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Photoreaction of Acetoacetate

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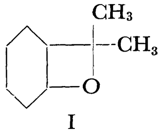
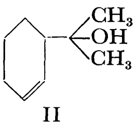
Methyl acetoacetate was irradiated in the presence of cyclohexene to afford methyl 3-cyclohexyl-3-hydroxybutyrate (VIII), methyl 3-cyclohexenyl-3-hydroxybutyrate (IX), two oxetanes (Xa and Xb), and cyclohexene dimers. In contrast to acetylacetone, acetoacetate behaves as a saturated ketone rather than as an α,β-unsaturated ester on photoreaction. We concluded that the n-π^* excitation of the enol-form of β-dicarbonyl compound is responsible for photo-cycloaddition, and no effective n–π^* excitation is accesisble on irradiaron of the enol-form of acetoacetate, since the enol form of acetoacetate has its n–π^* and π–π^* absorptions in the same region.

Ultraviolet irradiation of saturated ketone in the presence of olefin gives oxetanes. β-Diketone and olefin, on the other hand, give cyclobutanes under the same condition.

Bradshaw[1] reported the formation of oxetane I, unsaturated alcohol II, and olefin dimer III on irradiation of acetone in the presence of cyclohexene. De Mayo and Takeshita[2] reported that irradiation of acetylacetone in the presence of cyclohexene afforded cyclobutane derivative IV, which was transformed to diketone V by heat. This feature of 1,3-diketone can be accounted for by the excitation of the enol-form of acetylacetone, which is the predominant species under the reaction condition. β-Ketoester is also well known to enolize to a reasonably high extent in non-polar solvents.[3] If the enol-form of β-ketoester is responsible for the photo-cycloaddition, we may expect the formation of hydroxyester VI.


I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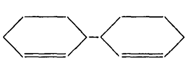
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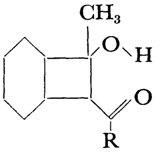
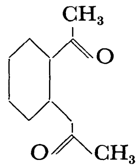
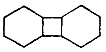

IV: R=CH$_3$
VI: R=OCH$_3$

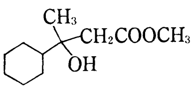

V

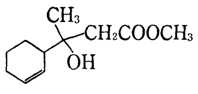
Our purpose in this work was to pursue the behaviour of acetoacetic ester, as saturated ketone or unsaturated ester, on irradiation in the presence of olefin.

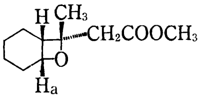
Results and Discussion

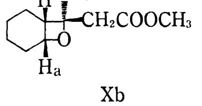
Irradiation of methyl acetoacetate and cyclohexene with a high pressure mercury lamp gave products which were separated into C$_{12}$-hydrocarbons and addition products between methyl acetoacetate and cyclohexene. The structures of C$_{12}$-hydrocarbons were assigned to be the two isomers of tricyclododecanes (VIIa and VIIb) and bicyclohexenyl (III) respectively. The structures of VIIa and VIIb were deduced mainly from the mass spectra which showed peaks at $m/e=164$ (molecular peak), 82, and 67 for both isomers. The last two peaks are characteristic of cyclohexene[4] which is formed by the ring opening of the tricyclododecanes. Hydrocarbon III was identified with bicyclohexenyl which was unambiguously synthesized. The fraction of the adducts between acetoacetate and cyclohexene consists mostly of four components; saturated hydroxy ester VIII, unsaturated hydroxy ester IX, and two isomers of oxetanes Xa and Xb in the ratio of *ca.* 1.0 : 1.5: 2.4 : 2.2.


VII


VIII


IX


Xa


Xb

Compound VIII was identified with methyl 3-cyclohexyl-3-hydroxybutyrate which was synthesized

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[1] J. S. Bradshaw, *J. Org. Chem.*, **31**, 237 (1966).

[2] P. de Mayo and H. Takeshita, *Can. J. Chem.*, **41**, 440 (1963).

[3] A. E. Gillam and E. S. Stern, "An Introduction to Electronic Absorption Spectroscopy in Organic Chemistry," Edward Arnold Ltd., London (1958), p. 259.

[4] H. Budzikiewicz, C. Djerassi and D. H. Williams, "Mass Spectrometry of Organic Compounds," Holden-Day, Inc., San Francisco (1967), p. 67.

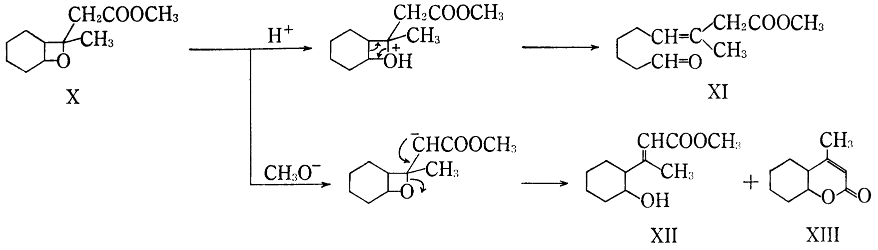

Fig. 1. Chemical behaviour of the oxetanes toward acid and base.

by the Reformatsky reaction between acetylcyclohexane and methyl bromoacetate. The structure of adduct IX was deduced to be methyl 3-(2-cyclohexenyl)-3-hydroxybutyrate from IR and NMR spectra, and was confirmed by the formation of adduct VIII by hydrogenation.

The oxetane-structures of adducts Xa and Xb were indicated by characteristic NMR signals[1] at 4.65 ppm due to the hydrogens attached to $C_6(H_a)$, and was further confirmed by the chemical behaviour toward acid and base. Acid treatment of the mixture of Xa and Xb gives two isomers of aldehyde XIa and XIb (IR: 2720, 1725 cm^{-1},NMR: 9.62 ppm) besides a small amount of methyl acetoacetate and cyclohexene (Fig. 1). The cleavage of oxetane by acid is well known.[5] Base treatment of Xa and Xb, on the other hand, produces the hydroxyester XII (3470, and 1725 cm^{-1}) and δ-lactone XIII (1710 cm^{-1}).

NMR signals of oxetane at 4.65 ppm due to H_a are a sextet with a half-band width of 14 Hz for Xa (Fig. 2) and a quintet with a half-band width of 17 Hz for Xb, respectively. Spin decoupling between C_5-methylene (H_c and H_d) and H_a of Xa gives a doublet for H_a with a coupling constant 7 Hz (J_{ab}). Oxetane Xb gives essentially the same result except for the coupling constant between H_a and H_b being 8 Hz.

These values of J_{ab} suggest that H_a and H_b are *cis* and the oxetane rings are *cis*-fused to cyclohexane ring. This feature is further supported by the half-band width of H_a-signal and the coupling constant between H_a and C_5-methylene: $J_{ac}=J_{ad}=2.5$ Hz for Xa, and $J_{ac}=J_{ad}=4.0$ Hz for Xb. If the ring junction were *trans*, both H_a and H_b would have to occupy *quasi*-axial conformation with respect to the cyclohexane ring. In this case H_a and one of the hydrogen of C_5-methylene (H_c or H_d) must be in the relation of *trans quasi*-diaxial regardless of the conformation of the cyclohexane ring, and the larger half-band width would be observed.[6] Thus the two oxetanes must be configurational isomers at C_8. The chemical shifts of methyls (1.50 ppm for Xa and 1.33 ppm for Xb)[1] and methylene bearing carbomethoxy groups (2.60 ppm for Xa and 2.72 ppm for Xb) are in good accordance with the struc-

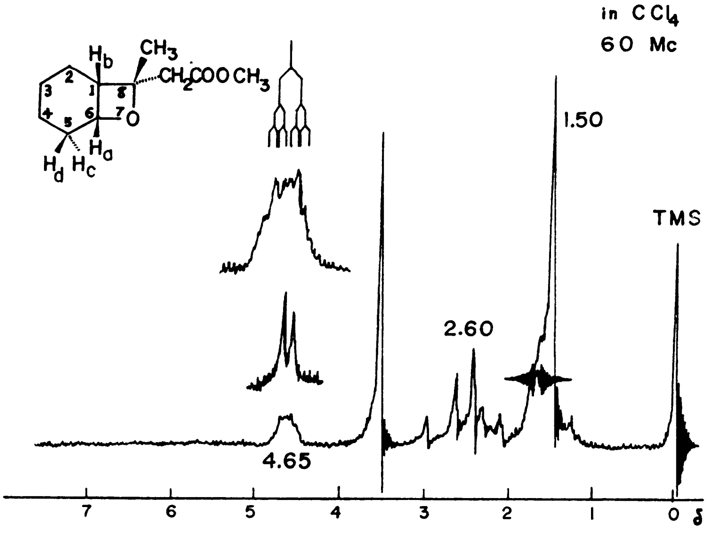

Fig. 2. NMR spectrum of oxetane Xa.

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5) G. Büchi, C. G. Inman and E. S. Lipinsky, *J. Amer. Chem. Soc.*, **76**, 4327 (1954).

6) N. S. Bhacca and D. H. Williams, "Applications of NMR Spectroscopy in Organic Chemistry: Illustrations from the Steroid Field," Holden-Day, Inc., San Francisco (1964), p. 51.

tures Xa and Xb. The anisotropic effect of C_1–C_2 bond would shift to a higher field the signals of the group which is *cis* to the C_1–C_2 bond. None of the *trans* isomers other than these *cis*-oxetanes was detected at least from VPC analysis.

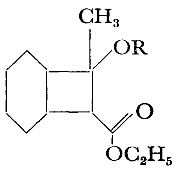
Types of products III, IX, Xa and Xb correspond to the irradiation products between acetone and cyclohexene reported by Bradshaw.[1] Thus the keto-form of acetoacetate must be responsible for the present photoreaction. We may expect the formation of adduct VI in the same fasion with acetylacetone, if the enol-form of acetoacetate is responsible in photoreaction. No such adduct, however, could be detected and the enol-form must be inert to the photo-cycloaddition under these irradiation.

During the course of confirming the inertness of the enol-form, the following results were obtained.

1) Irradiation of acetoacetate and cyclohexene in *n*-hexane, instead of benzene, gave the same results as in the case of the irradiation of the mixture in benzene, except for the lack of tricyclododecane (VII) in the product-mixture. Tricyclododecane was formed by the sensitization effect of benzene.

2) Irradiation with a low pressure mercury lamp (emitting strong line at 2537 Å) resulted in the production of the adducts in poor yield.

3) The enol-form of ethyl acetoacetate was fixed by making its ether (*β*-ethoxycrotonate), and acetate (*β*-acetoxycrotonate). Irradiation of these derivatives in the presence of cyclohexene did not give the expected adducts XIV and XV.



XIV: $R=C_2H_5$

XV: $R=COCH_3$

In view of these facts, it can be concluded that the enol-form of acetoacetate does not undergo cycloaddition at least by π–π^* excitation (246 mμ). Though n–π^* excitation of the enol-form might cause the cycloaddition, the effective n–π^* excited state is inaccessible in these systems.

Although acetylacetone (*ca.* 96% enol in *n*-hexane)[3] has a single absorption band at 272 mμ (Fig. 3), its enol ether discriminates the n–π^* band (308 mμ; $\varepsilon=70$) from the π–π^* band (248 mμ; $\varepsilon=15900$). Though we can not observe a distinct absorption maximum, the enol-form of acetylacetone must have n–π^* band in the same region as in the n–π^* band of its enol ether (308 mμ). This n–π^* excitation is believed to be responsible for the cycloaddition giving adduct IV though without rigorous evidence.[2] On the other hand, acetoacetate and its enol ether have π–π^* absorption at 246 mμ (due to enol-form, 51% in *n*-hexane)[3] and 230 mμ respectively, in *n*-hexane, and the n–π^*

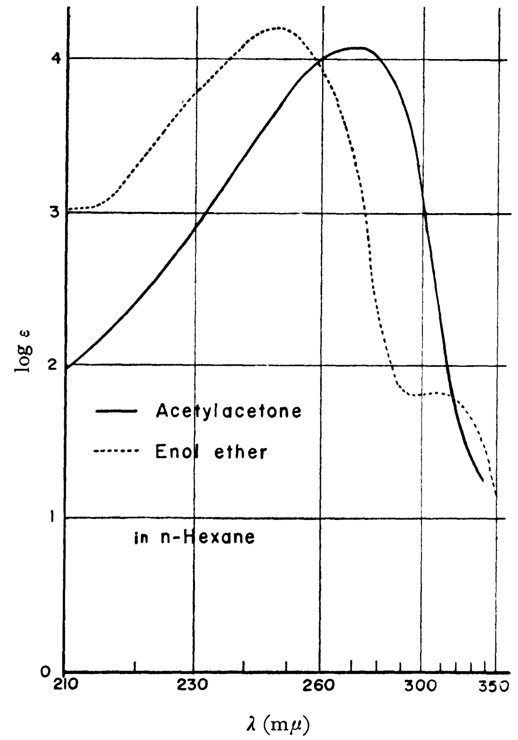


Fig. 3. UV spectra of acetylacetone and its enol ether.

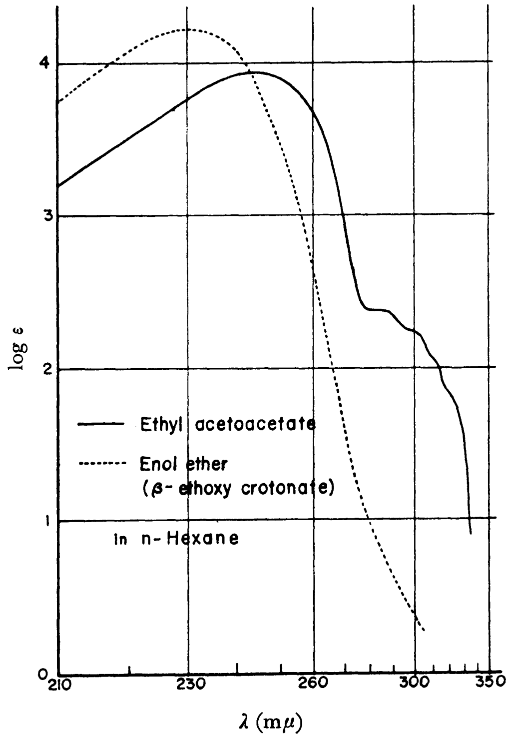


Fig. 4. UV spectra of ethyl acetoacetate and its enol ether.

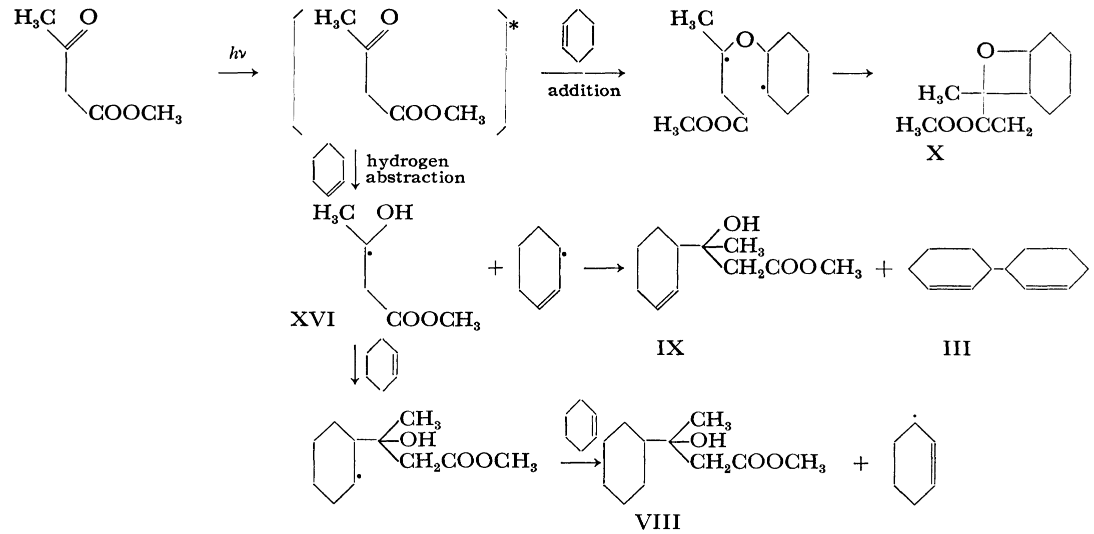


Fig. 5. Reaction scheme.

band of the enol-form can not be observed in both cases. An α,β-unsaturated ester usually has an n–π^* absorption around 240 mμ which is buried under the strong π–π^* absorption.[7] Attachment of hydroxy at β-position of α,β-unsaturated ester shifts the π–π^* absorption to longer wave length (*ca.* 40 mμ), while it possibly affects the n–π^* absorption a little.[8] The n–π^* absorption of the enol-form of acetoacetate, therefore, might be located in the same region as in its π–π^* absorption and the effective excited state (n–π^*) for the photo-cycloaddition can not be achieved.

UV spectrum of acetoacetate in n-hexane shows an absorption at 246 mμ (ε=8100) due to the π–π^* excitation of the enol-form and the shoulder at 285 mμ (ε=68) due to the n–π^* excitation of the keto-form. The latter excitation takes part in the formation of oxetane and the hydrogen abstraction from cyclohexene.

On the basis of the above discussion, the reaction of acetoacetate with cyclohexene can be rationalized as a process involving the n–π^* excitation of the keto-form of acetoacetate and can be represented by the scheme in Fig. 5. Formation of the saturated alcohol VIII can be envisaged by the initial coupling of the radical intermediate XVI and cyclohexene. The mechanism involving the coupling of cyclohexyl radical and the radical XVI can be eliminated by the fact that no bicyclohexyl can be detected in the reaction products.

Bicyclohexenyl (III) must originate from the coupling of two cyclohexenyl radicals formed by hydrogen abstraction. Formation of tricyclododecane (VII) is attributable to the sensitization by benzene used as solvent. This sensitization can be shown by the fact that cyclohexene itself gave VII on irradiation in benzene and the irradiation of acetoacetate and cyclohexene in n-hexane, instead of benezne, gave no tricyclododecane.

Experimental

Irradiation of Methyl Acetoacetate and Cyclohexene. Methyl acetoacetate (29.0 g) and cyclohexene (82.0 g) in 350 m*l* of benzene were internally irradiated with a 450 W high pressure mercury lamp (USHIO UM-452) through a quartz immersion well in the conventional manner. Most of acetoacetate disappeared after irradiation for 14 hr and the solvent was removed under reduced pressure.

Separation and Structure of Photo-products. The crude products were distilled into two fractions, A: bp 40—50°C/1.5 mmHg, 2.4 g, and B: bp 80—90°C/1.5 mmHg, 21.8 g. Fraction A showed mainly three peaks at 7.0 (VIIa), 8.5 (VIIb), and 14.5 min (III) in the ratio of 1 : 3 : 1 on VPC analysis (2.2 m × 6 mm, 10% PEG-20M on Chromosorb-W, 140°C). These products were separated and purified by preparative VPC. VIIa and VIIb were deduced to be tricyclo[6.4.0.0^{2,7}]dodecane. Product III was identified with the authentic sample of bicyclohexenyl.

VIIa. Mass: strong peaks at m/e=164 (M^+, $C_{12}H_{20}$), 82, 81, and 67 (base peak). IR (neat): 2850, 1445, 1340, 950 and 910 cm^{-1}. NMR (CCl_4): no olefinic hydrogen.

VIIb. Found: C, 87.62; H, 12.23%. Calcd for $C_{12}H_{20}$: C, 87.73; H, 12.27%. Mass: strong peaks at m/e=164 (M^+, $C_{12}H_{20}$), 82 (base peak), 81, and 67. IR (neat): 2850, 1449, 1320, 917, and 873 cm^{-1}. NMR (CCl_4): no olefinic hydrogen.

III. Found: C, 88.52; H, 11.17%. Calcd for $C_{12}H_{18}$: C, 88.82; H, 11.18%. IR (neat): 3010, 1650, 1435, 730, and 650 cm^{-1}. NMR (CCl_4): 5.6 ppm (4H, -CH=CH-).

Fraction B contains the adducts between acetoacetate and cyclohexene and shows four peaks at 13.4 (VIII),

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[7] W. D. Closson, S. P. Brady and P. J. Orenski, *J. Org. Chem.*, **30**, 2371 (1965).

[8] N. J. Turro, "Molecular Photochemistry," W. A. Benjamin, Inc., New York (1965), p. 139.

14.3 (IX), 16.3 (Xa), and 20.0 min (Xb) in the ratio of 1.0 : 1.5 : 2.4 : 2.2 on VPC analysis (2.5 m×6 mm, 10% PEG-20M on Chromosorb-W, 180°C). These adducts were separated by preparative VPC.

VIII. Found: C, 66.17; H, 9.90%. Calcd for $C_{11}H_{20}O_3$: C, 65.97; H, 10.07%. IR (neat): 3560, 1717, 1200, 1005, and 893 cm^{-1}. NMR (CCl_4):[*1] 3.63 ($-OCH_3$), 3.2 (-OH), 2.35 (q, J_{ab}=15 Hz, $-CH_2-COO-$), 1.10 ($-CH_3$), 0.8—2.0 ppm (11H).

IX. Found: C, 66.92; H, 9.43%. Calcd for $C_{11}H_{18}O_3$: C, 66.64; H, 9.15%. IR (neat): 3550, 3020, 1720, 1205, 1005, 893, and 725 cm^{-1}. NMR (CCl_4): 5.67 (diffused d, J=5 Hz, -CH=CH-), 3.63 ($-OCH_3$), 3.3 (-OH), 2.38 (q, J_{ab}=15 Hz, $-CH_2-COO-$), 1.2—2.3 (7H), 1.16 and 1.09 ppm ($-CH_3$, 1.5H for each of the two peaks, both singlet due to the diastereomeric nature of IX).

Xa. Found: C, 66.35; H, 8.89%. Calcd for $C_{11}H_{18}O_3$: C, 66.64; H, 9.15%. IR (neat): 1740, 1195, 1095, 995, 953, 925, and 883 cm^{-1}. NMR (CCl_4): 4.65 (sextet, >CH-O-), 3.60 ($-OCH_3$), 2.60 (q, J_{ab}=16 Hz, $-CH_2-COO-$), 2.4 (multiplet, >CH-), 1.50 ($-CH_3$), 1.2—1.9 ppm (8H).

Xb. Found: C, 66.32; H, 9.16%. Calcd for $C_{11}H_{18}O_3$: C, 66.64; H, 9.15%. Mass: m/e=198 (M^+, $C_{11}H_{18}O_3$). IR (neat): 1740, 1195, 1092, 1008, 940, and 885 cm^{-1}. NMR (CCl_4): 4.65 (quintet, >CH-O-), 3.60 ($-OCH_3$), 2.72 (q, J_{ab}=15 Hz, $-CH_2-COO-$), 2.6 (multiplet, >CH-), 1.33 ($-CH_3$), and 1.2—1.9 ppm (8H).

Irradiation of Methyl Acetoacetate and Cyclohexene in *n*-Hexane. Methyl acetoacetate (3.94 g) and cyclohexene (14.0 g) in 100 m*l* of purified *n*-hexane were internally irradiated with a 100 W high pressure mercury lamp (Rikosha, UVL-700) through a quartz jacket. After irradiation for 40 hr, most of the starting acetoacetate disappeared and VPC analysis showed that the composition of the adducts was the same as that from the irradiation using benzene as solvent.

Irradiation of Enol-ether of Methyl Acetoacetate. A mixture of ethyl β-ethoxycrotonate[9] (1.0 g), cyclohexene (3.0 g) and 10 m*l* of *n*-hexane was placed in a quartz tube and was externally irradiated with a 450 W high pressure mercury lamp. VPC analysis showed that essentially no change had occured in the starting mixture.

Irradiation by a Low Pressure Lamp. Methyl acetoacetate (3.94 g) and cyclohexene (14.0 g) in 100 m*l* of *n*-hexane were internally irradiated with a 30 W low pressure mercury lamp (Rikosha UVL-300). After irradiation for 6.5 hr, VPC analysis showed that less than two per cent of the starting ester had been converted to the photo-products.

Synthesis of Bicyclohexenyl (III). Bicyclohexenyl was synthesized by an allyl coupling of 3-bromocyclohexene *via* its Grignard reagent. The reaction was carried out in the conventional manner to prepare the Grignard reagent. A mixture of 3-bromocyclohexene (6.50 g), magnesium tunings (1.07 g) and catalytic amount of iodine in dry ether (50 m*l*) was stirred overnight at room temperature under nitrogen. Work up in the usual manner and alumina chromatography gave bicyclohexenyl (1.0 g), which was identical with the product III on IR and VPC analysis.

Found: C, 88.69; H, 11.28%. Calcd for $C_{12}H_{18}$: C, 88.82; H, 11.18%.

Methyl 3-Cyclohexyl-3-hydroxybutyrate (VIII). Acetylcyclohexane (2.58 g) and freshly distilled methyl bromoacetate (3.06 g) were dissolved in 20 m*l* of dry benzene - toluene (1 : 1). To the solution was added activated zinc powder (1.31 g) and trace amount of iodine, and the reaction mixture was refluxed for 3 hr. To the reaction mixture was added dilute sulfuric acid after cooling and the organic layer was separated. The aqueous layer was further extracted with benzene, and the combined extract was washed with aqueous sodium bicarbonate and water. Evaporation of the solvent and distillation of the products after drying over magnesium sulfate gave methyl 3-cyclohexyl-3-hydroxybutyrate; bp 98—99°C/2.5 mmHg, 1.05 g (25% yield). This product was identical with the adduct VIII on IR, NMR, and VPC analysis.

Hydrogenation of the Adduct (IX). The 1 : 1 mixture of the adducts VIII and IX (400 mg) in 5 m*l* of ethanol was hydrogenated over 10% palladium-charcoal (40 mg) in the usual manner. The product consists only of the adduct VIII on IR, NMR, and VPC analysis.

Base Treatment of Oxetanes (X). The mixture of the photo-adducts (4.30 g) was dissolved in 140 m*l* of 1% sodium methoxide - methanol and was stirred overnight at room temperature. After neutralization of the reaction mixture by bubbling carbon dioxide, the solvent was evaporated and the products were dissolved in ether. Distillation under reduced pressure separated the intact adducts (VIII and IX) (fraction A; bp 95—97°C/2.0 mmHg, 1.40 g) and the degradation products (XII and XIII) from oxetanes (fraction B; bp 110—120°C/2.0 mmHg, 1.20 g). No oxetane was detected in the product-mixture. Fraction A accompanied a small amount of the α,β-unsaturated esters which were formed from the adducts VIII and IX. Fraction B consisted of hydroxy-α,β-unsaturated esters (XII) and δ-lactone XIII, which were formed by the ring opening of the oxetanes, in the ratio of 1 : 1. XII and XIII were separated and purified by preparative VPC (2.2 m ×6 mm, 10% PEG-20 M on Chromosorb-W, 200°C).

XII. Found: C, 66.25; H, 8.77%. Calcd for $C_{11}H_{18}O_3$: C, 66.64; H, 9.15%. Mass: m/e=198 (M^+, $C_{11}H_{18}O_3$). IR (neat): 3470, 1725, 1642, 980, and 865 cm^{-1}. NMR (CCl_4): 5.65 (q, J=1.0 Hz, =CH-), 4.06 (diffused, >CH-O-), 3.66 ($-OCH_3$), 2.17 (d, J=1.0 Hz, $-CH_3$), and 1.2—2.4 ppm (10H).

XIII. Mass: m/e=166 (M^+, $C_{10}H_{14}O_2$). IR (neat): 1710, 1640, 990, and 856 cm^{-1}. NMR (CCl_4): 5.60 (q, J=1.5 Hz, =CH-), 4.40 (multiplet, >CH-O-), 1.95 (d, J=1.5 Hz, $-CH_3$), and 2.3—1.0 ppm (9H).

Acid Treatment of Oxetanes (X). A mixture of the photo-adducts (2.40 g) in 50 m*l* of methylene chloride was treated with *p*-toluenesulfonic acid (50 mg), and the mixture was stirred overnight at room temperature. The solvent was removed after neutralization of the solution with aqueous sodium bicarbonate and drying over magnesium sulfate. VPC analysis showed that the alcohol (VIII and IX) persisted on acid treatment and the oxetanes (X) were converted into aldehydes (XIa and XIb) in *ca.* 70% yield and to the hydroxy-α,β-unsaturated esters (XII), which were also formed by base treatment, in *ca.* 30% yield. The aldehydes

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[*1] The following abbreviations were used to show signal patterns. s: singlet, d: doublet, t: triplet, q: quartet.

9) E. E. Smissman and A. N. Voldeng, *J. Org. Chem.*, **29**, 3161 (1964).

were separated by distillation under reduced pressure (bp 90—100°C/2.0 mmHg) from the products-mixture and were purified by preparative VPC (2.2 m×6 mm, 10% PEG-20M on Chromosorb-W, 200°C).

XIa. Found: C, 66.65; H, 9.28%. Calcd for $C_{11}H_{18}O_3$: C, 66.64; H, 9.15%. IR (CCl_4): 2720, 1740, 1725, 1205, 1170, and 1015 cm^{-1}. NMR (CCl_4): 9.62 (t, J=2.0 Hz, -CHO), 5.32 (t, J=7.0 Hz, =CH–), 3.58 (-OCH_3), 2.90 (s, -CH_2-COO–), 2.36 (t, J=7.0 Hz, -CH_2⦣C=O), 1.98 (t, J=7.0 Hz, -CH_2⦣C=), 1.75 (-CH_3), and 1.2—1.7 ppm (4H).

XIb. Found: C, 66.28; H, 9.05. Calcd for $C_{11}H_{18}O_3$: C, 66.64; H, 9.15%. IR (CCl_4): 2720, 1740, 1725, 1260, 1160, and 1015 cm^{-1}. NMR (CCl_4): 9.62 (t, J=2.0 Hz, -CHO), 5.16 (t, J=7.0 Hz, =CH–), 3.58 (-OCH_3), 2.86 (s, -CH_2-COO–), 2.36 (t, J=7.0 Hz, -CH_2⦣C=O), 2.00 (t, J=7.0 Hz, -CH_2⦣C=), 1.66 (-CH_3), and 1.2—1.7 ppm (4H).

Aldehydes XIa and XIb were also formed during the VPC analysis when Chromosorb-P, instead of Chromosorb-W, was used as support for liquid phase (10% PEG-20M on Chromosorb-P, 160°C).

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