Methylene Analogs of Cyclobutenedione. VI.[1] Interconversion between 3,4-Dimethylcyclobut-3-ene-1,2-dione and 3,4-Dimethylenecyclobutane-1,2-dione

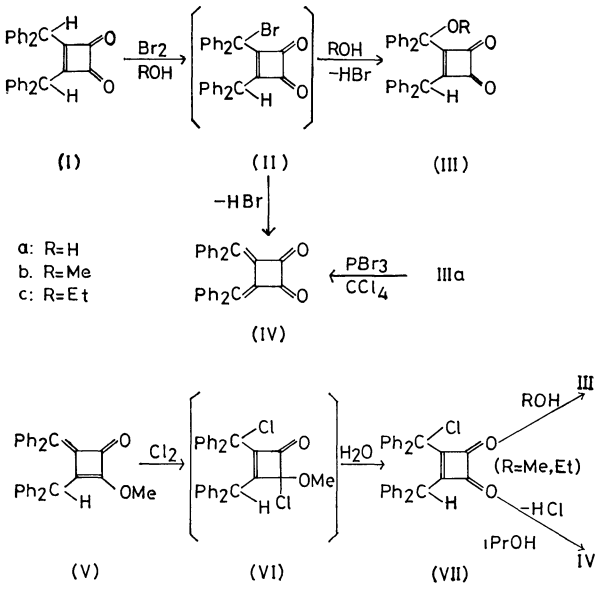
Fumio Toda and Nobuhiro Ooi

Department of Industrial Chemistry, Faculty of Engineering, Ehime University, Matsuyama 790

(Received July 10, 1972)

Treatment of 3,4-bis(diphenylmethyl)cyclobut-3-ene-1,2-dione (I) with bromine in ROH (R=H, Me, Et, and *i*-Pr) afforded 3,4-bis(diphenylmethylene)cyclobutane-1,2-dione (IV) and 3-diphenylmethyl-4-alkoxydiphenylmethylcyclobut-3-ene-1,2-dione (III) in various ratios depending on the steric bulkiness of R of ROH. Acidification of a solution of III in KOH–MeOH, in which III exists in the form of enolate anion (VIII), afforded III and IV in various ratios depending on the steric nature of the substituent R. Bromination of IV in 99% acetic acid afforded 3,4-bis(hydroxydiphenylmethyl)cyclobut-3-ene-1,2-dione (XI). Although the bromination of XI with phosphorus tribromide afforded IV, that with bromine afforded the 2,5-dihydrofuran derivative (XVII). The reaction of I with *o*-phenylenediamine to afford azamethylenecyclobutane derivatives XXV and XXVI is described.

The ring-hydrogen of 3-phenylcyclobut-3-ene-1,2-dione reacts with halogen to afford 4-halo-3-phenylcyclobut-3-ene-1,2-dione.[2-4] However, no reaction of hydrogen on the carbon bound to the cyclobutenedione ring has yet been reported. We have studied the reaction of 3,4-bis(diphenylmethyl)cyclobut-3-ene-1,2-dione (I) with electrophile and found that interconversion between I and 3,4-bis(diphenylmethylene)cyclobutane-1,2-dione (IV) occurs easily.



Scheme 1.

The reaction of I with bromine in 10% aqueous acetonitrile afforded 3-diphenylmethyl-4-hydroxydiphenylmethylcyclobut-3-ene-1,2-dione (IIIa) in a 45% yield. In methanol, 3-diphenylmethyl-4-methoxydiphenylmethylcyclobut-3-ene-1,2-dione (IIIb) was obtained in a 53% yield. On the other hand, the reaction of I with bromine in ethanol afforded 3-diphenylmethyl-4-ethoxydiphenylmethylcyclobut-3-ene-1,2-dione (IIIc) and IV in 39 and 13% yields, respectively, but that in 2-propanol afforded IV as the sole product (47% yield).

The reactions can be interpreted by assuming 3-diphenylmethyl-4-bromodiphenylmethylcyclobut-3-ene-1,2-dione (II) to be an intermediate. It is understandable that substitution of bromine of II with hydroxylic or alkoxylic nucleophile to afford III is in competition with the elimination of hydrogen bromide from II to afford IV (Scheme 1). The intermediacy of II is likely, since the bromination of IIIa with phosphorus tribromide in carbon tetrachloride afforded IV in a 52% yield. In order to confirm the intermediacy of II, preparation of its chloro-analog (VI) was attempted. Bubbling of chlorine through a solution of 2-methoxy-3-diphenylmethyl-4-diphenylmethylenecyclobut-2-en-1-one (V)[5] in ether afforded an oil. This was identified to be 3-diphenylmethyl-4-chlorodiphenylmethylcyclobut-3-ene-1,2-dione (VII) by means of IR and UV spectra, though the oil was too unstable for further purification. The strong IR absorption bands of VII, 1785 (νC=O) and 1640 cm^{-1} (νC=C), are charactaristic of cyclobutenedione derivatives as shown by I, III, and X. A possible reaction mechanism for the formation of VII is the hydrolysis of VI initially produced by the 1,4-addition of chlorine to V, since it has been established that α-halo-α-alkoxycyclobutanone is easily hydrolyzed into cyclobutenedione.[5] The reaction of VII with methanol and ethanol at room temperature afforded IIIb and IIIc in 64 and 59% yields, respectively. The reaction of VII with 2-propanol afforded IV in a 32% yield. It is thus reasonable to assume that II is an intermediate of the reaction of I with ROH in the presence of bromine. The reason for the difference between the reaction of VII with ethanol to afford IIIc and that of I with ethanol in the presence of bromine to afforded IIIc and IV is not clear.

UV spectra of IIIa, IIIb, and IIIc in 5% KOH–MeOH, 324 (18900), 323 (16000), and 323 nm (ε, 4700), respectively, were comparable with the spectrum of I in the same solvent, 330 nm (ε, 21700).[6]

1) Part V: F. Toda and J. Fujita, This Bulletin, **45**, 1928 (1972).

2) M. P. Cava and M. J. Mithchell, "Cyclobutadiene and Related Compounds," Academic Press, New York and London (1967), p. 128.

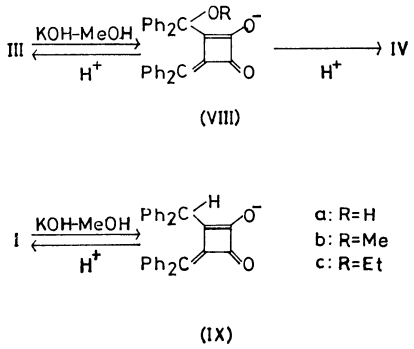
3) E. J. Smutny and J. D. Roberts, *J. Amer. Chem. Soc.*, **77**. 3420 (1955).

4) E. J. Smutny, M. E. Caserio, and J. D. Roberts, *ibid.*, **82**, 1793 (1960).

5) F. Toda and Y. Takehira, This Bulletin, **45**, 1816 (1972).

6) F. Toda and N. Ooi, This Bulletin, **45**, 1820 (1972).

Since it has been established that I dissolved in KOH–MeOH in the form of enolate anion (IX), the enolate form of III is considered to be VIII. The wavelength of the absorption band of VIII is slightly smaller than that of IX. The greater the sterical bulkiness of R in VIII, the smaller the molecular extinction coefficient ε. This suggests that the steric crowding between alkoxydiphenylmethyl and diphenylmethylene moieties increases the transition energy but decreases the probability of the electronic excitation of VIII.

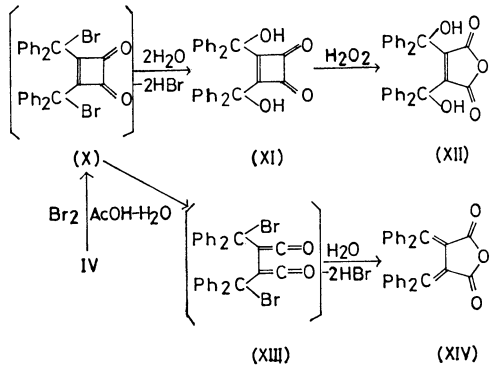


Scheme 2.

Acidification of IX affords I quantitatively,[6] but that of VIII was found to afford III and IV (Table 1). Major products obtained by the acidification of VIIIa and VIIIb were IIIa and IV, respectively. It seems possible that the ketonization of VIII leading to IV is predominant when R is relatively bulky. However, the ketonization of VIIIc afforded IIIc predominantly. A possible interpretation for the anomaly is that the ethoxy and enolate anion groups in IIIc are prevented from being arranged on an effective coplane for elimination.

Table 1. Yields (%) and products obtained by the ketonization of VIII

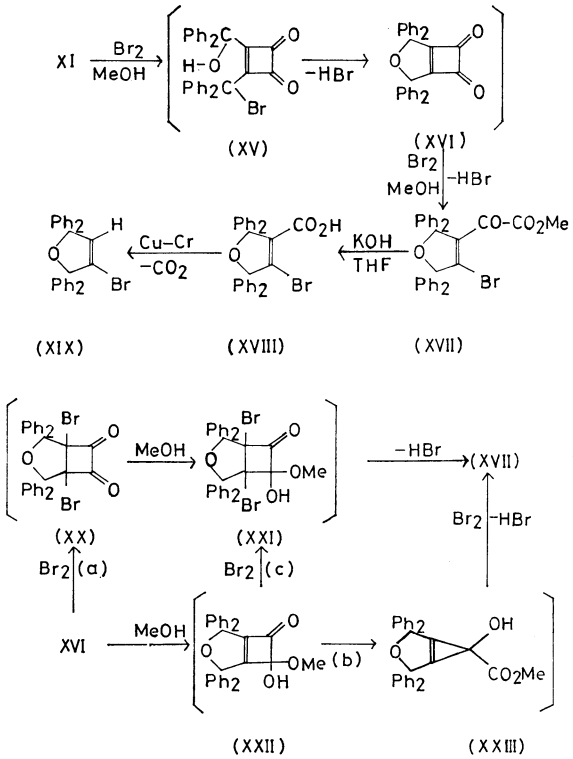
Enolate anion	Products (%)	
VIIIa	IIIa (60)	IV (5)
VIIIb	IIIb (25)	IV (56)
VIIIc	IIIc (83)	IV (8)



Scheme 3.

We reported that the reaction of IV with water in carbon tetrachloride in the presence of bromine affords 3,4-bis(diphenylmethylene)succinic anhydride (XIV) *via* the cyclobutenedione derivative (X) and the bisketene (XIII) successively[1] (Scheme 3). By means of a similar reaction in a protic solvent, one can expect the isolation of a stable cyclobutenedione derivative produced by the substitution of one or two bromines of X with nucleophile, instead of the conversion of X into XIII. The reaction of IV with bromine in 99% acetic acid afforded 3,4-bis(hydroxydiphenylmethyl)cyclobut-3-ene-1,2-dione (XI) and XIV in 55 and 6% yields, respectively. The formation of XI can be explained by the reaction of water and X initially produced by the 1,4-addition of bromine to IV. The production of X as an intermediate is supported by the isolation of XIV, though in a low yield (Scheme 3). The intermediacy of X was also confirmed by the reaction of XI with phosphorus tribromide in carbon tetrachloride to afford IV in a 43% yield. The reaction also gives structural evidence for XI. The structure of XI was further identified by its oxidation with hydrogen peroxide[2] to afford 3,4-bis(hydroxydiphenylmethyl)maleic anhydride (XII).

In order to prepare 3,4-bis(methoxydiphenylmethyl)-cyclobut-3-ene-1,2-dione, XI was made to react with methanol in the presence of bromine. However, 2,2,5,5-tetraphenyl-3-bromo-4-methoxalyl-2,5-dihydrofuran (XVII) was isolated in a 45% yield. The structure of XVII was identified by means of spectral data, and by its conversion into the known compound (XIX). Decarboxylation of 2,2,5,5-tetraphenyl-3-bromo-4-carboxy-2,5-dihydrofuran (XVIII), obtained by base-catalyzed hydrolysis followed by decarbonylation of XVII, afforded 2,2,5,5-tetraphenyl-3-bromo-2,5-dihydrofuran (XIX). The spectral data of XIX were



Scheme 4.

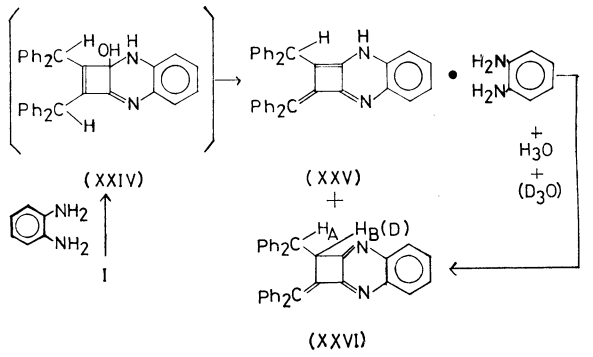
identical with those of an authentic sample.[7]

The reaction mechanism for the production of XVII can be explained by the intramolecular cyclization of XV into XVI followed by ring-opening, as shown in Scheme 4. The formation of the bicyclic intermediate (XVI) would precede the ring-opening of the cyclobutene-dione system, since the cyclobutenedione system was stable under the reaction conditions, as can be seen in the reaction of I with bromine in methanol to afford IIIb predominantly but not ring-opened product. The highly strained cyclobutenedione system of XVI would undergo ring-cleavage even under the acidic conditions of hydrogen bromide generated during the course of reaction, whereas the cyclobutenediones I and III were stable under such conditions (Scheme 2).

For the KOH-catalyzed ring-cleavage of phenylcyclobutenedione to afford benzylidenepyruvic acid, two mechanisms have been postulated, (a) addition-elimination[2,8] and (b) cyclopropenol mechanism.[2,9] However, (a) is unlikely since the addition of bromine to the double bond of cyclobutenedione system does not occur,[3,4] while (b) is also unlikely because of the highly strained nature of the bicyclic cyclopropene intermediate (XXIII). Another mechanism (c) can be applied to the present ring-cleavage of XVI. Since it is the ring-opening of XXI produced by the addition of bromine to XXII it might be considered the most probable mechanism.

Previous attempts to prepare the quinoxaline derivative having a fused cyclobutadiene ring, *i. e.*, 3,8-diazanaphtho[*b*]cyclobutadiene, have failed.[2,3,4,10] The reaction of I with *o*-phenylenediamine was carried out, with the expectation of obtaining the quinoxaline derivative of I. Contrary to expectation, the reaction afforded complex (XXV) and diazatrimethylenecyclobutane derivative (XXVI) in 15 and 17% yields, respectively. Their structures were identified by means of IR, UV, and NMR spectral data. The complex nature of XXV was confirmed by its acid-catalyzed reaction to afford XXVI in a 85% yield. Two protonation sites, β- and δ-carbon, are available for the protonation of dienamine.[11] The protonation on the β-carbon of XXV can afford XXVI. However, that on the δ-carbon of XXV which should produce the quinoxaline derivative of I, was not observed. The NMR spectrum of XXVI showed two AB-type doublets at 4.62 and 5.85 τ. Since the NMR spectrum of XXVI-d prepared by the reaction of XXV with DCl in D_2O showed one methine proton signal at 5.87 τ as a singlet, the structure of XXVI produced by the protonation on the β-carbon of XXV is determined.

The MS spectrum of the complex (XXV) showed the ion peak of each component at *m/e* 486 and 108, in addition to the parent ion peak at *m/e* 594. The



Scheme 5.

fragmentation pattern of the azadimethylenecyclobutene component of XXV was similar to that of XXVI. In both cases, fragment ion peaks, *m/e* 319 (M^+-Ph_2CH), *m/e* 152 (M^+-2Ph_2CH) and an intense peak at *m/e* 167 (Ph_2CH) were observed.

Experimental

All the melting points were uncorrected. IR and NMR spectra were measured in Nujol mull and $CDCl_3$ respectively, unless otherwise stated. Mass spectra were measured with an ionization energy of 70 eV.

Reactions of I with ROH in the Presence of Bromine. *With H_2O*: A solution of I[6] (0.30 g) and bromine (0.66 g) in 10% aqueous acetonitrile (10 ml) was heated under reflux for 3 hr. The cooled reaction mixture was diluted with benzene (100 ml), and washed successively with aqueous sodium thiosulfate and water, and dried over anhydrous sodium sulfate. The crude product remaining after evaporation of benzene was recrystallized from methanol to afford IIIa (0.14 g, 45%) as colorless prisms, mp 140—141 °C. IR: 1780 and 1765 (C=O) and 1570 cm^{-1} (C=C); λ_{max}^{EtOH}: 258 sh (10400), 265 sh (8900), 275 sh nm (ε, 7000); NMR: 2.3—3.1 (m, Ph, 20 H), 4.39 (s, CH, 1H), and 6.80 τ (s, OH, 1H).

Found: C, 83.42; H, 5.08%. Calcd for $C_{30}H_{22}O_3$: C, 83.70; H, 5.15%.

With MeOH: A solution of I (0.30 g) and bromine (0.66 g) in methanol (30 ml) was heated under reflux for 1 hr. The crude crystals remaining after the evaporation of methanol were recrystallized from methanol to afford IIIb (0.17 g, 53%) as colorless needles, mp 127—128 °C. IR: 1775 (C=O) and 1570 cm^{-1} (C=O); λ_{max}^{EtOH}: 259 sh (10500), 265 sh (9200), and 274 sh nm (ε, 7700); NMR (CCl_4): 2.5—3.0 (d, Ph, 20 H), 3.95 (s, CH, 1H), and 6.97 τ (s, OCH_3, 3H).

Found: C, 84.01; H, 5.46%. Calcd for $C_{31}H_{24}O_3$: C, 83.76; H, 5.44%.

With EtOH: A solution of I (0.30 g) and bromine (0.66 g) in ethanol (30 ml) was heated under reflux for 1 hr. Recrystallization from ethanol of the crude product obtained by evaporation of ethanol afforded a mixture of two crystalline forms, colorless and green crystals, which were separated mechanically. Recrystallization of the colorless crystals from ethanol afforded IIIc (0.13 g, 39%), mp 155—156 °C. IR: 1780 (C=O) and 1580 cm^{-1} (C=C); λ_{max}^{EtOH}: 260 sh (10300), 266 sh (9200), and 273 sh nm (ε, 7800); NMR (CCl_4): 2.4—3.1 (m, Ph, 20H), 3.91 (s, CH, 1H), 6.86 (q, J=7 Hz, CH_2, 2H), and 8.76 τ (t, J=7 Hz, CH_3, 3H).

Found: C, 84.09; H, 5.62%. Calcd for $C_{32}H_{26}O_3$: C, 83.82; H, 5.72%.

Recrystallization of the green crystals from acetonitrile

7) H. Tani and F. Toda, This Bulletin, **37**, 470 (1964).
8) A. T. Blomquist and E. A. LaLancette, *J. Amer. Chem. Soc.*, **84**, 220 (1962).
9) L. Skattbøl and J. D. Roberts, *ibid.*, **80**, 4085 (1958).
10) W. Ried and A. H. Schmidt, *Ann.*, **742**, 116 (1970).
11) G. H. Alt, "Enamines: Synthesis, Structure, and Reaction," ed. by A. G. Cook, Marcel Dekker, New York and London (1969), p. 118.

afforded IV (0.04 g, 13%) as green prisms, mp 206—207 °C (lit,[12] mp 206—207 °C).

With i-PrOH: A solution of I (0.30 g) and bromine (0.66 g) in 2-propanol (20 ml) was heated under reflux for 1 hr. The crude crystals separated out by the cooling of the reaction mixture were recrystallized from acetonitrile to afford IV (0.14 g, 47%) as green prisms, mp 206—207 °C.

The Reaction of IIIa with Phosphorus Tribromide. To a solution of IIIa (0.05 g) in carbon tetrachloride (3 ml) was added phosphorus tribromide (0.06 ml) at 0 °C, and the mixture was then stirred at 0 °C for 15 min. The crude product which crystallized out was recrystallized from acetonitrile to afford IV (0.025 g, 52%) as green prisms, mp 206—207 °C.

Synthesis of 3-Chlorodiphenylmethyl-4-diphenylmethylcyclobutene-1,2-dione (VII). Chlorine was bubbled through a solution of V[5] (0.30 g) in ether (20 ml) at room temperature for 5 min. The ethereal solution was washed successively with aqueous sodium thiosulfate and water, and dried over anhydrous sodium sulfate. Evaporation of the solvent afforded VII (0.30 g, 95%) as pale green oil. IR (liquid film): 1785 (C=O) and 1640 cm^{-1} (C=C); λ_{max}^{EtOH}: 243 sh (5700), 259 sh (3700), 266 sh (3300), and 273 sh nm (ε, 2900).

No satisfactory analytical data were obtained since the oil was too unstable for purification.

Reaction of VII with ROH. *With MeOH*: A solution of VII (0.30 g) in methanol (5 ml) was stirred at room temperature for 24 hr. The crude crystals separated out were recrystallized from methanol to afford IIIb (0.19 g, 64%) as colorless needles, mp 127—128 °C.

With EtOH: Treatment of VII (0.30 g) in ethanol (5 ml) by the same method as that employed for the reaction of of VII with methanol afforded IIIc, 0.18 g (59%) as colorless needles, after recrystallization from methanol, mp 155—156 °C.

With i-PrOH: Treatment of VII (0.30 g) in 2-propanol (5 ml) by the same method as that employed for the reaction of VII with methanol afforded IV, 0.09 g (32%) as green prisms, mp 206—207 °C, after recrystallization from acetonitrile.

Ketonization of The Enolate Anion VIII. To a solution of IIIa (0.1 g) in 10% methanolic potassium hydroxide (3 ml), was added concd hydrochloric acid (0.5 ml). The crude product separated out was washed with water. Recrystallization from methanol afforded a mixture of two crystalline forms, colorless needles and green prisms, which were separated mechanically. Recrystallization of the former from methanol afforded IIIa (0.06 g, 60%), mp 140—141 °C, while that of the latter from acetonitrile afforded IV (0.005 g, 5%), mp 206—207 °C.

The same treatment of IIIb and IIIc as that employed for IIIa afforded IV and the corresponding ketonization product (III), respectively, in the yields given in Table 1.

Reaction of IV with Bromine in Aqueous Acetic Acid. A mixture of IV (1.0 g), bromine (2.2 g) and 1% aqueous acetic acid (100 ml) was stirred at 70—75 °C for 1.5 hr. The reaction mixture was concentrated to dryness, and the residue was taken up in benzene (100 ml). The benzene solution was washed successively with aqueous sodium thiosulfate and water, and dried over anhydrous sodium sulfate. After removal of benzene, the residue was recrystallized from methanol to afford a mixture of two crystalline forms, colorless and red rhombs, which were separated mechanically. Recrystallization of the former from methanol afforded XI (0.6 g, 55%), mp 179—180 °C. IR: 3480 and 3360 (OH), 1810 and 1785 (C=O), and 1570 cm^{-1}.

Recrystallization of the latter from ethyl acetate afforded XIV (0.065 g, 6%), mp 230 °C (lit,[12] mp 230 °C).

Reaction of XI with Phosphorus Tribromide. To a solution of XI (0.1 g) in carbon tetrachloride (5 ml) was added phosphorus tribromide (0.12 ml) at 0 °C, and the mixture was then stirred at 0 °C for 15 min. Recrystallization from acetonitrile of the crude crystals which separated out afforded IV (0.04 g, 43%) as green prisms, mp 206—207 °C.

Oxidation of XI with Hydrogen Peroxide. A mixture of XI (0.15 g), 30% aqueous hydrogen peroxide (3 ml), and acetic acid (60 ml) was stirred at room temperature for 3 days. The crude crystals which separated out by the addition of water to the reaction mixture were washed with water. Recrystallization from methanol afforded XII (0.08 g, 51%) as colorless prisms, mp 205—206 °C. IR: 3480 and 3320 (OH), 1835 and 1770 (C=O), and 1590 cm^{-1} (C=C); λ_{max}^{EtOH}: 212 (24500), 255 (6700), and 285 sh nm (ε, 3500); NMR: 2.5—3.0 (m, Ph, 20 H) and 4.80 τ (s, OH, 2H).

Found: C, 78.06; H, 4.69%. Calcd for $C_{30}H_{22}O_5$: C, 77.91; H, 4.80%.

Reaction of IV with Bromine in Methanol. A solution of IV (0.11 g) and bromine (0.22 g) in methanol (10 ml) was heated under reflux for 45 min. The crude crystals formed by cooling the reaction mixture were recrystallized from acetone to afford XVII (0.06 g, 45%) as colorless prisms, mp 190—191 °C. IR: 1740 and 1690 (C=O), 1620 (C=C), 1235 (ester), and 1015 cm^{-1} (ether); $\lambda_{max}^{CHCl_3}$: 266 (8000) and 275 sh nm (ε, 7500); NMR: 2.6—2.9 (m, Ph, 20 H) and 6.20 τ (s, CO_2CH_3, 3H); MS: m/e 538 (M^+).

Found: C, 69.29; H, 4.15%. Calcd for $C_{31}H_{23}O_4Br$: C, 69.01; H, 4.26%.

Hydrolysis and Decarbonylation of XVII. A mixture of XVII (0.22 g), potassium hydroxide (0.42 g), tetrahydrofuran (8 ml) and acetone (7 ml) was heated under reflux for 7 hr. To the residue remaining after evaporation of the solvent of the reaction mixture to dryness was added dil hydrochloric acid and the crystalline solid obtained was washed with water. Recrystallization of the dried crude product from tetrahydrofuran–cyclohexane afforded XVIII (0.12 g, 61%), mp 278—279 °C. IR: 3000—2500 (CO_2H), 1690 (C=O), and 1600 cm^{-1} (C=C); λ_{max}^{EtOH} 238 sh (12400), 258 sh (5200), 264 sh (3500) and 268 sh nm (ε, 2400).

Found: C, 70.35; H, 3.94%. Calcd for $C_{29}H_{21}O_3Br$: C, 70.02; H, 4.22%.

Decarboxylation of XVIII. A mixture of XVIII (0.15 g), quinoline (5 ml), and a catalytic amount of copper chromite was heated under reflux for 4 hr. The cooled reaction mixture was diluted with ether (100 ml), and the ether solution was washed successively with dil hydrochloric acid and water, and dried over anhydrous sodium sulfate. The crude crystals obtained by evaporation of ether were recrystallized from methanol to afford XIX (0.08 g, 59%), mp 175 °C (lit,[7] mp 175 °C).

Reaction of I with o-Phenylenediamine. A mixture of I (1.00 g) and *o*-phenylenediamine (0.26 g) was allowed to remain at 130 °C for 40 min. The crude crystals obtained by the addition of methanol (1 ml) to the cooled reaction mixture were fractionated into two crystalline forms, pale yellow and yellow, by fractional recrystallization from tetrahydrofuran. Recrystallization of the former, relatively insoluble in tetrahydrofuran, from tetrahydrofuran–chloroform afforded XXV (0.22 g, 15%) as pale yellow prisms, mp 204—207 °C. IR: 3300 (NH) and 1610 cm^{-1} (C=N); $\lambda_{max}^{CHCl_3}$: 304 nm (ε, 5800); MS: *m/e* (rel intensity) 594 (4), 486 (23), 319 (9), 236 (18), 167 (100), 152 (8), and 108 (11).

Found: C, 84.75; H, 5.72; N, 9.39%. Calcd for

12) F. Toda and K. Akagi, *Tetrahedron*, **27**, 2801 (1971).

$C_{42}H_{34}N_4$: C, 84.85; H, 5.72; N, 9.43%.

Recrystallization of the latter, relatively soluble in tetrahydrofuran, from acetone afforded XXVI (0.2 g, 17%), mp 172—173 °C. IR: 1640 cm^{-1} (C=N); $\lambda_{max}^{CHCl_3}$: 275 (16800) and 385 nm (ε, 19000); NMR: 1.8—3.1 (m, Ph, 24H), 4.62 (d, J=2.5 Hz, H_B, 1H), and 5.85 τ (d, J=2.5 Hz, H_A, 1H); MS: *m/e* (rel intensity) 486 (34), 319 (10), 167 (100), and 152 (7).

Found: C, 88.67; H, 5.28%. Calcd for $C_{36}H_{26}N_2$: C, 88.86; H, 5.38%.

Reaction of XXV with Hydrochloric Acid. A suspension of XXV (0.1 g) in methanol (5 ml)–concd hydrochloric acid (0.6 ml) was stirred at room temperature for 30 min. The crude product obtained by concentration of the reaction mixture to dryness was suspended in water and then collected by filtration. The recrystallization of the dried crude product from acetone afforded XXVI (0.07 g, 85%), mp 172—173 °C. IR spectral data were identical with those of an authentic sample. Treatment of XXV (0.1 g) in methanol-d (2 ml)–concd deuteriochloric acid (0.6 ml) by the same method as that employed above, afforded XXVI-d (0.07 g, 85%). NMR: 1.8—3.1 (m, Ph, 24H) and 5.87 τ (s, H_A, 1H).