case.

The high strain in (3) is evident from the u.v. spectrum† [λ_{max} , 320 nm (log ϵ 3.15) as compared to λ_{max} , 275 nm (log ϵ



Scheme 3



Scheme 4

2.58) for (7)], and from its rapid rearrangement to (9) on irradiation which may proceed *via* the benzvalene (10); however, intermediates have not been detected (Scheme 4).

In contrast to (1),¹ (3) was unreactive towards tetracyanoethene in an attempted Diels-Alder reaction. According to models, this unexpected¹¹ lack of reactivity is again due to extreme steric hindrance by the *t*-butyl group which prevents approach of the dienophile. In this context, we want to point out that the 1H n.m.r. spectrum of (3) is temperature independent (from -75 to $+62^\circ C$) and shows (3) to occur in one conformation only. This conformation corresponds to that of (2) (exclusive conformer) and (1) (major conformer),³ with the pentamethylene bridge pointing with C-3 towards the *t*-butyl group [*cf.* the conformation drawn for (8)]. At first sight, this arrangement seems paradoxical in view of the crowding introduced by the *t*-butyl group. Apparently,^{2,3} the non-bonded interactions of the substituent at C-11 with the central methylene group (C-3) are less severe than those with the methylene groups closest to the benzene ring.

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