Synthetic Photochemistry. VI.[1] The Cycloaddition of Methyl Acetopyruvate with Cyclopentadiene: A Concomitant Formation of $(4+2)\pi$ and $(2+2)\pi$ Adducts

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The irradiation of methyl acetopyruvate in cyclopentadiene using a high-pressure mercury lamp yielded two $(4+2)\pi$ and two $(2+2)\pi$ adducts. These products were inert under the photochemical conditions.

Since the observation of stereospecific $(6+2)\pi$ and $(4+2)\pi$ cycloadditions together with an ene reaction in the UV-light induced reaction of methyl acetopyruvate (I) with tropylidene (II),[2] we have been interested in reaction of I with cyclic diene systems in order to examine the general reactions of I with conjugated olefins. The results obtained with cyclopentadiene (III) are herein described.

When I and III were irradiated in the usual manner, cycloadditions proceeded rapidly to give four products, IV (25.0), V (30.0), VI (8.9), and VII (13.7%) together with some amounts of a cyclopentadiene-dimer. Isolation of the products was achieved by fractional recrystallization and by means of preparative chromatographic techniques. One of the photo-products, IV easily crystallized out from the reaction mixture and its IR (ν: 3380, 1738, and 1695 cm^{-1}) and NMR [δ: 1.69 (H_{7a}, dq, J=9.0, 1.7 Hz), 2.15 (H_{7a}, br, d, J=9.0 Hz), 2.19 (3H, s), 2.85 (H_1, br), 3.10 (H_4 and H_6, overlapping, br. d, J=1.7 Hz), 3.79 (3H, s), 3.84 (OH, s), 5.99 (H_2, ddd, J=5.5, 3.0, 0.8 Hz) and 6.32 (H_3, ddd, J=5.5, 2.8, 0.8 Hz)] spectra suggested that it was a norbornene derivative, a $(4+2)\pi$ adduct, since the splitting patterns of the olefinic protons were symmetrical, and since the presence of an aldol group was certain. In addition, the following observations provided further evidence for its structure: An irradiation of IV under the formation conditions caused no change, resulting in its complete recovery, but when IV was heated at 160 °C for 30 min, I was regenerated by a *retro*-Diels-Alder reaction. The catalytic reduction of IV gave a dihydro-derivative (VIII), in whose NMR spectrum the H_6-signal had $J_{6,7}$=2 Hz. Therefore, VIII and IV have an *endo*-H_6. When VIII was reduced by sodium borohydride at room temperature, an epimeric mixture of 1,3-glycols (IX and X) was produced. However the same reduction at 0 °C afforded only IX. An oily formal (XI) was obtained from IX by the reaction of dimethyl formal in the presence of a trace amount of *p*-toluenesulfonic acid and subsequent silica-gel column chromatography. In the NMR spectrum, the *gem*-protons of the formal group of XI appeared as a pair of AB-type doublets, and the magnitude of *gem*-coupling constant coincided well with that of a strain-free 1,3-dioxane system.[3] Therefore, the *cis*-relationship for the hydroxyl group and 1'-hydroxyethyl group of IX was verified, and the whole stereochemistry of IV was established as depicted.

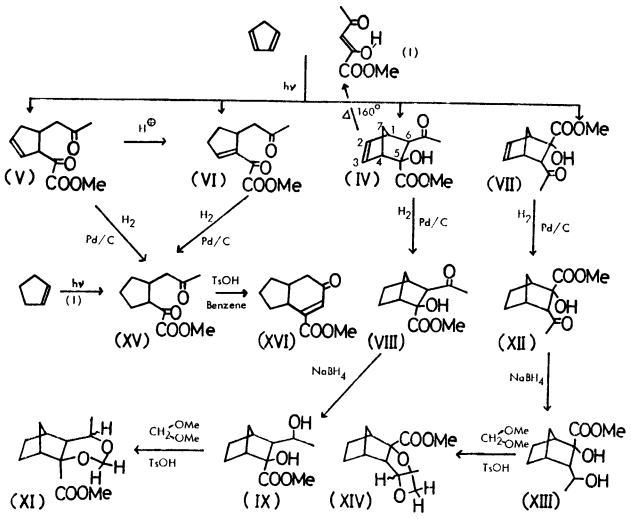
The product VII also exhibited symmetrical olefinic proton signals in its NMR spectrum [δ: 1.5—1.8 (2H, m), 2.10 (3H, s), 2.50 (1H, m), 3.10 (1H, m), 3.61 (1H, d, J=3 Hz), 3.81 (3H, s), 4.32 (1H, s, OH), 6.14 (1H, dd, J=6, 3 Hz), 6.46 (1H, dd, J=6, 3 Hz)]. In VII and its dihydro-derivative (XII), NMR splittings indicated that H_6 had an *exo*-orientation. The rest of the sterochemistry was deduced by a similar sequence to that for IV, *i.e.*, the formation of the strain-free formal (XIV) from XIII, a stereoselective sodium borohydride reduction product of XII.[4] The structure of VII is therefore as shown.

It is interesting to note that the structures of IV and VII suggest that the $(2+4)\pi$ photocycloaddition is non-stereo-selective, and the configurations of IV and VII are determined by the original geometry of I in the ground state.[5]

In this respect, there have been a couple of examples of the photo-cycloaddition of III and butadiene with α-acetoxyacrylonitrile;[6] the photochemical step of this reaction was however non-stereoselective and interpreted in terms of stepwise cyclization *via* a stable 1,4-biradical intermediate. The present results show some contrasts with this, and furthermore contrasts with the results of our previous study on the cycloaddition of I and II. Since the $(4+2)\pi$ addition in this case was stereospecific (expressed as $({}_s4+{}_s2)\pi$), but non-stereoselective, forming the *exo*- and *endo*-adducts, while the $(4+2)\pi$ addition in the case of I and II was also stereospecific (as $({}_s4+{}_s2)\pi$), but stereoselective with regard to the *exo-endo*-relationship, and non-regiospecific, giving a pair of double-bond isomers.[2]

V and VI were both shown to be $(2+2)\pi$ adducts; they gave the same dihydro-derivative (XV) which was identical with the adduct of cyclopentene and I. XV was dehydrated to an α,β-unsaturated keto-ester (XVI),[7] which was characterized by formation of a crystalline DNP. V and VI were separated by silica-gel column chromatography, but V was isomerized under mild conditions to VI. The NMR spectrum of VI revealed a characteristically broadened signal at δ: 7.08 (1H, m) which was ascribable to an α,β-unsaturated glyoxaloyl group (ν: 1680, 1700, 1740, and 1620 (strong) cm^{-1}). Thus, the structures of VI, an artifact formed during the work up, and V were deduced as follows.

Obviously, a merit of the photochemical addition reaction for synthetic purposes is an easy C–C bond formation at an unactivated C=C group, but an oridnary cycloaddition affords a cyclobutane derivative which sometimes reduces the usefulness of the process unless the transformation of the ring system can be achieved.



In this regard, the present results show that the utility of the photocycloaddition reaction may be extended to systems that are usually obtained by Diels-Alder-type reactions, and that the skeletal transformation of the adducts can be performed as having suitable functional groups.

In the present experiment, we could not detect an ene product, whose formation was a predominant process in the case of I and II.[2] This sharp contrast could be a reflection of a difference in chemical properties of the allylic methylenes, *i.e.*, the methylene hydrogens of III, being more acidic than that of II, would be unfavorable for abstraction by an electron-deficient n,π^*-excited carbonyl of I. Finally, a facile reaction with a cyclic diene such as those frequently used as triplet quenchers,[6] would be of theoretical interest in connection with the stereoelectronic factor of product formation.

Experimental

The NMR spectra were measured in deuteriochloroform solutions with either a Hitachi R-20 Model (60 MHz) or a JEOL PS-100 Model (100 MHz) spectrometer. Some of the NMDR experiments were carried out on a Varian HA-100 Model spectrometer owned by the Department of Chemistry, Tohoku University. The IR spectra were measured as a liquid film or in a KBr disk. Elemental analyses were performed by Mr. A. Abe, Division of Elemental Analyses, Kyushu University, stationed in the Department of Chemistry.

Photochemical Reaction of Methyl Acetopyruvate (I) with Cyclopentadiene (III). Isolation of the endo-*(4+2)π Adduct(IV) from the Product Mixture*: I (3.0 g) was dissolved in III (50 ml) and internally irradiated by a 450 W high-pressure mercury lamp for 4 hr. Then, the excess III was evaporated *in vacuo*, and the residue (16.7 g) was briefly passed through a silica-gel column to separate a hydrocarbon fraction, mainly a photodimer of III (13.7 g), and the product mixture, from which a crystalline mass, IV (680 mg), was separated out by refrigeration. Specimen of IV for analysis, colorless needles, mp 95—96 °C, was obtained by recrystallization from benzene-*n*-hexane. (Found: C, 62.80; H, 6.70%. Calcd for $C_{11}H_{14}O_4$: C, 62.84; H, 6.71%. *m/e*: 210 (M^+)).

Chromatographic Separation of the Mixture. Isolation of the (2+2)π Adducts, V and VI, and Enrichment of the exo-*(4+2)π Adduct (VII)*: The combined filtrate of IV was then fractionated by a silica-gel column chromatography to give V (a colorless liquid, 1.31 g), VI (a colorless liquid, 390 mg), an additional amount of IV (214 mg) and VII (a colorless liquid, 800 mg, a mixture with 25% of IV). V and VI were extremely sensitive to air, and easily polymerized.[8]

Catalytic Hydrogenation of IV. Formation of VIII: A methanol solution of IV (100 mg) was reduced in the presence of 5% palladium charcoal (200 mg) to give a colorless crystals (VIII), mp 98—99.5 °C (from benzene-*n*-hexane). (Found: C, 62.04; H, 7.55%. Calcd for $C_{11}H_{16}O_4$: C, 62.25; H, 7.60%. δ: 1.0—1.7 (6H, m), 2.10 (3H, s), 2.0—2.3 (1H, m), 3.20 (1H, d, J=2 Hz), 3.2—3.8 (1H, br., OH), and 3.80 (3H, s). ν: 3380, 1735, and 1708 cm^{-1}).

The DNP of VIII was obtained as yellow needles. Mp 195—198 °C (Found: C, 52.17; H, 5.10; N, 14.22%. Calcd for $C_{17}H_{20}O_7N_4$: C, 52.04; H, 5.14; N, 14.28%. δ: 1.97 (3H, s), 3.83 (3H, s), 7.80 (1H, d, J=9.5 Hz), 8.17 (1H, dd, J=9.5, 2.5 Hz), 8.95 (1H, d, J=2.5 Hz), and 10.85 (1H, br.s, NH). λ_{max}^{MeOH}: 363 nm(ε: 20800). ν: 3450, 3320, 1720, 1620, and 1598 cm^{-1}).

Sodium Borohydride Reduction of VIII. Isolation of a Dihydroxy-Ester (IX): a) VIII (48.3 mg) was dissolved in methanol (2 ml) and reduced with sodium borohydride (7.2 mg) for 3 hr at room temperature. The mixture was then acidified with hydrochloric acid and extracted by ether. A colorless oil (38 mg), initially obtained by cold-finger distillation, was gradually crystallized to give colorless needles (IX), mp 98—99 °C (from *n*-hexane). (Found: C, 61.48; H, 8.45%. Calcd for $C_{11}H_{18}O_4$: C, 61.66; H, 8.47%. δ: 1.23 (3H, d, J=6.5 Hz), 1.0—1.6 (6H, m), 2.0—2.5 (3H, m), 3.40 (2H, s, OH), 3.78 (3H, s), and 4.12 (1H, qd, J= 6.5, 3.3 Hz). ν: 3370 and 1745 cm^{-1}). The filtrate showed the presence of an epimeric glycol, X (δ: 1.26 (3H, d, J=6.5 Hz) and 3.78 (3H, s)), but no further characterization was attempted.

b) VIII (343 mg) was dissolved in cold methanol (4 ml) and reduced by sodium borohydride (22.1 mg) overnight at 0 °C. Then, the mixture was washed with dilute hydrochloric acid and extracted with benzene. Crystalline IX (128 mg) was obtained by silica-gel column chromatography in order to remove the recovered VIII. An absence of X in the mixture was assured by NMR spectral analysis.

Formation of a Formal-Derivative (XI) from IX: IX (28 mg) was dissolved in dimethyl formal (0.5 ml) and benzene (0.5 ml) in the presence of a catalytic amount of *p*-toluenesulfonic acid and refluxed for 3 hr. The mixture was then washed with water and extracted with benzene. A colorless liquid (23 mg) was obtained by cold-finger distillation of the extract. (Found: C, 63.77; H, 8.13%. Calcd for $C_{12}H_{18}O_4$: C, 63.70; H, 8.02%. δ: 1.28 (3H, d, J=7 Hz), 1.0—1.7 (5H, m), 1.9—2.5 (4H, m), 3.80 (3H, s), 3.7—4.1 (1H, m), 4.58 (1H, d, J=6 Hz), and 4.95 (1H, d, J=6 Hz). ν: 1732 cm^{-1}).

Catalytic Reduction of VII. Formation of a Dihydro-Derivative (XII): VII (170 mg, containing *ca.* 25% of IV) was dissolved in methanol (5 ml) and reduced by 5% palladium charcoal (300 mg) for 50 min, then the usual work up of the mixture afforded a colorless oil (124 mg) which appeared as a single peak on a gas-liquid chromatogram, but the NMR analysis indicated the presence of the dihydro-derivative (XII) and the previously characterized VIII in the same ratio as IV to VII in the starting material. (δ: 1.0—1.8 (6H, m), 2.15 (3H, s), 2.4—2.8 (2H, m), 3.25 (1H, br.d, J=3 Hz), 3.77 (3H, s), and 5.65 (1H, br., OH)).

Sodium Borohydride Reduction of XII: XII (125 mg, contaminated by *ca.* 25% VIII) was dissolved in methanol

(5 ml) and reduced with sodium borohydride (26.8 mg) for 5 hr. Then the mixture was acidified by dilute hydrochloric acid and extracted with benzene. The extract was subsequently passed through a silica-gel column to separate the desired glycol (XIII) from the less polar fraction as a colorless liquid (51 mg). (Found: C, 61.94; H, 8.45%. Calcd for $C_{11}H_{18}O_4$: C, 61.66; H, 8.47%. δ: 1.17 (3H, d, J=6.2 Hz), 1.0—2.6 (9H, m), 2.87 (2H, br. s, OH), 3.83 (3H, s), and 4.03 (1H, dq, J=7.5, 6.2 Hz). ν: 3525 and 1730 cm^{-1}).

Formation of a Formal-Derivative (XIV) from XIII: XIII (35 mg) was dissolved in dimethyl formal (0.5 ml) and benzene (0.5 ml) with a small amount of *p*-toluenesulfonic acid and heated under reflux for 2 hr. The mixture was then washed with water and extracted with ether to give a colorless liquid (30 mg) which showed a single peak on a gas-liquid chromatogram (Found: C, 63.57; H, 8.05%. Calcd for $C_{12}H_{18}O_4$: C, 63.70; H, 8.02%. δ: 1.33 (3H, d, J=7 Hz), 1.2—4.0 (10H, m), 3.79 (3H, s), 4.75 (1H, d, J=6.2 Hz), and 5.03 (1H, d, J=6.2 Hz). ν: 1740 cm^{-1}).

Isomerization of V into VI: A benzene solution of V (30 mg) was held on a silica-gel column for 48 hr, and subsequently eluted with benzene–ether (10: 1) mixture. The NMR spectrum showed that consisted solely of VI.

Catalytic Hydrogenation of V. Formation of a Dihydro-Derivative (XV): V (37.6 mg) was dissolved in methanol (2 ml) and reduced by 5% palladium charcoal (75 mg) to give XV as a faint yellow liquid (21.1 mg) (Found: C, 62.20; H, 7.63%. Calcd for $C_{11}H_{16}O_4$: C, 62.25; H, 7.60%. δ: 1.0—3.0 (10H, m), 2.02 (3H, s), and 3.80 (3H, s). ν: 1735 cm^{-1} (very strong)).

Catalytic Hydrogenation of VI. Formation of XV: VI (37.4 mg) was similarly hydrogenated to give XV (23 mg) which had an NMR spectrum identical with the previous sample of XV.

Photochemical Reaction of Cyclopentene with I. Formation of XV: I (503 mg) was dissolved in cyclopentene (5 ml) and externally irradiated by means of a high-pressure mercury lamp through a Pyrex glass filter for 8 hr. The excess olefin was then evaporated and the residue separated by silica-gel column chromatography. After elution of a hydrocarbon fraction (a cyclopentene-dimer), a pale yellow fraction (330 mg) was collected and purified by cold-finger distillation to give a faint yellow liquid which was identical with authentic XV obtained from V.

Acid-Induced Dehydration of XV. Formation of the α,β-Unsaturated Keto-Ester (XVI): XV (34 mg) was dissolved in benzene (5 ml) containing a small amount of *p*-toluenesulfonic acid and refluxed for 3 hr. The solution was washed with water and extracted with benzene. Removal of the solvent afforded a pale yellow residue which was further purified by cold-finger distillation to give a pale yellow liquid (27 mg). (*m/e*: 194 (M^+), 166, 163, 162, 152, 135 (base), 134, 107, 93, 91, 80, 79, 78, 67, 65, and 59. λ_{max}^{MeOH}: 209 nm(ε: 3640), 241 (5460). δ: 1.0—3.0 (10H, m), 3.76 (3H, s), and 6.50 (1H, br. s). ν: 1730 and 1680 cm^{-1}).

The DNP of XVI was obtained as bright-yellow needles. Mp 173—174 °C (Found: C, 54.16; H, 4.90; N, 14.83%. Calcd for $C_{17}H_{18}O_6N_4$: C, 54.54; H, 4.85; N, 14.97%. $\lambda_{max}^{CHCl_3}$: 380 nm(ε: 28800).

Further Irradiation of IV: IV (30 mg) was dissolved in deuteriochloroform and externally irradiated under its formation conditions. After 8 hr, no reaction has been detected by NMR spectral analysis.

Attempted Thermal Reaction of I and III: I (32.7 mg) and III (2 ml) were kept at room temperature for 4 hr, but no detectable reaction occurred other than slight dimerization of III. Then, the same mixture was heated on a steam bath for 1 hr, but evaporation of the olefin left unreacted I and the dimer of III.

Pyrolysis of IV: a) IV (31.3 mg) was dissolved in benzene (0.5 ml) and heated for 1 hr at 80 °C. IV was recovered quantitatively.

b) IV (33.4 mg) was dissolved in dichlorobenzene (0.4 ml) and heated for an hour at 160 °C. Silica-gel column chromatography of the mixture afforded a hydrocarbon fraction (oligomeric mixture of III) and colorless needles (15 mg) which were found to be I by mixed-mp, NMR, and IR comparisons.

Further Irradiation of V: V (35 mg) was dissolved in deuteriochloroform and externally irradiated under its formation conditions for 5 hr. NMR spectral analysis revealed no reaction.

Further Irradiation of VII. VII (60 mg, containing *ca.* 25% of IV) was dissolved in deuteriochloroform and irradiated under the formation conditions. No detectable reaction was observed after 4 hr.

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References

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2) H. Takeshita, A. Mori, and S. Itô, *ibid.*, **47**, 1767 (1974).

3) M. Anteunis, G. Swaelens, F. Anteunis-de Ketelaere, and P. Dirinck, *Bull. Soc. Chim. Belg.*, **80**, 409 (1971).

4) According to the NMR analysis, the diastereomeric carbinol of XIII was not formed. This might be a reflection of the *endo*-configuration for the acetyl-group of XII.

5) We thank a referee for his comment on the possible isomerization of an aldol to another aldol *via* ring-opened diketo-ester derivative under our reaction conditions resulting in the exclusive formation of the thermodynamically stable product, IV or VII. However, we think that this possibility can be eliminated since (a) IV and other $(4+2)\pi$ and $(6+2)\pi$ adducts of I have showed no tendency to cleave their aldol linkage by treatment with toluenesulfonic acid,[2] (b) the recyclization of such a diketo-ester to a strained norbornene frame-work with adjacent bulky substituents under our conditions seems improbable, and (c) no isomeric aldol has been detected during the pyrolysis of IV (NMR and glc analyses).

6) *e.g.*, W. L. Dilling and R. D. Kroening, *Tetrahedron Lett.*, **1968**, 5601; **1968**, 5101.

7) XVI was free from the stereoisomers judging from its NMR spectrum (see Experimental). The configuration of XVI was ascribed as *cis*-fused.

8) Correct figures for elemental analyses were not obtained despite an intensive effort.