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

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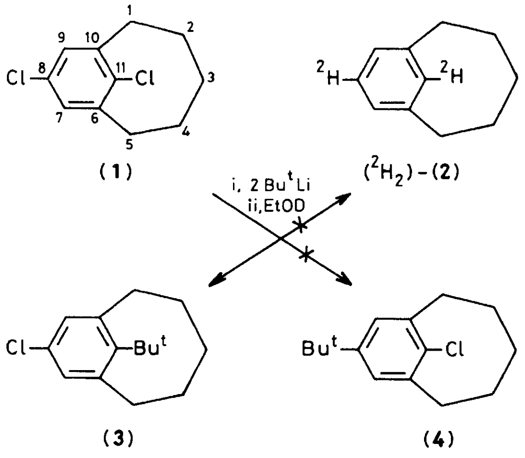
The reaction of 8,11-dichloro[5]metacyclophane with t-butyl-lithium gave the very crowded title compound in an unusual substitution reaction at the most hindered position of the molecule, C-11.

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 deuteriation (Scheme 1), (**1**) was converted in an unusual and efficient substitution reaction into the highly crowded 11-t-butyl-8-chloro[5]metacyclophane (**3**).



Scheme 1

A solution of (**1**) in tetrahydrofuran was cooled to −70 °C and treated with two equivalents of Bu^{t}Li 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 ($^2H_2$)-(**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 ^{1}H n.m.r. singlet at δ 1.38 proved the substitution of one chlorine by the t-butyl group; the great similarity of the ^{1}H 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**) are in accord with these data. A distinction in favour of (**3**) can be made by the rapid and clean rearrangement at room temperature to (**5**) under the catalytic influence of CF_3CO_2D in $CDCl_3$; (**5**) was the only product observed and was characterized by its spectral properties.† The mechanistic considerations 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 (^{1}H 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 (Δδ +15.4 compared to the value calculated by additivity rules[5]); 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^{t}Li, 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'

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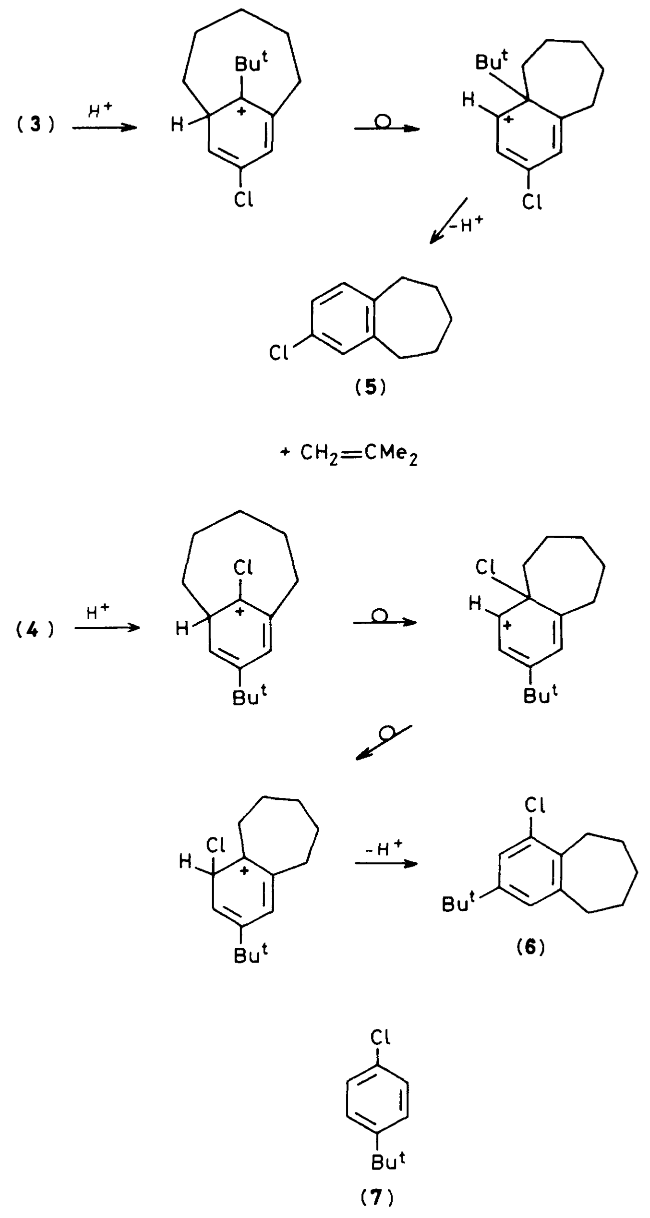
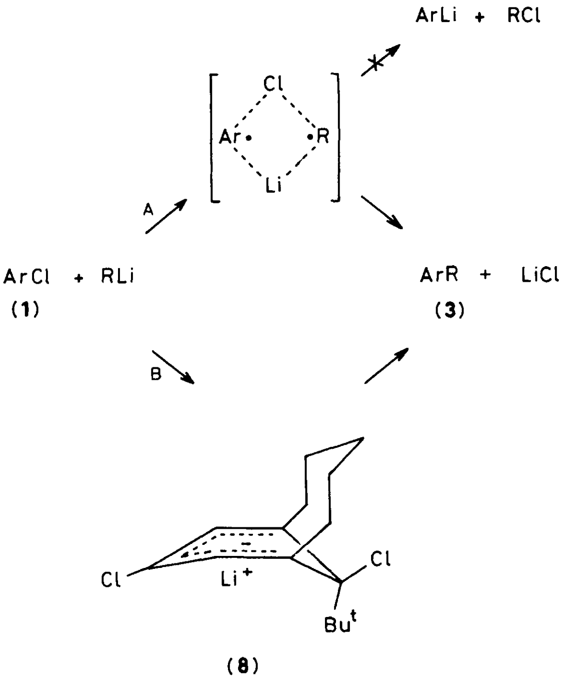
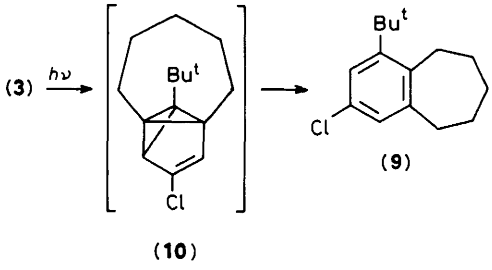
† (**3**): Mass spectrum *m*/*z*(%) 238(3.9), 236(13), (**3**)$^{\cdot+}$; 57(100); calcd. for $C_{15}H_{21}(^{35}Cl)$: 236.1332, found: 236.1325. ^{1}H N.m.r. (250 MHz, $CDCl_3$, δ) 6.56 (s, 2H), 3.14 (ddd, ^2J, ^3J 12.1, ^3J 3.3 Hz, 2H), 2.60 (ddd, ^2J 12.3 Hz, ^3J, ^3J 3.3 Hz, 2H), 1.83 (m, 2H), 1.50 (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-*C*Me$_3$), 35.6 (q, *J* 129.0 Hz, 11-C*Me*$_3$), 23.5 (t, *J* 121.8 Hz, C-3). U.v. [cyclohexane, $\lambda_{max.}$ in nm (log ε)] 270(3.45), 280(3.40), 320(3.15). (**5**): Mass spectrum *m*/*z*(%) 182(12), 180(42), (**5**)$^{\cdot+}$; 145(100); calcd. for $C_{11}H_{13}(^{35}Cl)$ 180.0706, found: 180.0691. ^{1}H 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



Scheme 3



Scheme 4

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 $S_{RN}1$ mechanism[8] 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 mechanism[10] (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† [$\lambda_{max.}$ 320 nm (log ε 3.15) as compared to $\lambda_{max.}$ 275 nm (log ε 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 unexpected[11] 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 ^{1}H n.m.r. spectrum of (**3**) is temperature independent (from −75 to +62 °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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