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Normal- and High-Pressure Diels-Alder Reactions of *p*-Tropoquinone with Furans

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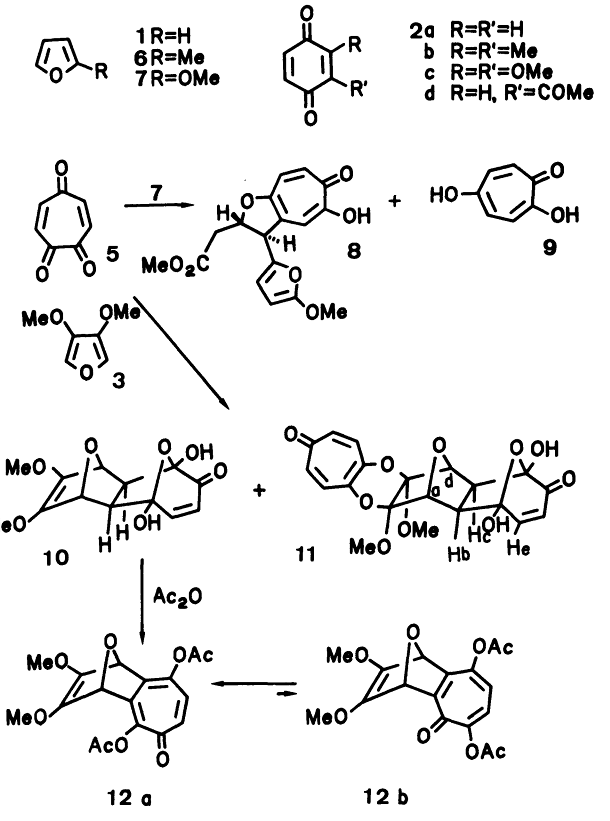
Synopsis. The Diels-Alder reactions of *p*-tropoquinone with furans were investigated under normal- and high-pressure conditions. With furan or 2-methylfuran, no cycloadduct was obtained at all, but with 2-methoxyfuran, a double Michael adduct was isolated from the reaction under the atmospheric pressure, and its structure was elucidated mainly by ^{1}H NMR analysis. With 3,4-dimethoxyfuran, an exo-1 : 1-adduct and its further reacted 2 : 1-adduct were isolated.

Because of the poor reactivity of furan (**1**) towards dienophiles,1) there is no successful example of a reaction with simple *p*-benzoquinone (**2a**) and its derivatives (such as **2b** and **2c**) under atmospheric pressure. However, furans became accessible to the reaction under the high-pressure conditions; with 3,4-dimethoxyfuran (**3**), formations of the endo- and exo-adducts were exemplified in the reaction with various dienophiles.2–4) Recently, we have succeeded in obtaining the Diels-Alder adducts of tropone (**4**) with **1** under high-pressure conditions,5) and with a continuing interest to the chemistry of tropoquinones as well as high-pressure cycloaddition reactions in troponoids, we have carried out the reaction with *p*-tropoquinone (**5**), and the results obtained therefrom are described briefly as illustrated in Scheme 1.

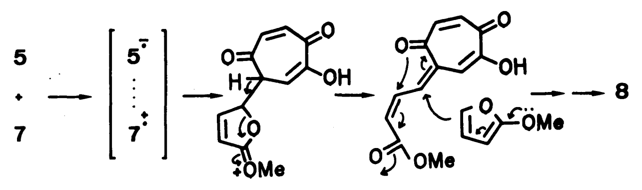


Scheme 1.

When the reaction of **5** with **1** or 2-methylfuran (**6**) was performed under 2800 bar at 40 °C, no identifiable product was formed. The reaction of **5** with 2-methoxyfuran (**7**) at room temperature gave a single adduct (**8**) in 24% yield with some amounts of 5-hydroxytropolone (**9**), which was inevitably formed by reduction of **5**. The molecular ion peak of **8** at $m/z=332$, in the mass spectrum was indicated as being a 2 : 1-adduct of **7** with **5**. The IR spectrum of **8** still disclosed the presence of a tropone ring system and a newly-formed ester carbonyl function. The ^{1}H NMR spectrum revealed the signals ascribable to the ester methyl, at $\delta=3.80$, ethereal methyl on the furan ring, 3.69, and two furan ring protons, at 5.08 and 6.17, as well as four aliphatic proton signals, at 2.83 (2H), 4.41, and 5.11. In addition to these, there were three troponoid proton signals; at 7.12, which only spin-coupled to a proton on a sp^3-carbon, and an *AB*-pair at 6.94 and 7.24 ($J=11$ Hz). Analyses of these observations led to the assignment of the structure, 3-(5-methoxy-2-furyl)-5-hydroxy-2-methoxycarbonylmethyl-2,3-dihydro-1-oxaazulen-6-one. Presumably, the formation of **8** could be explained by a Michael-type addition of **7** to **5**, a furan-ring-cleavage, and a further Michael addition of **7** (as illustrated in Scheme 2).

This preferential occurrence of a Michael addition over a Diels-Alder reaction is of interest; since a distinct coloration occurred immediately after mixing **7** and **5** a charge-transfer complex should have been formed. Also, the recombination of the cation radical and the anion radical initiated a series of the subsequent C-C bond formations.6) In this case, 5-hydroxytropolone was isolated in 33% from the reaction mixture. In this respect, a Michael addition of furans and thiophenes had a precedence in a benzenoid quinone, acetyl-*p*-benzoquinone (**2d**).7)

On the other hand, the reaction of **5** with **3** under ordinary pressures afforded a 1 : 1-adduct (**10**) in 49% yield. Under 3000 bar at room temperature, the reac-



Scheme 2.

tion afforded an additional product (**11**) in 17% yield together with **10** in 59% yield. However, the yield of **11** under 2900 bar at 40 °C improved to 58% and that of **10** decreased to 18%. Hence, **10** is a precursor of **11**. The ^{1}H NMR spectrum of **10** immediately identified its structure to be an exo-Diels-Alder product on the basis of a lack of the vinyl protons on the furan ring: The proton signals ascribable to the ethereal carbons were doublets (J=1 Hz) at δ=4.90 and 4.99 which indicated the exo-orientation, and two mutually-coupled (J=9.5 Hz) olefinic proton signals at 5.97 and 7.33 were appropriate for the α,β-unsaturated keto group. These NMR data closely resembled those of 8-oxabicyclo[3.2.1]oct-3-en-2-one derivatives,[8] and suggested the formation of the same framework via an intramolecular hemiacetalization.[9] This was verified when **10** was treated with acetic anhydride in pyridine, a diacetate **12** was obtained and it possessed a 2,5-diacetoxytropone structure. The proton signals on the ethereal carbons caused a down-field shift, δ=5.31 and 5.49, and the observed magnitude of the coupling constant for the vicinal protons on the troponoid ring was J=13 Hz, from which, the α-acetoxy keto function could be expressed as depicted (**12a**).[10] It is interesting to point out that **12** showed no tendency of an "acetotropy" which is common in the 2-acetoxytropones.[11] Probably, a bond strain from the fused oxanorbornene framework might disfavor the contribution of the isomeric form, **12b**. Indeed, the ^{13}C NMR of **12** has not revealed any appreciable broadening of the signals at room temperature.

The structure of **11** was also elucidated by the NMR spectral data: Its ^{1}H NMR spectrum resembled that of **10**, other than the additional signals at 6.94 (2H) and 7.40 (2H), ascribable to the overlapped tropone ring protons. Furthermore, the methoxyl signal moved to an up-field region. Therefore, **11** was assumed to be a secondary adduct of **5** with the dimethoxyethylene moiety of **10**. In this case, the α-dioxo group of **5** worked as the 4π component in the Diels-Alder reactions; as a cyclic α-diketone, this also has a precedence.[12] The stereochemistry of the methoxyl groups was assigned to be anti to two ether bridges on the basis of the positive nuclear Overhauser effect (NOE)[13] between the methoxyl and the methine proton signals (H_b and H_c), and between the β-proton (H_e) of the enone part and the H_b, respectively. This stereopreferential formation was parallel to other examples of the 7-oxabicyclo[2.2.1]heptene system.[14]

Consequently, the Diels-Alder reaction of **5** with **3** under normal- and high-pressure conditions gave a single exo-$[4+2]\pi$ adduct, which was a thermodynamically controlled product. In the case of **2a** with **3**, the endo-$[4+2]\pi$ adduct was the sole product under the ordinary pressure, but under the high-pressure conditions, e.g., 7000 to 19000 bar, the exo-$[4+2]\pi$ adduct gradually increased.[4] This contrast in the stereoselectivity is noteworthy.

Experimental

Reaction of 5 with 7 under Ordinary Pressure. A benzene solution (1 cm^3) of **5** (68 mg) and **7** (213 mg) was kept at room temperature for 1 h. The resultant precipitate was filtered to collect **9** [22.8 mg; 33%], whose identity with the authentic sample was confirmed by direct comparisons. Silica-gel column chromatography of the filtrate afforded **8** [yellow crystals, mp 138—139 °C, 26.1 mg; 24%. Found: C, 61.62; H, 4.92%; M.W., 332.0938. Calcd for $C_{17}H_{16}O_7$: C, 61.44; H, 4.85%; M.W., 332.0895. ^{1}H NMR $\delta^{15)}$=2.83 (2H, d, J=6 Hz), 3.69 (3H, s), 3.80 (3H, s), 4.41 (1H, dd, J=9, 1.5 Hz), 5.08 (1H, d, J=3.5 Hz), 5.11 (1H, dt, J=9, 6 Hz), 6.17 (1H, d, J=3.5 Hz), 6.94 (1H, d, J=11 Hz), 7.12 (1H, d, J=1.5 Hz), and 7.24 (1H, d, J=11 Hz). ^{13}C NMR δ=38.7, 50.6, 52.1, 57.8, 80.2, 81.9, 110.9, 118.4, 123.0 (2C), 139.0, 139.8, 158.6, 162.4, 166.5, and 170.2 (2C). IR ν 1740, 1585, 1460, and 1260 cm^{-1}. UV $\lambda_{\max}^{\mathrm{MeOH}}$ 232 nm (ε=26600), 238 (27100), 342 (10700), 386 (7000), 400 (7600), and 425 (3700)].

Reaction of 5 with 3 under Ordinary Pressure. A benzene solution (1.5 cm^3) of **5** (30 mg) and **3** (70.4 mg) was kept at room temperature for 5 h. Silica-gel column chromatography of the mixture afforded **10** [colorless crystals, mp 129 — 131 °C (decomp), 30.5 mg; 49%. Found: C, 55.24; H, 5.11%. Calcd for $C_{13}H_{14}O_7$: C, 55.31; H, 5.01%. ^{1}H NMR (CD_3OD) δ=2.44 (1H, d, J=6.5 Hz), 2.70 (1H, d, J=6.5 Hz), 3.66 (3H, s), 3.68 (3H, s), 4.90 (1H, d, J=1 Hz), 4.99 (1H, d, J=1 Hz), 5.97 (1H, d, J=9.5 Hz), and 7.33 (1H, d, J=9.5 Hz). ^{13}C NMR (CD_3OD) δ=52.2, 57.2, 59.5 (2C), 78.4, 79.1, 101.4, 102.6, 127.4, 141.6, 142.3, 159.4, and 197.6. IR ν 3370, 3170, 1690, 1175, 1160, 1015, and 1005 cm^{-1}. UV $\lambda_{\max}^{\mathrm{MeOH}}$ 218 nm (ε=8350)].

Reaction of 5 with 3 under High-Pressure. a) An isopropylbenzene (IB) solution (2.5 cm^3) of **5** (55.2 mg) and **3** (53.7 mg) was kept at room temperature under 3000 bar for 5 h. The silica-gel column chromatography of the mixture afforded **10** [67.4 mg; 59%] and **11** [colorless crystals, mp 223 °C (decomp), 14.2 mg; 17%. Found: C, 57.47; H, 4.58%. Calcd for $C_{20}H_{18}O_{10}$: C, 57.41; H, 4.35%. ^{1}H NMR (CD_3OD) δ=2.58 (1H, d, J=7 Hz), 2.86 (1H, d, J=7 Hz), 3.39 (3H, s), 3.43 (3H, s), 5.02 (1H, d, J=1 Hz), 5.07 (1H, d, J=1 Hz), 6.09 (1H, d, J=10 Hz), 6.94 (2H, d, J=12.5 Hz), 7.36 (1H, d, J=10 Hz), and 7.40 (2H, d, J=12.5 Hz). ^{13}C NMR (CD_3OD) δ=48.5, 49.4, 51.4, 52.9, 83.2, 84.4, 101.9, 103.3, 108.4 (2C), 128.3, 135.1 (2C), 137.6 (2C), 148.2, 148.5, 159.3, 187.8, and 197.0. IR ν 3020, 1705, 1550, 1510, 1212, 1180, 1110, and 1015 cm^{-1}. UV $\lambda_{\max}^{\mathrm{MeOH}}$ 232 nm (ε=19500) and 337 (12000)].

b) An IB solution (3 cm^3) of **5** (54 mg) and **3** (62 mg) was kept at 40 °C under 2900 bar for 5 h. The silica-gel column chromatography of the mixture afforded **10** [19.9 mg; 18%] and **11** [48.2 mg; 58%].

Acetic Anhydride Treatment of 10. An Ac_2O solution (2.5 cm^3) of **10** (100.4 mg) and pyridine (2.5 cm^3) was kept at room temperature for 1 d. Evaporation of the solvent in vacuo revealed the formation of **12** [pale yellow crystals, 134 — 136 °C, 84.4 mg; 68%. Found: C, 58.45; H, 4.68%. Calcd for $C_{17}H_{16}O_8$: C, 58.62; H, 4.63%. ^{1}H NMR δ=2.29 (3H, s), 2.34 (3H, s), 3.71 (3H, s), 3.73 (3H, s), 5.31 (1H, d, J=2 Hz), 5.49 (1H, d, J=2 Hz), 6.77 (1H, d, J=13 Hz), and 6.94 (1H, d, J=13 Hz). ^{13}C NMR δ=20.4, 20.5, 59.2 (2C), 80.0, 80.5, 135.2, 136.3, 138.7, 142.1, 142.9, 143.7, 144.2, 147.2, 167.8, 168.8, and 177.9. IR ν 1770, 1675, 1600, 1230, 1185, 1165, 1115, and 1085 cm^{-1}. UV $\lambda_{\max}^{\mathrm{MeOH}}$ 216 nm (ε=23650) and 302 (13800)].

Attempted Reaction of 5 with 1. A mixture of **5** (62 mg) and **1** (332 mg) was kept at 40 °C under 2800 bar for 12 h, no appreciable change occurred, and 21.8 mg (35%) of **5** was recovered.

Attempted Reaction of 5 with 6. A mixture of **5** (62 mg) and **6** (391 mg) was similarly kept at 40 °C under 2800 bar for 12 h. TLC of the mixture indicated no formation of the adduct, and silica-gel column chromatography furnished no isolable material.

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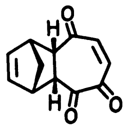

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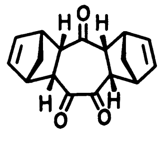

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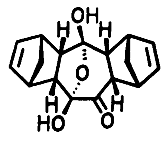

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