[Chem. Pharm. Bull. 21(1) 25-33 (1973)]

UDC 547.567.04 : 547.313.04

# The Substituent Effect on the Addition Course of the Diels-Alder Reaction of 2-Methyl-5-substituted-1,4-benzoquinones with Butadiene

TAKASHI HARAYAMA, MITSUAKI OHTANI, MASAHARU OKI, and YASUO INUBUSHI

*Faculty of Pharmaceutical Sciences, Kyoto University*[1]

(Received April 22, 1972)

The substituent effect on the addition course of the Diels–Alder reaction of butadiene with 2-methyl-1,4-benzoquinones which carry the cyano (V), dimethylcarbamoyl (VI), $\beta$-ethoxycarbonylethyl (VII), $\beta$-cyanoethyl (VIII), ethoxycarbonyl-*trans*-vinyl (IXa) group at the $C_5$ position, respectively, was examined. The addition of V and VI occurred one-sidedly at the ethylene linkage carrying the electronwithdrawing cyano and dimethylcarbamoyl group. In the compound (VII and VIII), butadiene added at both ethylene linkages giving a mixture of adducts in the ratio of XXXIIa/XXXIIb=2/3 and XXXIIIa/XXXIIIb=1/1, respectively. The reaction of 2-methyl-5-(ethoxycarbonyl-*trans*-vinyl)-1,4-benzoquinone (IXa) with butadiene furnished the adduct (XXXIVa), indicating that the addition occurred at the ethylene linkage bearing the unsaturated ester group.

In connection with the synthesis of serratinine (A),[2] the compounds (B), of which the angular substituent R carries the $C_3$ unit or is capable of extending it to the $C_3$ unit, were required to be synthesized by the Diels–Alder reaction of 2-methyl-5-substituted-1,4-benzoquinones with butadiene. To this end the effect of the substituents at $C_5$ in several 1,4-benzoquinones on the addition course of the Diels–Alder reaction was investigated.

In the Diels–Alder reaction of 1,4-benzoquinones with butadiene, it is known that the addition course of butadiene is affected by the substituent of the benzoquinones.[3] Thus, 2-methyl-5-methoxycarbonyl-1,4-benzoquinone (I) bearing the electronwithdrawing group at $C_5$ reacts with butadiene to give the sole addition product (II) possessing the methoxycarbonyl group at the angluar position.[4] In addition, Fieser, *et al.*[5] reported that the product from the reaction of 2-methyl- (IIIa) or 2-($\gamma$-carboxypropyl)-1,4-benzoquinone (IIIb) with butadiene was almost the type (IV) compound. The present paper deals with the results obtained from the Diels–Alder reaction of butadiene with 2-methyl-1,4-benzoquinones which carry the cyano (V), dimethylcarbamoyl (VI), $\beta$-ethoxycarbonylethyl (VII), $\beta$-cyanoethyl (VIII), and ethoxycarbonyl-*trans*-vinyl group (IXa) at the $C_5$ position, respectively. Further, in order to compare with the result from IXa the reaction of 2-($\beta$-ethoxycarbonyl-*trans*-vinyl)-1,4-benzoquinone (IXb) bearing no methyl group was also examined. Among these compounds, it is anticipated that the addition of butadiene to the compound (V and VI) will occur one-sidedly at the ethylenic linkage carrying the electronwithdrawing CN and $CONMe_2$ group in the similar way as the compound (I) and that butadiene will add to the compound (IXa) with some selectivity at the ethylenic linkage bearing the ethoxycarbonyl-*trans*-vinyl group.

---

[1] Location: *Yoshida-Shimoadachi-cho, Sakyo-ku, Kyoto.*

[2] Y. Inubushi, H. Ishii, B. Yasui, M. Hashimoto, and T. Harayama, *Chem. Pharm. Bull.* (Tokyo), **16**, 82, 92, 101 (1968); K. Nishio, T. Fujiwara, K. Tomita, H. Ishii, Y. Inubushi, and T. Harayama, *Tetrahedron Letters*, **1969**, 861.

[3] L.W. Butz, "Organic Reactions," Vol. 5, 1949, p. 136; A.S. Onishchenko, "Diene Synthesis," Israel Program for Scientic Translations, Jerusalem, 1964; M.F. Ansell, B.W. Nash, and D.A. Wilson, *J. Chem. Soc.*, **1963**, 3012.

[4] W. Nudenberg, A.M. Gaddis, and L.W. Butz, *J. Org. Chem.*, **8**, 500 (1943).

[5] L.F. Fieser, M.D. Gates, and G.W. Kilmer, *J. Am. Chem. Soc.*, **62**, 2966 (1940).

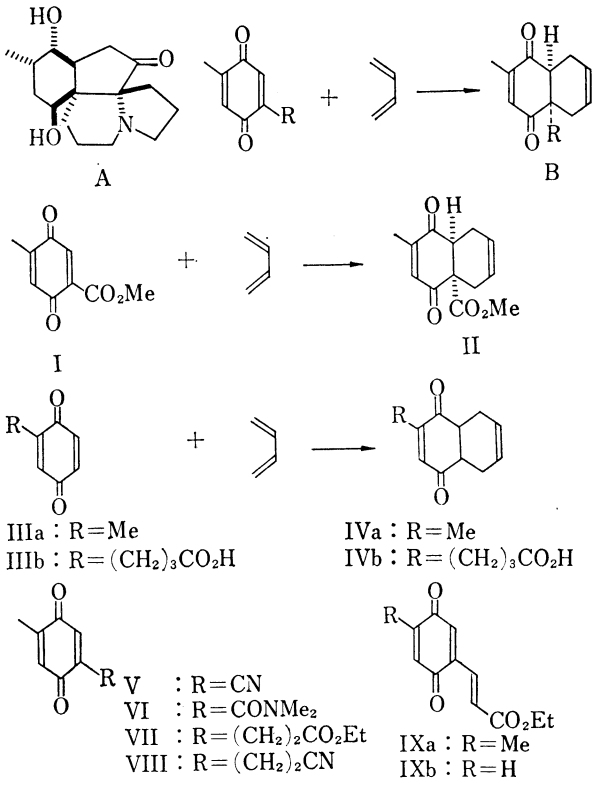

Chart 1

## Preparation of Quinones

### 2-Methyl-5-cyano-1,4-benzoquinone (V)

2-Methyl-5-methoxycarbonyl hydroquinone (Xa) was benzylated with benzyl chloride and $K_2CO_3$ in dimethyl formamide (DMF) to afford the dibenzyl ether (XI), mp 78—79°, in 90% yield. Hydrolysis of XI with alkali gave the carboxylic acid (XII), mp 142—143°, which was treated successively with $SOCl_2$ and ammonia gas to provide the amide (XIV), mp 196—198°, in 90% yield from XI. The cyano dibenzyl ether (XV), mp 131—132°, was obtained by dehydration of XIV with $POCl_3$–pyridine in 93% yield. Hydrogenolysis of XV on Pd-C gave quantitatively 2-methyl-5-cyano-hydroquinone (XVI), mp 244—246°, which was oxidized with $Ag_2O$ to give the quinone (V).

### 2-Methyl-5-dimethylcarbamoyl-1,4-benzoquinone (VI)

Reaction of the acid chloride (XIII) with dimethylamine gas gave the N-dimethyl amide (XVII), mp 146—148°, in 81% yield. Debenzylation of XVII gave the hydroquinone amide (XVIII), mp 165—170°, which was oxidized with $Ag_2O$ to provide the quinone (VI).

### 2-Methyl-5-(β-ethoxycarbonylethyl)-1,4-benzoquinone (VII)

Reduction of XI with LAH gave the primary alcohol (XIX), mp 102—103°, which was oxidized with Collins' reagent[6] to furnish the aldehyde (XX), mp 120°. The Wittig reaction of XX with diethyl carbethoxymethyl phosphonate[7] gave the $\alpha,\beta$-unsaturated ester (XXI), mp 101—103°, in 82% yield from XI. Hydrogenolysis and hydrogenation of XXI afforded the hydroquinone (XXII), mp 79—80°, which was oxidized with $Ag_2O$ to the corresponding quinone (VII).

### 2-Methyl-5-(β-cyanoethyl)-1,4-benzoquinone (VIII)

The Wittig reaction of the aldehyde (XX) with diethyl cyanoethyl phosphonate gave in 98% yield the cyano olefine (XXIII), mp 94—96°, which was hydrogenated to afford 2-methyl-5-(β-cyanoethyl)-1,4-hydroquinone (XXIV), mp 138—139°, in 76% yield. Oxidation of XXIV with $Ag_2O$ gave the quinone (VIII).

### 2-Methyl-5-(2-ethoxycarbonyl-*trans*-vinyl)-1,4-benzoquinone (IXa)

Since all attempts to remove the benzyl groups in XXI with various acids were unsuccessful, the methoxymethyl group was chosen as the phenolic hydroxyl-protecting group

---

[6] J.C. Collins, W.W. Hesse, and F.J. Frank, *Tetrahedron Letters*, **1968**, 3363.

[7] A.K. Bose and R.T. Dahill, Jr, *J. Org. Chem.*, **30**, 5051 (1965); H. Takahashi, K. Fujiwara, and M. Ohta, *Bull. Chem. Soc.*, **35**, 1498 (1962); W.S. Wadsworth, Jr and W.D. Emmons, *J. Am. Chem. Soc.*, **83**, 1733 (1961).

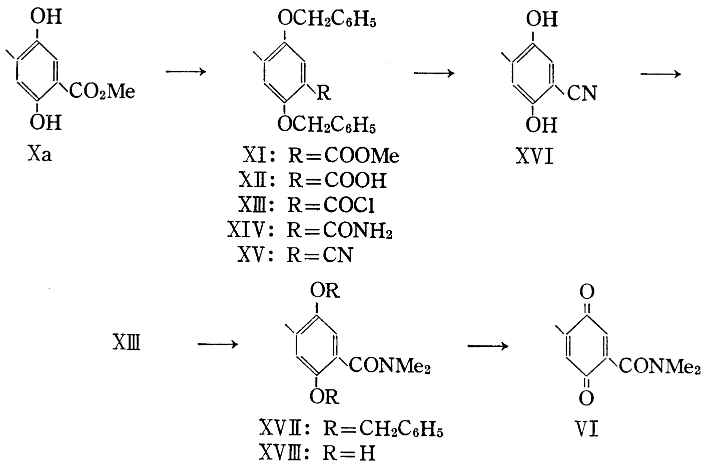

Chart 2

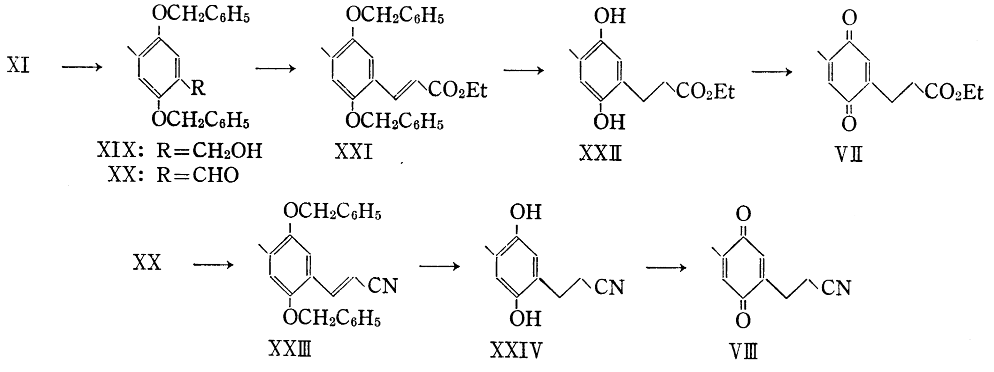

Chart 3

because it is easily cleaved by acids. Thus, treatment of the hydroquinone (Xa) with NaH and $ClCH_2OCH_3$ in DMF gave the methoxymethyl ether (XXVa) which was reduced to the alcohol (XXVIa), mp 74—75°. Oxidation of (XXVIa) with Collins' reagent afforded the aldehyde (XXVIIa), mp 51—52°, which was derived to the $\alpha,\beta$-unsaturated ester (XXVIIIa), mp 62—63°, by the Wittig reaction with $NaNH_2$ and diethyl carbethoxymethyl phosphonate in THF in 86% yield from Xa. The nuclear magnetic resonance (NMR) spectrum of (XXVIIIa) showed signals due to *trans* olefinic protons at 3.57$\tau$ (1H, d, $J$=16 Hz) and 2.00$\tau$ (1H, d, $J$=16 Hz). Treatment of XXVIIIa with HCl gave quantitatively the desired hydroquinone (XXIXa), mp 161—163°, which was converted to the quinone (IXa) by oxidation with $FeCl_3$ in ethanol.

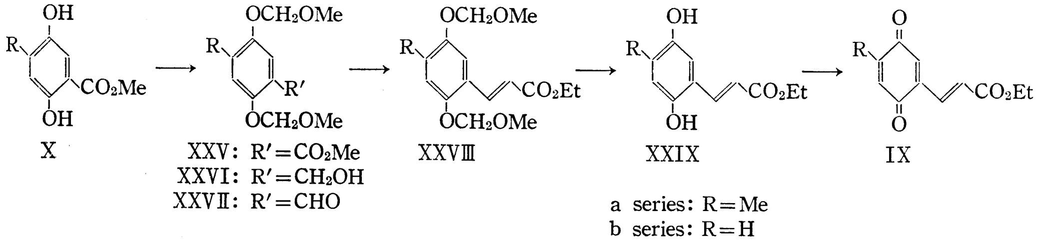

Chart 4

### 2-(ethoxycarbonyl-*trans*-vinyl)-1,4-benzoquinone (IXb)

The compound (IXb) was obtained from 2-methoxycarbonylhydroquinone (Xb) in 55% yield in analogy with the compound (IXa).

## Result and Discussion

All quinones without any purification were subjected to the Diels–Alder reaction with butadiene in dry benzene.

### Reaction of V with Butadiene

Treatment of V with butadiene in a sealed tube at room temperature for two days provided quantitatively the addition product (XXX), mp 85—88°. Its nuclear magnetic resonance (NMR) spectrum exhibited signals due to a vinyl methyl at 7.92$\tau$ (d, $J$=1.5 Hz) and one olefinic proton at 3.35 $\tau$ (q, $J$=1.5 Hz). These spectral data reveal that the addition of butadiene occurred one-sidedly to the ethylene linkage bearing the cyano group.

### Reaction of VI with Butadiene

Heating of VI with butadiene in a sealed tube at 90° afforded quantitatively the adduct (XXXI) whose NMR spectrum showed signals attributable to a vinyl methyl at 8.00 $\tau$ (d, $J$=1.5 Hz) and one olefinic proton at 3.50 $\tau$ (q, $J$=1.5 Hz). From this observation the structure of the adduct can be represented by the formula (XXXI), suggesting that the addition of butadiene occurred at the ethylenic linkage carrying the amide group. Under the same reaction condition as that employed in V, a part of the starting material (VI) was recovered unchanged. This fact shows that the dimethylcarbamoyl group causes a decrease in reactivity compared with the cyano group.

### Reaction of VII with Butadiene

Heating of VII with butadiene in a sealed tube at 100° for 20 hr afforded quantitatively two kinds of adducts which showed one spot on thin-layer chromatography (TLC). In the NMR spectrum, the following signals were observed; 8.70 $\tau$ (s, tertiary methyl) and 8.00 $\tau$ (d, $J$=1.5 Hz, vinyl methyl). This fact reveals that the adduct is a mixture of XXXIIa and XXXIIb in the ratio of 2/3. Thus, addition of butadiene in this case occurred in two directions.

### Reaction of VIII with Butadiene

Similarly, heating of VIII with butadiene in a sealed tube at 120° for 20 hr gave quantitatively the adduct (XXXIII), the NMR spectrum of which exhibited a singlet attributable to a tertiary methyl at 8.65 $\tau$ and a doublet ($J$=1.5 Hz) due to a vinyl methyl at 7.98 $\tau$. This fact reveals that the adduct is a mixture of XXXIIIa and XXXIIIb in the ratio of 1:1.

### Reaction of (IXa) with Butadiene

The adduct (XXXIVa), mp 114—115°, was obtained from IXa and butadiene by allowing a reaction mixture to stand overnight at room temperature in 39% yield. Its NMR spectrum showed signals due to a vinyl methyl at 8.00 $\tau$ (3H, d, $J$=1.5 Hz) and *trans* olefinic protons at 4.15 $\tau$ (1H, d, $J$=16 Hz) and 3.05 $\tau$ (1H, d, $J$=16 Hz). This observation indicates the one-sided addition of butadiene to an ethylene linkage carrying the $\alpha,\beta$-unsaturated ester group in IXa. Chromatography of the mother liquor from the filtration of the crystalline (XXXIVa) gave a small amount of a yellow substance (XXXV), $M^+$ 270, mp 90—93°, which revealed an ester carbonyl band at 1725 cm$^{-1}$ and a ketonic band at 1670 cm$^{-1}$ in the IR spectrum and signals attributable to a vinyl methyl at 7.80 $\tau$ (3H, d, $J$=1.5 Hz), an olefinic proton at 3.12 $\tau$ (1H, q, $J$=1.5 Hz) and two benzene protons at 1.75 $\tau$ (1H, s) and 1.54 $\tau$ (1H, s) in the NMR spectrum. In addition to these signals, the presence of a vinyl group was shown by signals at 4.42 $\tau$ (1H, d.d, $J$=11 Hz, $J$=1 Hz), 4.08 $\tau$ (1H, d.d, $J$=

17 Hz, $J$=1 Hz) and 2.50 $\tau$ (1H, d.d, $J$=11 Hz, $J$=17 Hz). These results permit to assign the naphthoquinone structure (XXXV) for the yellow substance. Hydrogenation of XXXV on Pd-C furnished the dihydro derivative (XXXVI), $M^+$ 272, mp 71—73°, the NMR spectrum of which exhibited signals due to an ethyl group arised from reduction of the vinyl group in XXXV at 8.70 $\tau$ (3H, t, $J$=8 Hz), and 6.90 $\tau$ (2H, q, $J$=8 Hz). These results described above can be rationalized by assuming the reaction mechanism as shown in Chart 5. Thus, addition of one double bond of butadiene as a dienophile to the quinone (IXa), followed by dehydrogenation might give the compound (XXXV). Many spots other than those of XXXIVa and XXXV were observed on TLC but no other material was isolated.

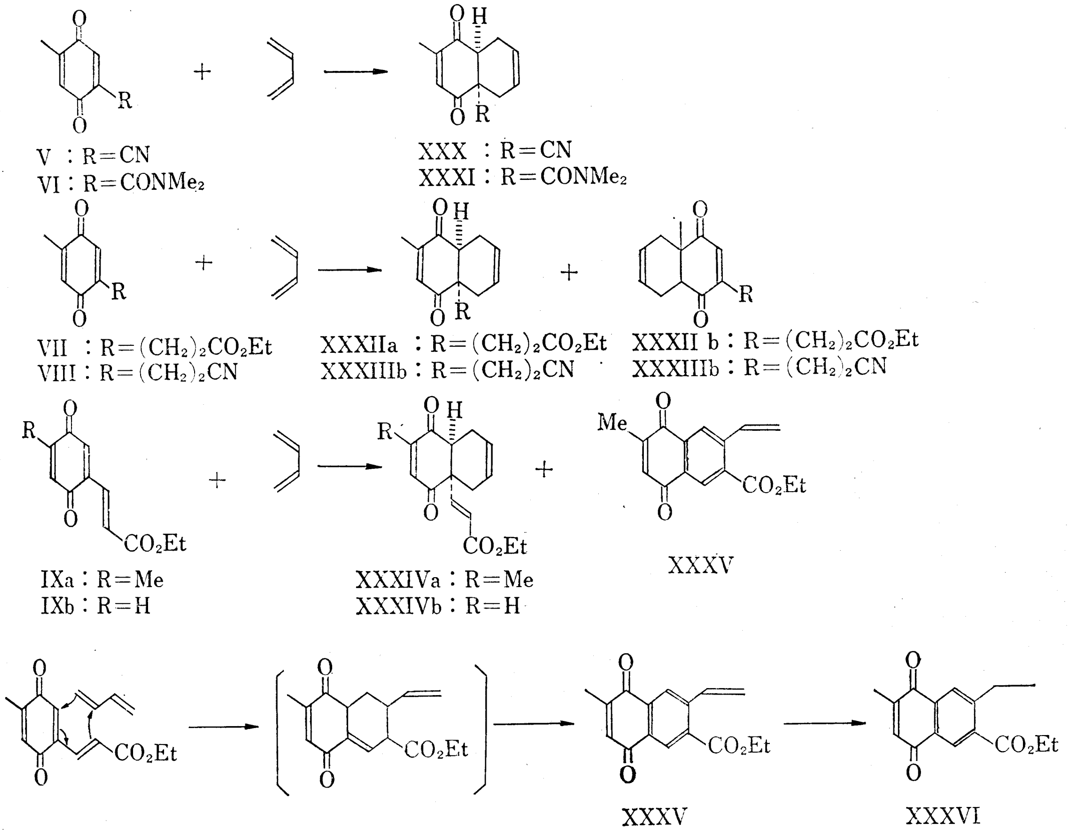

Chart 5

## Reaction of IXb with Butadiene

The adduct (XXXIVb), mp 97—98°, was obtained in 28% yield from IXb in analogy with IXa. Its NMR spectrum showed signals due to an active methine at 6.79 $\tau$ (1H, t, $J$=7.4 Hz) and *trans* olefinic protons at 4.14 $\tau$ (1H, d, $J$=16 Hz) and 3.03 $\tau$ (1H, d, $J$=16 Hz). Consequently, the structure of the adduct should be represented by the formula (XXXIVb), suggesting that butadiene added at the side of the double bond bearing the $\alpha,\beta$-unsaturated ester group in the quinone (IXb).[8]

Summarising the above results, the Diels–Alder addition of butadiene with 2-methyl-1,4-benzoquinones, (VII and VIII), carrying the saturated side chain at $C_5$, occurred at

---

[8] Although TLC of the mother liquor showed the presence of a yellow substance corresponding to the compound (XXXV) but the isolation of this compound was not achieved.

both ethylene linkages giving a mixture of adducts in the ratio of XXXIIa/XXXIIb=2/3 and XXXIIIa/XXXIIIb=1/1, respectively. In 2-methyl-benzoquinones, V and VI bearing the electronwithdrawing substituents at $C_5$, the addition of butadiene occurred one-sidedly at the ethylene linkage carrying these substituents to give quantitatively the adduct, (XXX) and (XXXI), respectively. Further, 2-methyl-1,4-benzoquinone (IXa) with the ethoxycarbonyl-*trans*-vinyl group at $C_5$ furnished the adduct (XXXIVa), indicating that the addition of butadiene occurred at the side of the ethylene linkage carrying the unsaturated ester group, although the yield was low.

## Experimental

All melting points were observed on a microscopic hotstage and uncorrected. All NMR spectra were obtained in $CDCl_3$ solution with tetramethylsilane as an internal standard on a Varian Associate A-60 recording spectrometer and infrared (IR) spectra were measured for solutions in $CHCl_3$ with Hitachi EPI spectrometer unless otherwise noted. Mass spectra were taken with a Hitachi RMU-6C spectrometer with a heated direct inlet system.

**The Dibenzyl Ether (XI)**——To a mixture of 9 g of the hydroquinone (Xa), 10 g of anhydr. $K_2CO_3$ and 20 ml of DMF, 15 g of benzyl chloride was added dropwise under heating with stirring. After 3 hr, the mixture was poured into ice water and extracted with ether. The extract was dried over $MgSO_4$ and evaporated. The residue was recrystallized from petroleum ether to give 16 g of XI as colorless pillars, mp 78—79°. IR $cm^{-1}$: $\nu_{C=O}$ 1710. NMR $\tau$: 2.40—2.75 (11H, m, benzene protons), 3.13 (1H, broad s, benzene proton), 4.90 (2H, s, $-OC\underline{H}_2-$), 4.95 (2H, s, $-OC\underline{H}_2-$), 6.12 (3H, s, $-COOC\underline{H}_3$) and 7.70 (3H, s, toluene Me). *Anal.* Calcd. for $C_{23}H_{22}O_4$: C, 76.22; H, 6.12. Found: C, 76.08; H, 6.00.

**The Carboxylic Acid (XII)**——To a solution of 2.1 g of XI in 20 ml of methanol was added a solution of 3 g of NaOH in 10 ml of water. The reaction mixture was refluxed for 3 hr on a steam bath, cooled, made acidic with 10% HCl and extracted with methylene chloride. The extract was dried over $MgSO_4$ and evaporated to give a crystalline mass. Recrystallization from acetone–ether gave 1.8 g of XII as colorless prisms, mp 142—143°. *Anal.* Calcd. for $C_{20}H_{20}O_4$: C, 75.84; H, 5.79. Found: C, 76.14; H, 5.69.

**The Cyano Dibenzyl Ether (XV)**——The reaction mixture of 3.4 g of the carboxylic acid (XII) in 50 ml of dry benzene and 5 ml of $SOCl_2$ was allowed to stand at room temperature overnight and evaporated to dryness *in vacuo*. Into a solution of the residue (XIII) in 10 ml of dry benzene was blown $NH_3$ gas. The reaction mixture was diluted with water and extracted with $CH_2Cl_2$. The extract was dried over $K_2CO_3$ and evaporated to leave crude crystals which were recrystallized from acetone–$CH_2Cl_2$ to afford 2.7 g of the amide (XIV), mp 196—198°. To a solution of 2.7 g of the amide (XIV) in 10 ml of pyridine was added 4 ml of $POCl_3$ under ice cooling. The mixture was allowed to stand at room temperature for 40 minutes, poured into ice water and extracted with $CH_2Cl_2$. The extract was washed with 5% HCl, dried over $MgSO_4$ and evaporated. The residue was chromatographed on silica gel and elution with $CH_2Cl_2$ afforded 2.4 g of XV which was recrystallized from acetone–ether to give colorless prisms, mp 131—132°. IR $cm^{-1}$: $\nu_{C\equiv N}$ 2230. *Anal.* Calcd. for $C_{22}H_{19}O_2N$: C, 80.22; H, 5.81. Found: C, 80.17; H, 5.94.

**2-Methyl-5-cyano-hydroquinone (XVI)**——To a solution of 2.4 g of XV in 50 ml of AcOEt was added 200 mg of 10% Pd-C. The mixture was stirred under hydrogen at room temperature and atmospheric pressure. After the absorption of hydrogen had ceased, the catalyst was filtered off and the filtrate was evaporated to dryness. The residue was recrystallized from AcOEt to give 1.0 g of XVI as colorless prisms, mp 244—246°. IR $cm^{-1}$: $\nu_{O-H}$ 3300; $\nu_{CN}$ 2250 (Nujol). *Anal.* Calcd. for $C_8H_7O_2N$: C, 64.42; H, 4.73. Found: C, 64.22; H, 4.43.

**The Adduct (XXX)**——To a solution of 400 mg of the hydroquinone (XVI) in 20 ml of dioxane was added 1 g of dry silver oxide and the mixture was stirred at 45° for 20 minutes. After cooling, the solid was filtered off and the filtrate was concentrated into dryness to give 300 mg of the quinone V. A solution of 300 mg of V and 1 g of butadiene in 5 ml of dry benzene was allowed to stand at room temperature for 2 days in a sealed tube. Removal of the solvent gave 0.36 g of the crude adduct (XXX) which was chromatographed on silica gel. The eluate with $CHCl_3$ was recrystallized from ether–petroleum ether to afford (XXX) as colorless prisms, mp 85—88°. IR $cm^{-1}$: $\nu_{CN}$ 2260; $\nu_{C=O}$ 1690; $\nu_{C=C}$ 1670 and 1620. NMR $\tau$ 3.35 (1H, q, $J=1.5$ Hz, olefinic proton), 4.22 (2H, m, olefinic protons) and 7.92 (3H, d, $J=1.5$ Hz, vinyl methyl). *Anal.* Calcd. for $C_{12}H_{11}O_2N$: C, 71.62; H, 5.51. Found: C, 71.80; H, 5.32.

**The N-Dimethylamide (XVII)**——Into a solution of 1.5 g of the acyl chloride (XIII) in 50 ml of dry benzene was bubbled $NHMe_2$ gas. The mixture was allowed to stand at room temperature overnight, diluted with water and extracted with $CH_2Cl_2$. The extract was dried over $MgSO_4$. Removal of the solvent left the crude product, which was recrystallized from acetone to provide 1.27 g of the amide (XVII) as colorless prisms, mp 146—148°. IR $cm^{-1}$: $\nu_{C=O}$ 1630. *Anal.* Calcd. for $C_{24}H_{25}O_3N$: C, 76.77; H, 6.71. Found: C, 76.62; H, 6.61.

**2-Methyl-5-dimethylcarbamoyl-hydroquinone (XVIII)**——A solution of 150 mg of the amide (XVII) in 10 ml of AcOEt was hydrogenolyzed over 100 mg of 10% Pd-C at atmospheric pressure and room temperature until the absorption of hydrogen had ceased. The catalyst was removed by filtration and the filtrate was evaporated to dryness. The residue was crystallized from AcOEt to afford colorless prisms (XVIII), mp 165—170°. IR $cm^{-1}$: $\nu_{O-H}$ 3350; $\nu_{C=O}$ 1610. *Anal.* Calcd. for $C_{10}H_{13}O_2N$: C, 61.52; H, 6.71. Found: C, 61.46; H, 6.71.

**The Adduct (XXXI)**——To a solution of 560 mg of XVIII in 10 ml of dry benzene and 10 ml of dry dioxane were added 1.1 g of $Ag_2O$ and 1 g of $Na_2SO_4$, and the mixture was stirred at 50° for 40 minutes. After cooling, the precipitates were filtered off and the filtrate was concentrated to dryness *in vacuo* to give the quinone (VI). A solution of 470 mg of the quinone (VI) in 6 ml of dry benzene and 2 g of butadiene was heated in a sealed tube at 100° for 6 hr. The solvent was evaporated under reduced pressure to give 570 mg of the oily adduct (XXXI), $M^+$ 247. IR $cm^{-1}$: $\nu_{C=O}$ 1690 and 1640. NMR $\tau$: 3.50 (1H, q, $J=1.5$ Hz, olefinic proton), 4.30 (2H, m, olefinic protons), 7.05 (6H, s, $NMe_2$), 8.00 (3H, d, $J=1.5$ Hz, vinyl methyl).

**The Alcohol (XIX)**——To a solution of 8.4 g of the ester (XI) in 200 ml of dry ether was added 2.5 g of $LiAlH_4$ and the mixture was refluxed for 3 hr. Excess hydride was decomposed with AcOEt, followed by addition of wet ether, and the separated organic layer was dried over $MgSO_4$. Removal of the solvent gave 7.7 g of the crude crystalline mass which was recrystallized from ether and *n*-hexane to afford colorless pillars (XIX), mp 102—103°. IR $cm^{-1}$: $\nu_{O-H}$ 3550. *Anal.* Calcd. for $C_{22}H_{22}O_3$: C, 79.01; H, 6.63. Found: C, 79.02; H, 6.39.

**The Aldehyde (XX)**——To a solution of 7.7 g of the alcohol (XIX) in 600 ml of dry $CH_2Cl_2$ was added 3.5 g of $CrO_3$–2pyridine complex and the mixture was stirred for 4 hr. The brownish solid was filtered off and the filtrate was washed with water, dried over $MgSO_4$ and evaporated *in vacuo*. The residue was chromatographed on silica gel. The eluate with $CH_2Cl_2$ was recrystallized from ether to give 7.15 g of the aldehyde (XX) as pale yellow pillars, mp 120°. IR $cm^{-1}$: $\nu_{C-H}$ 2750; $\nu_{C=O}$ 1670. *Anal.* Calcd. for $C_{22}H_{20}O_3$: C, 79.49; H, 6.06. Found C, 79.53; H, 6.20.

**The $\alpha,\beta$-Unsaturated Ester (XXI)**——To a stirred suspension of 400 mg of $NaNH_2$ in 10 ml of dry THF was added dropwise a solution of 2.5 g of diethyl carbethoxymethyl phosphonate in 10 ml of dry THF under ice cooling. Then, the solution was stirred at room temperature under a slow stream of nitrogen to sweep out the evolved ammonia. To the solution was added dropwise 3 g of the aldehyde (XX) in 10 ml of dry THF with stirring at 0—5°. After 1 hr, the reaction mixture was diluted with water and extracted with ether. After drying over $MgSO_4$, the solvent was evaporated. Recrystallization of the residue from ether–*n*-hexane gave 3.2 g of the $\alpha,\beta$-unsaturated ester (XXI) as colorless flakes, mp 101—103°. IR $cm^{-1}$: $\nu_{C=O}$ 1700; $\nu_{C=C}$ 1630. NMR $\tau$: 1.95 (1H, d, $J=16$ Hz, olefinic proton), 3.58 (1H, d, $J=16$ Hz, olefinic proton), 5.75 (2H, q, $J=7$ Hz, $-O-C\underline{H}_2-CH_3$), 8.70 (3H, t, $J=7$ Hz, $-CH_2-C\underline{H}_3$).

**2-Methyl-5-($\beta$-ethoxycarbonylethyl)-hydroquinone (XXII)**——To a solution of 200 mg of XXI in 15 ml of AcOEt were added 100 mg of 10% Pd-C and a drop of 5% HCl. The mixture was stirred under hydrogen at room temperature and atmospheric pressure until the absorption of hydrogen had ceased. After removal of the catalyst by filtration, the filtrate was evaporated to leave 110 mg of the hydroquinone (XXII) which was recrystallized from ether–petroleum ether to afford colorless prisms, mp 79—80°. IR $cm^{-1}$: $\nu_{O-H}$ 3600; 3400, $\nu_{C=O}$ 1715. *Anal.* Calcd. for $C_{12}H_{16}O_4$: C, 64.27; H, 7.19. Found: C, 64.07; H, 7.46.

**The Adduct (XXXII)**——To a solution of 100 mg of XXII in 20 ml of dry benzene were added 250 mg of dry $Ag_2O$ and 200 mg of $Na_2SO_4$. The mixture was stirred at room temperature for 1 hr and the precipitates were filtered off. The filtrate was evaporated to leave 90 mg of the yellow oily quinone (VII) which was dissolved in 5 ml of dry benzene. To this solution was added 2 g of butadiene and the mixture was heated at 100° in a sealed tube for 20 hr. The solvent was evaporated to give 110 mg of the oily adducts which were the mixture of XXXIIa and XXXIIb in the ratio of 2: 3. IR $cm^{-1}$: $\nu_{C=O}$ 1730, 1680; $\nu_{C=C}$ 1625. NMR $\tau$: 3.55 (olefinic proton), 8.00 (vinyl methyl), 8.70 (tetirary methyl). *Anal.* Calcd. for $C_{16}H_{20}O_4$: C, 69.54; H, 7.30. Found: C, 69.54; H, 7.28.

**The Cyano Olefine (XXIII)**——To a suspension of 480 mg of $NaNH_2$ in 20 ml of dry THF was added dropwise a solution of 2.1 g of diethyl cyanomethyl phosphonate in 10 ml of dry THF with stirring under ice cooling. The solution was then stirred at room temperature under a slow stream of nitrogen to sweep out the evolved ammonia. Into the reaction mixture, a solution of 2 g of the aldehyde (XX) in 30 ml of dry THF was added dropwise at room temperature. After 30 minutes, the reaction mixture was diluted with water and extracted with ether. The extract was dried over $MgSO_4$ and evaporated. The residue was recrystallized from ether–petroleum ether to afford 2.1 g of the cyano olefine (XXIII), mp 94—96°, as colorless needles. IR $cm^{-1}$: $\nu_{CN}$ 2230. NMR $\tau$: 2.40 (1H, d, $J=16$ Hz, olefinic proton), 2.62 (10H, s., benzene protons), 3.15 (2H, s, benzene protons), 4.11 (1H, d, $J=16$ Hz, olefinic proton), 4.94, 4.96 (each 2H, s, $-OC\underline{H}_2-$) and 7.70 (3H, s, toluene methyl). *Anal.* Calcd. for $C_{21}H_{21}O_2N$: C, 81.10; H, 5.96. Found: C, 81.17; H, 5.75.

**The Adducts (XXXIIIa) and (XXXIIIb)**——To a solution of 1.5 g of the cyano olefine (XXIII) in 20 ml of EtOH and a drop of 5% HCl was added 500 mg of 10% Pd-C. Catalytic reduction as usual gave 570 mg of 2-methyl-5-($\beta$-cyanoethyl)-1,4-hydroquinone (XXIV) which was labile but could be recrystallized from ether–petroleum ether to give colorless flakes, mp 138—139°. IR cm$^{-1}$: $\nu_{\text{O-H}}$ 3100; $\nu_{\text{CN}}$ 2240 (Nujol). To a mixture of 340 mg of XXIV, 500 mg of $Na_2SO_4$ and 50 ml of dry ether was added 600 mg of dried $Ag_2O$. The reaction mixture was stirred at room temperature for 1 hr and after the precipitates were removed by filtration, the filtrate was evaporated to provide 300 mg of the crude quinone (VIII). To a solution of 300 mg of the quinone (VIII) in 5 ml of dry benzene was added 1 g of butadiene. The reaction mixture was heated in a sealed tube at 120° for 20 hr. Work-up as usual afforded 380 mg of the oily adduct (XXXIII), M$^+$ 229, which was shown a mixture of XXXIIIa and XXXIIIb by the following spectral data. IR cm$^{-1}$: $\nu_{\text{CN}}$ 2260; $\nu_{\text{C=O}}$ 1680 and $\nu_{\text{C=C}}$ 1620. NMR $\tau$: 3.42 (t, $J=1$ Hz, olefinic proton), 3.50 (q, $J=1.5$ Hz, olefinic proton), 7.98 (d, $J=1.5$ Hz, vinyl methyl), 8.65 (s, tertiary methyl).

**The Alcohol (XXVIa)**——To a suspension of 25 g of NaH (mineral oil free) in 100 ml of DMF was added a solution of 50 g of the hydroquinone (Xa) in 100 ml of DMF with stirring under ice cooling and nitrogen atmosphere. To the reaction mixture was added dropwise 100 g of $ClCH_2OCH_3$ during 30 minutes at 0—5°. After excess hydride was decomposed with wet ether, the mixture was diluted with water and extracted with ether. The ether extract was dried over $MgSO_4$ and evaporated to dryness under reduced pressure to give 75 g of the oily methoxy methyl ether (XXVa). To a solution of 75 g of XXVa in 450 ml of dry ether was carefully added 9 g of $LiAlH_4$. After the end of reaction, excess reagent was decomposed with AcOEt and wet ether. The organic layer was dried over $MgSO_4$ and evaporated. Recrystallization of the residue from ether provided 51 g of the alcohol (XXVIa) as colorless needles, mp 74—75°. IR cm$^{-1}$: $\nu_{\text{O-H}}$ 3450. NMR $\tau$: 2.97 (1H, s, benzene proton), 3.10 (1H, s, benzene proton), 4.85 (4H, s, $2\times O\text{-}C\underline{H}_2\text{-}O$), 5.35 (2H, s, $-C\underline{H}_2\text{-}OH$), 6.52 (6H, s, $2\times OC\underline{H}_3$) and 7.76 (3H, s, toluene methyl).

**The Aldehyde (XXVIIa)**——To a solution of 28 g of the alcohol (XXVIa) in 1.4 l of dry $CH_2Cl_2$ was added 80 g of $CrO_3$-2pyridine complex and the mixture was stirred at room temperature for 2 hr. Further, 30 g of the complex was added and after 2 hr, the solid was filtered off and the $CH_2Cl_2$ solution was washed with water and dried over $MgSO_4$. Removal of the solvent *in vacuo* gave the crude aldehyde which was chromatographed on silica gel. Eluate with $CH_2Cl_2$ was recrystallized from *n*-hexane to provide 26 g of the aldehyde (XXVIIa) as colorless prisms, mp 51—52°. IR cm$^{-1}$: $\nu_{\text{C=O}}$ 1670. *Anal.* Calcd. for $C_{12}H_{16}O_5$: C, 59.99; H, 6.71. Found: C, 59.91; H, 6.87.

**The $\alpha,\beta$-Unsaturated Ester (XXVIIIa)**——To a suspension of 4 g of $NaNH_2$ in 100 ml of dry THF was added dropwise with stirring a solution of 20 g of diethyl carbethoxymethyl phosphonate in 50 ml of dry THF under ice cooling. The solution was then stirred at room temperature under a slow stream of nitrogen to sweep out the evolved ammonia. Into the reaction mixture, a solution of 20 g of the aldehyde (XXVIIa) in 50 ml of dry THF was added dropwise during half an hour at room temperature. The solvent was removed under reduced pressure and then the residue was taken up in water. The aqueous solution was extracted with ether and the extract was dried over $MgSO_4$. Removal of the solvent left 25.5 g of the $\alpha,\beta$-unsaturated ester (XXVIIIa) which was recrystallized from *n*-hexane to give colorless prisms, mp 62—63°. IR cm$^{-1}$: $\nu_{\text{C=O}}$ 1695; $\nu_{\text{C=C}}$ 1630. NMR $\tau$: 2.00 (1H, d, $J=16$ Hz, olefinic proton), 3.57 (1H, d, $J=16$ Hz, olefinic proton), 5.73 (2H, q, $J=7$ Hz, $CO_2C\underline{H}_2CH_3$), and 8.66 (3H, t, $J=7$ Hz, $CO_2CH_2\text{-}C\underline{H}_3$). *Anal.* Calcd. for $C_{16}H_{22}O_6$: C, 61.92; H, 7.15. Found: C, 61.82; H, 7.34.

**2-Methyl-5-(2-ethoxycarbonyl-*trans*-vinyl)-1,4-hydroquinone (XXIXa)**——A solution of 50 g of the ether (XXVIIIa) in 150 ml of 99% EtOH and five drops of conc. HCl was refluxed for 4 hr under nitrogen. After cooling, the mixture was diluted with a large amount of water and extracted with ether. The ether extract was dried over $MgSO_4$ and evaporated to leave 35 g of the crystalline mass which was recrystallized from ether–benzene to afford pale yellow needles, mp 161—163°. IR cm$^{-1}$: $\nu_{\text{O-H}}$ 3350; $\nu_{\text{C=O}}$ 1690; $\nu_{\text{C=C}}$ 1620 (Nujol). *Anal.* Calcd. for $C_{12}H_{14}O_4$: C, 64.85; H, 6.35. Found: C, 64.61; H, 6.34.

**The Adducts (XXXIVa) and (XXXV)**——To a stirred solution of 50 g of the hydroquinone (XXIXa) in 250 ml of 99% EtOH was added dropwise a solution of 350 g of $FeCl_3$ in 250 ml of 99% EtOH under ice cooling. After 1.5 hr, ether was added and the ether solution was washed with water several times, dried over $MgSO_4$ and evaporated to give 48 g of the crude quinone (IXa). To a solution of 48 g of the quinone (IXa) in 50 ml of dry benzene was added 32 g of butadiene. The mixture was stirred in an autoclave at room temperature overnight and the solvent was evaporated under reduced pressure. When triturated with ether, the residue gave 24 g of the crystalline mass which was recrystallized from ether to provide colorless prisms (XXXIVa), mp 114—115°. IR cm$^{-1}$: $\nu_{\text{C=O}}$ 1710, 1680; $\nu_{\text{C=C}}$ 1640, 1620. NMR $\tau$: 3.05 (1H, d, $J=16$ Hz, olefinic proton), 3.47 (1H, q, $J=1.5$ Hz, olefinic proton), 4.15 (1H, d, $J=16$ Hz, olefinic proton), 4.30 (2H, m, olefinic protons), 5.80 (2H, q, $J=7$ Hz, $-OC\underline{H}_2CH_3$), 6.81 (1H, t, $J=6.5$ Hz, active methine), 8.00 (3H, d, $J=1.5$ Hz, vinyl methyl) and 8.72 (3H, t, $J=7$ Hz $CH_2C\underline{H}_3$). *Anal.* Calcd. for $C_{16}H_{18}O_4$: C, 70.05; H, 6.61. Found: C, 70.32; H, 6.65. The mother liquor was chromatographed on silica gel and elution with *n*-hexane–benzene (2:1) gave 400 ml of the yellow crystalline mass which was recrystallized from petroleum ether to furnish the naphtoquinone derivative (XXXV), mp 90—93°, M$^+$ 270. IR cm$^{-1}$: $\nu_{\text{C=O}}$ 1725, 1670; $\nu_{\text{C=C}}$ 1630, 1605. NMR $\tau$: 1.54 (1H, s, benzene proton), 1.75 (1H, s, benzene proton), 2.50 (1H, d.d, $J_1=11$ Hz, $J_2=17$ Hz, olefinic proton), 3.12 (1H, q, $J=1.5$ Hz, olefinic proton), 4.08 (1H, d.d, $J_2=17$ Hz, $J_3=1$ Hz, olefinic proton), 4.42 (1H, d.d, $J_1=11$ Hz, $J_3=1$ Hz, olefinic proton), 5.56 (2H, q, $J=7$ Hz, $OC\underline{H}_2CH_3$), 7.80 (3H, d, $J=1.5$ Hz, vinyl methyl), 8.56 (3H, t, $J=7$ Hz, $OCH_2C\underline{H}_3$).

**Hydrogenation of XXV**——A solution of 80 mg of XXXV in 5 ml of AcOEt was hydrogenated over 30 mg of 10% Pd-C. After the usual work up, recrystallization of the residue from petroleum ether gave yellow prisms (XXXVI), mp 71—73°, $M^+$ 272. IR $cm^{-1}$: $\nu_{C=O}$ 1720, 1670, $\nu_{C=C}$ 1630. NMR $\tau$: 1.55 (1H, s, benzene proton), 2.00 (1H, s, benzene proton), 3.13 (1H, q, $J=1.5$ Hz, olefinic proton), 5.56 (2H, q, $J=7$ Hz, $OC\underline{H}_2CH_3$), 6.90 (2H, q, $J=8$ Hz, $C\underline{H}_2CH_3$) 7.80 (3H, d, $J=1.5$ Hz, vinyl methyl), 8.56 (3H, t, $J=7$ Hz, $OCH_2C\underline{H}_3$) and 8.70 (3H, t., $J=8$ Hz, $CH_2C\underline{H}_3$).

**The Alcohol (XXVIb)**——A solution of 4.2 g of (Xb) in 10 ml of DMF was added to the stirred mixture of 1.8 g of NaH (mineral oil free) in 15 ml of DMF under ice cooling and nitrogen. After 30 minutes, 5.3 g of $ClCH_2OCH_3$ was added dropwise to the reaction mixture, and the mixture was further stirred for ten minutes. Excess hydride was decomposed by addition of cold wet ether with caution and a large amount of water was added. The mixture was extracted with ether and the extract was dried over $K_2CO_3$ and evaporated to dryness *in vacuo* to yield 6.3 g of the oily (XXVb). To a solution of 6.3 g of XXVb in 50 ml of dry ether was added 1.5 g of $LiAlH_4$ little by little under cooling. After reaction mixture was refluxed for 4 hr, excess hydride was decomposed with wet ether. Organic layer was separated, dried over $K_2CO_3$ and evaporated. Distillation of the residue gave 5.0 g of the alcohol (XXVIb), bp 151.5—154°/3 mmHg.

**5-(2-Ethoxycarbonyl-*trans*-vinyl)-1,4-hydroquinone (XXIXb)**——To a stirred solution of 60 g of XXVIb in 1.0 l of dry $CH_2Cl_2$ was added portionwise 474 g of $CrO_3$-2 pyridine complex. After 2 hr, the filtrate was washed with water and dried over $K_2CO_3$. The solvent was evaporated *in vacuo*, and the residue was chromatographed on silica gel and elution with $CHCl_3$ gave 50 g of the oily aldehyde (XXVIIb). IR $cm^{-1}$: $\nu_{C=O}$ 1681. To a suspension of 11 g of $NaNH_2$ in 150 ml of dry THF was added with stirring a solution of 61 g of phosphonate in 70 ml of dry THF under ice cooling. Then the solution was stirred at room temperature under a slow stream of nitrogen to sweep out the evolved ammonia. After 4 hr, a solution of 50 g of the aldehyde (XXVIIb) in 100 ml of dry THF was added dropwise during 20 minutes at room temperature. The reaction mixture was diluted with water and extracted with ether. After drying over $MgSO_4$, the solvent was evaporated to leave 65 g of the oily $\alpha,\beta$-unsaturated ester (XXVIIIb). IR $cm^{-1}$: $\nu_{C=O}$ 1701; $\nu_{C=C}$ 1630. NMR $\tau$: 2.00 (1H, d, $J=16$ Hz, olefinic proton), 3.53 (1H, d, $J=16$ Hz, olefinic proton), 5.73 (2H, q, $J=7.2$ Hz, $OC\underline{H}_2CH_3$) and 8.67 (3H, t, $J=7.2$ Hz, $OCH_2C\underline{H}_3$). A solution of 15.8 g of XXVIIIb in 55 ml of 99% EtOH and two droups of conc. HCl was refluxed for 7 hr under nitrogen. After cooling, water was added and the mixture was extracted with ether. The extract was dried over $MgSO_4$ and evaporated to dryness to yield 8.1 g of slightly yellow crystals. Recrystallization from ether gave the hydroquinone (XXIXb) as pale yellow crystals, mp 164—166°. IR $cm^{-1}$: $\nu_{O-H}$ 3318; $\nu_{C=O}$ 1680; $\nu_{C=C}$ 1620 (Nujol). *Anal.* Calcd. for $C_{11}H_{12}O_4$: C, 63.45; H, 5.81. Found: C, 63.27; H, 5.75.

**The Adduct (XXXIVb)**——A solution of 450 g of $FeCl_3$ in 370 ml of 99% EtOH was added to a solution of 31.4 g of XXIXb in 200 ml of 99% EtOH under ice cooling. The mixture was stirred for 5 hr and diluted with ether. The ether layer was washed with water and dried over $MgSO_4$. Removal of the solvent left 29.4 g of the crude quinone (IXb). To a solution of the above quinone in 30 ml of dry benzene was added 30 g of butadiene. The mixture was stirred in an autoclave at room temperature for 24 hr. Removal of the solvent and trituration of the residue with ether gave 10.4 g of the adduct. Recrystallization from ether gave colorless prisms, mp 97—98°. IR $cm^{-1}$: $\nu_{C=O}$ 1710, 1688; $\nu_{C=C}$ 1646. NMR $\tau$: 3.03 (1H, d, $J=16$ Hz, olefinic proton), 3.32 (2H, s, olefinic protons), 4.14 (1H, d, $J=16$ Hz, olefinic proton), 4.25—4.33 (2H, m, olefinic proton), 5.79 (2H, q, $J=7.2$ Hz, $OC\underline{H}_2CH_3$), 6.79 (1H, t, $J=7.4$ Hz, active methine), 8.70 (3H, t, $J=7.2$ Hz, $CH_2C\underline{H}_3$). *Anal.* Calcd. for $C_{15}H_{16}O_4$: C, 69.21; H, 6.20. Found: C, 69.33; H, 6.10.