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Studies on Ketene and Its Derivatives. LXVII.⁽¹⁾ Photoreaction of Benzophenone and Benzaldehyde with Diketene⁽²⁾

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Photoreaction of diketene with benzophenone gave 5,5-diphenyl-1,6-dioxaspiro[3.3]-heptan-2-one (IV), 2,5-dihydro-4-hydroxydiphenylmethylfuran-2-one (V), 2,2,5,5-tetraphenyl-1,6-dioxaspiro[3.3]heptane (VI), and 2,2-diphenyl-4-diphenylmethyleneoxetane (VII). Similar reaction of benzaldehyde gave *trans* (XVI) and *cis* (XVII) isomer of 5-phenyl-1,6-dioxaspiro[3.3]heptan-2-one.

Most of the reactions of diketene fall into the category of addition reactions with concomitant opening of the β-lactone ring to afford acetoacetyl derivatives or heterocyclic compounds.⁽⁴⁾ The mode of the reaction involves ionic mechanism. For instance, diketene reacted with ketone to give the 1:1 adduct, 2,2-disubstituted-4-methyl-6-oxo-1,3-dioxene (I).⁽⁵⁾ Also, Hurd and Roe⁽⁶⁾ reported that diketene reacted with aldehyde such as benzaldehyde in the presence of potassium acetate to give benzalacetone (III), and they postulated that α-benzhydrylacetoacetic acid (II) should be an appropriate intermediate. Both reactions

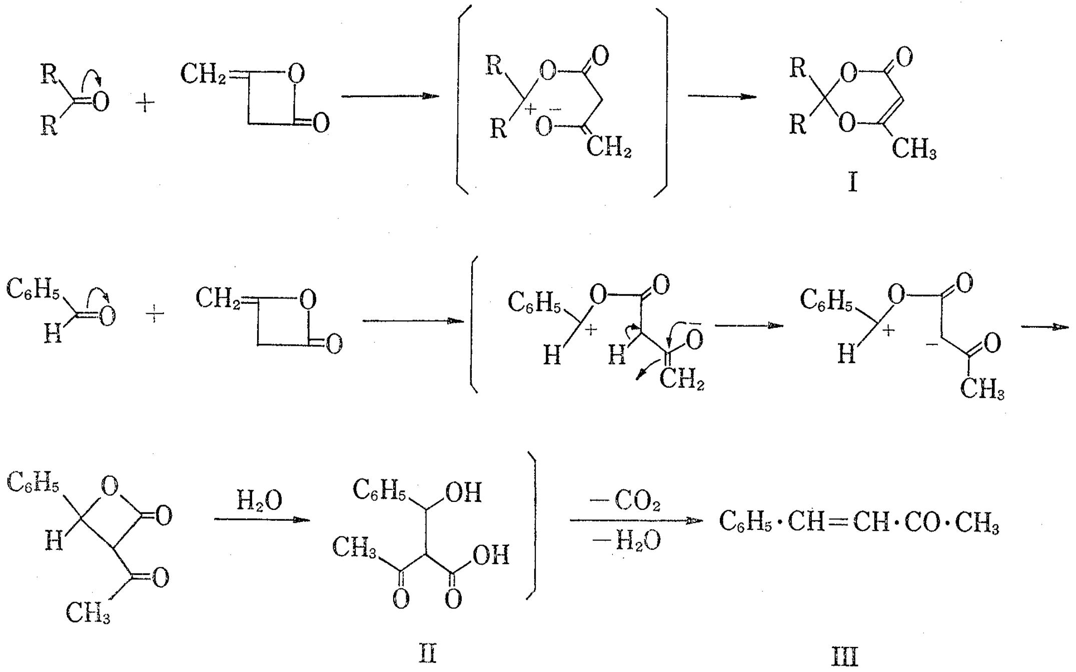

Chart 1

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1) Part LXVI: T. Kato and M. Noda, *Chem. Pharm. Bull.* (Tokyo), 22, 2947 (1974).
2) This was partly presented at the 93rd Annual Meeting of Pharmaceutical Society of Japan, Tokyo, April, 1973.
3) Location: *Aobayama, Sendai, 980, Japan.*
4) *e.g.*, T. Kato, *Yuki Gosei Kagaku Kyokai Shi*, **26**, 311 (1968).
5) M.F. Carroll and A.R. Bader, *J. Am. Chem. Soc.*, **75**, 5400 (1953).
6) C.D. Hurd and A. Roe, *J. Am. Chem. Soc.*, **61**, 3355 (1939).

can be explained by the heterolytic addition of diketene to a nucleophilic terminus (carbonyl oxygen) of ketone or aldehyde, followed by cyclization to give a six- or four-membered intermediate, respectively.

In contrast, little is known about reactions of the C=C double bond while maintaining the integrity of the β-lactone linkage. Reduction of diketene gave β-butyrolactone in good yield.[7] Benzonitrile oxide[8] and C-benzoyl-N-phenylazomethine oxide[9] underwent the similar reactions, for which intermediates maintaining of β-lactone linkage of diketene were proposed. Also, reactions of alkylthiols with diketene gave rise to γ-alkylthio-β-butyrolactones,[10] and these reactions usually involve radical intermediates.

In a previous paper of this series, we have reported the reaction of diketene with diazocompounds such as ethyl diazoacetate and diazoacetophenone gave rise to adducts keeping the β-lactone ring intact.[11] The present paper reports the photoreaction of diketene with benzophenone and benzaldehyde to give spiro compounds involving the addition to the olefinic moiety of diketene.

I. Reaction with Benzophenone

When benzophenone was allowed to react with diketene in benzene under irradiation with ultraviolet (UV) light with stirring, three crystalline products, 5,5-diphenyl-1,6-dioxaspiro[3.3]heptan-2-one (IV), 2,5-dihydro-4-(hydroxydiphenylmethyl)furan-2-one (V), and 2,2,5,5-tetraphenyl-1,6-dioxaspiro[3.3]heptane (VI), were isolated after purification by silica gel column chromatography. When the reaction was carried out under the nitrogen stream, a small amount of 2,2-diphenyl-4-diphenylmethyleneoxetane (VII) was obtained besides IV, V, and VI.

Structural assignments were made on the basis of elemental analysis, spectral data and chemical reactions. For instance, elemental analysis showed that IV is a 1:1 adduct of diketene and benzophenone. Infrared (IR) spectrum of IV showed a characteristic peak due to β-lactone carbonyl at 1850 cm^{-1}, indicating the maintaining of the β-lactone ring intact. Nuclear magnetic resonance (NMR) spectrum showed signals at 3.35 ppm (2H, singlet, β-lactone methylene) and 4.71—5.03 ppm (2H, AB_q, $J=8$ Hz, oxetane methylene) besides multiplet due to the benzene ring protons at 7.10—7.80 ppm. These data are well consistent with the structure of the spiro compound IV.

Elemental analysis and mass spectrum showed that compound V was also an adduct of diketene and benzophenone. IR spectrum indicated two carbonyl absorption bands at 1790 and 1755 cm^{-1}. In chloroform solution the band at 1790 cm^{-1} showed greater intensity than that at 1755 cm^{-1}, on the other hand, in carbon tetrachloride solution the intensities of the two bands were reversed *vise versa*. This observation suggested the structure of V being α,β-unsaturated γ-lactone derivative.[12] NMR spectrum also supported the furanone structure. Finally, V was reduced to the dihydro derivative (VIII). Heating of VIII with conc. sulfuric acid in benzene afforded the known compound of IX.[13]

Compound VI was already known, and properties such as melting point, IR and NMR spectral data are uniquely identical with those reported in the literature.[14]

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7) *a*) B.V. Aller, B. Patent 688269 (1953) [*A. C.*, **48**, 2767*c* (1954)]; *b*) J. Sixt, U. S. Patent 2763664 (1956) [*C. A.*, **51**, 5117*c* (1957)].

8) G.S. d'Alcontres, G. Cum, and M. Gattuso, *Ric. Sci.*, 37, 750 (1967).

9) M.C. Aversa, G. Cum, G.S. d'Alcontres, and N. Vccella, *J. Chem. Soc.* Perkin I, **1972**, 222.

10) G.A. Hull, F.A. Daniher, and T.F. Conway, *J. Org. Chem.*, **37**, 1837 (1972).

11) T. Kato and N. Katagiri, *Chem. Pharm. Bull.* (Tokyo), **21**, 729 (1973).

12) R.N. Jones, C.L. Angell, T. Ito, and R.J.D. Smith, *Can. J. Chem.*, **37**, 2007 (1959).

13) H. Matsuda, N. Ozawa, and S. Ohki, Abstracts of the 93rd Annual Meeting of Pharmaceutical Society of Japan, Tokyo, Vol. II, 146 (1973).

14) *e.g. a*) D.R. Arnold and A.H. Glick, *Chem. Commun.*, **1966**, 813; *b*) H. Gotthard, R. Steinmetz, and G.S. Hammond, *J. Org. Chem.*, **33**, 2774 (1968).

The structure of VII was characterized by elemental analysis, mass, IR and NMR spectral data. Thermal decomposition by gas chromatography of VII showed two peaks ascribable to 1,1-diphenylethylene (X) and diphenylketene (XI). Heating of VII with aniline at 150° resulted in the formation of diphenylacetanilide (XII), which was identified by gas chromatography. This observation also suggested the formation of XI as an intermediate. These data are well consistent with the structure of the oxetane derivative (VII).

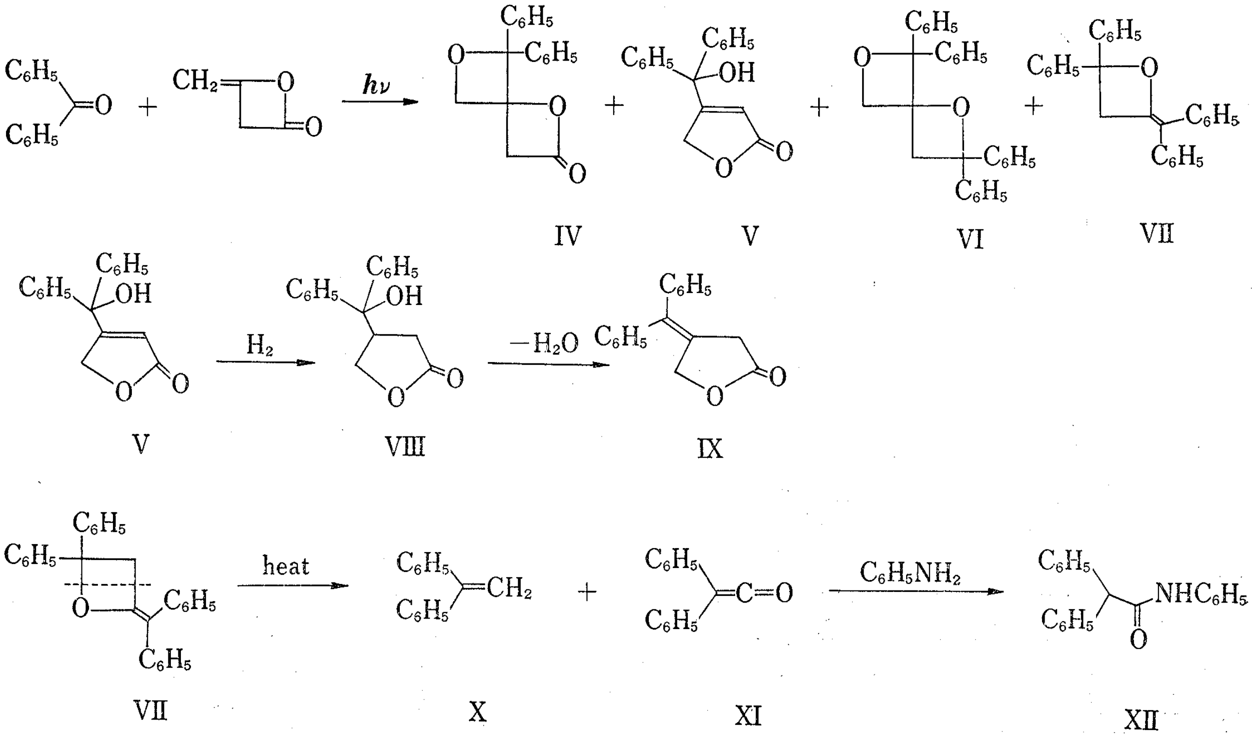

Chart 2

Though details of the mechanism of the formation of these products are not clear at present, likely pathways are shown in Chart 3. Namely, it is well documented fact that the photocycloaddition of a carbonyl compound to olefins gives oxetane derivatives.[15] Applying the mechanism proposed by Büchi, *et al.*,[14b] the attack of the electron-defficient oxygen atom of the carbonyl n-π^* excited state to the olefinic moiety of diketene produces a biradical intermediate (XIII), which cyclized to the spiro-oxetane compound (IV). Isomerization of IV along pathway a (by either radical or ionic reaction) gives the isomer V.

Decarboxylation of IV along pathway b affords 2,2-diphenyl-3-methyleneoxetane (XIV) as an intermediate, which adds to another molecule of benzophenone to give VI. This pathway is speculated on the basis of the reaction of benzonitrile oxide with diketene to give 3,3′-diphenyl-5,5′-spiro[2-isoxazoline], during which reaction 3-phenyl-5-methyleneisoxazoline was proposed as an probable intermediate.[8]

Compound VI is a known compound prepared by photoaddition of benzophenone to allene.[14] Since decomposition of diketene yields allene under certain conditions,[16] this is another possible mechanism of the formation of VI.

Elimination of formaldehyde from VI gives rise to VII.

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15) *e.g.* *a*) E. Paterno and G. Chieffi, *Gazz. Chim. Ital.*, 39, 341 (1909); *b*) G. Buchi, C.G. Inman, and E.S. Lipinsky, *J. Am. Chem. Soc.*, 76, 4327 (1954).

16) R.T. Conley and T.F. Rutledge, U.S. Patent 2818456 (1957) [*C.A.*, 52, 6391*f* (1958)].

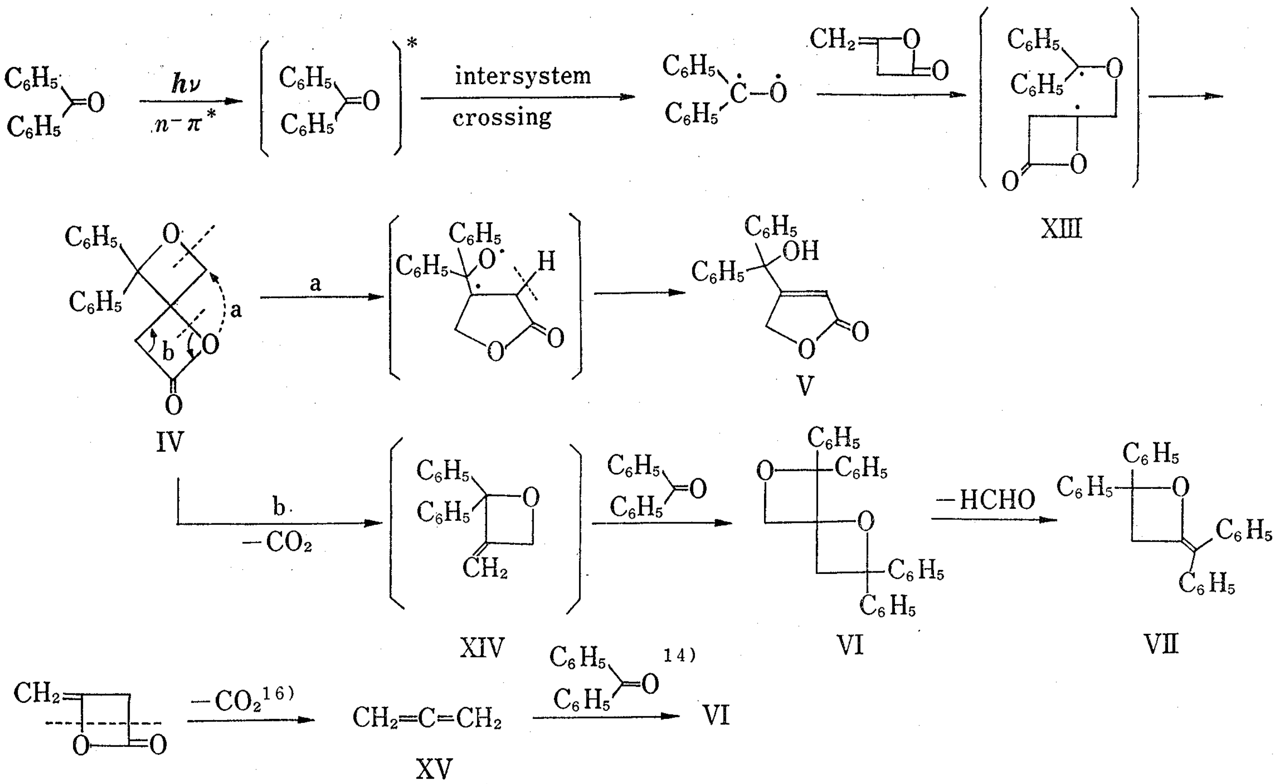


Chart 3

II. Reaction with Benzaldehyde

Similar reaction of benzaldehyde with diketene afforded two 1:1 adducts, a colorless oil of bp 92° (0.01 mmHg) (XVI) and colorless prisms of mp 71—72° (XVII), after purification by silica gel column chromatography. IR spectra of XVI and XVII showed carbonyl absorptions at 1848 and 1850 cm^{-1}, respectively, indicating the integrity of the β-lactone ring intact. Thus, *trans* and *cis* isomers of 5-phenyl-1,6-dioxaspiro[3.3]heptan-2-one are proposed as structures of these adducts.

Treatment of adducts, XVI and XVII, with ethanol in the presence of catalytic amount of sodium hydroxide afforded the esters, XVIII and XIX, respectively. The structure assignment was based on elemental analysis and spectral properties, which however, gave no interpretation for determination of *cis* and *trans* isomers.

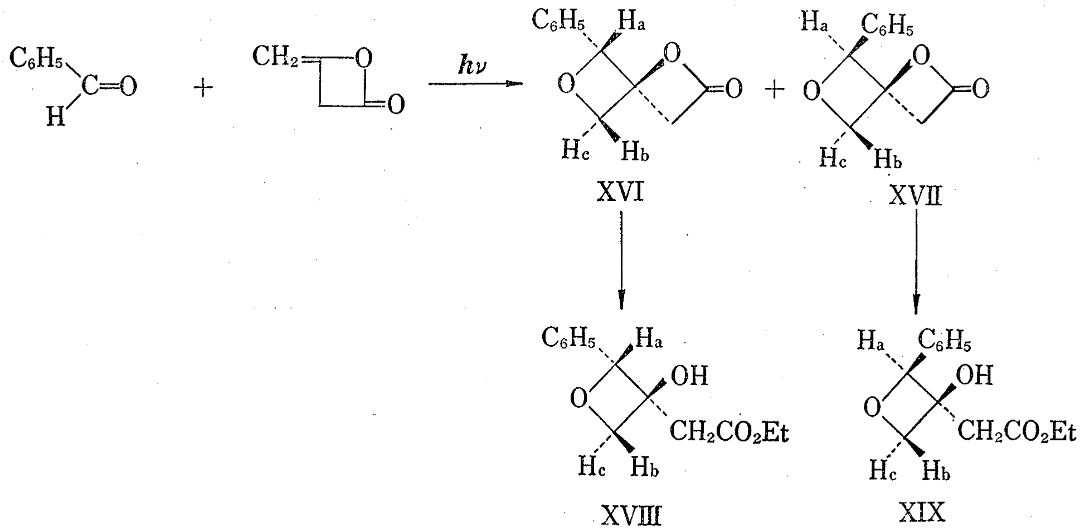
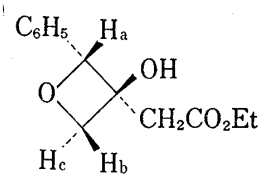


Chart 4

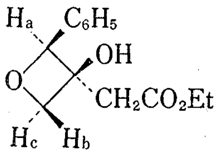
The use of an NMR shift reagent with the esters (XVIII and XIX) provided an indication of *cis* and *trans* stereoisomers. Namely, NMR spectra of XVIII and XIX were measured after successive addition of Eu(FOD)$_3$, and paramagnetic shifts of oxetane ring protons are shown in Table I. The signals of Ha and Hb protons of XVIII underwent larger shift than that of Hc proton, suggesting that Ha, Hb and OH group are located on the same site of the oxetane ring.

On the other hand, Ha proton of XIX showed lower shift than that of Hb proton, suggesting the phenyl and hydroxy groups being the same site. These findings provided evidence for the conclusion that XVIII is 3-ethoxycarbonylmethyl-(*trans*-3-hydroxy-2-phenyl)oxetane, and XIX is the *cis*-isomer. Accordingly, it is reasonably concluded that XVI is the *trans* derivative (phenyl and the oxygen of the β-lactone ring) and XVII is the *cis*-isomer.

Table I. Chemical and Paramagnetic Shifts with Eu(FOD)$_3$



XVIII



XIX

	XVIII			XIX		
	H$_a$	H$_b$	H$_c$	H$_a$	H$_b$	H$_c$
1	336	258	271	327	265	265
2	88	92	73	104	132	123
3	170	174	146	182	227	214

1: chemical shift (Hz) in CCl$_4$
2: paramagnetic shift calculated from the spectrum of sample (1×10^{-4} mole) and Eu(FOD)$_3$ (1×10^{-5} mole) in CCl$_4$
3: paramagnetic shift calculated from the spectrum of sample (1×10^{-4} mole) and Eu(FOD)$_3$ (2×10^{-5} mole) in CCl$_4$

Experimental

IR spectra were taken with a JASCO model IR-S spectrophotometer. NMR spectra were taken on a Hitachi R-20 instrument. Chemical shifts are reported on the δ scale, parts per million downfield from tetramethylsilan as an internal standard. Mass spectra were obtained on a Hitachi Double Focusing Mass Spectrometer RMU-7L. All melting points were uncorrected. The UV light source was a RIKO UVL-400H watercooled high pressure mercury lamp (Pyrex filter).

Reaction of Benzophenone with Diketene——1) A solution of benzophenone (9.1 g, 0.05 mole) and diketene (50 g, 0.6 mole) in benzene (50 ml) was placed in the UV reaction vessel equipped with a drying tube, and stirred at room temperature for 6 hr under irradiation with UV light, during which time CO$_2$ gas evolved. The reaction mixture was condensed *in vacuo*, and the resulting residue was submitted to silica gel column chromatography (Wakogel C-200, 35 cm × 3.5 cm), using petroleum ether (bp 40—50°) and ether as eluants. The petroleum ether eluted fraction gave crystalline substance. Recrystallization from MeOH gave colorless needles of mp 129—129.5° (VI) (lit. mp 129.5—130°,14a) mp 127—127.5° 14b)). Yield, 2.5 g (25%). *Anal.* Calcd. for $C_{29}H_{24}O_2$ (VI): C, 86.11, H, 5.98. Found: C, 85.79; H, 6.06. NMR (CCl$_4$): 2.76—3.36 (2H, AB$_q$, $J=12$ Hz), 4.40—4.81 (2H, AB$_q$, $J=7$ Hz), 6.65—7.70 (20H, m).

Elution was continued with the mixture of petroleum ether–ether (10: 1) to give a solid, which was recrystallized from CHCl$_3$–cyclohexane to colorless prisms of mp 123—124° (IV). Yield, 3.4 g (26%). *Anal.* Calcd. for $C_{17}H_{14}O_3$: C, 76.67; H, 5.30. Found: C, 76.51; H, 5.54. IR $\nu_{\max}^{\mathrm{CHCl_3}}$ cm^{-1}: 1850. NMR (CDCl$_3$): 3.35 (2H, s), 4.71—5.03 (2H, AB$_q$, $J=8$ Hz), 7.10—7.80 (10H, m). An oily residue obtained from this fraction was submitted again to silica gel column chromatography using CHCl$_3$ as an eluant giving V. Recrystallization from cyclohexane–ether gave colorless prisms of mp 116—117.5°. Yield, 1.3 g (9%). *Anal.* Calcd. for $C_{17}H_{14}O_3$ (V): C, 76.67; H, 5.30. Found: C, 76.88; H, 5.52. IR $\nu_{\max}^{\mathrm{CCl_4}}$ cm^{-1}: 1790, 1755, 1640. NMR (CCl$_4$–CDCl$_3$): 3.50—3.90 (1H, b), 4.75 (2H, broad s), 5.64 (1H, broad s), 7.25 (10H, s). Mass Spectrum *m/e*: 266 (M$^+$), 161, 105.

2) A solution of benzophenone (18.2 g, 0.1 mole) and diketene (84 g, 1 mole) in benzene (150 ml) was irradiated under N_2 stream to give VII (0.6 g, 1.5%) as colorless crystals from the petroleum ether eluted fraction. Use of the mixture of petroleum ether and ether afforded IV (6.2 g, 23%), V (0.1 g, 0.4%), and VI (0.5 g, 1%).

Compound VII was purified by recrystallization from MeOH to colorless prisms of mp 137—138° (decomp.). *Anal.* Calcd. for $C_{28}H_{22}O$ (VII): C, 89.80; H, 5.92. Found: C, 89.95; H, 6.03. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1670. NMR ($CDCl_3$): 3.85 (2H, s), 7.20—7.60 (20H, m). Mass Spectrum *m/e*: 374 (M^+), 194, 180.

Diphenylacetanilide (XII) and Diphenylethylene (X)——A mixture of VII (3 mg) and aniline (*ca.* 0.1 ml) was heated at 145—150° for 5 min. The mixture was dissolved in ether and washed with 10% HCl and then H_2O. After drying over Na_2SO_4, the ether solution was evaporated. The residue was submitted to gas chromatography using a JEOL JGO-20K gas chromatograph equipped with a 1 m by 3 mm column containing 10% SE-30 on chromosorb WAW 80—100 mesh at an oven temperature of 200°. XII and X were identified by the comparison of their retention times in gas chromatography with those of authentic samples of diphenylacetanilide and diphenylethylene. The flow rate was 26 ml/min at 23° and retention times follow: X, 1.1 min, XII, 21.6 min.

Thermal Decomposition of VII to give Diphenylethylene (X) and Diphenylketene (XI)——A solution of VII in acetone was submitted to gas chromatography under the same condition as described above, but the oven temperature and injection temperature were 120° and 170°, respectively. The retention times of X and XI were 9.2 min, 12.3 min, respectively.

4-(Hydroxydiphenylmethyl)tetrahydrofuran-2-one (VIII)——A mixture of V (0.53 g) and PtO_2 (0.1 g) in MeOH (20 ml) was shaken in H_2 until 57 ml of H_2 had been absorbed (theoretical amount 47 ml at 10°). Time required was about 40 min. The catalyst was filtered off and MeOH was distilled from the filtrate *in vacuo*. The residue was recrystallized from ether to give colorless prisms of mp 157—158° (VIII). Yield, 0.37 g (69%). *Anal.* Calcd. for $C_{17}H_{16}O_3$ (VIII): C, 76.10; H, 6.01. Found: C, 76.06; H, 6.19. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1765. NMR ($CDCl_3$): 2.43—2.65 (2H, ABX), 2.85 (1H, s), 3.40—4.0 (1H, ABX), 4.15—4.35 (2H, ABX), 7.10—7.40 (10H, m).

4-Diphenylmethylenetetrahydrofuran-2-one (IX)——To a solution of VIII (0.1 g) in dry benzene (10 ml) was added a drop of conc. H_2SO_4, and the mixture was refluxed for 1.5 hr. After washing with H_2O, the benzene solution was evaporated under reduced pressure. The residue was recrystallized from EtOH to colorless needles of mp 150—152° (IX), undepressed on admixture with an authentic sample prepared according to the procedure reported by Ohki.[13] Yield, 0.06 g (60%).

Reaction of Benzaldehyde with Diketene——Following the similar fashion given for benzophenone, a solution of benzaldehyde (10.6 g, 0.1 mole) and diketene (84 g, 1 mole) in benzene (150 ml) was irradiated with UV light. After 12 hr, the reaction mixture was condensed under reduced pressure. The resulting residue was extracted with hot ether. The ether soluble fraction was condensed, and the residue was purified by silica gel column chromatography using the mixture of petroleum ether and ether as an eluant. The petroleum ether–ether (10: 1) elution gave an oily product, which was vacuum distilled to give a colorless oil of bp 92° (0.01 mmHg) (XVI). Yield, 2.2 g (11%). *Anal.* Calcd. for $C_{11}H_{10}O_3$ (XVI): C, 69.46; H, 5.30. Found: C, 69.77; H, 5.58. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1848, NMR (CCl_4): 2.72—3.34 (2H, AB_q, $J=16.5$ Hz), 4.61—5.11 (2H, AB_q, $J=8$ Hz), 5.92 (1H, b), 7.32 (5H, s).

Elution was continued using a mixture of petroleum ether–ether (1: 2) to give colorless prisms of mp 71—72° (XVII). Yield, 1.9 g (10%). *Anal.* Calcd. for $C_{11}H_{10}O_3$ (XVII): C, 69.46; H, 5.30. Found: C, 69.51; H, 5.36. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1850. NMR (CCl_4): 3.43 (2H, s), 4.80 (2H, s), 5.68 (1H, s), 7.29 (5H, s).

3-Ethoxycarbonylmethyl-(*trans*-3-hydroxy-2-phenyl)oxetane (XVIII)——To a solution of XVI (0.1 g) in EtOH (3 ml) was added dropwise a solution of a trace of NaOH (*ca.* 1 mg) in EtOH (20 ml) with stirring in an NaCl-ice bath. After the addition was completed, the reaction mixture was neutralized with conc. HCl and evaporated *in vacuo*. The residue was dissolved in ether and washed with H_2O. The ether layer was dried over Na_2SO_4, filtered and the filtrate was evaporated. The residual solid was recrystallized from petroleum benzin to colorless prisms of mp 45—46.5° (XVIII). Yield, 0.08 g (65%). *Anal.* Calcd. for $C_{13}H_{16}O_4$ (XVIII): C, 66.08; H, 6.83. Found: C, 66.04; H, 6.78. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3480, 1710. NMR (CCl_4): 1.07 (3H, t, $J=7$ Hz), 2.32 (2H, s), 3.90 (2H, q, $J=7$ Hz), 4.17—4.65 (2H, AB_q, $J=6$ Hz), 4.39 (1H, b), 5.61 (1H, s), 7.26 (5H, s).

3-Ethoxycarbonylmethyl-(*cis*-3-hydroxy-2-phenyl)oxetane (XIX)——To a solution of XVII (0.1 g) in EtOH (3 ml) was added a solution of a trace of NaOH (*ca.* 1 mg) in EtOH (20 ml) with ice-cooling. Similar treatment as above afforded colorless needles of mp 55—57° (XIX). Yield, 0.08 g (65%). *Anal.* Calcd. for $C_{13}H_{16}O_4$ (XIX): C, 66.08; H, 6.83. Found: C, 66.01; H, 6.94. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3550, 1725. NMR (CCl_4): 1.25 (3H, t, $J=7$ Hz), 2.57 (1H, s), 2.60—3.15 (2H, AB_q, $J=15$ Hz), 3.92—4.28 (2H, q, $J=7$ Hz), 4.41 (2H, s), 5.44 (1H, s), 7.10—7.43 (5H, m).

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