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Synthetic Photochemistry. III.[1] The Addition Reaction of Methyl Acetopyruvate to Cycloheptatriene: An Ene Reaction and (4+2)π and (6+2)π Cycloadditions

Hitoshi Takeshita,* Akira Mori,* and Shô Itô**
*Research Institute of Industrial Science, Kyushu University, Hakozaki, Fukuoka 812
**Department of Chemistry, Tohoku University, Aramaki-Aoba, Sendai 980

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The irradiation of methyl acetopyruvate with cycloheptatriene by means of a high-pressure mercury lamp has yielded (6+2)π and (4+2)π cycloadducts, together with tropylcarbinol derivatives formed by a formal abstraction of allylic hydrogen by the excited carbonyl group, this being the major process in this reaction.

As part of our series of studies of the photo-cycloaddition reactions of α,β-unsaturated carbonyl compounds with functional substituents to olefins,[2] we have now extended the investigation to that of methyl acetopyruvate (I) with cycloheptatriene (II), a cyclic conjugated triene, in order to determine the generality of the reaction. One of our primary interests in this reactant is to ascertain whether or not we can see a (6+2)π cycloaddition.[3] At the same time, it will be valuable from the preparative point of view if we can see the hydrogen transfer process from a very reactive allylic methylene of II by an excited carbonyl group of I, since this should produce substituted tropylidenes, whose utilization might offer a novel entry to non-benzenoid aromatic systems. In fact, the experiments which will be described below have shown the occurrences of these two features.

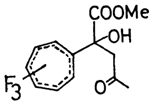
Results and Discussion

The irradiation of a mixture of I and II by a 450 W high-pressure mercury lamp with a Pyrex glass filter has slowly given a mixture of products.[4] After the completion of the reaction, as monitored by a ferric chloride test, the solvent was removed *in vacuo*; the residual oil was then chromatographed through a silica gel column to give as photoproducts III (a pale yellow liquid, 50%), IV (a faint yellow liquid, 14%), V (a faint yellow liquid, 14%), and VI (a faint yellow liquid, 5.8%). Their structure elucidation is as follows:

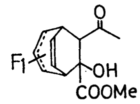
The Structure of III. The NMR of III indicates that it is an isomeric mixture, and repeated chromatographic fractionation of III afforded a practically pure 7-tropyl isomer, IIIa [δ: 2.12 (3H, s), 2.94 (1H, d, J=16 Hz), 3.12 (1H, d, J=16 Hz), 3.71 (3H, s), and 5.0—6.7 (6H, m)]. The mixture of III was then reduced to a single hexahydro-derivative (VII), which gave a 2,4-dinitrophenylhydrazone (DNP), ($\lambda_{\text{max}}^{\text{MeOH}}$: 359 nm (ε: 19400)), confirming that they have the same carbon skeleton. When III was heated in a sealed tube for 190 °C, a dealdolized product, VIII, was obtained after the fractionation of the pyrolysate.[5] According to the NMR spectral analysis, VIII was again shown to be an isomeric mixture of VIIIa, VIIIb, and VIIIc, the components differing in the positions of the double bonds, and through an extensive fractionation by silica gel column chromatography, an enriched sample of the VIIIa isomer was obtained. The rest of the isomers, however, could not be separated. VIIIa revealed the presence of a glyoxaloyl group in the IR ($\nu_{C=O}$: 1723, 1670 cm^{-1}) and the NMR [δ: 2.70 (2H, d, J=6.8 Hz), 3.86 (3H, s), and 5.3—7.45 (5H, complex m)] spectra. Since the presence of a tropyl chromophore is evident from the UV ($\lambda_{\text{max}}^{\text{MeOH}}$: 287 (ε: 4000) and 301 nm (3900)) spectrum as well as from the above NMR evidence, VIIIa is deduced to be methyl 1-tropylglyoxalate. VIIIb and VIIIc are considered to be 2-tropyl- and 3-tropyl-derivatives on the basis of NMR spectral evidence.[6] A mixture of VIII was easily hydrogenated to a single octahydro-derivative (IX), which was then hydrolyzed to a crystalline carboxylic acid. IX was oxidized by potassium permanganate to give pimelic acid, whose identity with an authentic specimen was proved by direct comparisons (IR and NMR spectra and glc of its methyl ester). In addition, the presence of unconjugated keto-groups ($\nu_{C=O}$: 1720 cm^{-1}) and a simple cyclic triene chromophore ($\lambda_{\text{max}}^{\text{MeOH}}$: 254 nm (ε: 3700)) clarifies that III is a methyl 2-tropyl-2-hydroxylevulinate.

The Structures of IV and V. IV and V were shown to be *cycloadducts* by the observed substitution patterns of the seven-membered rings, which exhibit four olefinic protons in the NMR. Since IV and V possess a hydroxyketo-ester function, they cannot be (2+2)π adducts. This was confirmed as follows: The independent hydrogenation of IV and V, using platinum oxide as the catalyst, resulted in the formation of the same tetrahydro-derivative (X), which gave a crystalline DNP ($\lambda_{\text{max}}^{\text{MeOH}}$: 362 nm (ε: 19500)). On the other hand, cycloheptene and I were irradiated in a similar manner to give the photo-adduct (XI) in a good yield together with a dimer of cycloheptene (a colorless liquid).[7] The non-identity of XI, which is a normal glyoxaloyl derivative, with X has been established by IR and NMR spectral comparisons. Therefore, IV and V should possess a bicyclo [3,2,2] nonadiene frame-work, derived by the (4+2)π cycloaddition process;otherwise, the occurrence of a positional isomerism of the double bond is impossible. Interestingly, neither the dehydration nor the dealdolization of X has been successful so far; always unreacted X has been recovered quantitatively, while XI gives a normal α,β-unsaturated keto-ester (XII, a colorless liquid), whose *mono*-DNP, ($\lambda_{\text{xeu}}^{\text{MeOH}}$: 377.5 nm (ε: 24600)) shows reasonable physical properties.

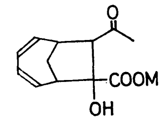
The Structure of VI. VI has also retained the aldolic moiety, as evidenced by its NMR [δ: 2.09 (3H, s), 3.60 (3H, s), and 5.85 (4H, br.s)] and IR (ν: 3500, 1723 (strong) cm^{-1}) spectra. The presence of cyclohepta-1,3-diene chromophore is confirmed by a measurement of the UV spectrum ($\lambda_{\text{max}}^{\text{MeOH}}$: 268 nm ($\varepsilon$: 3370)). On catalytic hydrogenation by platinum oxide, VI afforded a single tetrahydro-derivative (XIII, colorless liquid), which was further characterized by the formation of *mono*-DNP (yellow crystals, $\lambda_{\text{max}}^{\text{MeOH}}$: 360 nm ($\varepsilon$: 19200). XIII was not identical with either X or XI, judging from IR and NMR spectral comparisons. The remaining carbon skeleton for VI is, therefore, bicyclo [4,2,1] nonadiene, that of a $(6+2)\pi$ adduct.



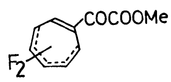
III



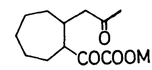
IV, V



VI



VIII



XI

In connection with the above results, a few points should be noted. First, the main product, III, was formed by an ene-reaction which was not previously observed in the photochemical reaction of I, but the phenomenon is not surprising since electron deficient oxygen of the n,π^* excited carbonyl group of I can abstract a partially-negative allylic hydrogen of II, leaving a symmetrical tropyl radical. Secondly, the mode of the concerted formation of IV and V has to be photochemically disallowed, and yet the formation of IV and V was stereospecific despite being not regiospecific, while the $(4+2)\pi$ photoaddition of the cyclopentadiene and α-acetoxyacrylonitrile has been reported to be non-stereospecific.[8] Third, the acquisition of VI constitutes, to the best of our knowledge, the first example of genuine $(6+2)\pi$ photocycloaddition, although a thermal $(6+2)\pi$ process has been reported in the reaction of acrylonitrile and II[9] and, in a formal sense, the intramolecular[3] and intermolecular photocycloadditions[10,11] of activated olefins and benzenes to give cyclobutanes are examples of the $(6+2)\pi$ process, as has been mentioned.[3] Finally, an apparent absence of the genuine $(2+2)\pi$ cycloadduct in the reaction mixture is in contrast with the photocycloadditions of ordinary olefins.

This complicated behavior itself makes the mechanistic analyses of the reaction difficult. However, at least one thing is clear; since the photoreaction is strongly concentration-dependent, *i.e.*, a slight dilution of II by an inert solvent diminishes the rate considerably, there is no involvement of a charge-transfer intermediate in this reaction. Other than this, since photoproducts are extremely unstable and sensitive to the air, and since addition of arylketones to the reaction system causes a consumption of the additives,[12] an intensive investigation will be needed to obtain a deeper understanding of the reaction.

Experimental

Reaction of Cycloheptatriene (II) and Methyl Acetopyruvate (I). a) I (7.24 g) was dissolved in II (200 ml) and was then internally irradiated by a 450 W high-pressure mercury lamp through a Pyrex glass filter under a nitrogen atmosphere for 54 hr. Then the reaction mixture was heated on an oil bath under reduced pressure to remove the II. The residual oil thus obtained was repeatedly fractionated by silica gel column chromatography, using hexane–benzene–ether system as eluant, to give as products III (a pale yellow oil; 5.9 g), IV (a pale yellow oil; 1700 mg), V (a faint yellow oil; 1700 mg), and VI (a faint yellow oil; 600 mg).

b) I (4.3 g) was dissolved in II (45 ml) and anhydrous ether (180 ml) and was then similarly irradiated. After 70 hr, the presence of I in the clean mixture was still recognized, but the crude mixture (*ca.* 2.1 g) obtained by the removal of the solvent and the unreacted I showed a similar product composition.

c) I (120 mg) was dissolved in II (3 ml) and externally irradiated by means of a high-pressure mercury lamp in the presence of various amount of benzophenone (10—100 mg). Every time, the formation of benzopinacol and a tropyl carbinol derivative exceeded that of the photoadducts.

Further Fractionation of III; Isolation of Methyl 2-(7-Tropyl)-2-hydroxylevulinate (IIIa). Above isomeric mixture of III (450 mg) was further chromatographed through a silica gel column; from the least polar fraction, a practically pure isomer, IIIa (a faint yellow oil; 30 mg), was obtained.

Hexahydro-derivative of III. III (98 mg) was dissolved in methanol and hydrogenated over platinum oxide to give a hexahydro-derivative (VII) as a colorless liquid in quantitative yield.

The DNP of VII was prepared in the usual manner as yellow needles; mp 168—168.5 °C (from ethanol-ethyl acetate) (Found: C, 53.81; H, 6.10; N, 13.46%. Calcd for $C_{19}H_{26}O_7N_4$: C, 54.02; H, 6.20; N, 13.26%).

Pyrolysis of III: Formation of Methyl Tropylglyoxalates (VIII). A degassed sample of III (305.7 mg) was heated in a sealed tube for 3 hr. The pyrolysate was then separated by silica gel column chromatography to yield, together with the recovered III (76 mg), 20 mg of a pale yellow liquid (VIII).

Fractionation of Isomeric Mixture of VIII; Enrichment of VIIIa. The above sample of VIII (120 mg) was further fractionated by silica gel column chromatography. The least polar fraction, eluted by hexane–benzene (1:10), consisted of VIIa (70% pure) as a pale yellow liquid after distillation on a cold finger (Found: C, 67.23; H, 5.75%. Calcd for $C_{10}H_{10}O_3$: C, 67.40; H, 5.66%).

Catalytic Reduction of VIII: Formation of Methyl Cycloheptylglycolate (IX). VIII (105 mg) was reduced in methanol over platinum oxide to give an octahydro-derivative, IX (bp 110—112 °C/3 mmHg) as a colorless liquid after a cold-finger distillation; the homogeneity of distillate was proven by glc (Found: C, 64.23; H, 9.59%. Calcd for $C_{10}H_{18}O_3$: C, 64.49; H, 9.74%. ν: 3500, 1740 cm^{-1}, δ: ~1.5 (13H, br.), 3.86 (3H, s), 3.93 (1H, d, $J=2$ Hz)).

Alkaline Hydrolysis of IX to Cycloheptylglycolic Acid. IX (20 mg) was treated with aqueous sodium hydroxide solution to give colorless needles, mp 88—90 °C (from ethanol–ethyl acetate) (Found: C, 62.72; H, 9.39%. Calcd for $C_9H_{16}O_3$: C, 62.76; H, 9.36%).

Potassium Permanganate Oxidation of IX; Formation of Pimelic Acid. IX (98.2 mg) was mixed with water (3 ml), and into the mixture aqueous potassium permanganate (330 mg in 10 ml) was added, drop by drop, at 0 °C, and then it was kept overnight. The mixture was subsequently acidified by hydrochloric acid and extracted with ether. An acidic material obtained by the re-extraction of the above was esterified by diazomethane to give dimethyl pimelate (40 mg (40%)) as a colorless liquid after cold-finger distillation. The sample showed essentially a single peak on a gas-liquid chromatogram and was identical with an authentic specimen (IR, NMR, and glc).

Catalytic Reduction of IV; *Formation of the Tetrahydro-derivative, X.* IV (155 mg) was dissolved in methanol and reduced with platinum oxide at room temperature. The product (X), a colorless liquid, was shown to be homogeneous; it consisted of a single peak on several gas-liquid chromatograms (ν: 3500, 1720, 1270, 1200 cm^{-1}. *m/e*: 240 (M^+), 95 (base peak)).

The DNP of X was obtained as yellow needles, mp 188—190 °C (Found: C, 54.04; H, 5.79; N, 13.37%. Calcd for $C_{19}H_{24}O_7N_4$: C, 54.28; H, 5.75; N, 13.33%).

Catalytic Reduction of V; *Formation of X.* V (255 mg) was similarly hydrogenated to give X, which was identical with those obtained from IV by a study of its IR and NMR spectra, glc, and a mixed-mp comparison with DNP.

Photochemical Reaction of I and Cycloheptene. I (115mg) was dissolved in cycloheptene (1 ml) and externally irradiated by a high-pressure mercury lamp through a Pyrex glass filter. After the evaporation of the excess olefin, the mixture was chromatographed through silica gel column to give a hydrocarbon and a 1: 1-cycloadduct (XI) (a colorless liquid (*m/e*: 240 (M^+), 95 (base peak), ν: 1730, 1270 cm^{-1})) which was not identical with either VII or X (IR, NMR, and glc).

Acid-Catalyzed Dehydration of XI; *Formation of the α,β-Unsaturated Keto-ester, XII.* XI (144 mg) was dissolved in benzene and heated with a small amount of *p*-toluenesulfonic acid to give XII (103 mg, 77.5%) as a colorless liquid ($\lambda_{\max}^{\mathrm{MeOH}}$: 245 nm ($\varepsilon$: 7100), ν: 1730, 1690, 1250 cm^{-1}).

The DNP of XII was obtained as orange-yellow needles; mp 180—181 °C (Found: C, 56.80; H, 5.53; N, 14.24%. Calcd for $C_{19}H_{22}O_6N_4$: C, 56.71; H, 5.51; N, 13.92%).

Catalytic Reduction of VI; *Formation of the Tetrahydro-Derivative XIII.* VI (83 mg) was dissolved in methanol and reduced over platinum oxide at room temperature. A single product (a colorless liquid), obtained after the usual work up, was characterized by the formation of crystalline DNP; yellow needles; mp 141—143 °C (Found: C, 54.33; H, 5.79; N, 13.29%. Calcd for $C_{19}H_{24}O_7N_4$: C, 54.28; H, 5.75; N, 13.33%).

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References and Notes

1) Part II: H. Takeshita, R. Kikuchi, and Y. Shoji, This Bulletin, **46**, 690 (1973).

2) H. Takeshita and S. Tanno, *ibid.*, **46**, 880 (1971).

3) A. S. Kushner, *Tetrahedron Lett.*, **1971**, 3275.

4) When the irradiation was also carried out in dioxane and in tetrahydrofuran solutions, a formation of polymeric material prevented the completion of the reaction, but the product distribution was similar to that of the present system.

5) The formation of azulenes has been observed. This will be the subject of another paper.

6) The NMR spectrum of VIII disclosed signals at δ: 3.87 (3H, s) and 2.47 (2H, t) for one isomer and at 3.89 (3H, s) and 2.40 (2H, t) for another isomer. However, the complexity of the overlapped vinyl proton signals prevented their distinguishment.

7) This showed no olefinic proton in the NMR, and no further study was carried out. However, it is interesting to note that its formation is attributable to the energy transfer of the triplet species of I to cycloheptene. This was not observed in the reaction of cyclohexene and I.

8) W. L. Dilling, and R. D. Kroening, *Tetrahedron Lett.*, **1968**, 5601. *cf.* T. S. Cantrell who also reported the formation of five photoadducts by the irradiation of cyclohexenone and cyclopentadiene; *Chem. Commun.*, **1970**, 1656.

9) D. Bellus, G. Helferich, and C. D. Weis, *Helv. Chim. Acta*, **54**, 463 (1971).

10) For example, a) H. J. F. Angus and D. Bryce-Smith, *Proc. Chem. Soc.*, **1959**, 326; b) D. Bryce-Smith, *Pure Appl. Chem.*, **16**, 47 (1968); c) H.-D. Scharf, and R. Klar, *Chem. Ber.*, **105**, 575 (1972).

11) H. E. Zimmerman, R. S. Givens, and R. M. Pagni, *J. Amer. Chem. Soc.*, **90**, 6096 (1968).

12) The results along this line will be reported in the future.