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Diels–Alder reactivity of *anti*-tricyclo[4.2.1.$1^{2,5}$]deca-3,7-diene derivatives

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ABSTRACT

The limited thermal stability of the polycyclic dione **1** can be circumvented by reacting its derivatives, hydroxyketone **3** and diol **4** with tetrachlorothiophene dioxide (**6d**) to yield the mono-Diels–Alder adduct **8** and rearranged polycyclic ether **11**, respectively. The structures of both new products were confirmed by X-ray structure determination.

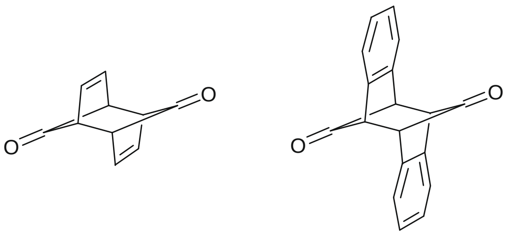
The synthesis of polycyclic compounds has been an important and stimulating area of organic chemistry, providing structurally unique molecules with unusual reactivities and novel properties, even leading to 'non-obtainable' molecular frameworks.[1] The *anti*-tricyclo[4.2.1.$1^{2,5}$]deca-3,7-diene scaffold has been investigated earlier in search of the elusive cyclopentadienone monomer,[2] as a starting material for the synthesis of heterocyclic oxadiamantane derivatives[3] and in the quest for non-classical carbocations.[4]

We are interested in dienedione **1** as a rigid molecular skeleton for the construction of more complex target compounds, in particular the unsubstituted indeneone dimer **2** (Fig. 1).[5] The chemistry of the title framework is challenging since not only chemo-, regio- and stereoselectivity have to be addressed[3] but, furthermore, the close proximity of functional groups gives rise to transannular reactions.[6] Despite the many reactions published by several groups,[3,7] no Diels–Alder cycloaddition of dienedione **1** or its derivatives, hydroxyketone **3** and diol **4** has been reported yet.

We prepared dienedione **1** in a three-step procedure from cyclopentadiene[8] and obtained the corresponding derivatives **3** and **4** by reduction with $NaBH_4$ in methanol/water[3c,9] and $LiAlH_4$ in THF[3c,4] in ca. 85% yield, respectively. The crystal structures of dienedione **1**[10] and the diol **4**[11] were recently reported by us.

Due to the thermally induced back isomerization of **1** to its *endo*-cyclopentadienone dimer **7**, that is, the substrate for the photochemical preparation of dienedione **1**,[8] it is not surprising that any attempt to react the latter (**1**) with dienes **6a–d**[12] (Fig. 2) at elevated temperatures furnished only isomer **7** and traces of unidentified material. After establishing the thermal stability of hydroxyketone **3** and diol **4** in refluxing toluene, we initially converted diol **4** with diene **6a** to a crude product that displayed a rather complex ^{1}H NMR spectrum. Similar observations were made when dienes **6b**[12a] and **6c**[12b] were employed. Unfortunately, we were not able to isolate any clean products from these conversions by either chromatography (silica gel, deactivated silica gel, basic alumina) or recrystallization.

Only upon reaction with tetrachlorothiophene dioxide (TCTD) **6d**,[12c] an established reagent for benzannulation, did we obtain a single product (yield: 81%) after refluxing the mixture in dry toluene for one day (Fig. 2). The ^{1}H NMR spectrum with ten signals did not display any olefinic signals, thus excluding a mono-Diels–Alder adduct of type **9**. The bis-DA-adduct was excluded by the number of proton resonances and the ^{13}C NMR data (Supplementary data). Infrared spectra revealed no broad OH band anymore and we concluded the formation of a transannular product, which is a racemic mixture of polycyclic ether **11**. The postulated structure was



1 **2**

Figure 1.

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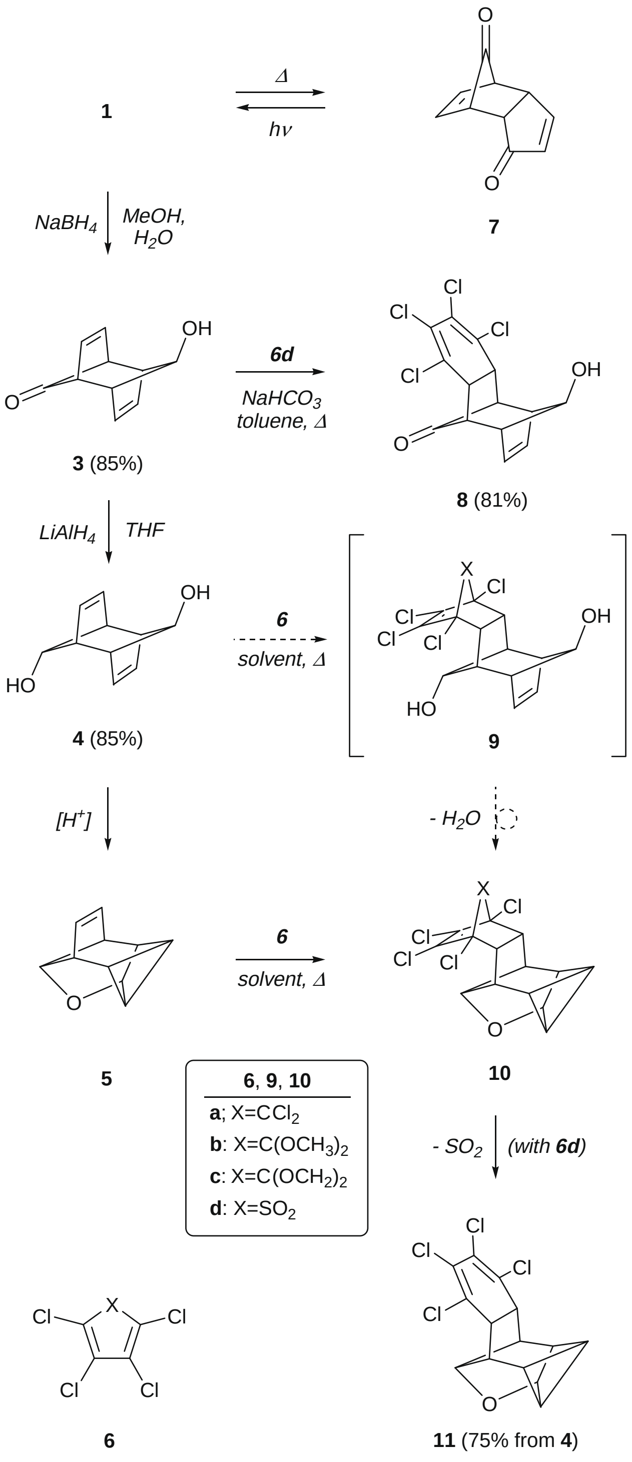

Figure 2.

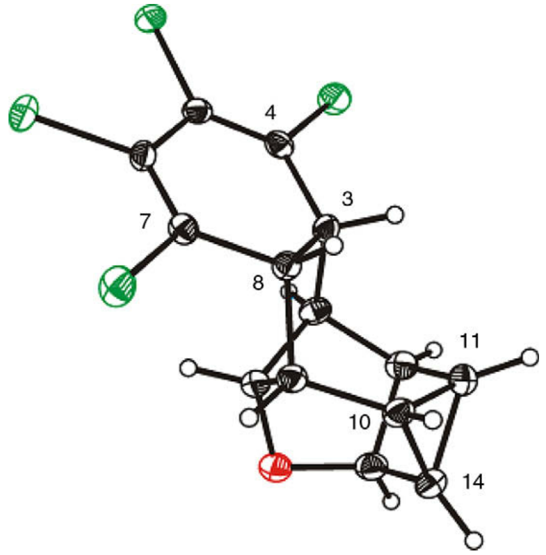

Figure 3. Crystal structure of polycyclic ether **11**; Thermal ellipsoids are shown at the 50% probability level.

confirmed by 2D NMR spectra (Supplementary data) and by X-ray structure determination (Fig. 3).[13] The structure displays an unusual framework with a bicyclo[2.1.0] subunit with the shortest C–C single bond distances found in the cyclohexadiene ring [C3–C4: 1.496(2) Å, C7–C8: 1.503(2) Å] and in the cyclopropane moiety [C10–C14: 1.503(2) Å, C10–C11: 1.502(2) Å].

The observed transannular reaction has been reported for the parent diol **4** under acid- or base-catalyzed conditions,[3,6] furnishing polycycle **5** with NMR chemical shifts that are in excellent agreement with the observed pattern of the relevant substructure in product **11** (Supplementary data). Furthermore, upon addition of dichlorocarbene on diol **4** a small amount of the corresponding rearranged product was found.[3b] We postulate the formation of racemic ether **11** to proceed via the sequence **4**→**5**→**10d**→**11**. Although a control experiment (sodium bicarbonate, diol **4**, toluene reflux) excluded any formation of polycycle **5**, we observed the latter by ^{1}H NMR spectroscopy as the first reaction intermediate when dienes **6a**–**d** were reacted with **4**, probably due to traces of acidic impurities in the reagents or formed in situ as SO_2 is extruded. Using a weak organic base (*N*,*N*-dimethylaniline) did not prevent the formation of transannular product **11**. Alternatively, the latter could be obtained in a control experiment from olefin **5** by Diels–Alder reaction with TCTD (**6d**) and subsequent cheletropic extrusion of SO_2 in high yield (85%). In case of dienes **6a**–**c** the reaction is once more initiated with a rearrangement and formation of adducts **9a**–**c** can be excluded (NMR). The subsequent Diels–Alder products **10a**–**c** can be observed in the ^{1}H NMR spectrum of each complex reaction mixture, albeit no isolation was possible (vide supra).

Conversely, the Diels–Alder reaction of hydroxyketone **3** was expected to proceed without concomitant transannular reaction. Surprisingly, no reaction occurred with an excess of dienes **6a**–**c** in refluxing toluene, whereas conversion with an excess of TCTD (**6d**) under the same conditions furnished exclusively monoadduct **8** in 75% yield (Fig. 2). Its ^{1}H and ^{13}C NMR spectra (Supplementary data) show the expected signal patterns for a compound with C_S symmetry, and the IR spectrum displays a prominent carbonyl band. Although the spectral data do not clearly indicate the cycloaddition of diene **6d** to the least-hindered double bond, that is, the olefin syn to the hydroxyl group, we obtained structural proof for the adduct **8** by X-ray structure determination (Fig. 4).[14] The crystal packing shows an extended network of individual molecules forming hydrogen bonds from the carbonyl group and the hydroxy group to neighboring molecules, respectively (Supplementary data).

The conversion of hydroxyketone **3**, or monoadduct **8**, under more forcing conditions (refluxing xylenes, excess of **6d**) furnished a reaction mixture that did not display olefinic signals in the NMR spectra anymore. We have not been able, though, to purify any clean products from the poorly soluble precipitate and can therefore only speculate on the formation of a bis-adduct. Compound

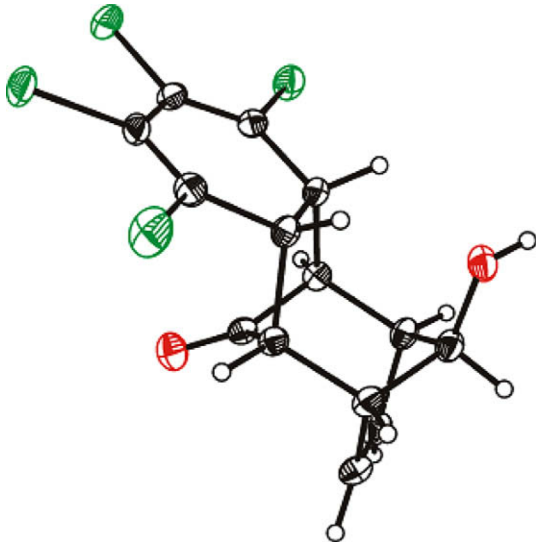

Figure 4. Crystal structure of mono-Diels–Alder adduct **8**; Thermal ellipsoids are shown at the 50% probability level.

8 also provides a suitable substrate for oxidation of the hydroxyl group and subsequent Diels–Alder reaction of the unreacted alkene subunit to yield a formal twofold DA adduct of the parent dienedione **1**. We will report our efforts on further synthetic transformations of **8** (aromatization, protective group chemistry, oxidation) in due course.

In conclusion, we have compared the Diels–Alder reactivity of three highly functionalized *anti*-tricyclo[4.2.1.1^{2,5}]deca-3,7-diene derivatives. We have obtained and structurally characterized two new polycyclic frameworks, the transannular reactivity derived ether **11** and a mono-Diels–Alder adduct **8**, from diol **4** and hydroxyketone **3**, respectively.

Acknowledgments

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Supplementary data

Supplementary data (experimental procedures, spectroscopic characterization, and X-ray crystallographic data with unit cell figures of mono-Diels–Alder adduct **8** and polycyclic ether **11**) associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2009.03.215.

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13. *Crystallographic data for* **11**: crystal dimensions $0.26 \times 0.17 \times 0.17\ \text{mm}^3$, $C_{14}H_{10}Cl_4O$, $M_r = 336.02$, triclinic, space group $P\bar{1}$, $a = 6.7578(9)$ Å, $b = 7.8027(11)$ Å, $c = 12.3333(17)$ Å, $\alpha = 91.430(21)$, $\beta = 100.908(2)$, $\gamma = 97.504(2)$, $V = 632.28(15)$ Å^3, $Z = 4$, $d_{calc} = 1.765\ \text{g cm}^{-3}$, $\mu = 0.921\ \text{mm}^{-1}$, $F(0\,0\,0) = 340$, reflections collected/unique = 7316/2815 [R(int) = 0.0140], refinement method = full-matrix least-squares on F^2, final R indices [$I > 2\sigma(I)$] $R_1 = 0.0267$, $wR_2 = 0.0661$, R indices (all data) $R_1 = 0.0305$, $wR_2 = 0.0681$, goodness of fit on $F^2 = 1.069$; Measurements were carried out at 153(2) K on a Bruker SMART APEX II diffractometer equipped with an APEX II 4 K charge-coupled device area detector and a sealed-tube X-ray source (graphite-monochromated Mo K$_\alpha$ radiation, $\lambda = 0.71073$ Å). A complete sphere of data was collected to better than 0.8 Å resolution. Processing was carried out by using the program SAINT (*SAINT+, Version 7.46A*; Madison, WI, 2007), which applied Lorentz and polarization corrections to three-dimensionally integrated diffraction spots. The program SADABS (Sheldrick, G. M. *SADABS, Version 2007/4*; Bruker AXS: Madison, WI, 2007) was used for the scaling of diffraction data, the application of a decay correction, and an empirical absorption correction based on redundant reflections. For structure determination, refinement and molecular graphics the solution all calculations were performed using the SHELXTL Plus package (Sheldrick, G. M. *SHELXTL 97*; University of Göttingen, 1997) for structure determination, refinement and molecular graphics: CCDC 724685.
14. *Crystallographic data for* **8**: crystal dimensions $0.28 \times 0.27 \times 0.18\ \text{mm}^3$, $C_{14}H_{10}Cl_4O_2$, $M_r = 352.02$, monoclinic, space group $P2_1/n$, $a = 10.9551(11)$ Å, $b = 12.0807(13)$ Å, $c = 21.2951(22)$ Å, $\beta = 103.885(1)$, $V = 2736.0(5)$ Å^3, $Z = 8$, $d_{calc} = 1.709\ \text{g cm}^{-3}$, $\mu = 0.86\ \text{mm}^{-1}$, $F(0\,0\,0) = 1424$, reflections collected/unique = 30,684/6236 [R(int) = 0.027], refinement method = full-matrix least-squares on F^2, final R indices [$I > 2\sigma(I)$] $R_1 = 0.0363$, $wR_2 = 0.0894$, R indices (all data) $R_1 = 0.0442$, $wR_2 = 0.0931$, goodness of fit on $F^2 = 1.114$; Measurements were carried out at 153(2) K on a Bruker SMART APEX II diffractometer equipped with an APEX II 4 K charge-coupled device area detector and a sealed-tube X-ray source (graphite-monochromated Mo K_α radiation, $\lambda = 0.71073$ Å). A complete sphere of data was collected to better than 0.8 Å resolution. Processing was carried out by using the program SAINT (*SAINT+, Version 7.46A*; Madison, WI, 2007), which applied Lorentz and polarization corrections to three-dimensionally integrated diffraction spots. The program SADABS (Sheldrick, G. M. *SADABS, Version 2007/4*; Bruker AXS: Madison, WI, 2007) was used for the scaling of diffraction data, the application of a decay correction, and an empirical absorption correction based on redundant reflections. For structure determination, refinement and molecular graphics the solution all calculations were performed using the SHELXTL Plus package (Sheldrick, G. M. *SHELXTL 97*; University of Göttingen, 1997) for structure determination, refinement and molecular graphics: CCDC 724686.