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Structures of New [4+2]-Cycloadducts from Diels–Alder Reactions of Methyl 2-Oxo-2*H*-pyran-5-carboxylate with 2-Methyl- and 2-Methoxy-1,3-butadienes[1)]

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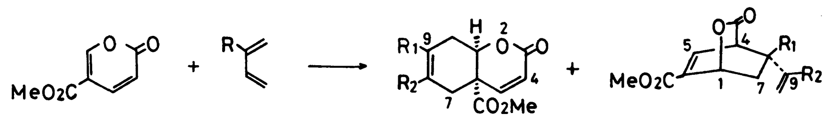
Synopsis. A Diels–Alder reaction of methyl 2-oxo-2*H*-pyran-5-carboxylate (**1**) with isoprene gave two stereoisomers, methyl 8-methyl-8-vinyl- and 8-isopropenyl-3-oxo-2-oxabicyclo[2.2.2]oct-5-ene-6-carboxylates. On the other hand, only a stereoisomer from a reaction of **1** with 2-methoxy-1,3-butadiene, methyl 8-methoxy-8-vinyl-3-oxo-2-oxabicyclo[2.2.2]oct-5-ene-6-carboxylate was obtained. The stereostructures of these adducts were determined by NMR spectral data and single-crystal X-ray analyses.

Diels–Alder reactions[2)] using 2-pyrones can be used to prepare such versatile products as various [4+2]-cycloadducts, polycyclic compounds, and benzene derivatives since 2-pyrones might serve as either dienes or dienophiles and the primary adducts undergo succeeding thermal conversions through their secondary reactions, e.g., decarboxylation, hydrogen migration, and intramolecular cycloaddition. In the course of our study on the thermal cycloaddition reactions of enone compounds, we became interested in the use of methyl 2-oxo-2*H*-pyran-5-carboxylate (**1**) as a substrate bearing two enone systems with the expectation that it might selectively react as a diene or a dienophile to the reaction partner and that the products potentially serve as synthetic intermediates. Previous papers[3)] have demonstrated that the Diels–Alder reactions of **1** with 2-substituted 1,3-butadienes **2** afford tetrahydrocoumarins **3—5** and that they can be used as one approach to the synthesis of trichothecane sesquiterpenes.[3b,4)] In addition to the documented products resulting from the reaction of **1** acting as a dienophile, we have tried to isolate hitherto unidentified cycloadducts of **1** as a diene. We now report on the structures of the newly isolated [4+2]-cycloadducts **6**, **7**,[5)] and **8**.



1

2 R=Me, OMe

3 R_1=Me, R_2=H
4 R_1=H, R_2=Me
5 R_1=OMe, R_2=H

6 R_1=Me, R_2=H
7 R_1=H, R_2=Me
8 R_1=OMe, R_2=H
9 R_1=H, R_2=OMe

Cycloadditions of **1** with isoprene or 2-methoxy-1,3-butadiene were carried out at 90—114 °C in an autoclave. The crude products were repeatedly column-chromatographed and recrystallized to afford three pure bicyclic lactones **6—8**, along with some other known products **3—5**. However, in the present reactions the regioisomer (**9**) of **8** could not be detected.[6)] The combined yield and the ratio of **6** to **7** were seriously effected by the reaction temperature since further conversions of these initial adducts occurred under applied conditions.[7)] As shown in Table 1, the IR and ^{1}H NMR spectra of the three compounds indicated characteristic of absorption bands (1635—1640 and 950—990 cm^{-1}) and signals

Table 1. IR and ^{1}H NMR Spectral Data for Cycloadducts

	6	**7**	**8**
IR/cm^{-1}	1750, 1715, 1635, 990, 970	1750, 1720, 1640, 990, 960	1760, 1720, 1640, 970, 950
NMR/δ			
C_1-H	5.46—5.77(m)	5.61—5.74(m)	5.44—5.66(m)
C_4-H	3.42(d, *J*=6)	3.78(dd, *J*=6, 2)	3.80(d, *J*=6)
C_5-H	7.26(dd, *J*=6, 2)	7.18(dd, *J*=6, 2)	7.17(dd, *J*=6, 2)
C_7-H	1.94(d, *J*=2)	2.42(dd, *J*=10, 4)	1.83(dd, *J*=14, 2)
	2.00(d, *J*=4)	2.67—2.84(m)	2.40(dd, *J*=14, 4)
C_8-H		1.62(ddd, *J*=10, 4, 2)	
C_9-H	5.46—5.77(m)		5.44—5.66(m)
C_{10}-H	4.84(dd, *J*=8, 2)	4.58(bs)	5.10(dd, *J*=8, 2)
	5.08(d, *J*=2)	4.79(bs)	5.32(d, *J*=2)
C–Me	1.32(s)	1.73(s)	
O–Me	3.79(s)	3.78(s)	3.69(s), 3.00(s)

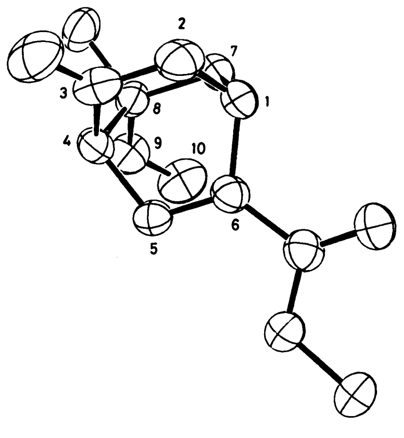


Fig. 1. ORTEP drawing of the molecular structure of **6**.

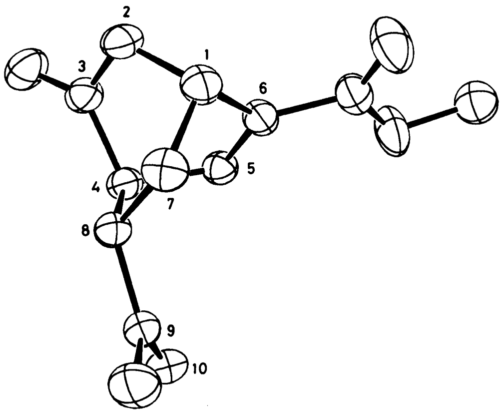


Fig. 2. ORTEP drawing of the molecular structure of **7**.

due to vinyl and isopropenyl groups. The ^{1}H NMR spectra also revealed the presence of one olefinic proton (C_5–H) at the lowest field with the splitting pattern of a doublet of doublets (J=6 and 2 Hz) and two methine protons (C_1–H and C_4–H) at positions α to the oxygen and carbonyl of the lactone. The similality of these spectral data indicates that they possess the same structural skeleton formed presumably by an endo addition; however, they differed in regiochemistry. Furthermore, the stereochemistry of **6** and **7** could be confirmed by X-ray crystal structure analyses; these were performed with single crystals prepared from methanol solutions. Perspective views are depicted in Figs. 1 and 2.[8] Thus, their structures were determined to be **6**, **7**, and **8**. The results obtained here show that **1** can react both as a dienophile and a diene toward 2-methyl- and 2-methoxy-1,3-butadienes to furnish [4+2]-cycloadducts **3**—**5** and **6**—**8**.

Experimental

Melting points are uncorrected. IR spectra were measured in $CHCl_3$ with a Hitachi 260-50 spectrometer. NMR spectra were obtained with JEOL JNM MH-100, JEOL JNM-PMX 60, and JEOL JNM-FX 60 spectrometers for ^{1}H and ^{13}C in $CDCl_3$, respectively. Chemical shifts are given in δ values (ppm) downfield from the internal TMS reference. Mass spectra were measured with a JEOL JMS-D 300S spectrometer. Column chromatography was performed with Fuji-Davison BW-300 silica gel.

Methyl 8-Methyl-8-vinyl- and 8-Isopropenyl-3-oxo-2-oxabicyclo[2.2.2]oct-5-ene-6-carboxylates (6 and 7). A mixture of 1.0 g (6.5 mmol) of **1** and 2.2 g (32 mmol) of isoprene in 100 ml of benzene was heated at 110—114 °C for 10 h in an autoclave under a nitrogen atmosphere. After removing the solvent and excess diene, the residue was chromatographed on silica gel with hexane–ethyl acetate (19:1) as an eluent to give a mixture of **6** and **7** (0.56 g; 50% yield based on **1** consumed) along with a mixture of **3** and **4** (0.32 g), and **1** (0.22 g). A mixture of **6** and **7** was repeatedly column-chromatographed and finally recrystallized from methanol to afford each pure compound (ratio of **6**/**7** was about 1:3); the elevation of the reaction temperature (above ca. 120 °C) led to a decrease of a total yield of **6** and **7**, and to change of the isomer ratio. The high reaction temperature also improved the yield of the known product, tricyclo[$3.2.1.0^{2,7}$]-octene compound.[3a] **6**: Mp 115—116 °C (methanol); MS: m/z 222 (M^+) and 223 $[M+1]^+$); Found: C, 64.65; H, 6.24%. Calcd for $C_{12}H_{14}O_4$: C, 64.85; H, 6.35%. **7**: Mp 106—106.5 °C (methanol); MS: 222 (M^+) and 223 $[M+1]^+$); Found: C, 64.80; H, 6.43%. Calcd for $C_{12}H_{14}O_4$: C, 64.85; H, 6.35%.

Methyl 8-Methoxy-8-vinyl-3-oxo-2-oxabicyclo[2.2.2]oct-5-ene-6-carboxylate (8) and the Related Adducts. A mixture of 5.0 g (32 mmol) of **1** and 5.1 g (60 mmol) of 2-methoxy-1,3-butadiene in 50 ml of toluene was heated at 90—100 °C for 3 h in an autoclave under a nitrogen atmosphere. Removing the solvent and excess diene gave 9.5 g of a yellow viscous oil. The crude products were column-chromatographed on silica gel using hexane–ethyl acetate (4:1) as an eluent to afford 9-methoxy-6-methoxycarbonyl-2-oxabicyclo-[4.4.0]deca-4,8-dien-3-one (**5**; 5.0 g), and its 9,10-dehydro isomer (0.78 g). The other fractions were further chromatographed under similar conditions to give **8** as a colorless solid (ca. 10% yield) together with unidentified materials. **5**: Mp 104.5—105.5 °C (hexane-acetone) (lit,[3b] mp 96—98 °C); IR: 1730—1740 and 1675 cm^{-1}; ^{1}H NMR: 2.15—2.95 (4H, m, 2×-CH_2-), 3.50 (3H, s, -OCH_3), 3.78 (3H, s, -CO_2CH_3), 4.67 (1H, m, $-CH_2\overset{|}{C}\underline{H}O-$), 5.02 (1H, dd, J=7 and 2 Hz, $-C\underline{H}=\overset{|}{C}OCH_3$), 6.04 and 6.94 (each 1H, d, J=11 Hz, -CH=CH-); ^{13}C NMR: 29.6, 31.4, 46.2, 53.0, 54.2, 77.0, 89.9, 121.0, 149.3, 152.2, 163.1, and 171.5; MS: m/z 238 (M^+). 9,10-Dehydro isomer of **5**: Mp 100—103 °C (hexane-ethyl acetate); IR: 1730—1740 and 1675 cm^{-1}; ^{1}H NMR: 1.72—2.24 (4H, m, 2×-CH_2-), 3.49 (3H, s, -OCH_3), 3.70 (3H, s, -CO_2CH_3), 4.72 (1H, d, J=5 Hz, $=CH\overset{|}{C}\underline{H}O-$), 5.38 (1H, d, J=5 Hz, $=C\underline{H}\overset{|}{C}HO-$), 5.91 and 6.57 (each 1H, d, J=11 Hz, -CH=CH-); MS: m/z 238 (M^+); Found: C, 60.41; H, 5.82%. Calcd for $C_{12}H_{14}O_5$: C, 60.49; H, 5.92%. This enol compound was transformed into the corresponding keto compound, 6-methoxycarbonyl-2-oxabicyclo[4.4.0]dec-4-ene-3,9-dione through the column chromatography using silica gel; mp 128—129 °C (ether) (lit,[3b] 121—122 °C); IR: 1730—1740 cm^{-1}; ^{1}H NMR: 2.00—2.89 (6H, m, 3×-CH_2-), 3.90 (3H, s, -CO_2CH_3), 5.18 (1H, t, J=4 Hz, $-CH_2\overset{|}{C}\underline{H}O-$), 6.09 and 7.00 (each 1H, d, J=11 Hz, -CH=CH-); ^{13}C NMR: 29.5, 37.3, 43.7, 46.8, 53.6, 78.7, 121.3, 148.0, 162.0, 171.1, and 205.0; MS: m/z 224 (M^+); Found: C, 58.79; H, 5.46%. Calcd for $C_{11}H_{12}O_5$: C, 58.92; H, 5.40%. **8**: Mp 105—106.5 °C (hexane-methanol); MS: m/z 208 ($[M+1]^+-31$) and 207 (M^+-31); Found: C, 60.70; H, 6.01%. Calcd for $C_{12}H_{14}O_5$: C, 60.50; H, 5.92%.

X-Ray Analyses of 6 and 7.⁽⁹⁾ The single crystals used for X-ray analyses were recrystallized from methanol solutions. The diffraction data for compounds **6** and **7** were collected on an Enraf-Nonius CAD-4 automated four-circle diffractometer with graphite-monochromated Mo $K\alpha$ radiation (λ=0.71073 Å). The unit-cell constants and diffraction intensities were measured by the ω–2θ scan method. The intensities were corrected for the Lorentz and polarization factors, but no corrections were made for the absorption. The structures were solved by direct method using the program MULTAN 82⁽¹⁰⁾ and the refinement were done by full-matrix least-squares method with anisotropic temperature factors for the non-H atoms and isotropic temperature factors, B=5, for the H atoms. The atomic-scattering factors taken from the International Tables for Crystallography⁽¹¹⁾ were used on a SDP program package.⁽¹²⁾ The crystal data are as follows.

6: $C_{12}H_{14}O_4$, M=222.24, colorless single-crystal size 0.4×0.1×0.05 mm³, monoclinic, space group $P2_1/n$, a=6.150(6), b=6.7759(8), c=26.680(3) Å, γ=95.91(3)°, V=1106(1) Å³, Z=4, D_C=1.335 g cm⁻³, μ(Mo $K\alpha$)=0.936 cm⁻¹. A total of 3228 reflections in the range $2°<2\theta<60°$ were collected for the structure analysis. The final R value was R=0.049, R_W=0.053 for 145 valiables and 1007 reflections with $I>3.0\sigma(I)$.

7: $C_{12}H_{14}O_4$, M=222.24, colorless single-crystal size 0.8×1.0×0.3 mm³, triclinic, space group $P\bar{1}$, a=6.234(2), b=7.91(1), c=12.248(5) Å, α=101.93(5), β=97.41(3), γ=107.76(4)°, V=551(1) Å³, Z=2, D_C=1.340 g cm⁻³, μ(Mo $K\alpha$)=0.985 cm⁻¹. A total of 4827 reflections in the range $2°<2\theta<70$ were collected for the structure analysis. The final R value was R=0.104, R_W=0.136 for 144 valiables and 3074 reflections with $I>3.0\sigma(I)$. The molecules of **7** take randomly one of the two possible conformations which differ in the methyl group orientation around the C–O ester linkage.

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5) Preparation of **7** has been reported, but no description on the stereochemistry has been found, see: Ref. 3d.

6) The addition in which **1** functions as a diene is predicted to occur at its 3,6-positions with both 2,1- and 3,4-positions of isoprene and 2-methoxy-1,3-butadiene on the basis of their molecular orbital coefficients (HOMO for **1**, LUMO for dienes) by the Hückel method.

7) The conversion reactions of the primary adducts are under investigation and the results will be described in detail elsewhere.

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