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The Stereochemistry of Diels-Alder Adduct of 5-Methyl-2-cyclohexene-1-one with Butadiene

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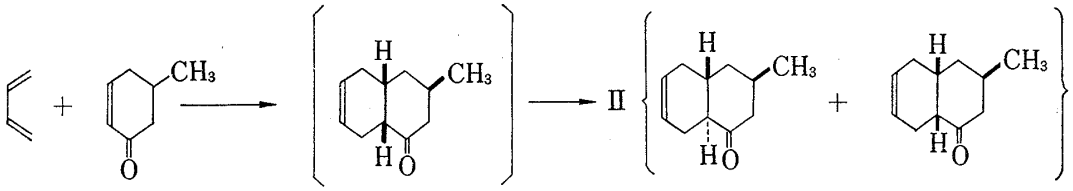
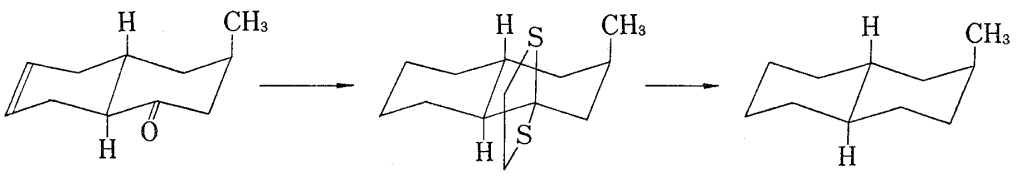
The Diels-Alder reaction of 5-methyl-2-cyclohexene-1-one (I) with butadiene was examined. It was concluded that addition of butadiene to the dienophile (I) took place from the opposite side to a secondary methyl side to give initially the *cis* adduct (IIb), which then epimerizes mostly to the *trans* derivative (IIa).

Only a few papers,[2] have been recorded of the Diels-Alder reaction of 5-alkyl-cyclohexene-1-ones with butadiene. Since this type of reactions is considered to be most useful for the construction of the carbon skeleton of some sesquiterpenes and others, we are interested in studying the structure and the stereochemistry of the product obtained from the reaction of the structurally simplest dienophile of this series, 5-methyl-2-cyclohexene-1-one (I),[3] with butadiene.

Treatment of I with butadiene in the presence of BF_3·etherate provided the crude adduct (II), bp 73—75°/2 mmHg, in 46% yield. The gas chromatography (GC) of II showed two peaks in a IIa/IIb=5/1 ratio and only the major product (IIa) was isolated as a crystalline pure state, mp 42.5—43.5°. The minor product (IIb), however, could not be isolated as a pure state.



I IIa IIb



IIa III IV

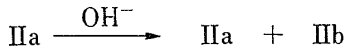
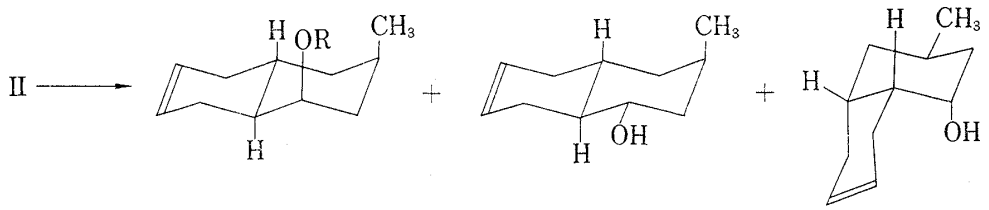


Chart 1

1) Location: *Yoshida-Shimoadachi-cho, Sakyo-ku, Kyoto.*
2) K. Yamamoto, I. Kawasaki, and T. Kaneko, *Tetrahedron Letters*, **1970**, 4859; F. Nerdel and H. Dahl, *Ann. Chem.*, **710**, 90 (1967).
3) H.O. House and W.F. Fischer, Jr., *J. Org. Chem.*, **33**, 949 (1968).

Catalytic hydrogenation of IIa, followed by dithioketalization with ethanedithiol gave the dithioketal (III) in 72% yield. On reduction over Raney nickel, the compound (III) provided the hydrocarbon (IV), whose nuclear magnetic resonance (NMR) spectrum was identical with that of an authentic sample of *trans*-anti-2-methyldecalin.[4] Consequently, the structure of the major product (IIa) can be now represented by the formula (IIa). The pure major product (IIa) was equilibrated in 10% NaOH solution in MeOH and the GC of the equilibrium mixture showed two peaks, each retention time of which was identical with that of IIa and IIb, respectively, in the GC of the crude product (II). Thus, the compound (IIb) is assumed to be the *cis*-decalone derivative (IIb).

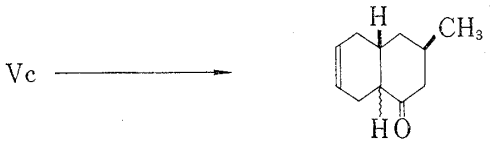
In order to confirm the above structural assignment, the following experiments were undertaken. The reduction product of the crude adduct (II) with $NaBH_4$ showed three peaks (Va: Vb: Vc=3: 2: 1) in the GC, and the chromatographic separation of this product gave an oily alcohol A (Va) and two crystalline alcohols, the alcohol B (Vb, mp 108—109°) and the alcohol C (Vc, mp 67—68°). On the other hand, the reduction product of the pure major product (IIa) with $NaBH_4$ revealed two peaks in the GC in 5/3 ratio and each retention time of these peaks was identical with that of Va and Vb, respectively. Since oxidation of Va and Vb with Jones' reagent provided the same ketone (IIa), the alcohol A (Va) and the alcohol B (Vb) are described as a pair of epimers with respect to a hydroxyl group. Accordingly, it can be deduced that the compound (Vc) must arise from the minor product (IIb) by reduction. The NMR spectrum of Va showed signals due to a secondary methyl group at δ 1.20 (d., J= 7 Hz) and a proton geminal to an ax. hydroxyl group at δ 3.88 (m., $W_{1/2}$=8 Hz). The NMR spectrum of Vb exhibited signals attributable to a secondary methyl group at δ 1.01 (d., J=7 Hz) and a proton geminal to an eq. hydroxyl group at δ 3.51 (octet, J_1=11 Hz, J_2= 10 Hz and J_3=4.5 Hz). When compared the chemical shift of the signal due to a secondary methyl group in Va with that in Vb, it was noticed that the signal concerned in the former appeared at the lower field than that in the latter. This observation can be reasonably explained by assuming the 1,3-diaxial relationship between a secondary methyl group and a hydroxyl group. This diaxial relationship was also supported by the observation that the signal due to a secondary methyl group in the acetylated compound (VI) from Va appeared at δ 1.11 in the NMR spectrum.[5] The structures of the alcohol A and B can be represented by the formulas (Va) and (Vb), respectively.



Va : R=H
VI : R=Ac

Vb

Vc



VII {IIa and IIb}

Chart 2

4) E. Banas, A.W. Weitkamp, and N.S. Bhacca, *Anal. Chem.*, **38**, 1783 (1966).
5) Y. Kawazoe, Y. Sato, M. Natsume, H. Hasegawa, T. Okamoto, and K. Tsuda, *Chem. Pharm. Bull.* (Tokyo), **10**, 338 (1962); Y. Kawazoe, Y. Sato, T. Okamoto, and K. Tsuda, *ibid.*, **11**, 328 (1963).

The NMR spectrum of the alcohol C revealed signals attributable to a secondary methyl group at δ 0.94 (d., J=7 Hz) and a proton geminal to an ax. hydroxyl group at δ 4.00 (m., $W_{1/2}$=13 Hz). The product (VII) derived from Vc by Jones' oxidation showed two peaks corresponding to those of IIa and IIb, respectively, in a 1/1.7 ratio. After treatment of VII with a 10% NaOH solution in MeOH, the GC of the equilibrium mixture was examined. In this case, a ratio of two peaks corresponding to those of IIa and IIb, respectively, was 3/1. These results showed that Jones' oxidation of Vc gave the ketone (VII) containing mainly the *cis*-decalone derivative (IIb). After treatment with alkaline solution, a ratio of IIa/IIb varied and the equilibrium mixture contained mainly the *trans*-decalone derivative (IIa). Consequently, the alcohol C is now represented by the formula Vc.

Summarizing the above results, it can be concluded that addition of butadiene to the dienophile (I) takes place from the opposite side to a secondary methyl side to give initially the *cis* adduct (IIb), which then epimerizes mostly to the *trans* derivative (IIa).

Experimental

All melting points were observed on a microscopic hot stage and uncorrected. All NMR spectra were obtained in $CDCl_3$ solution with tetramethylsilane as an internal standard on a Varian A-60 spectrometer, and IR spectra were measured for a solution in $CHCl_3$ with a Hitachi EPI spectrometer, when otherwise noted. Mass spectra were taken with a Hitachi RMU-6C spectrometer with a heated direct inlet system. Gas chromatography was carried out on a 15% Reoplex 400 column (stainless steel 2 m×3 mm i.d., on 60—80 mesh chromosorb WNAW) at 150° with a Hitachi Gas Chromatograph Model 063 equipped with a hydrogen flame ionization detector. Nitrogen was used as a carrier gas (30 ml/min).

The Diels-Alder Adduct (II)——To a solution of 30 g of 5-methyl-2-cyclohexenone in 50 ml of dry benzene was added 20 g of BF_3·etherate, 400 mg of hydroquinone, and 40 g of butadiene. The mixture was allowed to stand at room temperature in a sealed tube for 6 days. The reaction mixture was diluted with water and extracted with $CHCl_3$. The extract was dried over anhydr. K_2CO_3 and evaporated. Distillation of the residue gave 20.6 g of the adduct (II), bp 73—75°/2 mmHg. Gas chromatography of the distillate (II) showed two peaks at the retention time of 8.4 min and 10.4 min in a ratio of 5: 1. The distillate solidified on standing and recrystallization from *n*-pentane gave 3.1 g of IIa as colorless plates, mp 42.5—43.5°. IR cm^{-1}: ν_{CO} 1700 and $\nu_{C=C}$ 1655. NMR δ: 0.97 (3H, br. d., J=7 Hz, >CH–CH_3), 5.67 (2H, m., olefinic protons). *Anal.* Calcd. for $C_{11}H_{16}O$: C, 80.44; H, 9.83. Found: C, 80.52; H, 9.82. In the GC, the compound (IIa) revealed one peak corresponding to a peak due to a major component in the GC of II.

***trans*-Anti-2-methyldecalin (IV)**——To a solution of 866 mg of IIa in 60 ml of EtOH was added 240 mg of 10% Pd on C. The mixture was stirred under hydrogen at room temperature and atmospheric pressure. After the absorption of hydrogen had ceased, the catalyst was filtered off and the filtrate was evaporated to leave 866 mg of the ketone. IR cm^{-1}: ν_{CO} 1700; M^+ 166. To a solution of 866 mg of the ketone in 30 ml of $CHCl_3$ was added 1.64 g of ethanedithiol and ten drops of BF_3·etherate. The mixture was allowed to stand at room temperature for 4 days and diluted with water and extracted with CH_2Cl_2. The extract was washed with 3% NaOH solution and dried over $MgSO_4$. After filtration, the filtrate was evaporated and the residue in *n*-hexane was chromatographed on Al_2O_3. Elution of the column with the same solvent gave 921 mg of the oily dithioketal (III). M^+ 242. NMR δ: 1.15 (3H, d., J=7 Hz, >CH–CH_3), 3.23 (4H, m., –S–CH_2–CH_2–S–). To a solution of 921 mg of IV in 30 ml of ethanol was added 12 g of Raney Ni W2 and the mixture was refluxed for 6 hrs. The filtrate was diluted with water and extracted with *n*-pentane. The extract was dried over $MgSO_4$ and evaporated to leave 327 mg of IV. M^+ 152. NMR δ: 0.95 (3H, d., J=7 Hz, >CH–CH_3).

Reduction of the Adduct (II) with $NaBH_4$——To a solution of 8 g of II in 150 ml of ethanol was added portionwise 4 g of $NaBH_4$ and the mixture was stirred under ice cooling for 1 hr. The reaction mixture was diluted with water and extracted with $CHCl_3$. The extract was dried over $MgSO_4$ and evaporated to dryness *in vacuo*. Gas chromatography of the residue showed three peaks at the retention time 10 min, 11.4 min, and 13.7 min, respectively, in a ratio 1: 3: 2, which corresponded to the alcohol C, alcohol A and alcohol B, respectively. The residue in $CHCl_3$ was chromatographed on silica gel and elution with the same solvent gave 2.8 g of the oily alcohol A (Va) in the earlier eluate. M^+ 166. IR cm^{-1}: ν_{OH} 3620, 3500, $\nu_{C=C}$ 1660. NMR δ: 1.20 (3H, d., J=7 Hz, >CH–CH_3), 3.88 (1H, m., $W_{1/2}$=8 Hz, >CH–OH) and 5.67 (2H, m., olefinic protons). Continued elution of the column with the same solvent left a crystalline mass which was recrystallized from *n*-pentane to provide 250 mg of the alcohol C (Vc) as colorless needles, mp 67—68°. IR cm^{-1}: ν_{OH} 3550, and $\nu_{C=C}$ 1653. NMR δ: 0.94 (3H, d., J=7 Hz, >CH–CH_3), 4.00 (1H, m,. $W_{1/2}$=13 Hz, >CH–OH), and 5.75 (2H, br. s., olefinic protons). *Anal.* Calcd. for $C_{11}H_{18}O$: C, 79.46; H, 10.92. Found: C, 79.49; H, 10.76. Further elution of the column with the same solvent gave a crystalline mass which was recrystallized

from *n*-hexane to afford 1 g of the alcohol B (Vb) as colorless needles, mp 108—109°. IR cm^{-1}: ν_{OH} 3600, 3450 and $\nu_{C=C}$ 1655. NMR δ: 1.01 (3H, d., J=7 Hz, >CH–CH_3), 3.51 (1H, octet, J_1=11 Hz J_2=10 Hz and J_3=4.5 Hz, >CH–OH), and 5.69 (2H, m., olefinic protons). *Anal.* Calcd. for $C_{11}H_{18}O$: C, 79.46; H, 10.92. Found: C, 79.16; H, 11.07.

Reduction of IIa with $NaBH_4$——To a solution of 70 mg of IIa in 5 ml of EtOH was portionwise added 70 mg of $NaBH_4$. The mixture was stirred for 30 min. After the usual work-up, gas chromatography of the residue showed two peaks in a ratio of 5: 3, whose retention times were identical with those of the alcohol A (Va) and alcohol B (Vb), respectively.

Oxidation of the Alcohol A (Va) and the Alcohol B (Vb)——To a solution of 100 mg of the alcohol A (Va) in 10 ml of acetone was added 0.5 ml of Jones' reagent. The mixture was stirred under ice cooling for 20 min. The excess of reagent was decomposed by addition of methanol and the reaction mixture was diluted with water and extracted with ether. The extract was dried over K_2CO_3 and evaporated. The residue in $CHCl_3$ was filtered on silica gel to afford 80 mg of crystalline mass which was identical with an authentic sample of IIa in all respects. Similarly, oxidation of the alcohol B (Vb) with Jones' reagent gave IIa.

Acetylation of the Alcohol A (Va)——A solution of 400 mg of the alcohol A (Va), 10 ml of Ac_2O and 30 mg of *p*-TsOH was heated on a water bath for 4 hr. The reaction mixture was diluted with water and extracted with ether. The ethereal solution was washed with aq. Na_2CO_3 solution and dried over K_2CO_3 and evaporated. The residue in $CHCl_3$ was chromatographed over silica gel and elution with the same solvent afforded 230 mg of the acetate (VI). M^+ 208. IR cm^{-1}: $\nu_{C=O}$ 1720, $\nu_{C=C}$ 1660, and ν_{C-O} 1250. NMR δ: 1.11 (3H, d., J=7 Hz, >CH–CH_3), 2.03 (3H, s., $OCOCH_3$), 5.01 (1H, m,. $W_{1/2}$=7 Hz, >CH–OAc) and 5.68 (2H, m., olefinic protons).

Oxidation of the Alcohol C (Vc)——To a solution of 40 mg of the alcohol C (Vc) in 4 ml of acetone was added 0.2 ml of Jones' reagent. The mixture was stirred under ice cooling for 20 min. After the usual work-up, the residue in $CHCl_3$ was filtered on silica gel. Gas chromatography of the product (VII) revealed two peaks in a ratio of 1: 1.7, retention times of which were identical with those of IIa and IIb, respectively.

Treatment of IIa and VII with 10% Solution in MeOH——1) A solution of 30 mg of (IIa) in 10% NaOH solution in MeOH was allowed to stand at room temperature overnight and diluted with water and extracted with ether. The extract was dried over K_2CO_3 and evaporated. Gas chromatography of the residue showed two peaks in a ratio of 3: 1 whose retention times were identical with those of IIa and IIb, respectively.

2) A solution of 40 mg of VII in 10% NaOH in MeOH was treated with a similar manner mentioned above. IR and GC of the residue were identical with those of the equilibrium mixture obtained from IIa by the procedure 1).