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## Diels-Alder Reactions involving 1,2-Isopropylidenedioxy-3-trifluoromethylcyclohexa-3,5-diene

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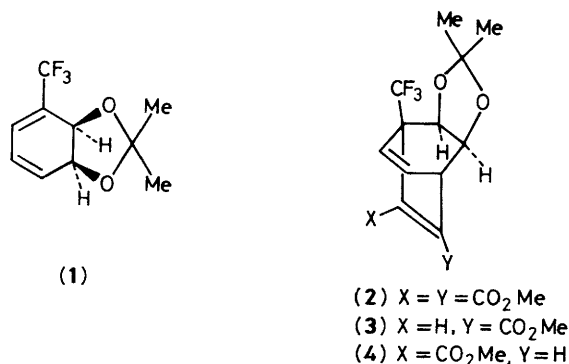
The title compound was treated with several dienophiles to give cycloadducts resulting from addition to the less hindered face of the molecule. An exceptional case was provided by *N*-ethylmaleimide which added in *endo*-fashion to both faces of the diene. 1,2-Isopropylidenedioxy-3-trifluoromethylcyclohexa-3,5-diene acted as a dienophile on addition to cyclopentadiene and underwent dimerization to give a stable [4 + 2] adduct.

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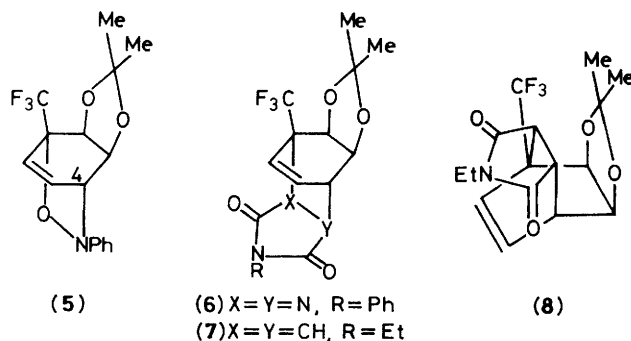
The microbial oxidation of benzene (and derivatives) using *Pseudomonas* sp. gives (3-substituted) *cis*-cyclohexadiene-1,2-diol.<sup>1</sup> While the chemistry of *cis*-cyclohexadiene-1,2-diol<sup>2</sup> and *cis*-3-methylcyclohexadiene-1,2-diol<sup>3</sup> has received some attention, the properties of other 3-substituted cyclohexadienediols produced by this fascinating series of biotransformations have not been reported heretofore. We report that the acetal (1) is readily prepared from the corresponding diol<sup>4</sup> and undergoes some interesting Diels–Alder reactions.

## Discussion

Reaction of the diene (1) with dimethyl acetylenedicarboxylate furnished the adduct (2) (m.p. 95 °C) in 83% yield while with methyl propiolate it gave two isomers in the ratio 3:1 (54%).

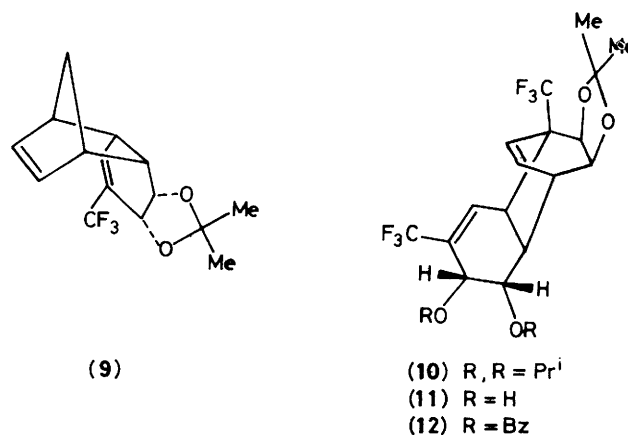


The major product was the ester (3) (m.p. 64.5 °C) (with the trifluoromethyl group and the ester moiety distant) and this compound was distinguished from compound (4) (m.p. 104–106 °C) by the coupling pattern of the lowfield alkene proton. Cycloaddition of the diene (1) and nitrosobenzene proceeded at room temperature to produce the adduct (5) (m.p. 80–81 °C) as needle-like crystals in 90% yield. Similarly, cycloaddition of the diene (1) with 4-phenyl-1,2,4-triazoline-3,5-dione gave the adduct (6) (60.5%), while *N*-ethylmaleimide gave two products, one formed by *endo*-addition to the open face of the diene [(7), 50% yield] and the other produced by *endo*-addition to the hindered face of the diene [(8), 38% yield].



Not only can the alkene (1) enter into Diels–Alder reactions as the diene component but it can also act as a dienophile. Reaction of compound (1) with cyclopentadiene gave the adduct (9) albeit in low yield. The reactive nature of the acetal (1) as diene and dienophile is reflected in the ready dimerization of the compound when kept at 0–5 °C. The dimer (10), m.p. 157–158 °C was identified by conversion into the partially deprotected material (11) and the dibenzoate (12), followed by detailed n.m.r. studies.

In most cases, complete assignment of all <sup>1</sup>H and <sup>13</sup>C



resonances was possible including individual methyl peaks. This was achieved by combination of homonuclear <sup>1</sup>H{<sup>1</sup>H} decoupling, selective heteronuclear <sup>13</sup>C{<sup>1</sup>H} decoupling and observation of <sup>19</sup>F-<sup>13</sup>C coupling constants. Any structural ambiguities were resolved by n.O.e.-difference spectroscopy. For example, the structure of compound (5) was proved by observation of a massive enhancement of the signal from 4-H when the aromatic region was irradiated. Saturation of the protons in the methine groups bonded to oxygen atoms in compound (7) led to a very large (ca. 20%) enhancement of the signals associated with protons in the methine groups labelled X and Y. For adduct (8) a through-space interaction was found between the lower field methyl group and the methine protons of the succinimide moiety. In addition both the regio- and stereochemistry of compound (11) were confirmed by finding through-space connections between the two methyl groups and neighbouring methine and alkene protons. Similarly, compound (9) was found to be in the *endo* rather than the *exo* form by observation of n.O.e. correlations between the pair of methylene protons and the pair of bridge methine protons.

**Selected Experimental Data.**—Column chromatography was carried out under pressure on MN-Kieselgel 60 230–400 mesh with the eluant specified in parentheses. The benzene used as solvent was dried with sodium wire. Chemical shifts are reported in  $\delta$  values relative to Me<sub>4</sub>Si as an internal standard. Accurate mass determinations were made on compounds estimated to be >95% pure by H<sup>1</sup> n.m.r. spectroscopy and thin layer chromatography.

**Preparation of the Cycloadduct (2).**—The acetal (1) (0.11 g, 0.5 mmol) and dimethyl acetylenedicarboxylate (0.5 ml) were dissolved in dry benzene (3.0 ml). The mixture was refluxed for 75 h under an atmosphere of nitrogen. The benzene was removed by distillation at reduced pressure to give a yellow oil. The oil was subjected to column chromatography over silica gel. Elution with ethyl acetate in light petroleum (b.p. 60–80) (1:4, v/v) afforded compound (2) (0.15 g, 83%, m.p. 95 °C).  $\delta_{\text{H}}$ (250 MHz) (CDCl<sub>3</sub>) 1.28 (3 H, s, CH<sub>3</sub>), 1.35 (3 H, s, CH<sub>3</sub>), 3.77 (3 H, s, CH<sub>3</sub>), 3.82 (3 H, s, CH<sub>3</sub>), 4.44 (1 H, m, CH), 4.47 (1 H, m, CH), 4.62 (1 H, dm, *J* 7 Hz, CH), 6.37 (1 H, dm, *J* 7.6 Hz, C=CH), and 6.56 (1 H, ddm, *J* 7.6 and 7.5 Hz, C=CH) [Found: (*M* + NH<sub>4</sub>)<sup>+</sup> 380.1327. C<sub>16</sub>H<sub>17</sub>F<sub>3</sub>O<sub>6</sub> requires (*M* + NH<sub>4</sub>) 380.1321].

**Preparation of the Cycloadducts (7) and (8).**—The acetal (1) (0.22 g, ca. 1.0 mmol) was dissolved in dry benzene (2.5 ml) and *N*-ethylmaleimide (0.12 g ca. 1.0 mmol) in dry benzene (2.5 ml) was added. The resultant mixture was refluxed under nitrogen for 72 h. Work-up as described above furnished the crude product (0.40 g) as a white crystalline solid. The crude product

was subjected to chromatography over silica gel [eluant ethyl acetate–light petroleum (b.p. 60–80 °C) (1:3, v/v)]. The first component eluted from the column was the adduct (**8**) (0.13 g, 38%, m.p. 119–123 °C);  $\delta_{\text{H}}$ (CDCl<sub>3</sub>) 1.06 (3 H, t, CH<sub>3</sub>), 1.35 (3 H, s, CH<sub>3</sub>), 1.50 (3 H, s, CH<sub>3</sub>), 3.48 (5 H, m, NCH<sub>2</sub>, CH  $\times$  3), 4.23 (1 H, dd, *J* 8.1 and 3.5 Hz, CH), 4.3 (1 H, d, *J* 8.1 Hz, CH), 6.08 (1 H, d, *J* 8.5 Hz, C=CH), and 6.28 (1 H, dd, *J* 8.5 and 6.6 Hz, C=CH) [Found: (*M* + NH<sub>4</sub>)<sup>+</sup>, 363.1528. C<sub>16</sub>H<sub>18</sub>F<sub>3</sub>NO<sub>4</sub> requires (*M* + NH<sub>4</sub>)<sup>+</sup> 363.1531]. The more polar compound was the adduct (**7**) (0.17 g, 50%, m.p. 169 °C);  $\delta_{\text{H}}$ (CDCl<sub>3</sub>) 1.08 (3 H, t, CH<sub>3</sub>), 1.29 (3 H, s, CH<sub>3</sub>), 1.33 (3 H, s, CH<sub>3</sub>), 2.88 (2 H, m, CH  $\times$  2), 3.48 (2 H, q, NCH<sub>2</sub>), 3.57 (1 H, m, CH), 4.39 (2 H, m, CH  $\times$  2), 6.08 (1 H, d, *J* 8.7 Hz, C=CH), 6.22 (1 H, dd, *J* 8.7, 6.4 Hz, C=CH) [Found: (*M* + NH<sub>4</sub>)<sup>+</sup>, 363.1528. C<sub>16</sub>H<sub>18</sub>F<sub>3</sub>NO<sub>4</sub> requires (*M* + NH<sub>4</sub>)<sup>+</sup> 363.1531].

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