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From the *anti*-tricyclo[4.2.1.1^{2,5}]deca-3,7-diene framework to 4,5,6,7-tetrachloro-isoindenone derivatives

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ABSTRACT

Two formal trapping products of 4,5,6,7-tetrachloro-isoindenone (**1b**) can be obtained from the polycyclic precursor (**4**) in a multi-step sequence, thus guaranteeing the *anti*-orientation of the arene and alkene/arene units. Compound **2b** was synthesized without the in situ generation of 4,5,6,7-tetrachloro-isoindenone **1b** or cyclopentadiene and has been fully characterized. Furthermore, progress toward dibenzo derivative **3b**, the poorly soluble [4+4] dimer of **1b**, was made along analogous synthetic steps. In addition, the structures of two crucial intermediates were determined by X-ray crystallography.

Previous studies on isoindenone (indene-2-one) **1a** and its derivatives focused on their unique reactivity,[1–3] as implied by their possible resonance structures **1a** (*o*-quinodimethane; cyclopentadienone) and **1′a** (oxyallyl structure). Once generated, and in the absence of an olefinic scavenger, isoindenones display a unique dimerization behavior which is dependent on steric and electronic factors, that is, the number and position of substituents as well as the degree of aromatic annulation of parent compound **1**. The molecular architecture **3** depicts only one of the many possible isoindenone dimerization products (e.g., norbornenone, dioxane, and 2-oxabicyclo[3.2.1]oct-6-en-8-one derivatives) that were previously reported (Fig. 1).[1–3] Herein, we wish to disclose the synthesis of two new polycycles that are formally derived from the unknown 4,5,6,7-tetrachloro-isoindenone **1b**. We prepared the *anti*-monobenzo derivative **2b** and the *anti*-dibenzo compound **3b** via a short multi-step sequence from dienedione **4**, thus circumventing the synthesis of a suitable precursor for the in situ generation of compound **1b**. This indirect approach from dienedione **4** guaranteed access to the unique target compounds, benzoenedione **2b**, a formal [4+4]-adduct of two intrinsically reactive species (isoindenone **1b** and cyclopentadienone) and the *anti*-dibenzo derivative **3b**, one of the several dimers of compound **1b**. The multi-step approach implies no isomerization of the crucial tricyclic framework along the entire sequence (vide infra) whereas the two target compounds are intriguing substrates for thermally initiated isomerization reactions and photochemical studies.

Dienedione **4** cannot be benzannulated directly as isomerization to **5** occurs rapidly upon thermal activation.[4] Fortunately,

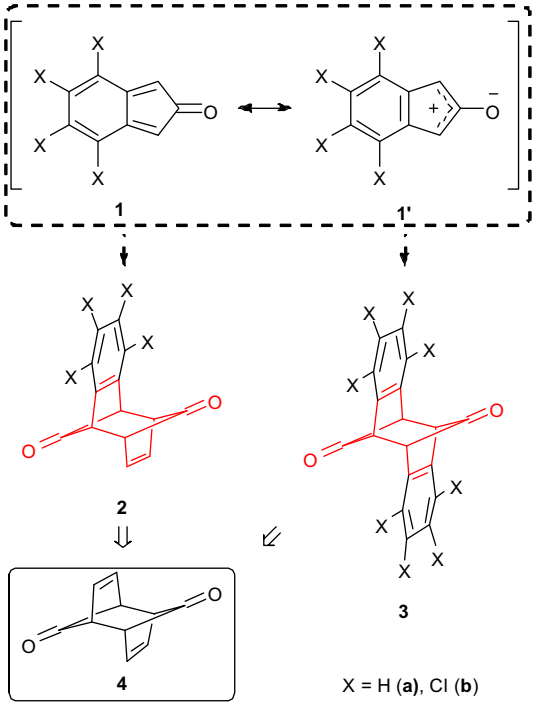

Figure 1. Two potential routes to rigid arene-scaffolds.

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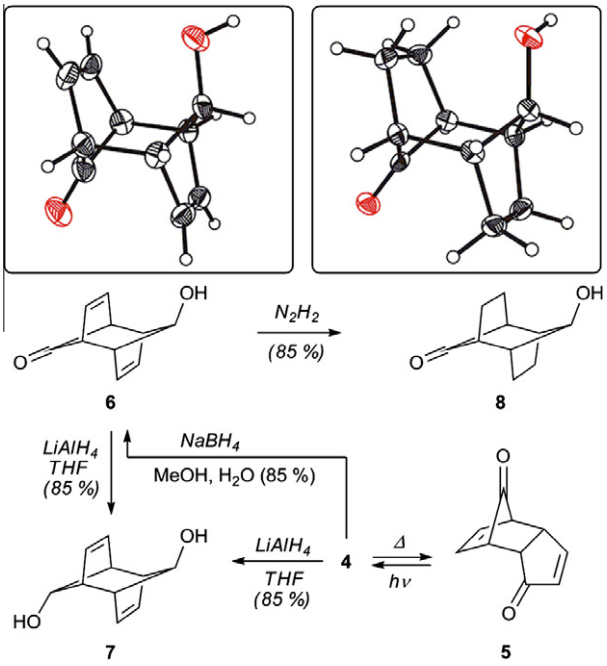

Figure 2. The *anti*-tricyclo[4.2.1.1^{2,5}]deca-3,7-diene framework is a versatile platform for further functionalization; crystal structures of hydroxyketones **6**[9] and the saturated derivative **8**[10]—thermal ellipsoids are shown at the 50% probability level.

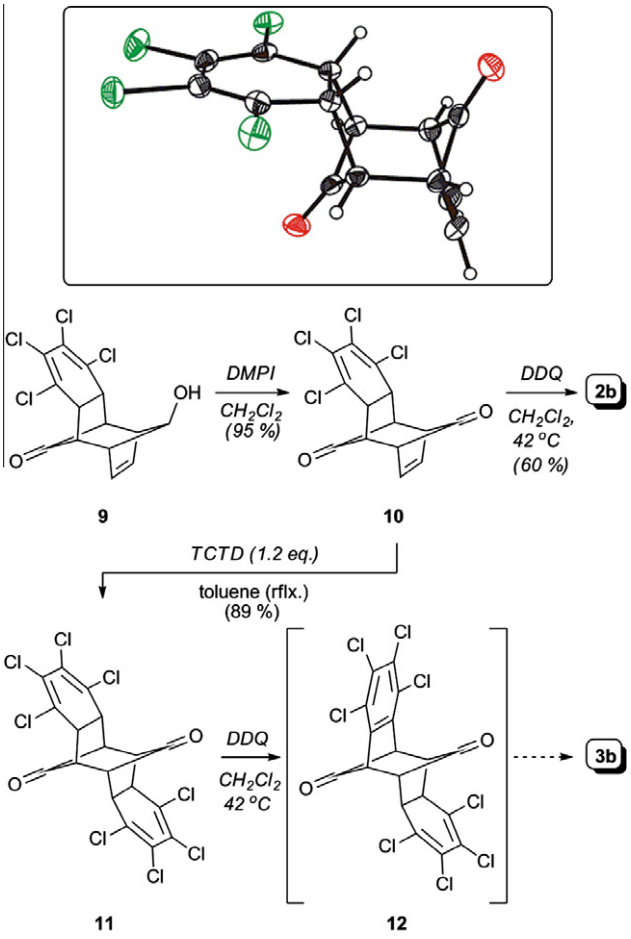

Figure 3. Synthesis of formal tetrachloro-isoindenone derivatives **2b** and **3b**; crystal structure of adduct **10**[13]—thermal ellipsoids are shown at the 50% probability level.

the thermally stable hydroxyketone **6**[5] and diol **7**[5a,6] can be easily prepared as alternative substrates for a Diels–Alder cycloaddition, pending oxidation of the corresponding hydroxyl functionality at a later stage of the synthetic route. We were successful in determining the crystal structure of hydroxyketone **6** (Fig. 2), thus obtaining the last structure within the series **4** → **6** → **7**.[7] The structure is closely related to the saturated derivative **8**[5b] (Fig. 2) which we obtained by diimide reduction.[8] Table 1 compares selected crystallographic data for the tricyclic compounds **4** and **6**–**8**.

As we reported recently, the Diels–Alder reaction of diol **7** with tetrachlorothiophene dioxide (TCTD) led to the transannular product that was not suitable for further conversion toward scaffolds **2b**–**3b**, whereas hydroxyketone **6** furnished exclusively the mono-adduct **9**.[11] Oxidation of adduct **9** with the Dess–Martin periodinan (DMPI)[12] occurred almost instantaneously at room temperature and dione **10** was isolated in excellent yield after chromatography on silica gel. The structure of dione **10**,[13] a formal mono-Diels–Alder adduct of dienedione **4**, was confirmed by X-ray structure determination (Fig. 3). The subsequent aromatization[14] to benzoenedione **2b** with dichlorodicyano-*p*-benzoquinone

Table 1
Crystallographic data for the tricyclic scaffolds **4**, **6**, **8**, **7**, and compound **15**

	Dienedione **4**[7a]	Hydroxyketone **6**[9]	Hydroxyketone **8**[10]	Diol **7**[7b]	Diketone **10**[13]
Chemical formula	$C_{10}H_8O_2$	$C_{10}H_{10}O_2$	$C_{10}H_{14}O_2$	$C_{10}H_{12}O_2$	$C_{14}H_8Cl_4O_2$
Formula weight, g mol^{-1}	160.16	162.18	166.21	164.2	350.00
Temperature, K	295(2)	153(2)	153(2)	295(2)	153(2)
Crystal size, mm^3	0.3 × 0.2 × 0.2	0.24 × 0.22 × 0.17	0.39 × 0.10 × 0.04	0.5 × 0.5 × 0.5	0.31 × 0.19 × 0.16
Crystal system, space group	Triclinic, $P\bar{1}$	Monoclinic, $P2_1$	Triclinic, $P\bar{1}$	Monoclinic, $P2_1/c$	Monoclinic, $P2_1/n$
a, Å	6.448(7)	12.069(2)	6.3499(7)	10.3730(14)	6.1335(6)
b, Å	6.6120(6)	10.2935(18)	10.9715(11)	9.8494(14)	21.944(2)
c, Å	8.9758(6)	18.656(3)	12.3707(13)	7.7128(11)	10.2927(10)
α, °	81.671(8)	90	98.2750(10)	90	90
β, °	79.176(10)	92.911(2)	104.3880(10)	91.850(11)	107.1330(10)
γ, °	84.745(8)	90	92.7830(10)	90	90
Volume, Å^3	370.96(6)	2314.6(7)	822.92(15)	787(19)	1323.8(2)
Z	2	12	4	4	4
ρ_{calc}, mg m^{-3}	1.434	1.396	1.342	1.385	1.756
R_1[a]	0.037	0.0474	0.0442	0.039	0.0250
wR_2[b]	0.088	0.0824	0.1033	0.099	0.0635
Largest diff. peak/hole, e Å^{-3}	0.2 and −0.15	0.28 and −0.19	0.31 and −0.20	0.25 and −0.19	0.36 and −0.21

[a] R_1 is defined as $\sum||F_o| - |F_c||/\sum|F_o|$ for $I > 2\sigma(I)$.
[b] wR_2 is defined as $[\sum[w(F_o^2 - F_c^2)^2]/\sum w(F_o^2)^2]^{1/2}$ for $I > 2\sigma(I)$.

(DDQ) was carried out under very mild conditions (CH_2Cl_2, 42 °C) to prevent any thermally induced rearrangement of the product. Thus, the complete conversion of scaffold **9** to target **2b** typically required several days, as easily monitored by ^{1}H NMR spectroscopy: The C_s-symmetrical product **2b** displayed only three resonances for the corresponding olefin and the two bridgehead hydrogen environments. After aqueous work-up and column chromatography on silica gel we obtained pure **2b** as colorless crystals. Compound **2b** is moderately soluble in most organic solvents and was fully characterized. Contrary to other isoindenone derivatives,[1–3] the mass spectrometric data (EI, 70 eV) show the parent molecular ion peak with the characteristic isotope pattern, but no prominent fragment for isoindenone **1b** or cyclopentadienone was observed.

An alternative route to product **2b** by DDQ-facilitated aromatization of precursor **9**, followed by Dess–Martin oxidation was attempted, but failed in the first step when no aromatization of compound **9** could be achieved under mild conditions. Currently, the reactivity of **2b** toward thermolysis and photochemically initiated conversions is under investigation and we will report the rather complex behavior in due course.

As anticipated, the *anti*-dibenzo derivative **3b** proved to be a more challenging target compound: we had already experienced the extremely poor solubility of the product(s) that formed upon another cycloaddition of TCTD to adduct **9**, preventing any meaningful characterization, not to mention product isolation.[11] Furthermore, NMR spectroscopic evidence for compound **3a**, the dimer of the parent isoindenone **1a**, was discussed in the literature without providing any analytical data.[1a]

On dione **10**, though, the second Diels–Alder reaction with TCTD was carried out successfully and furnished the marginally soluble bis-adduct **11** in 90% yield. The C_{2h}-symmetrical compound **11** displays only the two remaining bridgehead proton resonances in the ^{1}H NMR spectrum whereas the characterization by ^{13}C NMR spectroscopy in a variety of solvents (CD_2Cl_2, $CDCl_3$, C_6D_6, acetone-d_6, DMSO-d_6, C_6D_5Cl) was thwarted by the compound's poor solubility, even at higher temperatures. Nevertheless, infrared spectroscopy, mass spectrometry, and elemental analysis data support the assigned structure. The last oxidative step to the dibenzo derivative **3b** required the aromatization of precursor **11**, once more carried out in dilute solution and under mild conditions. The reaction proceeds only slowly and any attempts to isolate intermediate **12** or target compound **3b** from the mixture yielded only impure fractions. Nevertheless, the ^{1}H NMR spectroscopic evidence for intermediate **12** is unequivocal with two characteristic doublets for the bridgehead atoms in the central framework and a singlet for the tetrachlorocyclohexadiene subunit in the molecule's lower half. A new singlet at 4.05 ppm (Supplementary data) has been tentatively assigned to the isoindenone dimer **3b**.

In conclusion, we have achieved a selective synthesis of benzoenedione **2b** from dienedione precursor **4** along a four-step protocol. Furthermore, we established the synthesis of TCTD-bis-adduct **11** *en route* to the dibenzo derivative **3b**. Both polycyclic target compounds are formal [4+4] cycloaddition products of the unknown 4,5,6,7-tetrachloroisoindenone **1b**: compound **2b**, an adduct with another fleeting intermediate (cyclopentadienone) and *anti*-dibenzo derivative **3b**, the corresponding isoindenone dimer. A thorough investigation of **2b**, (**3b**) with regard to thermal stability, photochemical behavior, and toward various trapping reagents is currently in progress. These investigations will provide mechanistic details relating to the elusive parent compound, 4,5,6,7-tetrachloro-isoindenone **1b**.

Acknowledgments

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Supplementary data

Supplementary data (experimental procedures and spectroscopic characterization of all new products; X-ray crystallographic data for **6**, **8**, and **10**; unit cell figures for **6** and **8**) associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2010.09.045.

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9. Crystallographic details for hydroxyketone **6** have been deposited with the Cambridge Crystallographic Centre as a Supplementary Publication No. CCDC 793335.
10. Crystallographic details for hydroxyketone **8** have been deposited with the Cambridge Crystallographic Centre as a Supplementary Publication No. CCDC 793336.
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