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Studies on Ketene and Its Derivatives. LXXIV.[1] Carroll Reaction of 1,1-Diphenyl-2-propynyl Acetoacetate

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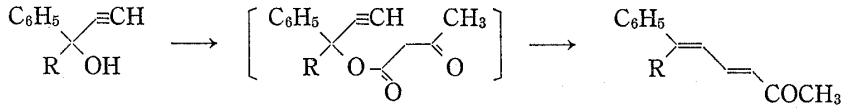
Carroll reaction of 1,1-diphenyl-2-propynyl acetoacetate results in the formation of 3,5-hexadien-2-one derivative (IIIc) besides 2,4-hexadienoic acid derivatives (IV and IV'). IV and IV' are proved to be geometrically isomers by the comparison of their nuclear magnetic resonance data. Other reactions are explained.

It is a well documented fact[3] that reaction of β-ketoester with β,γ-unsaturated alcohol in the presence of a basic catalyst gives rise to γ,δ-unsaturated ketone. Applying this reaction, considerable literatures have been published concerning a practical total synthesis for the essential oils such as pseudoionone, citral, geraniol, and so on, using ethynyl alcohols and diketene as starting materials.[4] On the other hand, only a few references are available dealing with the Carroll reaction of aromatic unsaturated alcohols with diketene. Carroll[5] reported that reaction of diketene with 1-phenyl-2-propyn-1-ol (Ia, R=H) and 2-phenyl-3-butyn-2-ol (Ib, R=CH_3) afforded 6-phenyl-3,5-hexadien-2-one (IIIa, R=H), and 6-phenyl-3,5-heptadien-2-one (IIIb, R=CH_3) respectively.

The present paper reports the Carroll reaction of 1,1-diphenyl-2-propyn-1-ol (Ic) and diketene to give 6,6-diphenyl-3,5-hexadien-2-one (IIIc) and 2-acetyl-5,5-diphenyl-2,4-pentadienoic acid (IV and IV'), which can be regarded as the intermediate of the Carroll reaction. In addition, during the course of this investigation we isolated the acetoacetates of 1-phenyl-2-propyn-1-ol and 2-phenyl-3-butyn-2-ol (IIa and IIb), which is another subject of this paper.



Ia, b — IIa, b — IIIa, b

a: R=H, b: R=CH_3

Chart 1

When 1-phenyl-2-propyn-1-ols (Ia, b, c: R=H, CH_3, C_6H_5) were allowed to react with diketene in $CHCl_3$ in the presence of triethylamine, corresponding acetoacetates (IIa, b, c) were obtained in *ca.* 60% yield.

Though the Carroll reaction of Ia and Ib gave only the sole products, IIIa and IIIb, heating of 1,1-diphenyl-2-propynyl acetoacetate (IIc) in toluene afforded colorless prisms of mp 72—74°, $C_{18}H_{16}O$ (IIIc), yellow prisms of mp 130—131°, $C_{19}H_{16}O_3$ (IV), and colorless prisms of mp 163—164°, $C_{19}H_{16}O_3$ (IV') in 20%, 25%, and 4.5% yield, respectively.

1) Part LXXIII: T. Kato and S. Masuda, *Chem. Pharm. Bull.* (Tokyo), **23**, 2251 (1975).
2) Location: *Aobayama, Sendai, 980, Japan.*
3) *e.g.*, M.F. Carroll, *J. Chem. Soc.*, **1940**, 704.
4) *e.g.*, W. Kimel, J.D. Surmatis, J. Weber, G.O. Chase, N.W. Sax, and A. Ofner, *J. Org. Chem.*, **22**, 1611 (1957).
5) M. Carroll, Brit. Patent 762656 (1956) [*C.A.*, **51**, 12143 (1957)].

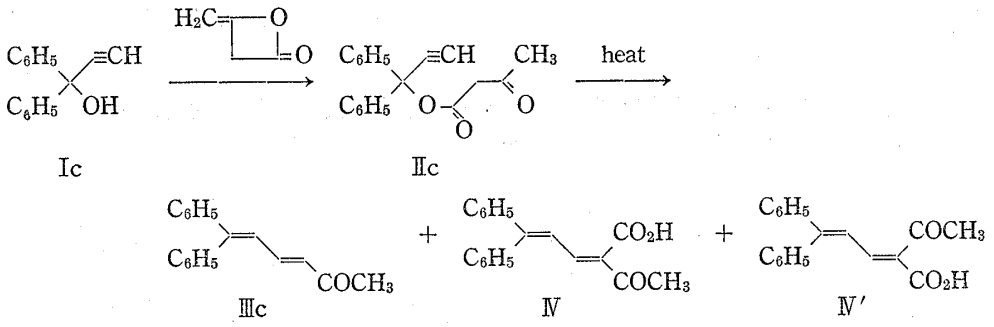


Chart 2

The infrared (IR) spectrum ($CHCl_3$) of IIIc showed the carbonyl absorption at 1655 cm^{-1}. The nuclear magnetic resonance (NMR) spectrum (CCl_4) indicated signals due to methyl protons at 2.08 ppm (3H, s), three olefinic protons at 6.15 ppm (1H, d, J=15.5 Hz), 6.84 ppm (1H, q, J=15.5 Hz), and 6.85 ppm (1H, d, J=15.5 Hz), and aromatic protons at 7.23 ppm (10H, m). Catalytic reduction of IIIc with Pd-C gave 6,6-diphenylhexan-2-one (V). These data indicated the structure of IIIc being 6,6-diphenyl-3,5-hexadien-2-one.

Both of compounds IV and IV′ were soluble in alkali, and IR spectra (KBr) indicated the presence of the carbonyl group at near 1700 cm^{-1}. When a solution of IV′ in $CHCl_3$ was allowed to stand at room temperature, IV′ was isomerized partly to IV. Heating of IV gave the compound IIIc. Catalytic reduction of IV and IV′ afforded V. Treatment of IV with $KMnO_4$ afforded β-phenylcinnamaldehyde (VI). On the basis of these data, it seemed to be reasonable to assume that IV and IV′ were stereoisomers, and both of them were characterized as 2-acetyl-5,5-diphenyl-2,4-pentadienoic acid. Treatment of IV with 5% $NaHCO_3$, followed by methylation with CH_3I afforded crystals of mp 75—76° (VII′) and mp 93—95° (VII), both of which were identified as methyl esters of IV. VII and VII′ were also prepared by the Knoevenagel reaction of methyl acetoacetate with β-phenyl cinnamaldehyde (VI). Catalytic reduction of both VII and VII′ with palladium-charcoal afforded methyl 2-acetyl-5,5-diphenylpentanoate (VIII). These observations were well consistent with the structure of the esters as the *cis* and *trans* isomer of methyl 2-acetyl-5,5-diphenyl-2,4-pentadienoate.

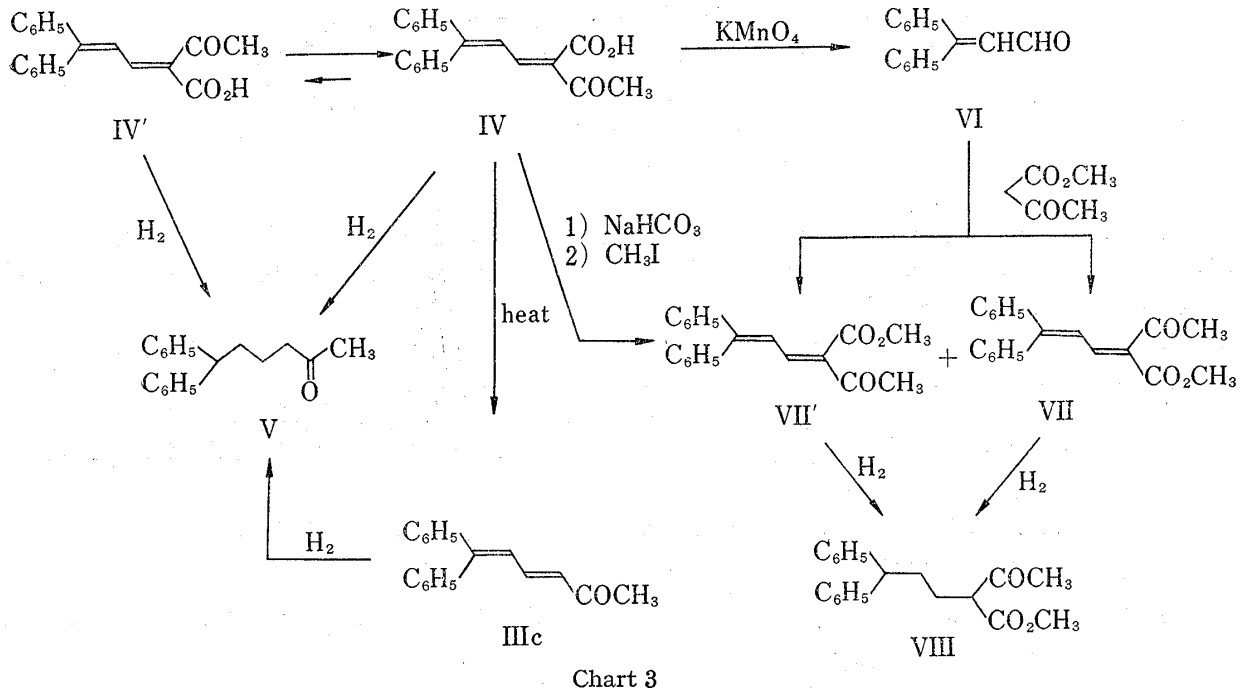
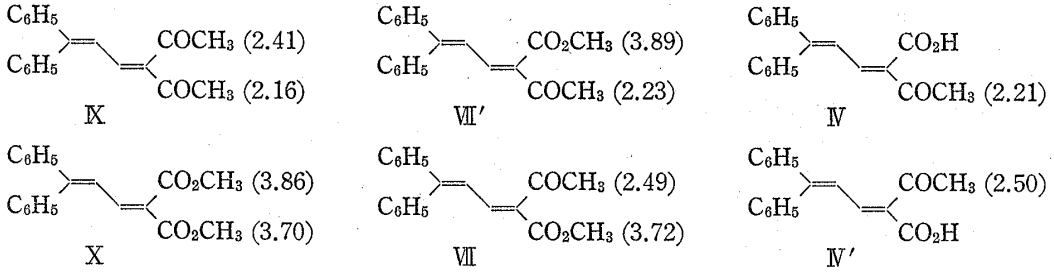


Chart 3

In order to determine the *cis-trans* isomeric structures of these products, model compounds such as 3-acetyl-6,6-diphenyl-3,5-hexadien-2-one (IX) and dimethyl γ-phenylcinnamylidene malonate (X) were prepared. Thus, acetylacetone and dimethyl malonate were allowed to react with β-phenylcinnamaldehyde (VI) to give a 71% yield of $C_{20}H_{18}O_2$ (IX), and a 90% yield of $C_{20}H_{18}O_4$ (X), respectively. As mentioned in experimental section, the spectral data of the products suggested the structure being IX and X, respectively.



NMR ($CDCl_3$) ppm

Chart 4

In the NMR spectrum of IX two singlet signals owing to two acetyl methyl groups appeared at 2.16 ppm and 2.41 ppm. Similarly, ester methyl protons of X appeared at 3.70 ppm and 3.86 ppm as singlets. On consideration of anisotropy effect of the β-phenylstyryl group, signals at 2.41 ppm of IX and 3.86 ppm of X should be assigned to *cis*-acetyl and *cis*-ester methyl which were affected by the β-phenylstyryl moiety of IX and X, respectively.

It seems to be reasonable to consider the acetyl methyl of VII' and IV to be located at *trans* position to the β-phenylstyryl group, while that of VII and IV' being at *cis* positions.

A likely mechanism for the formations of these products is shown in Chart 5. Namely, the migration of Ic gives rise to the allene derivative as an intermediate, which on prototropy transforms to either IV or IV'. The migration of Ic with concomitant decarboxylation affords IIIc directly, which is also obtained by heating of IV.

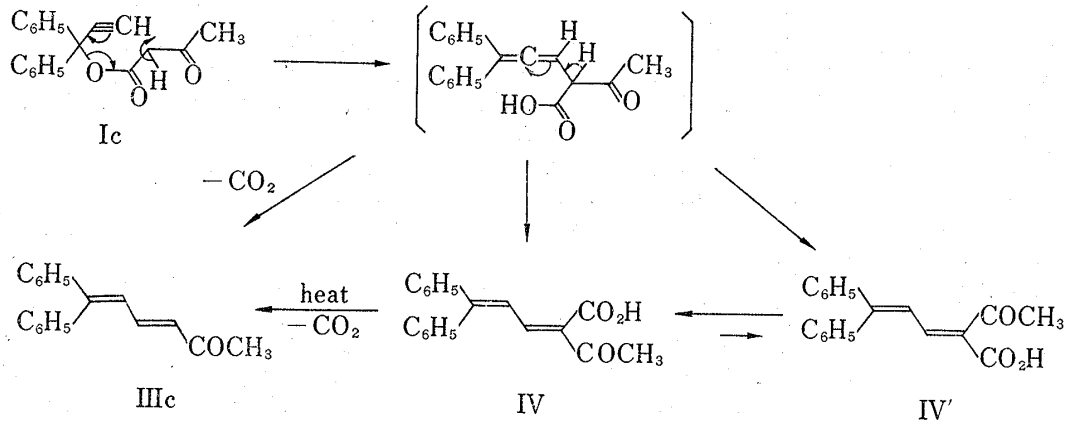


Chart 5

Experimental

All melting points were uncorrected. IR spectra were measured by a Nippon-Bunko Model IR-S spectrophotometer. NMR spectra were taken on a Hitachi-Perkin Elmer R=20 spectrophotometer at 60 MHz. Values are given in ppm. Abbreviations are as follows: s=singlet, d=doublet, t=triplet, q=quartet, m=multiplet, br=broad.

1-Phenyl-2-propynyl Acetoacetate (IIa)——To a mixture of 1-phenyl-2-propyn-1-ol (Ia)[6] (1.3 g), and a catalytic amount of triethylamine (2 drops) in $CHCl_3$ (15 ml), was added a solution of diketene (1 g) in $CHCl_3$

6) D. Papa, F.J. Villani, and H.F. Ginsberg, *J. Am. Chem. Soc.*, **76**, 4446 (1954).

(5 ml) dropwise under reflux during the period of 30 min. After heating for an additional 3 hr. The reaction mixture was condensed *in vacuo*. The oily residue was purified by vacuum distillation to give a colorless oil of bp 93—95° (0.003 mmHg). Yield, 1.3 g (60%). *Anal.* Calcd. for $C_{13}H_{12}O_3$ (IIa): C, 72.21; H, 5.59. Found: C, 72.08; H, 5.64. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3280, 1740, 1715, 1650, 1625, 1130. NMR (CCl_4) ppm: 1.90 (1H, s, enol-CH_3), 2.21 (2H, s, keto-CH_3), 2.30 (1.3H, s, keto-CH_2), 2.51 (1H, t, $J=3$ Hz, acetylene H), 4.90 (0.35H, s, enol-CH=), 6.40 (1H, t, $J=3$ Hz, >CH), 7.30 (5H, m), 11.75 (0.35H, s, enol-OH).

1-Methyl-1-phenyl-2-propynyl Acetoacetate (IIb)——Following the procedure described above, 2-phenyl-3-butyn-2-ol (Ib) (0.9 g) was treated with diketene (0.6 g) in the presence of triethylamine to give a colorless oil of bp 102—106° (0.01 mmHg). Yield, 0.7 g, (58%). *Anal.* Calcd. for $C_{14}H_{14}O_3$ (IIb): C, 73.02; H, 6.13. Found: C, 73.45; H, 6.19. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3270, 1750, 1720, 1630, 1160. NMR (CCl_4) ppm: 1.68 (0.7H, s, enol-CH_3), 1.89 (2.3H, s, keto-CH_3), 2.11 (3H, s, CH_3), 2.70 (1H, s, acetylene H), 3.26 (1.5H, s, keto-CH_2), 5.80 (0.25H, s, enol-CH=), 7.4 (5H, m), 11.7 (0.25H, s, enol-OH).

1,1-Diphenyl-2-propynyl Acetoacetate (IIc)——According to the similar procedure given for IIa, reaction of 1,1-diphenyl-2-propyn-1-ol (Ic) (2.1 g) with diketene (1.0 g) in $CHCl_3$ afforded colorless needles of mp 100—101° (ether). Yield, 1.8 g (65%). *Anal.* Calcd. for $C_{19}H_{16}O_3$ (IIc): C, 78.06; H, 5.52. Found: C, 77.90; H, 5.79. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3280, 1755, 1740, 1660, 1620, 1150. NMR (CCl_4) ppm: 2.25 (3H, s, CH_3), 3.02 (1H, s, acetylene H), 3.52 (2H, s, CH_2), 7.4 (10H, m).

Thermal Reaction of 1,1-Diphenyl-2-propynyl Acetoacetate (IIc)——A solution of IIc (4.5 g) in toluene (25 ml) was refluxed for 4 hr. The reaction mixture was washed with a saturated $NaHCO_3$ solution. The organic layer was washed with H_2O, dried over Na_2SO_4, and condensed *in vacuo*. The resulting oily residue was purified by vacuum distillation to give an oil, bp 130—140° (0.001 mmHg), which on allowing to stand, solidified to give a crystalline substance. Recrystallization from ether–petroleum ether afforded colorless prisms (IIIc) of mp 72—74°. Yield, 0.65 g (20%). *Anal.* Calcd. for $C_{18}H_{16}O$ (IIIc): C, 87.06; H, 6.50. Found: C, 87.42; H, 6.60. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1655. NMR (CCl_4) ppm: 2.80 (3H, s), 6.15 (1H, d, $J=15.5$ Hz), 6.84 (1H, q, $J=15.5$ Hz), 6.85 (1H, d, $J=15.5$H z), 7.23 (10H, m).

The saturated $NaHCO_3$ washing was acidified with 10% HCl, and extracted with $CHCl_3$. The $CHCl_3$ soluble fraction was condensed *in vacuo* to give a crystalline residue. Recrystallization from ether gave yellow prisms of mp 130—131° (IV). Yield, 0.7 g (25%). The mother liquor was condensed, and crystalls separated was recrystallized from ether to colorless prisms of mp 163—164° (IV′). Yield, 0.12 g (4.5%). *Anal.* Calcd. for $C_{19}H_{16}O_3$ (IV): C, 78.06; H, 5.52. Found: C, 77.50; H, 5.39. IR ν_{max}^{KBr} cm^{-1}: 3500—2500, 1710, 1700 (sh). NMR ($CDCl_3$) ppm: 2.21 (3H, s), 7.38 (10H, m), 7.73 (1H, d, $J=11.5$ Hz), 8.45 (1H, d, $J=11.5H_2$), 11—12 (1H, br). *Anal.* Calcd. for $C_{19}H_{16}O_3$ (IV′): C, 78.06; H, 5.52. Found: C, 78.27; H, 5.53. IR ν_{max}^{KBr} cm^{-1}: 3500—2500, 1700, 1660. NMR ($CDCl_3$) ppm: 2.50 (3H, s), 7.2—7.5 (10H, m), 10.9—11.2 (1H, br).

6,6-Diphenylhexan-2-one (V)——1) A suspension of IV (0.5 g) and 5% Pd-C (0.1 g) in EtOH (30 ml) was shaken under the H_2 stream until the absorption of H_2 had been completed. After removal of the catalyst by filtration, the filtrate was condensed at reduced pressure. The residue was distilled *in vacuo* to give a colorless oil of bp 140° (2 mmHg). Yield, 0.34 g (70%). *Anal.* Calcd. for $C_{18}H_{20}O$ (V): C, 85.67; H, 7.99. Found: C, 85.40; H, 8.05. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1705. NMR ($CDCl_3$) ppm: 1.2—1.9 (4H, m), 2.05 (3H, s), 2.40 (2H, t, $J=8$ Hz), 3.86 (1H, t, $J=8$ Hz), 7.19 (10H, s).

2) A suspension of IV′ (0.15 g) and 5% Pd-C (0.05 g) in EtOH (10 ml) was shaken under the H_2 stream until the absorption of H_2 had been completed. After removal of the catalyst by filtration, the filtrate was condensed at reduced pressure. The residue was distilled *in vacuo* to give a colorless oil (V) of bp 140° (2 mmHg). Yield, 0.08 g (63%).

3) IV (0.1 g) was placed in a test tube and the tube was heated in an oil bath at 130—140° for 7 hr. The reaction mixture was dissolved in $CHCl_3$, and washed with a saturated $NaHCO_3$ solution. The $CHCl_3$ layer was condensed *in vacuo*, and the residue was purified by silica gel column chromatography. The petroleum ether elution gave IIIc. Yield, 0.01 g (12%). A mixture of IIIc (0.42 g) and 5% Pd-C (0.1 g) in EtOH (30 ml) was shaken under H_2 stream until 100 ml of H_2 had been absorbed. After removal of the catalyst by filtration, the filtrate was condensed *in vacuo*. The residue was distilled *in vacuo* to give a colorless oil (V) of bp 140° (2 mmHg). Yield, 0.38 g (88%).

β-Phenylcinnamaldehyde (VI)——To a solution of IV (0.13 g) in acetone (5 ml) was added dropwise, a solution of $KMnO_4$ (0.1 g) in acetone (15 ml) with stirring. After stirring for an additional 30 min, the mixture was filtered and the filtrate was condensed *in vacuo*. The residue was extracted with ether. The ether layer was purified by silica gel column chromatography using petroleum ether as an eluant. The elution was condensed to give colorless prisms (petroleum ether) of mp 74—75°. Yield, 0.056 g (66%).

Methyl 2-Acetyl-5,5-diphenyl-2,4-pentadienoate (VII and VII′)——1) A mixture of Na–salt of IV (0.22 g) and CH_3I (0.2 g) in dimethylformamide (DMF) (5 ml) was stirred at room temperature for 1 hr. After removal of the solvent by vacuum distillation, the residue was extracted with ether. The ether solution was condensed, and the resulting residue was purified by silica gel column chromatography using petroleum ether and ether as eluants. The petroleum ether–ether (9: 1) elution gave colorless needles of mp 93—95°

(VII). Yield, 0.03 g (15%). *Anal.* Calcd. for $C_{20}H_{18}O_3$ (VII): C, 78.41; H, 5.92. Found: C, 78.09; H, 5.87. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1700. NMR ($CDCl_3$) ppm: 2.49 (3H, s), 3.72 (3H, s), 7.2—7.5 (12H, m).

The elution was continued using the same solvent giving pale yellow prisms (ether–petroleum ether) of mp 75—76°. Yield, 0.1 g (48%). *Anal.* Calcd. for $C_{20}H_{18}O_3$ (VII′): C, 78.41; H, 5.92. Found: C, 78.14; H, 5.97. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1715, 1680. NMR ($CDCl_3$) ppm: 2.23 (3H, s), 3.89 (3H, s), 7.2—7.5 (12H, m).

2) A solution of β-phenylcinnamaldehyde (VI) (2 g), methyl acetoacetate (1.1 g), and 3 drops of piperidine in benzene (40 ml) was refluxed for 3 hr. The reaction mixture was condensed *in vacuo*, and the residue was purified by silica gel column chromatography and recrystallization from petroleum ether and ether giving VII and VII′ in 30% (1.0 g) and 33% (1.1 g) yield, respectively.

Methyl 2-Acetyl-6,6-diphenylpentanoate (VIII)——1) A mixture of VII (0.15 g) and 5% Pd-C (0.05 g) in EtOH (30 ml) was shaken under H_2 stream until 30 ml of H_2 had been absorbed. After filtration, the EtOH solution was condensed *in vacuo*. The residue was recrystallized from ether–petroleum ether to colorless prisms of mp 73—74°. Yield, 0.08 g (60%). *Anal.* Calcd. for $C_{20}H_{22}O_3$ (VIII): C, 77.39; H, 7.14. Found: C, 77.48; H, 7.27. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1730, 1700. NMR ($CDCl_3$) ppm: 1.6—2.1 (4H, m), 2.11 (3H, s), 3.40 (1H, t, $J=7$ Hz), 3.68 (3H, s), 3.89 (1H, t, $J=7$ Hz), 7.20 (10H, s).

2) The compound derived from the reduction of VII′ (0.15 g), in the same manner as above, was identical with the reduction product of VII. Yield, 0.08 g (60%).

3-Acetyl-6,6-diphenyl-3,5-hexadien-2-one (IX)——To a solution of VI (0.5 g) and acetylacetone (0.24 g) in benzene (15 ml) was added 3 drops of piperidine. After refluxing for 3 hr, the reaction mixture was condensed *in vacuo*. The residue was purified by recrystallization from ether and petroleum ether to yellow needles of mp 86—87.5°. Yield, 0.5 g (71%). *Anal.* Calcd. for $C_{20}H_{18}O_2$ (IX): C, 82.73; H, 6.25. Found: C, 82.46; H, 6.38. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1680, 1650. NMR ($CDCl_3$) ppm: 2.16 (3H, s), 2.41 (3H, s), 7.2—7.4 (12H, m).

Dimethyl γ-Phenylcinanmylidenemalonate(X)——Following the similar fashion as described above, reaction of VI (0.5 g) with dimethyl malonate (0.32 g) afforded colorless needles (ether–petroleum ether) of mp 85—86°. Yield, 0.8 g (90%). *Anal.* Calcd. for $C_{20}H_{18}O_4$ (X): C, 74.52; H, 5.63. Found: C, 74.41; H, 5.87. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1710, 1700. NMR ($CDCl_3$) ppm: 3.70 (3H, s), 3.86 (3H, s), 7.2—7.6 (12H, m).

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