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Cope Rearrangement versus a Novel Tandem Retro-Diels–Alder–Diels–Alder Reaction with Role Reversal†

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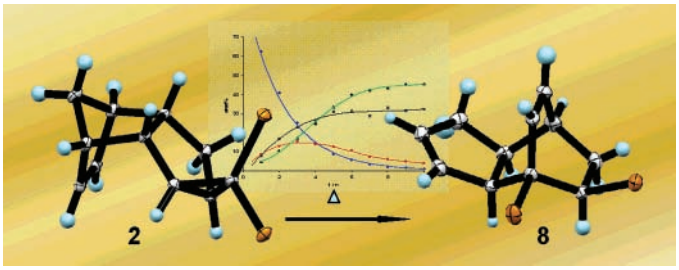
ABSTRACT



A reinvestigation of the thermolysis of 4,4-dibromotetracyclo[6.2.1.0^{2,7}.0^{3,5}]undec-9-ene (2) affords diene 8 with a completely rearranged hydrocarbon skeleton via the isolable intermediate 4, along with cyclopentadiene and bromobenzene. DFT calculations show that the novel tandem retro-Diels–Alder–Diels–Alder reaction *with role reversal* is slightly less favored than the overall single-step Cope rearrangement.

Organic chemists have always been fascinated by rearrangements in which relatively simple compounds are being transformed into more complex structures. The rigorous clarification of the detailed reaction mechanism for such conversions remains a challenging task.

According to an earlier report,[1] heating of 4,4-dibromotetracyclo[6.2.1.0^{2,7}.0^{3,5}]undec-9-ene (**2**), the product resulting from a dibromocarbene addition to dicyclopentadiene (**1**), [2] at 130 °C for 1 h leads to the ring-opened[3] compound **4** (Scheme 1). In addition, cyclopentadiene (**5**) and bromobenzene (**7**)[4] are formed. A reinvestigation of the thermolysis of **2**, however, finds *rac*-(1*R*,2*S*,6*R*,7*R*,10*R*)-1,10-dibromotricyclo[5.2.2.0^{2,6}]undeca-3,8-diene (**8**, 33% isolated yield), **5**, and **7** (42%, via GC calibration) as products. Moreover, **8** comprises ^{1}H NMR and IR data identical with those reported for **4**.

A single-crystal X-ray analysis of **2** confirms the structure of the starting material (Figure 2). Next, **2** was thermolized in refluxing *m*-xylene (138 − 139 °C). In order to monitor the thermolysis, every hour a sample for GC analysis was taken. In Figure 1, peak areas of relevant signals are plotted against reaction time.

The decrease of starting material **2** is unimolecular and obeys first-order kinetics. The ring-opening product **4** is an intermediate in the formation of final product **8**. The experiments were also performed at 111 °C with toluene as

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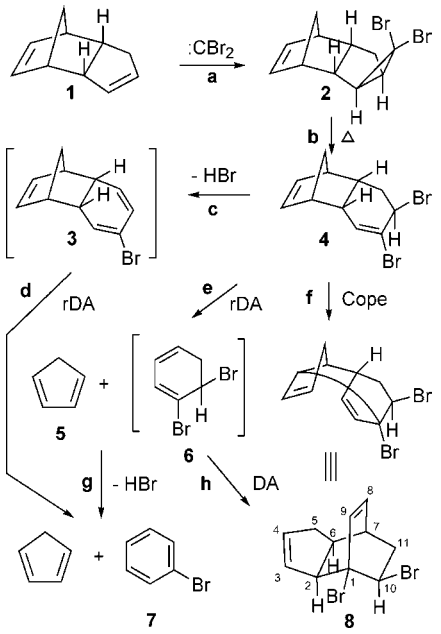
Scheme 1



solvent and afforded the same product distribution. Because of toluene's lower boiling point, the reaction rate is lower. While the half-life of **2** in refluxing *m*-xylene is 1.5 h, it is 14.4 h in toluene. Both structures **4** and **8** were established unequivocally by single-crystal X-ray analysis (Figure 2).

As expected, the ring opening of **2** to **4** proceeds according to the Woodward−Hoffmann−DePuy rule[5] in a stereoselective manner. The spectroscopic data obtained for **4** proved to be totally different from NMR and IR data published earlier.[1] To corroborate the fact that **4** is an intermediate, it was refluxed under the conditions applied for **2**. The conversion **4** → **8** also follows first-order kinetics. Furthermore, under the reaction conditions, isolated product **8** was found to be almost completely stable (94%).

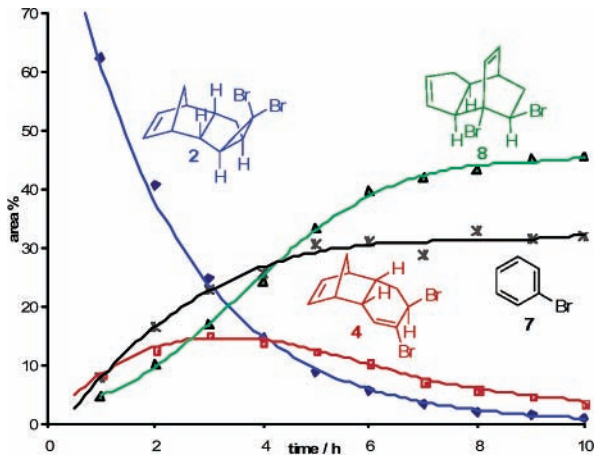


Figure 1. Time-dependent decomposition of **2** in refluxing *m*-xylene.

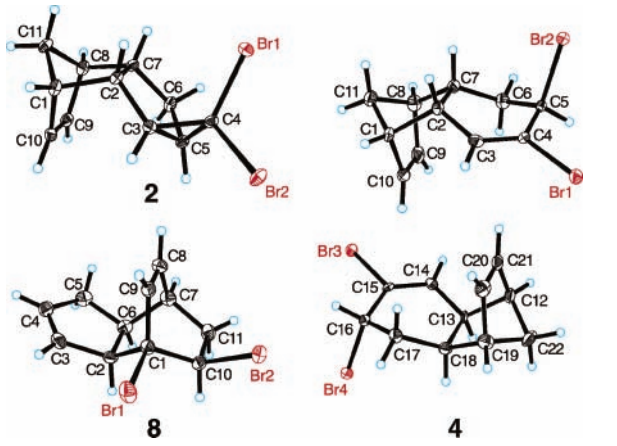


Figure 2. ORTEP representations of the single-crystal X-ray diffraction structures of **2**, **4** (crystallized in a 1:1 ratio of enantiomers), and **8**.

A plausible mechanism for the formation of bromobenzene (**7**) encompasses a retro-Diels−Alder (rDA) reaction of **4** to give **6** and a subsequent elimination of HBr (Scheme 1). A mere Diels−Alder (DA) reaction[6] of **6** and cyclopentadiene (**5**) leads to **8**. To our knowledge, the consecutive sequence **4** → **5** + **6** → **8** represents a novel tandem rDA−DA reaction[7] *with role reversal*. An alternative possible pathway to **8** consists of a stereoselective Cope rearrangement[8] in **4**.

Computations of the transition states for both pathways using density functional theory (B3LYP/6-31G(d))[9] suggest that the Cope rearrangement **4** → **8** (ΔG_{412} = 30.6 kcal/mol) is energetically preferred over the rDA reaction **4** → **5** + **6** (ΔG_{412} = 34.2 kcal/mol) by 3.6 kcal/mol (Table 1). Moreover, when compared with the Cope rearrangement, the DA reaction **5** + **6** → **8** has a significant unfavorable entropic contribution and should not occur at such high temperatures (ΔG_{412} = 40.4 kcal/mol; ΔE_0 = 22.8 kcal/mol). Therefore, if at all, the tandem rDA−DA reaction should be responsible for the formation of only a very small fraction of **8**. The calculations also confirm that **8** is the kinetically favored product of the DA reaction of cyclopentadiene with **6**.[10] In the tandem pathway (**e**, **h**), a rDA reaction is followed by a DA reaction in a new recombination of cyclopentadiene (**5**) and **6**.

In an attempt to corroborate this tandem pathway, 6,6-dibromobicyclo[3.1.0]hex-2-ene (**9**) was synthesized at −60

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(10) For example, for the formation of the isomeric compound **10** a barrier needs to be overcome that is 3.2 kcal/mol higher in energy than the one leading to **8**.

Table 1. Relative Energies of Compounds **2**, **3** + HBr, **8**, **10**, and Transition States for Conversions **b**−**f**, **h** (Scheme 1) in Comparison to **4**[a]

	ΔE_0 (kcal/mol)	ΔG_{412} (kcal/mol)
2	+16.3	+17.1
b: **2** → **4**	+52.2	+51.1
3 + HBr	+15.3	+1.4
4	0.0	0.0
e: **4** → **5** + **6**	+36.0	+34.2
c: **4** → **3** + HBr	+38.5	+37.3
f: **4** → **8**	+30.4	+30.6
d: **3** + HBr → **5** + **7** + HBr	+36.5	+21.5
5 + **7** + HBr	−5.7	−37.8
5 + **6**	+10.9	−8.4
h: **5** + **6** → **8**	+33.7	32.0
8	−7.9	−7.3
10	−7.8	−7.1

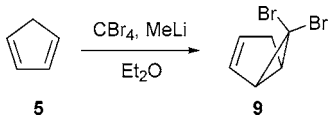
[a] Values in kcal/mol from B3LYP/6-31G(d) calculations.

to 0 °C[11] and treated with cyclopentadiene (**5**) in order to obtain **8**. This experiment failed; instead, decomposition and cleavage of HBr is favored and intermediate **6**, which would result from **9**, could not be detected. Moreover, attempts to trap **6** with 1,3-diphenylisobenzofuran did not succeed.

The thermal treatment of **2** in a closed apparatus (pressure tube) at about 200 °C for 2 h afforded two isomeric products **8** (22%) and **10**[12] (5%). Isomer **10** could be the DA adduct of **5** and **6**, with a different orientation of diene and dienophile. The fact that neither **10** nor any of the other possible DA adducts were found under the standard conditions (*m*-xylene reflux, open apparatus) is a further indication for a Cope rearrangement in **4**.

Thermolysis of **8** in *m*-xylene with added HBr gas at ∼200 °C in the closed apparatus (Scheme 2) yielded almost

Scheme 2



a 1:1 ratio of isomers **8** (25%) and **10** (24%) along with HBr addition product **11** (16%) and bromobenzene (**7**, 14%).

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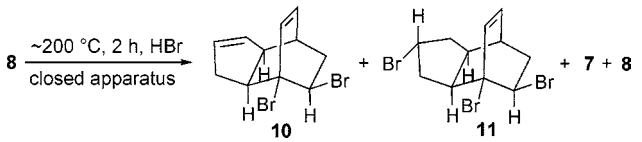
(12) Structural verification by X-ray analysis.

According to B3LYP/6-31G(d) calculations, HBr catalyzes the shift of the double bond by a concerted proton exchange. Since this reaction is reversible and **10** ($\Delta E_0 = -7.8$ kcal/mol in comparison to **4**) possesses nearly the same relative energy as **8** ($\Delta E_0 = -7.9$ kcal/mol) (Table 1), a statistical distribution is obtained. Compound **11** formally derives from a protonation of the double bond at C3 of the five-membered ring in **8** followed by capture of the resulting cation by the bromide ion from the *exo*-side (Scheme 3). However, **11** does

Scheme 3



not originate from the most stable carbenium ion that can be generated from **8** by HBr attack at the double bond of the cyclohexene moiety. Instead, the addition of HBr occurs at the most electron-rich double bond (C3−C4) of **8** in a concerted, strongly asymmetric fashion. Compound **11** proved to be stable under the reaction conditions (200 °C, 2 h, closed apparatus, without HBr), and both **8** and **10** were not even formed in traces.

In conclusion, the thermal treatment of **2** leads to the rearranged product **8** through isolable intermediate **4** along with cyclopentadiene (**5**), and bromobenzene (**7**), by a deep-seated rearrangement[13] of the initial hydrocarbon skeleton. In an earlier publication,[1] structure **4** was mistaken for final product **8**. One mechanistic alternative, a novel tandem rDA−DA reaction[7] *with role reversal*, is slightly less favored than the one-step Cope rearrangement **4** → **8**. Furthermore, while the thermal reaction in an open vessel exclusively provides **8**, in a closed apparatus in addition its double bond isomer **10** is formed from **8** by HBr catalysis.

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Supporting Information Available: Materials and methods, experimental procedures, spectral data, NMR spectra, crystallographic data of **2**, **4**, **8**, and **10**, and computational data. This material is available free of charge via the Internet at http://pubs.acs.org.

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