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Methylene Analogs of Cyclobutenedione. III.¹⁾ The Reaction of 2-Bromo- and 2,2-Dibromo-3,4-bis(diphenylmethylene)cyclobutanone with Alcoholic Potassium Hydroxide

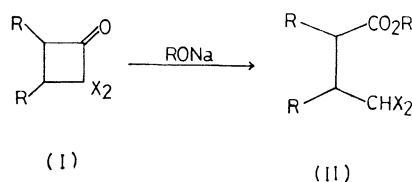
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The reactions of 2-bromo-3,4-bis(diphenylmethylene)cyclobutanone (III) with methanolic and 2-propanolic potassium hydroxide afforded methyl 4-methoxy-2,3-bis(diphenylmethylene)butyrate (VIII) and 3,4-bis(diphenylmethylene)- γ -lactone (XXI) respectively. The reaction of the 2,2-dibromo analog of III (XXV) with methanolic potassium hydroxide afforded methyl 4-methoxy-4-bromo-2,3-bis(diphenylmethylene)butyrate (XXVIIIa) and methyl 4,4-diphenyl-3-formyl-2-diphenylmethylenebut-3-enate (XXIIIa) in approximately equal yields. However, the reaction of XXV with 2-propanolic potassium hydroxide afforded XXIIIc exclusively. The reaction mechanism was disclosed to be that the haloester intermediates V and XXVII initially formed from III and XXV respectively, by the addition of alcohol to the carbonyl followed by the ring-opening, react with the alkoxy and hydroxy anions competitively.

It has been reported that the reaction of 2-halo-,²⁾ 2,4-dihalo,²⁾ and 2,2-dihalocyclobutanone³⁾ with a base affords the corresponding cyclopropane carboxylic acid *via* a Favorskii transformation. It has also been reported that the treatment of 2,2-dihalocyclobutanone (I) with a base affords the ring-opened product (II).³⁻⁶⁾



1) Part II: F. Toda and K. Akagi, *Tetrahedron*, **27**, 2801 (1971). Note the change in the title of the series of publications to "Methylene Analogs of Cyclobutenedione" instead of the previously-used "Methylene Analogs of Cyclobutadienequinone." Since cyclobutadiene is not an aromatic compound, its dicarbonyl derivative is not a real quinone.

2) J. L. Ripoll, *Ann. Chim. (Paris)*, **2**, 233 (1967).

3) V. Fletcher and A. Hassner, *Tetrahedron Lett.*, **1970**, 1071.

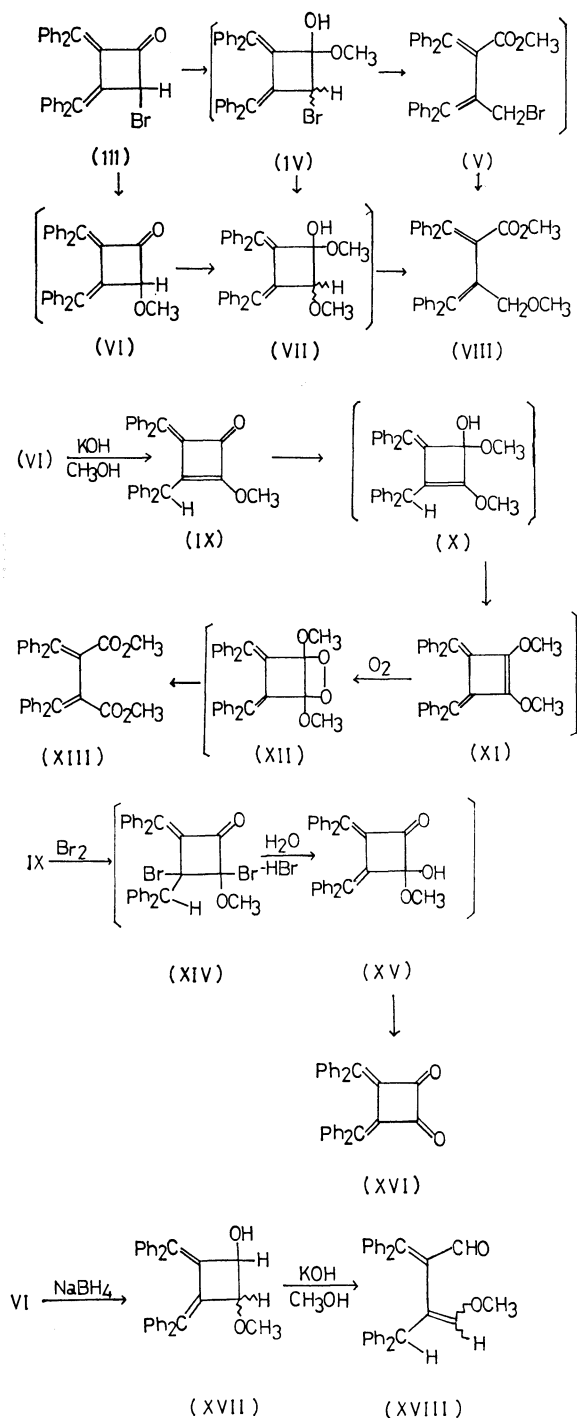
4) J. M. Conia and J. L. Ripoll, *Bull. Soc. Chim. Fr.*, **1963**, 763.

5) L. Ghosez, R. Montarzine, and P. Mollet, *Tetrahedron Lett.*, **1966**, 135.

6) T. R. Patts and R. E. Harmon, *J. Org. Chem.*, **34**, 2792 (1970).

In connection with these facts, we are interested in the reaction of 2-bromo- (III) and 2,2-dibromo-3,4-bis(diphenylmethylene)cyclobutanone(XXV) with alcoholic potassium hydroxide. The actual products were compounds that were derived by the reaction of both the carbonyl and the bromine of III and XXV with the base. Therefore, of particularly interest to us the determination of the reaction site which the base attacks initially.

The reaction of III¹⁾ with methanolic potassium hydroxide at room temperature for 6 hr afforded VIII in a 93% yield. The structure of VIII was determined



Scheme 1.

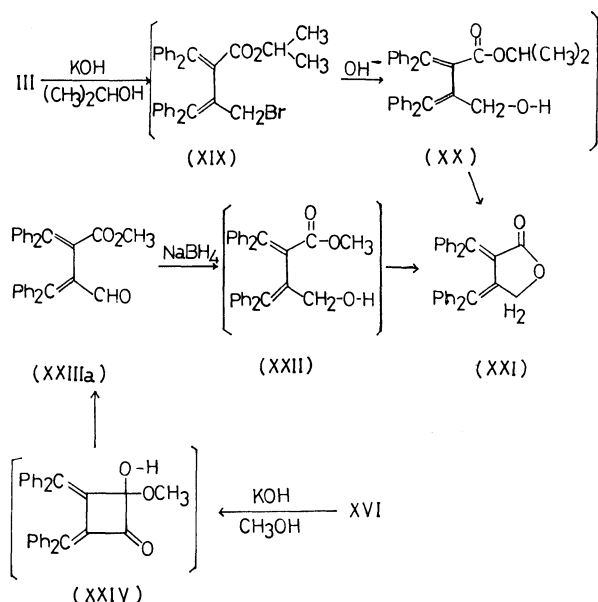
by means of the spectral data described in the Experimental section. For the reaction, the two main paths are considerable, as is shown in Scheme 1. One of them proceeds *via* the VI produced by the substitution. The other one proceeds *via* the IV produced by the addition. However, any possibility of the formation of VI in the reaction is neglected, since the reaction of VI, prepared according to a previously-reported method,¹⁾ with methanolic potassium hydroxide afforded IX and XIII in 30 and 43% yields respectively, but no detectable VIII. The structure of IX was identified by means of the spectral data shown in the Experimental section. The UV spectrum of IX in C₂H₅OH, 293 nm (ϵ , 17600), was comparable to that of the analogous compound, 4-diphenylmethylene-3-diphenylhydroxymethylcyclobut-2-enone in C₂H₅OH, 280 nm (ϵ , 15400).^{1,7)} The structure of IX was further identified by the reaction with bromine in chloroform to afford XVI¹⁾ in a 30% yield. The reaction may proceed *via* XIV and XV, as is shown in Scheme 1. The structure of XIII was identified by a comparison of its spectral data with those of an authentic sample prepared by the reaction of XVI with methanol in the presence of a catalytic amount of bromine.⁸⁾

It was proven that the IX initially produced by the 1,3-hydrogen shift of VI reacts further with sodium methoxide in the presence of oxygen and finally affords XIII, probably *via* X, XI, and XII. When VI was treated with sodium methoxide under nitrogen, IX was obtained in a 65% yield, besides a small amount of XIII (1%). The treatment of IX with the base under oxygen afforded XIII exclusively. It is probable that XI reacts with oxygen and affords XIII, since it has been established that the analogous compound, 3,4-bis(diphenylmethylene)cyclobutene, reacts with oxygen rapidly even in the course of recrystallization and affords 3,4-bis(diphenylmethylene)butanedial.⁹⁾

On the basis of the results obtained above, the reaction path which proceeds *via* IV was established as reasonable. Nevertheless, there is still the problem to be resolved of whether the conversion of IV into VIII proceeds *via* V or VII. The possibility that VII is an intermediate can, however, be ruled out, since XVII, which is analogous to VII, showed a different type of reaction with the base. The reaction of XVII, prepared by the sodium borohydride reduction of VI, with the base afforded the vinyl ether XVIII, but no compound analogous to VIII.¹⁰⁾

The reaction of III with 2-propanolic potassium hydroxide to afford XXI exclusively can also be interpreted by assuming XIX as an intermediate. The hydroxy ester, XX, produced by the reaction of XIX with the hydroxy anion undergoes intramolecular cyclization to XXI. The cyclization of XX to XXI is reasonable, since the sodium borohydride reduction of XXIIIa prepared by the reaction of XVI with

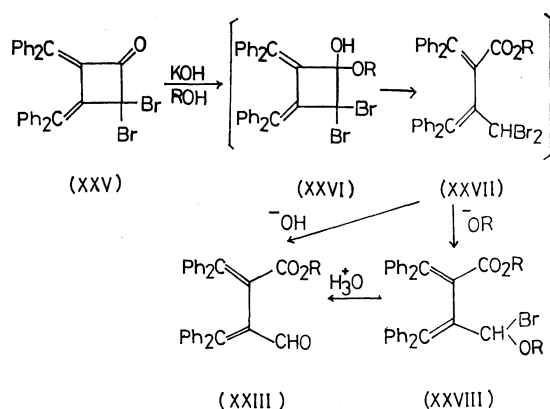
7) F. Toda and K. Akagi, *Tetrahedron Lett.*, **1970**, 5289.8) F. Toda and J. Fujita, *This Bulletin*, **45**, 1928 (1972).9) F. Toda, M. Higashi, and K. Akagi, *Chem. Commun.*, **1969**, 1219.10) F. Toda and N. Ooi, *This Bulletin*, **45**, 1820 (1972).



methanolic potassium hydroxide afforded XXI quantitatively, probably *via* XXII, which is analogous to XX, and since it has been established that the sodium borohydride reduction of γ -keto ester afford γ -lactones.^{11,12)}

Finally, the most reasonable path from III to VIII is that which proceeds successively *via* IV and V. Therefore, the reaction type of III with the base is similar to that of I to afford II.³⁻⁶⁾

The reaction of XXV¹⁾ with methanolic potassium hydroxide at room temperature for 6 hr afforded XXVIIIa and XXIIIa in 48 and 52% yields respectively. The structure of XXVIIIa was identified by means of the spectral data described in the Experimental section.

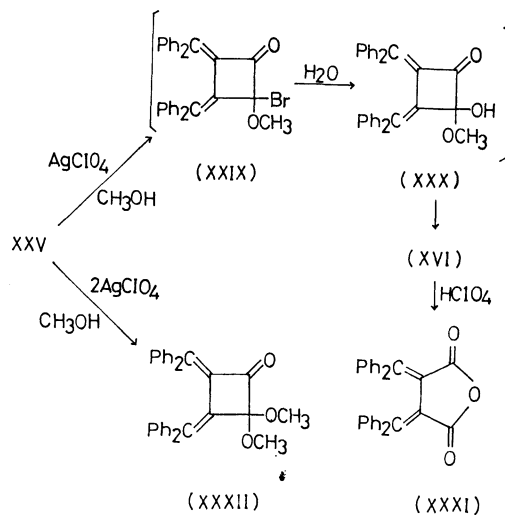


- a : R = CH₃
 b : R = C₆H₅
 c : R = CH(CH₃)₂

Scheme 3.

Under the reaction conditions employed for XXV, XXVIIIa was not converted to XXIIIa, but was recovered unchanged, even though the heating of XXVIIIa with hydrochloric acid in methanol afforded XXIIIa in a 52% yield.

Since XXVIIIa is analogous to the VIII produced by the reaction of III with methanolic potassium hydroxide, a similar reaction mechanism is applicable. As is shown in Scheme 3, the XXVI initially produced by the attack of the methoxy anion on the carbonyl of XXV undergoes ring-opening to afford XXVII. The two competing reactions of XXVII with the methoxy and hydroxy anions afford XXVIII and XXIII respectively. Evidence for the presence of the competing reactions was obtained by the following experiments. When XXV was treated with ethanolic potassium hydroxide, XXVIIIb and XXIIIb were isolated in 15 and 85% yields respectively. However, the same treatment of XXV with 2-propanolic potassium hydroxide afforded XXIIIc exclusively (80% yield). The spectral data of XXVIIIb (Experimental section) were comparable to those of XXVIIIa. The spectral data of XXIIIb and XXIIIc (Experimental section) were also comparable to those of XXIIIa.



The type of the reaction of XXV with the base to afford XXVIII and XXIII *via* XXVII is also similar to that of III and of I. The monomethoxy ketone XXIX, analogous to VI, which was ruled out as a possible intermediate in the reaction of III, is probably not an intermediate for the following reasons. The reaction of XXV with an equimolar amount of silver perchlorate in wet methanol at room temperature afforded XVI and XXXI in 16 and 30% yields respectively. A reasonable reaction path is that shown in Scheme 4, since the reaction of XXV with two molar amounts of silver perchlorate in wet methanol afforded XXXII in a 55% yield, and since the oxidation of XVI into XXXI by perchloric acid has been established.¹⁾ The high reactivity of the bromine of XXIX

11) R. Gelin and M. Chiguac, *C. R. hebdomadaire des Séances Acad. Sci.*, **258**, 3313 (1964).

12) P. de Mayo, E. Y. Spencer, and R. W. White, *Can. J. Chem.*, **41**, 2996 (1963).

13) All the IR and NMR spectra were measured in Nujol mull and CDCl₃ respectively.

in the acidic media suggests that XXIX in methanolic potassium hydroxide affords a halogen-free product instead of XXVIIIa.

Experimental¹³⁾

The Reaction of III with Methanolic Potassium Hydroxide. A suspension of finely-powdered III¹⁾ (0.35 g) in 5% methanolic potassium hydroxide (30 ml) was stirred at room temperature for 6 hr. The crude product obtained by the addition of water to the reaction mixture was collected by filtration, washed with water, and dried. The crude product was recrystallized from cyclohexane to afford VIII as colorless prisms; 0.25 g (93%); mp 152–153°C. IR, 1710 (C=O), 1435 (ester CH₃), 1265 and 1245 (ester) and 1105 cm⁻¹ (C–O–C); UV, (CHCl₃), 234 (26400), 260 sh (16200) and 314 nm (ϵ , 8400); NMR, 2.7–3.2 (m, C₆H₅, 20H), 6.03 (s, CH₂, 2H), 6.53 (s, CO₂CH₃, 3H) and 6.63 τ (s, OCH₃, 3H).

Found: C, 83.38; H, 5.99%. Calcd for C₃₂H₂₈O₃: C, 83.48; H, 6.10%.

The Reaction of VI with Methanolic Potassium Hydroxide. A suspension of finely-powdered VI¹⁾ (0.5 g) in 5% methanolic potassium hydroxide (20 ml) was stirred at room temperature for 20 hr. The yellow crystals which separated out were collected by filtration, washed with methanol, and recrystallized from acetone to afford XIII as yellow needles; 0.24 g (43%); mp 233–234°C (lit.⁸⁾ 233–234°C). The spectral data were identical with those of an authentic sample prepared by a separate method.⁸⁾

The addition of water to the mother liquor remaining after the separation of the crude crystals of XIII by filtration afforded crude crystals. The recrystallization of the crude crystals from cyclohexane afforded IX as colorless prisms; 0.15 g (30%); mp 126–127°C. IR, 1760 (C=O), 1650 (*exo* C=C), 1590 (*endo* C=C), 1290 (=C–O–) and 1080 and 1060 cm⁻¹ (C–O–C); UV (C₂H₅OH), 293 nm (ϵ , 17600); NMR, 2.6–3.2 (m, C₆H₅, 20H), 5.33 (s, CH, 1H) and 5.95 τ (s, CH₃, 3H).

Found: C, 86.27; H, 5.51%. Calcd for C₃₁H₂₄O₂: C, 86.89; H, 5.65%.

When a suspension of VI (0.2 g) in 5% methanolic potassium hydroxide (50 ml) was stirred for 24 hr at room temperature under nitrogen, and when the reaction mixture was then treated as above, 0.13 g (65%) of IX and 2 mg (1%) of XIII were isolated.

The Reaction of IX with Methanolic Potassium Hydroxide under Oxygen. A solution of IX (0.12 g) in 5% methanolic potassium hydroxide (20 ml) was stirred at room temperature under oxygen for 24 hr. The yellow crystals which separated out were collected and recrystallized from acetone to afford XIII as yellow needles; 0.05 g (40%); mp 233–234°C.

The Reaction of IX with Bromide. One drop of bromine was added to a solution of IX (0.05 g) in chloroform (5 ml). The crude product which remained after the evaporation of the solvent was recrystallized from cyclohexane to afford XVI as green needles; 0.015 g (30%); mp 206–207°C (lit.¹⁾ 206–207°C). The spectral data were identical with those reported.¹⁾

The Preparation of XXIIIa. A suspension of XVI¹⁾ (0.4 g) in 5% methanolic potassium hydroxide (20 ml) was heated under reflux for 10 min. The crude product obtained by the addition of water to the reaction mixture was collected by filtration, washed with water, and dried. The recrystallization of the crude product from cyclohexane afforded XXIIIa as pale yellow prisms; 0.35 g (80%); mp 160–

161°C. IR, 2780 (CHO), 1700 (ester C=O), 1660 (aldehyde C=O) and 1265 cm⁻¹ (ester); UV (CH₃OH), 236 (20500), 289 (13700) and 335 nm (ϵ , 7500); NMR, 0.52 (s, CHO, 1H), 2.5–3.1 (m, C₆H₅, 18H), 3.35 (m, C₆H₅, 2H) and 6.50 τ (s, CH₃, 3H).

Found: C, 83.41; H, 5.38%; Mol wt (benzene), 436. Calcd for C₃₁H₂₄O₃: C, 83.76; H, 5.44%. Mol wt, 444.

The Preparation of XXI. To a solution of XXIIIa (0.55 g) in tetrahydrofuran (10 ml), we added an excess of sodium borohydride (0.2 g). The reaction mixture was decomposed with water and extracted with benzene. The benzene solution was washed with water and dried over sodium sulfate. The crude product obtained by the evaporation of the solvent was recrystallized from methanol to afford XXI as yellow prisms; 0.32 g (62%); mp 221–222°C. IR, 1750 (C=O), 1580 (C=C) and 1130 cm⁻¹ (lactone); UV (C₂H₅OH), 258 (22200) and 388 nm (ϵ , 9200); NMR, 2.5–3.6 (m, C₆H₅, 20 H) and 5.02 τ (s, CH₃, 2H).

Found: C, 86.37; H, 5.28%; Mol wt (*m/e*), 414. Calcd for C₃₀H₂₂O₂: C, 86.93; H, 5.35%; Mol wt, 414.

The Reaction of III with 2-propanolic Potassium Hydroxide. A suspension of finely-powdered III (0.5 g) in 5% 2-propanolic potassium hydroxide (50 ml) was stirred at room temperature for 4 hr. The recrystallization of the crude product obtained by the addition of water to the reaction mixture from cyclohexane afforded XXI as yellow prisms; 0.15 g (35%); mp 221–222°C. Its spectral data were identical with those described above.

The Reaction of XXV with Methanolic Potassium Hydroxide. A suspension of finely-powdered XXV (0.58 g) in 5% methanolic potassium hydroxide was stirred at room temperature for 6 hr. The crude product thus formed was collected by filtration, washed with water, and recrystallized from benzene-petroleum ether (bp 70–80°C) to afford XXVIIIa as colorless prisms; 0.28 g (48%); mp 182–183°C. IR, 1720 (C=O), 1240 (ester) and 1090 and 1080 cm⁻¹ (C–O–C); UV (CHCl₃), 272 nm (ϵ , 9100); NMR, 2.6–3.0 (m, C₆H₅, 20H), 3.65 (s, CH, 1H), 6.85 (s, CH₃, 3H) and 7.08 τ (s, CH₃, 3H).

Found: C, 71.34; H, 5.36%; Mol wt (benzene), 525. Calcd for C₃₂H₂₇O₃Br: C, 71.14; H, 5.04%; Mol wt, 539.

The mother liquor remaining after the separation of the crude XXVIIIa by filtration was diluted with water. The crude crystals which separated out were recrystallized from cyclohexane to afford XXIIIa as pale yellow prisms; 0.28 g (52%); mp 160–161°C. Its spectral data were identical with those recorded for an authentic sample prepared from XVI.

The Reaction of XXV with Ethanolic Potassium Hydroxide. When a suspension of XXV (0.46 g) in 5% ethanolic potassium hydroxide (50 ml) was treated by the same procedure employed for the reaction of XXV with methanolic potassium hydroxide, 0.07 g (15%) of XXVIIIb, mp 175–176°C and 0.35 g (85%) of XXIIIb, mp 165–166°C were obtained.

The structure of XXVIIIb was identified by means of the following spectral and analytical data. IR, 1695 (C=O), 1250 (ester) and 1065 cm⁻¹ (C–O–C); UV (CHCl₃), 275 nm (ϵ , 8700); NMR, 2.5–3.2 (m, C₆H₅, 20 H), 3.65 (s, CH, 1H), 6.35 (q, $J=7.5$ Hz, CH₂, 2H), 7.08 (q, $J=7.5$ Hz, CH₂, 2H), 8.93 (t, $J=7.5$ Hz, CH₃, 3H), and 9.25 τ (t, $J=7.5$ Hz, CH₃, 3H).

Found: C, 71.24; H, 5.09%; Mol wt (benzene), 549. Calcd for C₃₄H₃₁O₃Br: C, 71.86; H, 5.49; Mol wt, 567.

The structure of XXIIIb was identified by means of the following spectral and analytical data. IR, 2720 (CHO), 1690 (ester C=O), 1650 (aldehyde C=O) and 1260 cm⁻¹

(ester); UV (C_2H_5OH), 236 (19300), 289 (12100) and 332 sh nm (ϵ , 6700); NMR, 0.94 (s, CHO, 1H), 2.85 (m, C_6H_5 , 18H), 3.40 (m, C_6H_5 , 2H), 6.01 (q, $J=7.5$ Hz, CH_2 , 2H) and 9.15 τ (t, $J=7.5$ Hz, CH_3 , 3H).

Found: C, 84.35; H, 5.62%. Calcd for $C_{32}H_{26}O_3$: C, 83.84; H, 5.68%.

The Reaction of XXV with 2-Propanolic Potassium Hydroxide. A suspension of finely-powdered XXV (0.5 g) in 5% 2-propanolic potassium hydroxide (50 ml) was stirred at room temperature for 6 hr. The crude product formed by the addition of water to the reaction mixture was recrystallized from cyclohexane to afford XXIIIc as pale yellow prisms; 0.3 g (80%); mp 115–116°C. IR, 2720 (CHO), 1685 (ester C=O) 1650 (aldehyde C=O) and 1260 cm^{-1} (ester). The IR spectrum was comparable to those of XXIIIa and XXIIIb.

Found: C, 83.65; H, 5.82%. Calcd for $C_{33}H_{28}O_3$: C, 83.87; H, 5.97%.

The Acid-catalyzed Hydrolysis of XXVIII. A solution of XXVIIIa (0.15 g) in methanol (50 ml) containing five drops of concentrated hydrochloric acid was heated under reflux for 3 hr. The crude product which remained after the evaporation of the solvent to dryness was recrystallized from cyclohexane to afford XXIIIa; 0.064 g (52%).

The same treatment of XXVIIIb (0.21 g) afforded XXIIIb; 0.1 g (60%).

The Reaction of XXV with Methanol in the Presence of Silver Perchlorate. To a solution of XXV (0.6 g) in methanol (5 ml) - tetrahydrofuran (5 ml), we added an equimolar

amount of silver perchlorate (0.2 g). After the removal of the silver bromide formed by filtration, the filtrate was evaporated to dryness. The residue was taken up in ether (100 ml), and the ether solution was washed successively with aqueous sodium chloride and water and dried over sodium sulfate. The evaporation of the solvent afforded a mixture of red and green crystals. After the recrystallization from cyclohexane, this mixture was separated mechanically into components. Each component was further recrystallized from cyclohexane. Red rhombs (0.14 g (30%)) were identified as the anhydride XXXI by a comparison of its spectral data with those recorded for an authentic sample¹¹. Green needles (0.07 g (16%)) were found to be the diketone XVI¹¹ by the same spectroscopic method.

When XXV (0.6 g) was treated with two molar amounts of silver perchlorate (0.4 g) by the same procedure as that employed for the reaction of XXV with an equimolar amount of silver perchlorate, 0.27 g (55%) of XXXII was obtained as the sole product. The structure of XXXII was identified by a comparison of its spectral data with those of an authentic sample prepared according to a previously-reported method.¹¹

The authors wish to express their thanks to Mr. Shoichi Kato for the elemental analyses, to Miss Shizuko Konomi for her measurement of the NMR spectra, and to Miss Sayumi Asakawa for her measurement of the UV spectra.