

## Tandem Diels–Alder–Diels–Alder Reaction Displaying High Stereoselectivity: Reaction of Hexachlorocyclopentadiene with Naphthalene

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The Diels–Alder reaction is one of the most intensively studied and used reactions in organic chemistry.<sup>1</sup> The reasons for this success lie in the very wide scope of the reaction,<sup>2</sup> in puzzling aspects of its regio- and stereoselectivity,<sup>3</sup> in some hotly debated aspects of its timing<sup>4</sup> and mechanism,<sup>5</sup> as well as in its outstanding ability to introduce simultaneously several asymmetric centers either intermolecularly<sup>6</sup> or intramolecularly.<sup>7</sup>

In the process of exploring the scope of the new concept 'holosynthons' in synthetic schemes<sup>8</sup> our attention was attracted by a reaction reported in the 1950s<sup>9</sup> and very seldom cited since.<sup>10</sup> It involves the reaction at 160°C of naphthalene and hexachlorocyclopentadiene for 120 h [eqn. (1)].

In terms of holosynthons this is a fascinating reaction because it adds, in one step, four more rings and 12 potential functionalities to a given substrate, although presently in low yield (25%).

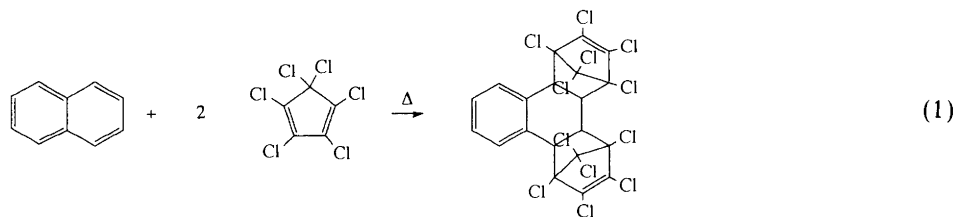
The original<sup>9</sup> and following reports<sup>10</sup> were however, very light on structural proof (there are a great number of other isomeric possibilities for the formula C<sub>20</sub>H<sub>8</sub>Cl<sub>12</sub>) and, on the stereospecificity of the reaction. We therefore decided to reinvestigate this reaction to check the

proposed structure, and the stereoselectivity of the reaction.

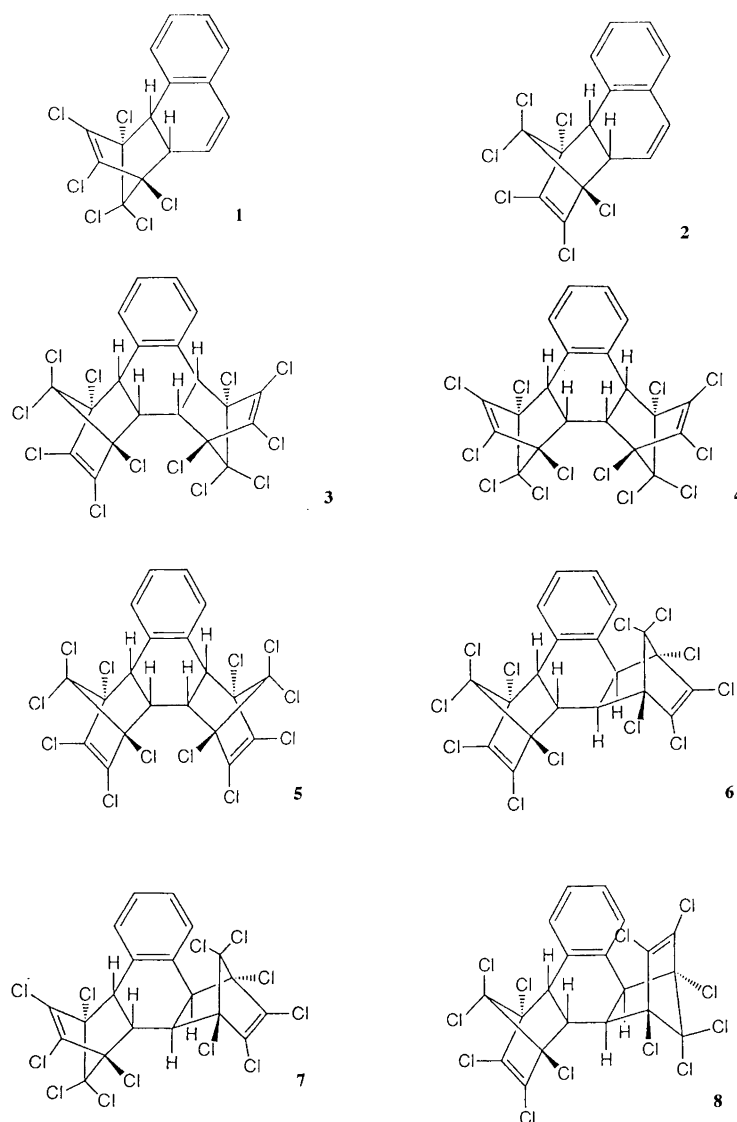
The experimental process described in Ref. 9 yielded 25% of a white solid (m.p. 244°C; Calc. for C<sub>20</sub>H<sub>8</sub>Cl<sub>12</sub>: C, 35.61; H, 1.19; Cl, 63.20. Found: C, 36.06; H, 1.66; Cl, 58.96). The rather poor fit is due to the large number of Cl atoms which reduce the quality of the analysis. The NMR spectrum of the reaction mixture analyzed at 400 MHz showed only tiny signals other than those corresponding to the starting material and the final product. Traces of mono Diels–Alder adduct **1** were detected (Scheme 1). This observation probably follows from the fact that the first Diels–Alder reaction has to break aromaticity and thus is slower than the second one.

The <sup>1</sup>H NMR spectrum of the final product (solvent CDCl<sub>3</sub>; internal reference Me<sub>4</sub>Si; chemical shift, integration, coupling constants, position) displayed the following signals: 7.8 ppm (2 H), dd, *J* = 3 and 6 Hz (C4); 7.35 ppm (2 H), dd, *J* = 3 and 6 Hz (C5); 4.06 ppm (2 H), d, *J* = 9 Hz (C2); 3.60 ppm (2 H), d, *J* = 9 Hz (C1).

The <sup>13</sup>C NMR spectrum (solvent: CDCl<sub>3</sub>; internal reference: Me<sub>4</sub>Si) was characterized by peaks at δ 41.5, 47 (carbons 1 and 2); 82, 85 (carbons 9 and 6); 101 (carbon



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**Scheme 1.** Possible stereoisomers for the tandem Diels–Alder reaction between naphthalene and hexachlorocyclopentadiene (compounds **4** and **5** are optically inactive).

10), 127.6, 123.4 (carbons 4 and 5); 128.1, 128.6 (carbons 7 and 8); 133.4 (carbon 3) (for the numbering, see Fig. 1). These assignments were based on the chemical shifts and on APT and DEPT experiments. These NMR data do not make possible an unambiguous assignment of the signals to any of the stereoisomers displayed in Scheme 1. They do show, however, that only one couple of enantiomers out of the 10 possible stereoisomers is formed during this reaction.

A structure determination by single crystal X-ray diffraction methods ( $R=0.038$ ) removed the ambiguities of the NMR studies.<sup>11</sup> The structure obtained (Fig. 1) proved that the reaction product corresponded to the pair of enantiomers of formula **8** (Scheme 1). Therefore, the main factor at work in the high stereoselectivity of this Diels–Alder reaction seems to be a steric effect. In the first step the transition state **A** (Scheme 2) involves far more steric hindrance than does the transition state **B**. The



**Scheme 2.**

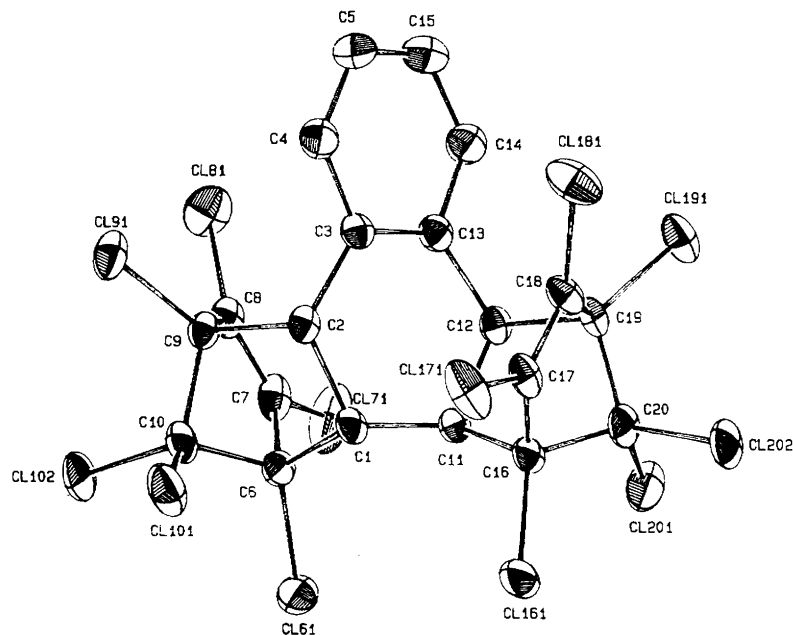


Fig. 1.

secondary orbital effects sometimes invoked to rationalize *endo* vs. *exo* selectivity<sup>12</sup> do not seem to be needed here.

In the second Diels–Alder step the only active face of the substituted naphthalene is the one free of steric hindrance. On this unhindered face the same type of steric factors involved in the first Diels–Alder reaction explain the total predominance of formation of the *exo* isomer.

We have tried to find milder conditions for the formation of **8** using photochemical stimulation,<sup>13</sup> or LiClO<sub>4</sub> salt effects.<sup>14</sup> None of these conditions has yet led to marked improvement, although electron transfer catalysis<sup>15</sup> has yielded encouraging preliminary results. We are presently exploring the best ways of exploiting the 12 functionalities present in the stereoisomer obtained particularly using metal vapor solution synthesis.<sup>16</sup>

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