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Synthetic Photochemistry. I. The Cycloaddition Reaction of Methyl Acetopyruvate with Olefins

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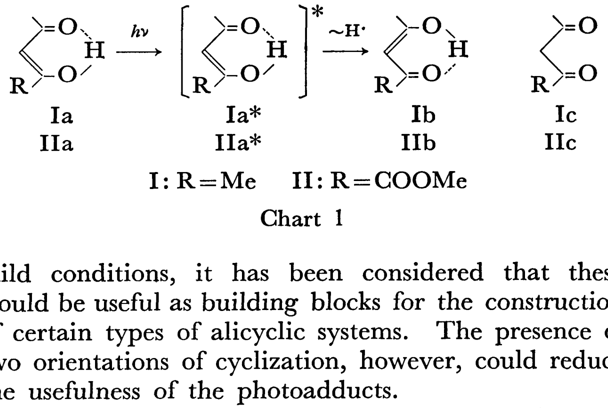
The photochemical cycloaddition reaction of methyl acetopyruvate, an unsymmetrical β-diketone, with olefins afforded the single 1 : 1 molar adducts in good yields. A ready method of the cyclization of the adducts to the β-methoxycarbonyl-$\Delta^{\alpha,\beta}$-cyclohexenones has preparative values.

Unsaturated carbonyl compounds with various types of structural modifications have been reported to undergo a cycloaddition reaction with olefins upon ultraviolet light irradiation, and the mechanistic features of this method have been intensively investigated.[1,2] The cycloaddition reaction of acetylacetone (I), a typical enolizable β-diketone, has also been shown to yield aldolic adducts which dealdolyze spontaneously to heptane-2,6-diones.[3,4]

The absence of intermolecular hydrogen abstraction from the olefins or solvents, a distinctive feature of this particular instance, was in sharp contrast with the phenomenon observed in ordinary carbonyl irradiations, and could be interpreted as the intervention of intramolecular γ-hydrogen abstraction. Since I is a symmetrical molecule, one could not distinguish the difference between Ia and Ib; it is thus not possible to ascertain the reactivity of Ib, a species derived after the hydrogen shift, for the photochemical reaction.

In addition, since the photochemical adducts were convertible to cyclohexenone derivatives under very mild conditions, it has been considered that these would be useful as building blocks for the construction of certain types of alicyclic systems. The presence of two orientations of cyclization, however, could reduce the usefulness of the photoadducts.



I: R=Me II: R=COOMe

Chart 1

We have carried out a study of the photochemical cycloaddition reaction of methyl acetopyruvate (II) with various types of olefins in connection with the above points and have obtained some new findings, which will be described herein.

Results and Discussion

The irradiation of an ethereal solution of II in cyclohexene with high-pressure mercury lamp through a Pyrex glass filter smoothly afforded a single photoadduct (III) in a nearly quantitative yield.[5] The presence of an acetyl group as well as a methoxycarbonyl group in III was evident from the NMR[δ 2.03 (3H, s) and 3.82 (3H, s)] and IR[$\nu_{C=O}$ 1730—1710

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[1] P. E. Eaton, *Accounts Chem. Res.*, **1**, 50 (1968).

[2] P. de Mayo, *ibid.*, **4**, 41 (1971).

[3] P. de Mayo and H. Takeshita, *Can. J. Chem.*, **40**, 440 (1963).

[4] Since our early investigation was made, several reports on the photochemical cycloaddition of enolizable β-diketones appeared. Ref. 4a has shown the reaction occurred *via* n–π^* triplet of I by quenching experiment. 4a) H. Nozaki, M. Kurita, T. Mori, and R. Noyori, *Tetrahedron*, **24**, 1821 (1968). 4b) G. Büchi, J. A, Carlson, J. F. Powell, Jr., and L. F. Tietze, *J. Amer. Chem. Soc.*, **92** 2165 (1970).

[5] In this case, the formation of 3,3-bi(cyclohexenyl), due to the intermolecular hydrogen abstraction by an n–π^* triplet, was not recognized (gas-liquid chromatogram).

cm^{-1} (strong)] spectra. The former also indicated the composition of II to be that of a 1 : 1 adduct. The cyclization of III in the presence of catalytic amounts of *p*-toluenesulfonic acid yielded IV, which was shown to be an epimeric mixture of β-methoxycarbonyl-$\Delta^{\alpha,\beta}$-cyclohexenone derivatives by the IR[$\nu_{C=O}$ 1730 and 1667 cm^{-1}, and δ_{CH_2} 1413 cm^{-1}] and NMR[δ 3.76 (s) and 3.78 (s), the total of both the signals integrated for 3H, 6.53 (br. s) and 6.28 (d, J=2.1 Hz), the total of the two signals integrated for 1H] spectra, although a silica-gel, thin-layer chromatogram showed only one spot. These observations permitted us to suggest the structure IVa or IVb for the cyclization product; those structures are analogous to those for the adducts from the reaction with I. The selection of the correct structure from the above two was made on the basis of the following evidence, first, zinc, and acetic acid reduction of IV afforded a dihydro-derivative (V) which subsequently gave a mixture of deuterio-derivatives by the ordinary procedure and by subsequent reesterification. The occurrence of a pentadeuterio-derivative among the products, confirmed by mass-spectral analysis, requires that Va be at least one of the components of V, even when it consists of an undetectable mixture of isomers. Secondly, palladium dehydrogenation after the lithium aluminum hydride reduction of IV yielded α-methylnaphthalene as the sole aromatized compound, which was characterized as the picrate. Since it has been established that the mixture of α- and β-methylnaphthalenes can not be fractionated by this procedure,6) the absence of β-methylnaphthalene clearly excludes the possibility of the structures of III, IV, and V being IIIb, IVb, and Vb respectively.

A similar reaction of II with cyclohexa-1,4-diene afforded the corresponding photoadduct (VI), which was then catalytically reduced to III. The acid cyclization of VI yielded the corresponding cyclohexenone (VII), parallel to the case of the conversion of III to IV. The spectral data of VI[δ 2.03 (s) and 2.06 (s), the total of these two integrated for 3H, 3.82 (3H, s) and 5.63 (2H, br.), $\nu_{C=O}$ 1735 cm^{-1} (strong)] and VII[δ 3.78 (s) and 3.79 (s), the total of these two signals also integrated for 1H, $\nu_{C=O}$ 1738 and 1675 cm^{-1}, and δ_{CH_2} 1412 cm^{-1}] also supported the respective structures as depicted.

As examples of the unsymmetrical olefins, vinyl acetate and isobutyl vinyl ether were taken for the reaction with II; they again afforded the single adducts, VIII and IX, in each case.7) Their structures were clearly deduced from the spectral evidence. In particular, the appearance of the triplets at δ 5.63 (1H, J=7 Hz) in VIII and at δ 4.32 (1H, J=7 Hz) in IX excluded the alternative structures. This electronic selectivity in the reaction is remarkable, and it may have a potential usefulness in synthesis.

Now, obvious points of interest in the relation between the structures of the products and the major tautomer of II in the ground state have to be considered.8)

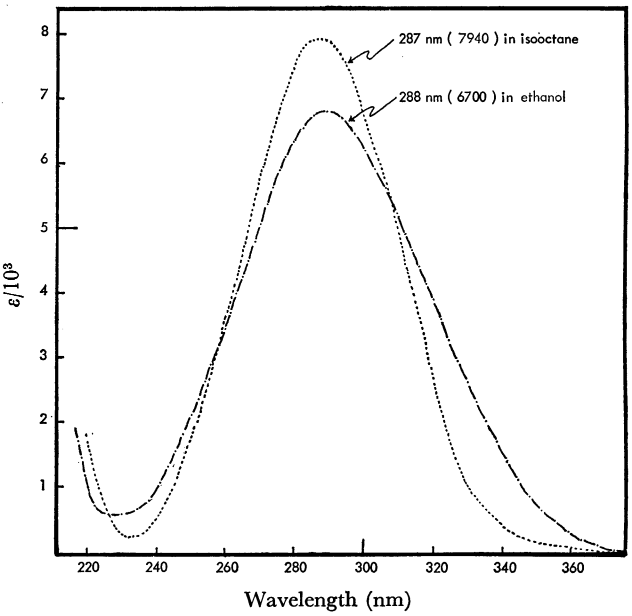

Fig. 1. UV absorption spectrum of II.

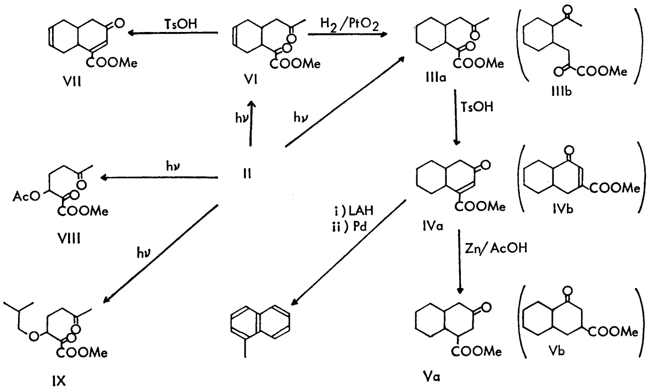

Chart 2.

The NMR spectrum of II [δ 2.22 (3H, s), 3.83 (3H, s), 6.27 (1H, s), and 13.5 (1H, br.)] in a carbon tetrachloride solution indicates that II is at least 95% enolized, showing no signal due to the diketonic tautomer (IIc). In addition to this, the UV spectrum of II (Fig. 1) in an isooctane solution showed an absorption maximum at 287 nm (ε=8000), suggesting that, even in a dilute solution, the enol form is substantial. Since the linearly conjugated tautomer (IIa) should be more stable than the other one (IIb),9) it can be concluded that all of the above adducts were derived from the reaction of the major tautomer (IIa) in a straightforward manner, and that IIb, produced after a possible intramolecular hydrogen shift through photochemically-excited IIa, was being deactivated and was unreactive. The exclusive formation of VIII and IX from the oxygen-bearing olefins, a result in contrast with the reaction of I and isopropenyl acetate, might, with the reactants, be attributable to a hydrogen-bonding or

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6) R. Meyer and H. Fricke, *Ber.*, **47**, 2770 (1914).

7) No indication for the intermolecular hydrogen abstraction. process was obtained in the reaction of II with cyclohexa-1,4-diene, vinyl acetate or isobutyl vinyl ether.

8) The reactive state of the reaction will be a subject of independent studies.

9) There would be no reason to reveal a marked difference in the contents of enolic tautomers between I and II, if II indeed exists as IIb.

a dipole-dipole interaction; II could form a more rigid complex than I leading to photoadducts with the observed orientation.

Finally, it may be mentioned that the yields of the products are quite high; even in the case of cyclohexa-1,4-diene, the 1 : 1 adduct VI was obtained in satisfactorily high yield. Since these adducts possess only one acetyl group, the cyclization naturally leads to a single product in each case. These two points make this procedure practical for certain alicyclic syntheses.

Experimental

The mps, determined with a Fisher-Jones apparatus, were uncorrected. The UV spectra were measured in a methanol solution unless otherwise stated. The IR spectra were obtained for either KBr disks or a carbon tetrachloride solution. The NMR spectra were determined at 60 MHz for a solution in carbon tetrachloride, with tetramethylsilane as the internal standard, and the chemical shifts were expressed in δ values.

The Reaction of Methyl Acetopyruvate (II) and Cyclohexene; The Formation of Methyl 2-Acetonylcyclohexylglyoxalate (III). II (5.76 g) was dissolved in a mixture of cyclohexene (40 ml) and ether (120 ml) and irradiated by a 450 W high-pressure mercury lamp through a Pyrex glass filter in a nitrogen atmosphere; the reaction was monitored by submitting an aliquot to a color reaction with a ferric chloride solution. After the completion of the reaction, the mixture was evaporated *in vacuo*; the residual oil was purified by distillation to yield a colorless liquid; bp 128°C/2 mmHg; 8.58 g (95%).

Found: C, 63.55; H, 8.21%. Calcd for $C_{12}H_{18}O_4$: C, 63.70; H, 8.02%. λ_{max} 232 nm (8700).

The Bis-Semicarbazone of III. Colorless needles; mp 240—242°C (from ethanol).

Found: C, 49.22; H, 6.95; N, 24.23%. Calcd for $C_{14}H_{24}O_4N_6$: C, 49.40; H, 7.11; N, 24.69%.

The Dehydration of III; The Formation of 4-Methoxycarbonyl-Δ^3-octalone-2 (IV). III (800 mg) was heated with *p*-toluenesulfonic acid (10 mg) in a benzene solution for 5 hr; then, the reaction mixture was passed through an alumina column and evaporated. The distillation of the residue on a cold finger yielded a colorless liquid; bp 105°C/0.2 mmHg (bath temp.); 750 mg (86%). This was homogeneous in gas-liquid chromatograms.

Found: C, 68.89; H, 7.58%. Calcd for $C_{12}H_{16}O_3$: C, 69.21; H, 7.74%.

The 2,4-Dinitrophenylhydrazone of IV. Yellow-orange needles; mp 176—177°C (from ethanol).

Found: C, 55.11; H, 6.30; N, 14.09%. Calcd for $C_{18}H_{24}O_6N_4$: C, 55.09; H, 6.17; N, 14.28%. λ_{max} 385 nm (18800).

The Reduction of IV by Zinc and Acetic Acid; The Formation of 4-Methoxycarbonyldecalone-2 (V). IV (200 mg) was reduced by an excess amount of zinc in acetic acid to give a colorless liquid; 140 mg; bp 125°C/0.2 mmHg (bath temp.).

Found: C, 68.41; H, 8.55%. Calcd for $C_{12}H_{18}O_3$: C, 68.54; H, 8.63%.

The 2,4-Dinitrophenylhydrazone of V. Yellow needles; mp 121—123°C (from ethanol).

Found: 55.49; H, 5.77; N, 14.11%. Calcd for $C_{18}H_{22}O_6N_4$: C, 55.38; H, 5.68; N, 14.35%. λ_{max} 363 nm (18100).

The Deuterium Oxide Treatment of V. V (60 mg) was converted to a mixture of deuterio-derivatives by the use of deuterium oxide (0.2 ml) in dioxane (1.2 ml) containing a trace amount of sodium deuteroxide. After the reesterification of the product by diazomethane, a colorless liquid (43 mg) was obtained by cold-finger distillation.

Mass spectrum: M^+/e; 210 (7.7), 211 (13.2), 212 (24.0), 213 (31.2), 214 (19.7), and 215 (4.2%).

The Dehydrogenation of the Lithium Aluminum Hydride Reduction Product of IV. IV (200 mg) was reduced by the use of lithium aluminum hydride (50 mg) in ether. After the usual work-up, the product was placed in a dehydrogenation tube containing 5% palladium carbon (500 mg) and heated at 220°C for 16 hr in a nitrogen atmosphere. Then, the mixture was extracted by ethanol and filtered. A saturated solution of picric acid was poured into the extract to precipitate naphthalenes. The yellow crystals (45 mg) thus obtained were purified by recrystallization from ethanol to give fine yellow needles; mp 141—142°C, which was undepressed on admixture with authentic α-methylnaphthalene picrate. Every fraction of the recrystallizations showed the absence of β-methylnaphthalene on NMR-spectral analysis.

The Photochemical Reaction of II with Cyclohexa-1,4-diene; The Formation of Methyl 2-Acetonylcyclohex-4-enylglyoxalate (VI). II (2.88 g) was dissolved in a mixture of cyclohexa-1,4-diene (50 ml) and ether (70 ml) and irradiated similarly as in the case of cyclohexene. The product was then purified by distillation to yield a colorless liquid (bp 132°C/0.2 mmHg (bath temp.)), whose homogeneity was proved by gas-liquid chromatograms; 4.08 g (91%).

Found: C, 64.55; H, 7.38%. Calcd for $C_{12}H_{16}O_4$: C, 64.26; H, 7.19%.

The Bis-Semicarbazone of VI. Colorless needles; mp 235—237°C (from methanol).

Found: C, 49.81; H, 6.43; N, 24.60%. Calcd for $C_{14}H_{22}O_4N_6$: C, 49.69; H, 6.55; N, 24.84%.

The Catalytic Reduction of VI. *a)*: VI (25 mg) was hydrogenated in an ethyl acetate solution containing 10% palladium carbon (50 mg). After the reaction had ceased, the product was isolated by the filtration of the catalyst and by distillation with a cold finger to give a colorless liquid (15 mg), which was a 50 : 50 mixture of III and IV, as confirmed by NMR-spectral and gas-liquid-chromatographic analyses.

b): VI (55 mg) was reduced in acetic acid with platinum oxide. The product isolated after the usual work-up afforded a colorless liquid (45 mg) which was found to be homogeneous by gas-liquid-chromatographic determination and which was identified as IV.

The 2,4-Dinitrophenylhydrazone of the Reduction Product of VI. A part of the above sample was converted to 2,4-dinitrophenylhydrazone, which was identified with that of IV by a direct comparison.

The Acid Catalyzed Cyclization of VI; The Formation of 4-Methoxycarbonyl-$\Delta^{3,6}$-hexalone (VII). VI (200 mg) was heated with *p*-toluenesulfonic acid (5 mg) in benzene for 3 hr, and the product purified by cold-finger distillation was a colorless liquid (165 mg) which was gas-liquid chromatographically homogeneous.

Found: C, 70.21; H, 6.55%. Calcd for $C_{12}H_{14}O_3$: C, 69.88; H, 6.84%. λ_{max} 231 nm (7300).

The 2,4-Dinitrophenylhydrazone of VII. Yellow-orange needles; mp 176—177°C (from ethanol).

Found: C, 55.67; H, 4.37; N, 14.82%. Calcd for $C_{18}H_{18}O_6N_4$: C, 55.95; H, 4.70; N, 14.50%. λ_{max} 387 nm (19400).

The Photochemical Reaction of II with Vinyl Acetate; The Formation of Methyl 3-Acetoxy-2,6-dioxoheptanoate (VIII). II (77 mg) was sealed in a Pyrex glass tube with vinyl acetate (7 ml) and placed for an external irradiation. After 3 hr, the mixture was evaporated and the residue was distilled on a cold finger to yield a colorless liquid; 95 mg (82%). This was homogeneous in thin-layer chromatograms and in NMR spectroscopic analysis.

Found: C, 52.22; H, 6.27%. Calcd for $C_{10}H_{14}O_6$: C, 52.17; H, 6.13%.

The Photochemical Reaction of II with Isobutyl Vinyl Ether; The Formation of Methyl 2,6-Dioxo-3-isobutoxyheptanoate (IX). II (77 mg) was dissolved in a mixture of isobutyl vinyl ether (2 ml) and ethyl acetate (5 ml) and was externally irradiated in a sealed Pyrex tubing. A colorless liquid; 103 mg (84%), obtained after a cold-finger distillation, was homogeneous in thin-layer chromatograms and in NMR spectral analysis. Found: C, 58.81; H, 8.33%. Calcd for $C_{12}H_{20}O_5$: C, 59.00; H, 8.25%.

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