[Chem. Pharm. Bull. 21(3) 528—537 (1973)]

UDC 547.567.04 : 615.33.011.5

# Synthetic Study of Siccanin, an Antifungal Antibiotic. III.[1] Some Diels-Alder Adducts of 2-Methoxy-5-methoxycarbonylbenzoquinone[2]

Sadao Oida, Yoshihiko Ohashi, and Eiji Ohki

*Central Research Laboratories, Sankyo Co., Ltd.*[3]

(Received August 28, 1972)

The Diels–Alder reaction of 2-methoxy-5-methoxycarbonylbenzoquinone (**6**) with various 1-substituted isoprenes (**5a—d**) was studied and the 8$\beta$-substituted *cis*-tetrahydronapthoquinone-8a$\alpha$-carboxylates (**19a—d**) were obtained and characterized. Some of the latter compounds are important intermediates for synthesis of the A and B rings of siccanin (3), an antifungal antibiotic.

In Part II[1] of this series, we reported that acid-catalyzed cyclization of an 8$\alpha$, 8a$\alpha$-disubstituted *cis*-decalin (**1**) gave a perhydrobenzo[*a*]xanthene (**2**) with a ring juncture of *cis*/*anti*/*cis*. This result made the approach unsuitable for a synthesis of siccanin[4] (**3**), an antifungal antibiotic, with a *cis*/*syn*/*cis* ring juncture. Accordingly, attention was directed to the possibility of a synthesis by stereospecifically constructing an angular substituted *cis*-octalin like **4**. This octalin would have a double bond occupying the 7 position and $\beta$-oriented substituent at the 8 position suitable for attaching the D ring in the later steps of synthesis in order to yield the required *cis*/*syn*/*cis* ring juncture. This paper deals with the development of this alternate approach to siccanin (**3**).

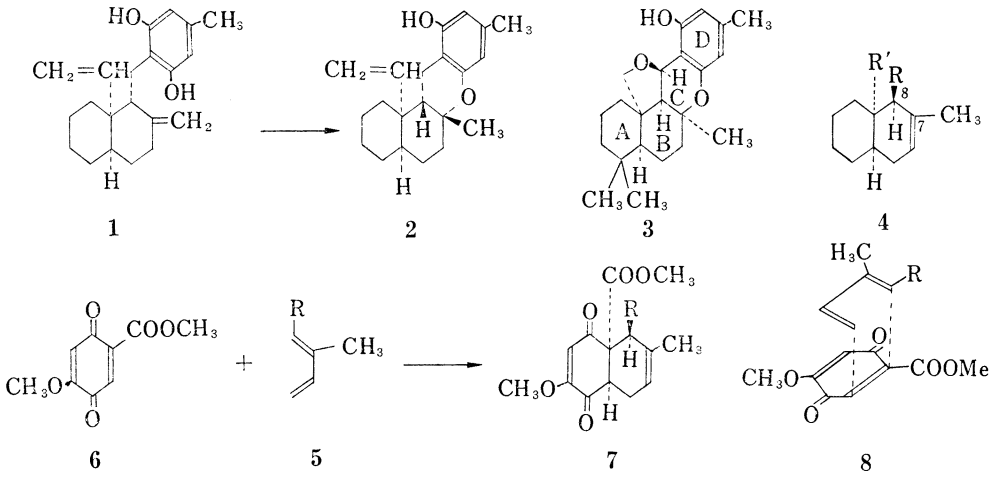


Chart 1

As the first step in synthesizing the *cis*-octalin (**4**), we chose the reaction of some substituted isoprenes (**5**) with 2-methoxy-5-methoxycarbonylbenzoquinone[5] (**6**). Selection of

1) Part II: A. Yoshida, S. Oida, Y. Ohashi, C. Tamura, and E. Ohki, *Chem. Pharm. Bull.* (Tokyo), **20**, 2642 (1972).
2) Presented at the 91st Annual Meeting of the Chemical Society of Japan, April 1971, Tokyo.
3) Location: *Hiromachi, Shinagawa-ku, Tokyo.*
4) K. Ishibashi, K. Hirai, M. Arai, S. Sugawara, A. Endo, A. Yasumura, H. Masuda, and T. Muramatsu, *Ann. Sankyo Res. Lab.*, **22**, 1 (1970) and references cited therein.
5) M.F. Ansell, J.W. Lown, D.W. Turner, and D.A. Wilson, *J. Chem. Soc.*, **1963**, 3036.

the quinone (**6**) was due to the favorable effects of the attached substituents with reference to the preceding work of Ansell, *et al.*[6]: The electron-attracting methoxycarbonyl group will activate one ethene linkage of **6**, while the electron-donating methoxy group will deactivate the other one, encouraging a Diels–Alder reaction of the diene, which forms the adduct (**7**) with an angular carbon substituent. Further, the resultant adduct (**7**) would incorporate all the structural requirements of the 8$\beta$-substituted *cis*-octalin (**4**) because of the well-known stereospecificity of the Diels–Alder reaction. This enabled us to assume that the two rings of the adduct (**7**) would be *cis*-oriented and that the hydrogen atom of the asymmetric center created at the 8 position in this reaction would be on the same side of the molecular plane as the substituents at the points of ring juncture. This is because of the reaction proceeding through an *endo*-transition state (**8**) of the geometrical type which is generally accepted for the Diels–Alder reaction.

The quinone (**6**) was synthesized by a modification of the published procedure,[5] because the reported yields[7] in some stages of preparing 2,5-dihydroxy-4-methoxybenzoic acid were not found to be reproducible. The hydroxy group of 2-methoxy-5-acetylhydroquinone[8] (**9**) was protected with methoxymethyl groups and the resulting ether (**10**) was oxidized with bromine, yielding a benzoic acid derivative (**11**) which had lost one of the protecting groups. Following the method of Ansell, *et al.*[5] acid-catalyzed esterification of **11** gave the hydroquinone (**12**) whose oxidation with silver oxide in benzene gave the quinone (**6**) in good yield.

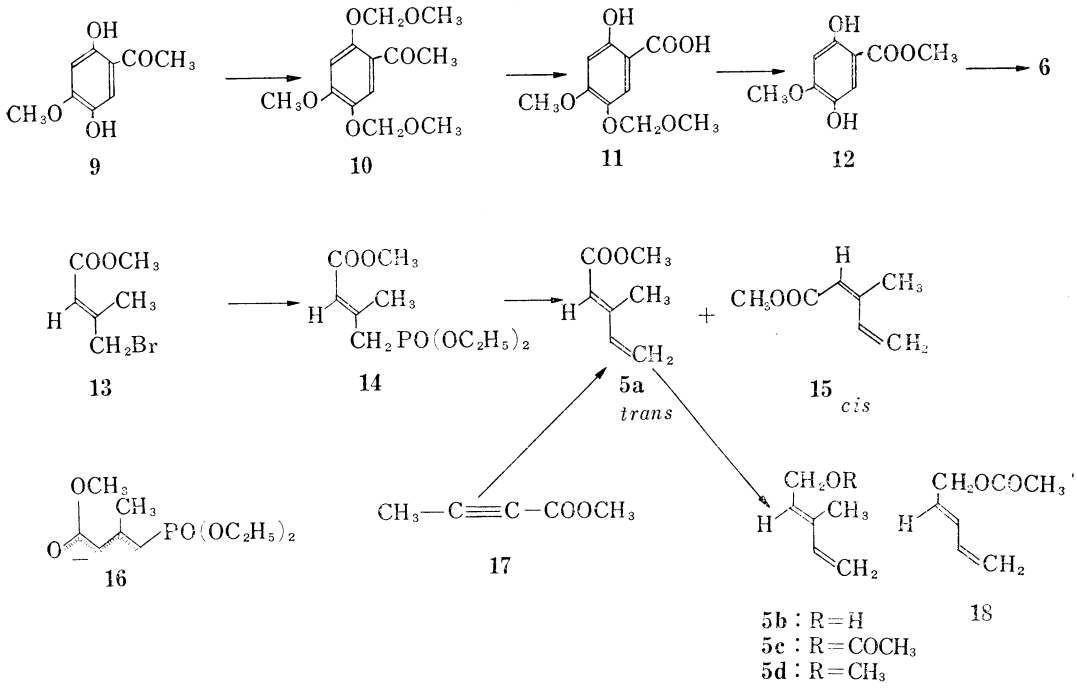



Chart 2

Synthesis of the isoprene derivatives (**5**) to be utilized in the Diels–Alder reaction was carried out in the following way. It was particularly important that the substituents in

6) M.F. Ansell, B.W. Nash, and D.A. Wilson, *J. Chem. Soc.*, **1963**, 3012.
7) P. Yates and G.H. Stout, *J. Am. Chem. Soc.*, **80**, 1691 (1958); S. Rafagopalan, T.R. Seshadri, and S. Varadarajan, *Proc. Indian Acad. Sci.*, **30A**, 265 (1949).
8) E. Hardegger, K. Steiner, E. Widmer, H. Corrodi, Th. Schmidt, H.P. Knoepfel, W. Rider, H.J. Meyer, F. Kugler, and H. Gempeler, *Helv. Chim. Acta*, **47**, 1996 (1964).

the 1 position of these dienes were *trans*-oriented against the 3—4 double bond because of the stereochemical requirement of the adduct (**7**) as mentioned above. First, methyl *trans*-4-bromo-3-methylbut-2-enoate[9] (**13**), prepared from methyl $\beta$-dimethylcrotonate, was treated with triethyl phosphite to give a phosphono compound (**14**), $bp_{0.9}$ 125—127°, in good yield. The Wittig reagent generated by treating **14** with sodium hydride reacted with paraformaldehyde, affording a mixture of *cis* and *trans* dienoates (**15** and **5a**). Based on the reaction sequence, predominant formation of a *trans* dienoate (**5a**) was expected in this reaction, but nuclear magnetic resonance (NMR) spectrum of the reaction product indicated an abundance of a *cis* dienoate (**15**): Ester carbonyl function affects a quartet absorption due to the C-4 vinyl proton in the case of the *cis* dienoate (**15**) and shifts it to a lower field centering at 7.83 ppm than that of the *trans* dienoate (**5a**) at 6.44 ppm. A comparison of these signal areas indicated the ratio of the *cis* and *trans* dienoates as being about 2:1; and this was also supported by the vapor phase chromatography of the reaction product over diethyleneglycol succinate. The predominant formation of the *cis* dienoate (**15**) from the *trans*-substituted starting material (**14**) may be ascribed to a carbanion (**16**) resulting from a reaction of **14** with bases, whose equilibrium may be favorable to the formation of a thermally-stable *cis* dienoate (**15**).[10]

Recently, Siddall, *et al.*[12] reported that the conjugate addition reaction of lithium dialkylcuprate to $\alpha\beta$-acetylenic esters was conducted with a fair stereospecificity at a low temperature, resulting in a predominant formation of a *trans* acrylate by the addition of an alkyl group and a hydrogen across the triple bond in a *cis* manner. Accordingly, we carried out a treatment of methyl tetrolate (**17**) with lithium divinylcuprate[13] at a low temperature. NMR analysis of the resulting dienoate mixture indicated its composition as *cis*:*trans*=1:2 with a predominant formation of the desired *trans* compound (**5a**).[14] An exhaustive purification of **5a** thus obtained was found to be wasteful and **5a** was still contaminated with a fairly large amount of its *cis* isomer (**15**). However, **5a** was good enough to be able to serve as a starting material for the following Diels–Alder reaction, because the reaction rate of the *cis* dienoate (**15**) with the quinone (**6**) is quite low compared to that of the *trans* isomer (**5a**) and **15** would cause no disturbance in the addition reaction of **5a**.[15] Lithium aluminum hydride reduction of **5a** yielded 3-methyl-2,4-pentadienol (**5b**), $bp_{15}$ 75—84°, whose acetylation afforded a dienylacetate (**5c**), $bp_{13}$ 71—76°. On the other hand, **5b** was treated with methyl iodide in the presence of sodium hydride, giving a dienyl methyl ether (**5d**), $bp_{95}$ 75—79°. These diene compounds, still contaminated by the corresponding *cis* isomers, were used in the reaction with the quinone (**6**) as will be described below. Moreover, 2,4-pentadienyl acetate (**18**) easily obtainable by the known method[16] was used in some cases of the preliminary study owing to its availability.

First, the reaction of the quinone (**6**) with methyl *trans*-3-methyl-2,4-pentadienoate (**5a**) was studied. This reaction was conducted smoothly and afforded a 1:1 adduct (**19a**) as an intractable syrup in fair yield. The adduct (**19a**) was found to be unstable, and its purification

9) W.S. Johnson, T. Li, D.J. Faulkner, and S.F. Campbell, *J. Am. Chem. Soc.*, **90**, 6225 (1968).

10) On the other hand, an acid-catalyzed rearrangement of 3-methyl-1,4-pentadien-3-ol reported by Oroshnik[11] yielded a 3-methyl-2,4-pentadienol mixture which was analyzed by NMR spectrometry. Its composition was shown as *cis*: *trans*=9: 1, also indicating a predominant formation of the thermally stable *cis* derivative.

11) W. Oroshnik, *J. Am. Chem. Soc.*, **78**, 2651 (1956).

12) J.B. Siddall, M. Biskup, and J.H. Fried, *J. Am. Chem. Soc.*, **91**, 1853 (1968); Also see J. Klein and R.M. Turbel, *ibid.*, **91**, 6186 (1969); E.J. Corey, and J.A. Katzenellenbogen, *ibid.*, **91**, 1851 (1969).

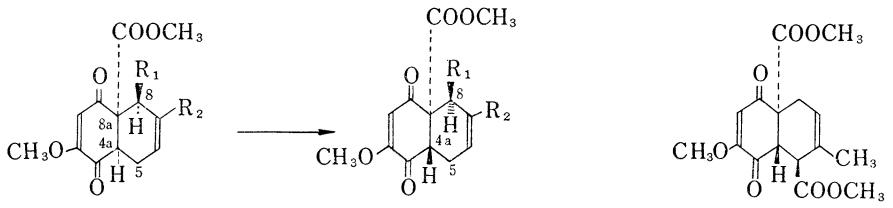
13) G.M. Whitsides, W.F. Fisher, Jr., J.S. Filippo, R. W.Bashe, and H.O. House, *J. Am. Chem. Soc.*, **91**, 4871 (1969).

14) Application of this method with lithium divinylcuprate to $\alpha\beta$-acetylenic esters were independently carried out and announced during this study. See E.J. Corey, C.U. Kim, R.H. K. Chen, and M. Takeda, *J. Am. Chem. Soc.*, **94**, 4395 (1972).

15) J.G. Martin and R.K. Hill, *Chem. Rev.*, **61**, 540 (1961).

16) S. Oida and E. Ohki, *Chem. Pharm. Bull.* (Tokyo), **17**, 1990 (1969).

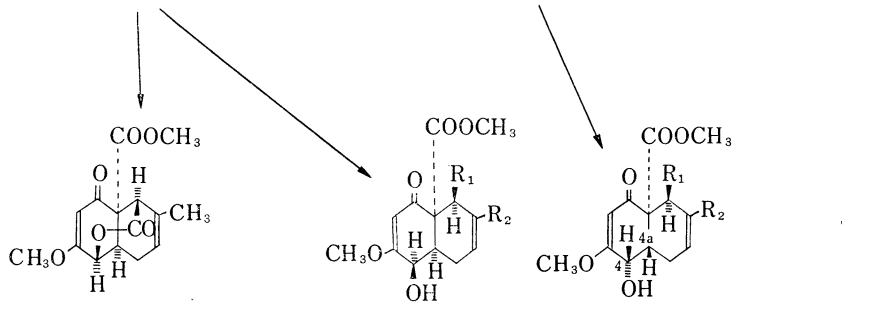
on silica gel made it easily converted into a crystalline isomeric adduct (**20a**), mp 133—134°. These adducts exhibited a characteristic ultraviolet absorption at 271—273 mμ, which was consistent with the published data,[6] due to the presence of a methoxy-substituted conjugated endione system in these molecules. As shown in Table I, the NMR spectrum of the isomerized adduct (**20a**) showed a marked quartet absorption at 4.14 ppm with $J$=7.5 and 8.5 Hz due to a C-4a angular proton. This absorption was indicative of the presence of two protons at the neighboring C-5 carbon atom, suggesting the structure of **20a** as shown in Chart 3 and ruling out the alternate possible formula (**21**). In 1963, Ansell, *et al.*[5] studied an analogous Diels–Alder reaction between several pentadienes and quinones and reported that NMR spectrometry served as a reliable tool for assigning gross structures to the adduct. The above mentioned coupling constants of the quartet absorption in the NMR spectrum of **20a** due to the C-4a proton are consistent with their published data, suggesting that **20a** has a *trans*-4*a*,5,8,8*a*-tetrahydro-1,4-naphthoquinone skeleton as shown in Chart 3. Consequently, the structure of the unstable adduct (**19a**) initially obtained in this reaction would be deduced as a *cis* isomer. Further, sodium borohydride reduction of the *trans* adduct (**20a**) gave a monohydroxy derivative (**22a**), mp 154—155.5°, whose NMR data were illustrated as shown



**19a** : $R_1$=$COOCH_3$, $R_2$=$CH_3$
**19b** : $R_1$=$CH_2OCOCH_3$, $R_2$=H
**19c** : $R_1$=$CH_2OCOCH_3$, $R_2$=$CH_3$
**19d** : $R_1$=$CH_2OCH_3$, $R_2$=$CH_3$

**20a** : $R_1$=$COOCH_3$, $R_2$=$CH_3$
**20b** : $R_1$=$CH_2OCOCH_3$, $R_2$=H
**20c** : $R_1$=$CH_2OCOCH_3$, $R_2$=$CH_3$
**20d** : $R_1$=$CH_2OCH_3$, $R_2$=$CH_3$

**21**



**23**

**24a** : $R_1$=$COOCH_3$, $R_2$=$CH_3$
**24b** : $R_1$=$CH_2OCOCH_3$, $R_2$=H
**24c** : $R_1$=$CH_2OCOCH_3$, $R_2$=$CH_3$
**24d** : $R_1$=$CH_2OCH_3$, $R_2$=$CH_3$

**22a** : $R_1$=$COOCH_3$, $R_2$=$CH_3$
**22b** : $R_1$=$CH_2OCOCH_3$, $R_2$=H
**22d** : $R_1$=$CH_2OCH_3$, $R_2$=$CH_3$

Chart 3

in Table I. It is to be noted that the coupling constant, $J$=5.7 Hz, of the doublet-doublet absorption due to the newly-built C-4 proton would be indicative of its *cis* relation against the neighboring C-4a angular proton. This suggests that the attack of the hydride ion in the reduction of **20a** would be from the unhindered β-side, forming the α-hydroxy derivative (**22a**).[17]

17) This newly-built hydroxyl function in **22a** and **24a** was supposedly associated with the neighboring ester carbonyl group through hydrogen bonds. This was suggested by associated infrared absorptions or by a doublet-split NMR absorption due to these hydroxyl groups.

On the other hand, an analogous reduction of the crude *cis* adduct (**19a**) gave a lactone (**23**), mp 181—182.5°, along with an isomeric monohydroxy derivative (**24a**), mp 113.5—116.5°.[17] The latter compound (**24a**) was easily converted into the lactone (**23**) on treatment with an acid. Similar to the case of **22a**, the NMR spectrum of the isomeric hydroxy compound (**24a**) exhibits a doublet-doublet absorption due to the C-4 proton, whose coupling constant, $J$=5.5 Hz, would also suggest its *cis* relation against the angular C-4a proton. Thus, the newly built hydroxy group of **24a** is supposedly $\beta$-oriented and, further, the facile lactone formation of **24a** into **23** involves an evidence for the 8$\beta$-orientation in the ester side chain in **24a**. These facts imply that the reaction between **5a** and **6** was conducted as postulated above, giving the 8$\beta$-substituted *cis*-tetrahydronaphthoquinone (**19a**).

Next, assuming that the C-8 ester function in the adduct (**19a**) is not distinguishable from that of the C-8a angular ester group in its successive transformation and, in addition, may affect the C-8 configuration to be isomerized with bases, the introduction of some other groups not amenable to isomerization at the 8 position was desired. Consequently, the reaction of the quinone (**6**) with 2,4-pentadienyl acetate (**18**) was tested. This reaction also proceeded under rather mild conditions and gave a *cis* adduct (**19b**) as a syrup which was also easily converted into a *trans* adduct (**20b**), mp 162—166°, on treatment with silica gel. Sodium borohydride reductions of the *cis* and *trans* adducts gave a corresponding monohydroxy derivative (**24b**), mp 170—171.5°, and its isomer (**22b**), mp 139—140°, respectively. These compounds exhibited physical data similar to the series with a 8$\beta$-methoxycarbonyl group as mentioned above: For instance, as shown in Table I, the NMR spectrum of the *trans* adduct (**20b**) showed a charateristic quartet absorption at 3.38 ppm, $J$=9.0 and 7.8 Hz, due to the C-4a angular proton, also suggesting that the acetoxymethyl side chain is attached at the 8 position. Structures of the newly-built hydroxyl groups obtained by the reduction were also designated as shown in Chart 3 by means of NMR analysis (Table I). This suggests that the hydride attack occurred from the corresponding unhindered side.[18]

Next, the reaction between the quinone (**6**) and 3-methyl-2,4-pentadienyl acetate (**5c**) was studied and was found to be more complicated. This reaction itself proceeded smoothly, but gave a fairly large amount of a phenolic isomeric compound, mp 150—156°, which was not identified, along with the requisite *cis* adduct (**19c**). The *cis* adduct (**19c**) was quite unstable on standing and isomerized into the same phenolic compound. Treatment of the *cis* adduct (**19c**) with silica gel also afforded a *trans* adduct (**20c**), mp 153—157°. Sodium borohydride reduction of the crude *cis* adduct (**19c**) yielded an analogous 4$\beta$-hydroxy derivative (**24c**) as crystals of mp 170.5—171.5°. These structures of **20c** and **24c** thus obtained were also assigned on the basis of their NMR data (Table I).

The 8$\beta$-substituted *cis*-tetrahydronaphthoquinone (**19c**) and its derivative (**24c**) thus obtained were expected to be promising starting materials for building up the A and B rings of siccanin (**3**); but it was found that the synthetic route starting with them faced insurmountable obstacles in some steps of the transformations as will be described in our next paper. Therefore we carried out a reaction of the quinone (**6**) with 3-methyl-2,4-pentadienylmethyl ether (**5d**), expecting a formation of a tetrahydronaphthoquinone with a stable side chain. This reaction also proceeded under mild conditions and gave the requisite *cis* adduct (**19d**), mp 120—122°, in 66% yield. Sodium borohydride reduction of **19d** followed by acetylation gave an acetate of a 4$\beta$-hydroxy derivative (**24d**), mp 151.5—153°. On the other hand, treatment of the *cis* adduct (**19d**) with silica gel afforded a *trans* adduct (**20d**), mp 147—152°, whose sodium borohydride reduction afforded a 4$\alpha$-hydroxy compound (**22d**), mp 141—142.5°.

18) Similar to the cases (**22a** and **24a**) suggested earlier in footnote 17, the newly-built hydroxy group of **22b** derived from the *trans* adduct (**20b**) has a hydrogen bond as shown by infrared or NMR spectrometry, while that of **24b** from the *cis* adduct (**19b**) does not. This suggests that the 4$\alpha$-hydroxy group is close to the angular ester carbonyl in the case of **22b**, but not in the case of **24b**. It also gives supplementary support to the structural discussion.

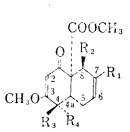
TABLE I. NMR Data of Substituted 1,4,4*a*,5,8,8*a*-Hexahydronaphthalene-8*a*-carboxylates[a)]

| Compound | $R_1$ | $R_2$ | $R_3$ ($\beta$) | $R_4$ ($\alpha$) | 4aH | 2H | $3CH_3O$ | 4H | 4OH |
|---|---|---|---|---|---|---|---|---|---|
| **20a** | $CH_3$ | $COOCH_3$ | CO | | $\beta$ | 5.93 s | 3.85 s | — | — |
| **22a** | $CH_3$ | $COOCH_3$ | H | OH | $\beta$ | 5.45 s | 3.83 s | 4.23 dd (11.2, 5.7)[b)] | 5.19 d (11.2)[c)] |
| **23** | $CH_3$ | CO ——— | O | H | $\alpha$ | 5.36 d (1.4) | 3.80 s | 4.77 dd (2.0, 1.4) | — |
| **24a** | $CH_3$ | $COOCH_3$ | OH | H | $\alpha$ | 5.41 s | 3.67 s | 4.24 dd (10.6, 5.5)[d)] | 4.70 d (10.6)[b)] |
| **20b** | H | $CH_2OCOCH_3$ | CO | | $\beta$ | 5.94 s | 3.67 s | — | — |
| **22b** | H | $CH_2OCOCH_3$ | H | OH | $\beta$ | 5.45 s | 3.83 s | 4.17 dd (11.2, 4.7)[e)] | 5.41 d (11.2) |
| **24b** | H | $CH_2OCOCH_3$ | OH | H | $\alpha$ | 5.35 d (1.2) | 3.78 s | 4.69 dd (4.7, 1.2) | — |
| **20c** | $CH_3$ | $CH_2OCOCH_3$ | CO | | $\beta$ | 5.88 s | 3.83 s | — | — |
| **24c** | $CH_3$ | $CH_2OCOCH_3$ | OH | H | $\alpha$ | 5.36 d (1.2) | 3.76 s | 4.61 dd (5.0, 1.2) | 3.8 br. |
| **20d** | $CH_3$ | $CH_2OCH_3$ | CO | | $\beta$ | 5.92 s | 3.63 s | — | — |
| **22d** | $CH_3$ | $CH_2OCH_3$ | H | OH | $\beta$ | 5.45 s | 3.71 s | 4.13 dd (11.0, 5.0)[f)] | 5.46 d (11.0)[b)] |
| Acetate of **24d** | $CH_3$ | $CH_2OCH_3$ | $OCOCH_3$ | H | $\alpha$ | 5.39 d (1.5) | 3.70 s | 5.89 dd (4.8, 1.5) | — |

| Compound | 4aH | 5H | 6H | $7CH_3$ | 8H | $COOCH_3$ | | Other |
|---|---|---|---|---|---|---|---|---|
| **20a** | 4.14 dd (8.5, 7.5) | 2.5 | 5.58 | 1.86 | 4.16 | 3.67 s 3.75 s | | — |
| **22a** | 3.49 ddd (1.2, 5.7, 5.5) | 2.4 br. | 5.63 m | 1.86 m | 4.18 br. s | 3.72 s 3.69 s | | — |
| **23** | 3.17 m | — | 5.48 m | 1.85 m | 3.49 d (2.0) | 3.77 s | | — |
| **24a** | 3.09 ddd (6.5, 5.5, 4.0) | 2.27br. | 5.72 m | 1.74 m | 4.11 br. | 3.77 s | | — |
| **20b** | 3.38 dd (9.0, 7.8) | 2.5 br. | 5.8 m | — | — | 3.85 s | $-CH_2O-$ | 4.10 dd (11.3, 5.4) 4.42 dd (11.3, 4.5) |
| | | | | | | | $-OCOCH_3$ | 2.01 s |
| **22b** | — | — | 5.82 m | — | — | 3.75 s | $-OCOCH_3$ | 2.02 s |
| **24b** | 3.15 ddd (10.7, 6.0, 4.7) | — | 5.70 br. | — | — | 3.81 s | $-CH_2O-$ $-OCOCH_3$ | 4.54 d (6.6) 2.03 s |
| **20c** | 3.45 dd (9.5, 8.2) | 2.5 m | 5.43 m | 1.77 m | 3.4 br | 3.61 s | $-CH_2O-$ | 4.06 dd (12.0, 3.8) 4.51 dd (12.0, 4.8) |
| | | | | | | | $-OCOCH_3$ | 1.96 s |
| **24c** | 3.11 ddd (9.3, 7.0, 5.0) | 2.2 br. | 5.40 m | 1.81 m | — | 3.79 s | $-CH_2O-$ $-OCOCH_3$ | 4.59 d (6.0) 2.01 s |
| **20d** | — | 2.45 m | 5.52 m | 1.80 m | — | 3.83 s | $-CH_2OCH_3$ | 3.24 s |
| **22d** | 3.01 ddd (11.0, 6.0, 5.0) | — | 5.50 m | 1.79 m | — | 3.81 s | $-CH_2OCH_3$ | 3.23 s |
| Acetate of **24d** | 3.09 ddd (9.8, 7.5, 4.8) | 2.2 m | 5.31 m | 1.77 m | — | 3.79 s | $-CH_2O-$ | 3.72 dd (10.4, 5.5) 3.98 dd (10.4, 6.6) |
| | | | | | | | $-OCH_2OCH_3$ | 3.28 s |

*a*) The spectra were determined on a Varian A-60A spectrometer. The solutions were *ca.* 15% solutions in $CDCl_3$ with 1% TMS ($\delta$ 0.0) added. The $\delta$ values for multiplets or broad absorptions are the centers. Coupling constants are given in parenthesis. By an addition with $D_2O$;

*b*) d(5.7); *c*) disappeared; *d*) d(5.5); *e*) d(4.7); *f*) d(5.0)



As illustrated in Table I, the NMR spectral data of these compounds certified the structures using the same criterion mentioned above.

Further transformation of the 4$\beta$-hydroxy compound (**24d**) thus obtained towards the A and B rings of siccanin (**3**) will be the subject of our subsequent paper.

## Experimental

Melting points are not corrected. Infrared (IR) spectra were determined on a Perkin–Elmer Model 221 or Perkin–Elmer Infracord, ultraviolet (UV) spectra on a Beckman Model DK-2, NMR spectra on a Varian A-60 spectrometer, and mass spectra on a JEOL JMS-OLSG spectrometer. Removal of solvent *in vacuo* was accomplished with a rotating flash evaporator at 20—30 mmHg and usually at 35—50°. Plates for thin-layer chromatograohy (TLC) were prepared with Silica Gel G (E. Merck AG) and visualization of the spots was effected by spraying iodine or a solution of $NH_4VO_3$ in 50% $H_2SO_4$ followed by heating. Columns for ordinary chromatography were prepared with Wako Gel Q-22 or Alumina II—III (E. Merck AG) and for dry column chromatography with Wako Gel C-200. The abbreviations used are as follows: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad; sh, shoulder.

**2,5-Bis(methoxymethyloxy)-4-methoxyacetophenone (10)**——Fifty percent NaH mineral oil suspension (7.68 g) was washed with hexane and dissolved in 80 ml of dimethylsulfoxide by warming at 75° under $N_2$ atmosphere. To an ice-cold, stirred solution of 14.6 g of 2,5-dihydroxy-4-methoxyacetophenone[8] (**9**) in 60 ml of dimethylsulfoxide, half the volume of this NaH solution was added dropwise during a 5 min period and the mixture was stirred for 15 min. Then, 7 g of methoxymethylchloride was added dropwise and the mixture was stirred for 15 min. Successively, the remaining NaH solution was added and, after stirring for 15 min, 7 g of methoxymethylchloride was added. The mixture was further stirred for 1 hr with cooling and then left overnight at room temperature. The reaction mixture obtained was diluted with cold water and extracted twice with ether. The combined ether extracts were washed with dil. aq. NaOH, then with $H_2O$ and dried. Removal of the solvent left 13.6 g of **10** as a syrup. An analytical sample was purified by silica gel column chromatography followed by recrystallization from ether–hexane as prisms, mp 56°. IR $\nu_{max}^{Nujol}$ $cm^{-1}$: 1656, 1604. NMR ($CDCl_3$) $\delta$ ppm: 2.55 (3H, s), 3.46 (3H, s), 3.48 (3H, s), 3.86 (3H, s), 5.10 (2H, s), 5.20 (2H, s), 6.72 (1H, s), 7.53 (1H, s). *Anal.* Calcd. for $C_{13}H_{18}O_6$: C, 57.77; H, 6.71. Found: C, 57.47; H, 6.71.

**2-Hydroxy-4-methoxy-5-methoxymethyloxybenzoic Acid (11)**——A NaOBr solution prepared by adding 34 g of $Br_2$ in 180 ml of 20% aq. NaOH was added dropwise to an ice-cold, stirred solution of 18.3 g of the crude **10** in 250 ml of dioxane. After being stirred for 20 min with cooling, the mixture was stirred at room temperature for 30 min and then was refluxed for 2.5 hr. To the cooled mixture was added a solution of 5 g of $KHSO_4$ and 5 g of NaOH in 150 ml of $H_2O$. The resulting mixture was shaken for 5 min, and extracted twice with ether. The aqueous layer was acidified with dil. HCl and extracted three times with ether. The combined extracts were dried and evaporated *in vacuo*, leaving 14.0 g (91%) of a crystalline mass, mp 142—153°, which was recrystallized from acetone–hexane to give **11** as needles, mp 151—153.5°. IR $\nu_{max}^{Nujol}$ $cm^{-1}$: 2650, 1648, 1625, 1590. NMR ($CDCl_3$) $\delta$ ppm: 3.56 (3H, s), 3.92 (3H, s), 5.18 (2H, s), 6.51 (1H, s), 7.50 (1H, s), 10.0 (2H, br). *Anal.* Calcd. for $C_{10}H_{12}O_6$: C, 52.63; H, 5.30. Found: C, 52.53; H, 5.34.

**Methyl 2,5-Dihydroxy-4-methoxybenzoate (12)**——The crude **11** (mp 142—153°, 12.3 g) was dissolved in 130 ml of MeOH and 10 ml of conc. $H_2SO_4$ was added. The mixture was refluxed for 12.5 hr. After cooling, the mixture was poured into 100 ml of ice-twaer and extracted with ether three times. The combined extracts were washed with dil. $NaHCO_3$, dried and evaporated *in vacuo* and the residue was recrystallized from benzene to give 6.12 g of **12**, mp 144—146° (reported[6] mp 145—147°). The mother liquor of the recrystallization was concentrated and left standing, giving 0.60 g of a second crop of **12**, mp 143—145°. The dil. $NaHCO_3$ solution used in washing the etheral extract of **12** was acidified with dil. HCl and extracted with ether three times. The combined extracts were dried and evaporated *in vacuo*, leaving o.61 g of 2,5-dihydroxy-4-methoxybenzoic acid, mp 205° (reported[7] mp 199—200°).

**Methyl *trans*-$\beta$(Diethylphosphonomethyl)-crotonate (14)**——A mixture of 6.4 g of methyl *trans*-$\beta$-(bromomethyl)-crotonate[9] (**13**) and 6.5 g of triethylphosphite was refluxed for 3.5 hr and the mixture was distilled, giving 7.1 g of **14**, $bp_{0.9}$ 125—127°. IR $\nu_{max}^{liq.}$ $cm^{-1}$: 1725, 1651. NMR ($CDCl_3$) $\delta$ ppm: 1.34 (6H, t, $J$=7.1 Hz), 2.31 (3H, dd, $J$=3.6, 1.2 Hz), 2.70 (2H, dd, $J$=23.6, 1.0 Hz), 3.71 (3H, s), 4.13 (4H, dq, $J$=8.3, 7.1 Hz), 5.82 (1H, br, d, $J$=5.2 Hz). *Anal.* Calcd. for $C_{10}H_{19}O_5P$: C, 48.00; H, 7.65; P, 12.38. Found: C, 47.76; H, 7.66; P, 12.46.

**Methyl *trans*-3-Methyl-2,4-pentadienoate (5a) and Its *cis* Isomer (15)**——(i) After being washed twice with hexane, 1.32 g of 50% NaH mineral oil dispersion was suspended in 30 ml of dimethoxyethane and to the suspension was added 6.65 g of **14** at 0° with stirring. After the mixture was stirred for 1 hr with cooling, 1.58 g of paraformaldehyde was added during a period of 30 min. The mixture was stirred for 30 min with cooling, and then at 60° for 3 hr. Then, the mixture was diluted with $H_2O$ and extracted with ether. The extract was washed with $H_2O$, dried and evaporated *in vacuo*. Distillation of the residue gave 0.71 g

of a mixture of **5a** and **15**, $bp_{20}$ 65—67°. IR $\nu_{max}^{liq.}$ $cm^{-1}$: 1720, 1639, 1605 (*trans*), 1595 (*cis*). NMR ($CDCl_3$) $\delta$ ppm: for *cis* (**15**): 2.01 ($CH_3$–C=, d, $J$=1.0 Hz), 3.71 ($CH_3OOC$–, s), 7.83 ($CH_2$=CH–, dd, $J$=17.5, 10.5 Hz); $\delta$ ppm for *trans* (**5a**): 2.27 ($CH_3$–C=, s), 3.70 ($CH_3OOC$–, s), 6.44 ($CH_2$=CH–, dd, $J$=17.5, 10.5 Hz). ii) To a cooled, stirred phenyllithium etheral solution prepared from 5 g of lithium and 52.3 g of bromobenzene according to the procedure of Gilman[19] was added 17.2 g of tetravinyltin and the mixture was stirred for 1 hr. The resulting precipitates of tetraphenyltin (25.2 g) was filtered off and the filtrate was added dropwise at −78° to a solution of 59.7 g of CuI-P($n$-Bu)$_3$ complex in 60 ml of tetrahydrofuran during a 30 min period. The solution was stirred at −78° for 15 min and 23.3 g of methyl tetrolate (**17**) was added during a 10 min period. After further stirring for 15 min with cooling, 15 ml of $H_2O$ was carefully added dropwise to the mixture at −78°. Then, the mixture was warmed to room temperature and extracted twice with ether. The combined extracts were dried and evaporated *in vacuo*. Distillation of the residue afforded 19 g of a mixture of **5a** and **15**. The NMR spectrum of this product showed that the relative ratio of **5a** and **15** was *ca.* 2: 1.

**3-Methyl-2,4-pentadienol (5b), Its Acetate (5c) and Its Methylether (5d)**——To a suspension of 15 g of $LiAlH_4$ in 350 ml of ether was added 47 g of the ester mixture (**5a** and **15**) obtained by the procedure-ii dropwise at −30° during a 40 min period and the mixture was stirred at 0° for 2 hr. The excess reagent was decomposed by careful addition of 25 ml of AcOEt and then of 50 ml of $H_2O$. After the addition of 200 ml of 20% dil. $H_2SO_4$, the organic layer was collected and the water layer was extracted twice with ether. The combined organic layer and extracts were dried and evaporated *in vacuo*. Distillation of the residue gave 29 2 g of **5b** as a colorless syrup, $bp_{13}$ 75—84°.

Acetylation of **5b** with $Ac_2O$–pyridine and distillation of the product gave its acetate (**5c**), $bp_{13}$ 71—76°.

Fifty percent NaH mineral oil suspension (15.6 g) was washed with hexane and dissolved in 160 ml of dimethylsulfoxide at 70°. To the ice-cold NaH solution was added dropwise 29.1 g of **5b** and the mixture was stirred for 10 min. Then, 57 g of methyliodide was added with cooling and the mixture was stirred for 15 min with cooling. The reaction mixture was diluted with $H_2O$ and extracted with ether. The extract was dried and evaporated and the residue was distilled, affording 23.6 g of the methylether (**5d**) as a colorless syrup, $bp_{95}$ 75—79°. *Anal.* Calcd. for $C_7H_{12}O$: C, 74.95; H, 10.78. Found: C, 74.23; H, 10.56.

**Reaction of Methyl *trans*-3-Methyl-2,4-pentadienoate (5a) with the Quinone (6)**——A mixture of 1.0 g of the quinone (**6**), 1.2 g of **5a**, and 6 ml of benzene was kept at 70° for 16 hr and the mixture was concentrated *in vacuo* to give 1.91 g of the crude *cis* adduct (**19a**), dimethyl 1,4-diketo-3-methoxy-7-methyl-1,4,4$a\alpha$,5,8$\alpha$,8 $a$-hexhydronaphthalene-8$\beta$,8$a\alpha$-dicarboxylate, as a syrup.

The crude *cis* adduct (**19a**) (0.83 g) was charged on 65 g of silica gel and eluted with AcOEt–hexane (3: 2, v/v). While being monitored by TLC chromatography, the main fraction was collected (630 mg) and recrystallized from EtOH, giving 350 mg of the *trans* adduct (**20a**), dimethyl 1,4-diketo-3-methoxy-7-methyl-1,4,4$a\beta$,5,8$\alpha$,8$a$-hexahydronaphthalene-8$\beta$,8$a\alpha$-dicarboxylate, as prisms, mp 131.5—134°. An analytical sample was obtained as plates by further recrystallization from the same solvent, mp 133—134°. IR $\nu_{max}^{Nujol}$ $cm^{-1}$: 1738, 1730 (sh.), 1665, 1615. UV $\lambda_{max}^{EtOH}$ 271.5 mx ($\varepsilon$ 10000). *Anal.* Calcd. for $C_{16}H_{18}O_7$: C, 59.62; H, 5.63. Found: C, 59.58; H, 5.57.

The mother liquor left by the recrystallization of **20a** was concentrated and left standing, giving 34 mg of an isomeric compound, mp 170—171.5° (from EtOH), along with 32 mg of a second crop of **20a**. IR $\nu_{max}^{Nujol}$ $cm^{-1}$: 1739, 1725, 1660, 1601. UV $\lambda_{max}^{EtOH}$ 273m$\mu$ ($\varepsilon$ 9500). NMR ($CDCl_3$) $\delta$ ppm: 1.67 (3H, m), 3.67 (3H, s), 3.82 (3H, s), 5.59 (1H, m), 5.91 (1H, s). *Anal.* Calcd. for $C_{16}H_{19}O_7$: C, 59.62; H, 5.63. Found: C, 59.77; H, 5.51.

**$NaBH_4$ Reduction of the *cis* Adduct (19a)**——The crude *cis* adduct (**19a**) (1.09 g) was dissolved in 10 ml of MeOH and 0.1 g of $NaBH_4$ was added with stirring. The mixture was left standing at room temperature for 10 min, then diluted with ether and $H_2O$, and extracted with ether. The extract was dried and evaporated *in vacuo*, leaving 727 mg of a syrup which was chromatographed over a dry column of 100 g of silica gel. From the fast-running fractions, 70 mg of a lactone (**23**), mp 177—180°, was obtained. An analytical sample in the form of leaflets was obtained by recrystallization from AcOEt, mp 181—182.5°. IR $\nu_{max}^{Nujol}$ $cm^{-1}$: 1747, 1665, 1629. UV $\lambda_{max}^{EtOH}$ 252 m$\mu$ ($\varepsilon$ 15000). *Anal.* Calcd. for $C_{15}H_{16}O_6$: C, 61.64; H, 5.52. Found: C, 61.66; H, 5.41.

Further, 109 mg of a monohydroxy derivative (**24a**), dimethyl 4$\beta$-hydroxy-1-keto-3-methoxy-7-methyl-1,4,4$a\alpha$,5,8,8$a$-hexahydronaphthalene-8$\beta$,8$a\alpha$-dicarboxylate, mp 113—116.5°, prisms (from AcOEt) were obtained as a more polar component. IR $\nu_{max}^{Nujol}$ $cm^{-1}$: 3480, 1750, 1735, 1647, 1597. UV $\lambda_{max}^{EtOH}$ 254 m$\mu$ ($\varepsilon$ 13000). *Anal.* Calcd. for $C_{16}H_{20}O_7$: C, 59.25; H, 6.22. Found: C, 59.34; H, 6.30.

A mixture of 34 mg of the monohydroxy derivative (**24a**) thus obtained, 2 ml of benzene and 3 mg of TsOH was refluxed for 30 sec. After addition of $NaHCO_3$ (solid) the mixture was filtered and evaporated *in vacuo*. The residue was recrystallized from AcOEt–hexane to give the lactone (**23**) (22 mg) as leaflets, mp 178—181°, which was identical with the sample obtained above.

19) H. Gilman, L. Sumners, and R.W. Leeper, *J. Org. Chem.*, **17**, 630 (1952).

**$NaBH_4$ Reduction of the *trans* Adduct (20a)**——The *trans* adduct (**20a**) (100 mg) was treated with 15 mg of $NaBH_4$ in 1.3 ml of MeOH as described above. The product was recrystallized from AcOEt–hexane, giving 31 mg of a monohydroxy derivative (**22a**), dimethyl 4α-hydroxy-1-keto-3-methoxy-7-methyl-1,4,-4aβ,5,8,8a-hexahydronaphthalene-8β,8aα-dicarboxylate, mp 155—156.5°. IR $\nu_{max}^{Nujol}$ $cm^{-1}$; 3380, 1733, 1699, 1657, 1617. UV $\lambda_{max}^{EtOH}$ 253.5 mμ (ε 15000). *Anal.* Calcd. for $C_{16}H_{20}O_7$: C, 59.25; H, 6.22. Found: C, 59.11; H, 6.10.

**Reaction of 2,4-Pentadienyl Acetate (18) with The Quinone (6)**——The quinone (**6**) (529 mg) and 514 mg of **18** was dissolved in 2 ml of benzene by warming briefly and the mixture was left at room temperature for 12 hr. The mixture was concentrated *in vacuo*, giving 940 mg of a syrupy residue whose TLC chromatogram did not reveral the presence of any unreacted **6** and whose NMR spectrum indicated that a main component of the product was a *cis* adduct (**19b**), methyl 8β-acetoxymethyl-1,4-diketo-3-methoxy-1,4,4aα,5,8,8a-hexahydronaphthalene-8aα-carboxylate. IR $\nu_{max}^{liq.}$ $cm^{-1}$: 1740, 1660, 1606. NMR ($CDCl_3$) δ ppm: 1.94 (3H, s), 3.82 (3H, s), 3.96 (1H, dd, $J$=12.0, 4.1 Hz), 4.25 (1H, dd, $J$=12.0, 5.0 Hz), 5.72 (2H, m), 5.95 (1H, s).

The crude **19b** (220 mg) was chromatographed on 6 g of silica gel. Fractions eluted with benzene–ether (10: 1, v/v) were evaporated and the residue was recrystallized from EtOH, giving 85 mg of a *trans* adduct (**20b**), methyl 8β-acetoxymethyl-1,4-diketo-3-methoxy-1,4,4aβ,5,8,8a-hexahydronaphthalene-8aα-carboxylate, as prisms, mp 162—166°. IR $\nu_{max}^{Nujol}$ $cm^{-1}$: 1748, 1725, 1670, 1613. UV $\lambda_{max}^{EtOH}$ 273 mμ (ε 11000). *Anal.* Calcd. for $C_{16}H_{18}O_7$: C, 59.62; H, 5.63. Found: C, 59.65; H, 5.88.

**$NaBH_4$ Reduction of the *cis* Adduct (19b)**——The crude *cis* adduct (**19b**) (433 mg) was treated with 50 mg of $NaBH_4$ in 5 ml of MeOH. By following the same procedure, described earlier, 313 mg of a crystalline mass of a crude monohydroxy derivative (**24b**), methyl 8β-acetoxymethyl-4β-hydroxy-1-keto-3-methoxy-1,4,4aα,5,8,8a-hexahydronaphthalene-8aα-carboxylate, were obtained. Recrystallization from AcOEt–hexane gave 199 mg of **24b**, mp 167—169.5°. An analytical sample of plates was obtained by further recrystallization from AcOEt, mp 170—171.5°. IR $\nu_{max}^{Nujol}$ $cm^{-1}$: 3470, 1738, 1649, 1600. UV $\lambda_{max}^{EtOH}$ 256 mμ (ε 15000). *Anal.* Calcd. for $C_{16}H_{20}O_7$: C, 59.25; H, 6.22 Found: C, 59.00; H, 6.24.

**$NaBH_4$ Reduction of the *trans* Adduct (20b)**——The *trans* adduct (**20b**) (150 mg) was treated with 20 mg of $NaBH_4$ in 2 ml of MeOH as described above. The product was recrystallized from AcOEt–hexane to give 60 mg of a monohydroxy derivative (**22b**), methyl 8β-acetoxymethyl-4α-hydroxy-1-keto-3-methoxy-1,4,4aβ,5,8,8a-hexahydronaphthalene-8aα-carboxylate, as fine needles, mp 139—140°. IR $\nu_{max}^{Nujol}$ $cm^{-1}$: 3350, 1738, 1693, 1656, 1613. UV $\lambda_{max}^{EtOH}$ 256 mμ (ε 15000). *Anal.* Calcd. for $C_{16}H_{20}O_7$: C, 59.25; H, 6.22. Found: C, 58.86; H, 6.19.

**Reaction of 3-Methyl-2,4-pentadienyl Acetate (5c) with the Quinone (6)**——A mixture of 2.53 g of the quinone (**6**), 3 g of **5c**, and 12 ml of benzene was refluxed for 4 hr and the mixture was evaporated *in vacuo* to give a crude *cis* adduct (**19c**), methyl 8β-acetoxymethyl-1,4-diketo-3-methoxy-7-methyl-1,4,4aα,5,8,8a-hexahydronaphthalene-8aα-carboxylate, as a syrup (4.57 g). NMR analysis of this product indicated that this product is a mixture of **19c** and the isomeric phenolic compound, which will be described below, in a relative ratio of 2: 1. Main absorption of the NMR spectrum of the *cis* adduct (**19c**) was shown as follows: ($CDCl_3$) δ ppm: 1.88 (3H, m), 3.75 (3H, s), 3.77 (3H, s), 4.22 (1H, dd, $J$=13.0, 5.0 Hz), 5.4 (1H, m), 5.92 (1H, s).

Pulverizing 548 mg of this reaction product in benzene–hexane gave 85 mg of the isomeric phenolic compound, mp 150—156°. IR $\nu_{max}^{Nujol}$ $cm^{-1}$: 3430, 1744, 1691, 1634, 1584. UV $\lambda_{max}^{EtOH}$ 232 mμ (ε 13000), 349 mμ (ε 3500). NMR ($CDCl_3$) δ ppm: 1.85 (3H, m), 1.95 (3H, s), 3.67 (3H, s), 3.93 (3H, s), 5.44 (1H, m), 5.48 (1H, s), 5.68 (1H, s, disappeared with addition of $D_2O$), 2.4—4.0 (5H, m). *Anal.* Calcd. for $C_{17}H_{20}O_7$: C, 60.71; H, 5.99. Found: C, 60.63; H, 5.89.

The solution of the *cis* adduct (**19c**) left by collection of the isomeric phenolic compound was concentrated *in vacuo* and chromatographed over 20 g of alumina. Fractions eluted with benzene were evaporated and the residue was recrystallized from MeOH to give 129 mg of a *trans* adduct (**20c**), methyl 8β-acetoxymethyl-1,4-diketo-3-methoxy-7-methyl-1,4,4aβ,5,8,8a-hexahydronaphthalene-8aα-carboxylate, as prisms, mp 153—157°. IR $\nu_{max}^{Nujol}$ $cm^{-1}$: 1748, 1725, 1660, 1610. UV $\lambda_{max}^{EtOH}$ 274 mμ (ε 10000). *Anal.* Calcd. for $C_{17}H_{20}O_7$: C, 60.71; H, 5.99. Found: C, 60.86; H, 5.98.

**$NaBH_4$ Reduction of the *cis* Adduct (19c)**——The crude *cis* adduct (**19c**) obtained by treatment of 0.5 g of **6** and 0.6 g of **5c** as described above was dissolved in 7 ml of MeOH and 0.11 g of $NaBH_4$ was added with stirring. The mixture was left standing at room temperature for 10 min, then diluted with ether and $H_2O$, and extracted with ether. The extract was dried and evaporated *in vacuo*, leaving 0.74 g of a crystalline syrup which was recrystallized from AcOEt to give 296 mg of a monohydroxy derivative (**24c**), methyl 8β-acetoxymethyl-4β-hydroxy-1-keto-3-methoxy-7-methyl-1,4,4aα,5,8,8a-hexahydronaphthalene-8aα-carboxylate, as prisms, mp 170.5—171.5°. IR $\nu_{max}^{Nujol}$ $cm^{-1}$: 3340, 1735, 1646, 1598. UV $\lambda_{max}^{EtOH}$ 252 mμ (ε 11000). *Anal.* Calcd. for $C_{17}H_{22}O_7$: C, 60.34; H, 6.55. Found: C, 60.37; H, 6.56.

The aqueous layer left by collection of **24c** was acidified with dil. HCl and extracted with $CHCl_3$. Evaporation of the extract gave 42 mg of the isomeric phenolic compound, mp 148—155°, which was identified with the sample obtained before by infrared spectrometry.

**Reaction of 1-Methoxymethyl-3-methyl-2,4-pentadiene (5d) with the Quinone (6)**——A solution of 3.1 g of the quinone (**6**) and 3 g of **5d** was left standing at 0° for 15 hr. Removal of the solvent left 5.23 g of a

crude *cis* adduct (**19d**), which crystallized on standing. Recrystallization from benzene–hexane gave 3.8 g of the *cis* adduct, methyl 1,4-diketo-3-methoxy-8$\beta$-methoxymethyl-7-methyl-1,4,4a$\alpha$,5,8,8a-hexahydronaphthalene-8a$\alpha$-carboxylate, as prisms, mp 120—122°. IR $\nu_{max}^{Nujol}$ cm$^{-1}$: 1743, 1722, 1660, 1610. NMR ($CDCl_3$) $\delta$ ppm: 1.75 (3H, m), 2.99 (3H, s), 3.13 (1H, dd, $J$=11.0, 5.0 Hz), 3.77 (3H, s), 3.83 (3H, s), 5.46 (1H, m), 5.94 (1H, s).

A mixture of the crude *cis* adduct (**19d**) (0.35 g), 3.5 g of alumina, and 7 ml of MeOH was shaken at room temperature overnight and filtered. Evaporation of the solvent from the filtrate gave a crystalline mass which was recrystallized from benzene–hexane to give 148 mg of the *trans* adduct (**20d**), methyl 1,4-diketo-3-methoxy-8$\beta$-methoxymethyl-7-methyl1,4,4a$\beta$,5,8,8a-hexahydronaphthalene-8a$\alpha$-carboxylate, as prisms, mp 142—149°. The analytical sample was obtained by recrystallization from EtOH as prisms, mp 147—152°. IR $\nu_{max}^{Nujol}$ cm$^{-1}$: 1743 (sh.), 1722, 1661, 1605. UV $\lambda_{max}^{EtOH}$ 272 m$\mu$ ($\varepsilon$ 10000). *Anal.* Calcd. for $C_{16}H_{20}O_6$: C, 62.32; H, 6.54. Found: C, 61.91; H, 6.57.

**$NaBH_4$ Reduction of the *cis* Adduct (19d)**——The crude *cis* adduct (10.87 g) thus obtained was dissolved in 100 ml of MeOH and, after cooling at 0°, 1.5 g of $NaBH_4$ was added in one portion. The mixture was stirred for 30 min with cooling and extracted twice with $CHCl_3$. The extract was dried and evaporated *in vacuo* to give 10.68 g of a crude monohydroxy compound (**24d**), methyl 4$\beta$-hydroxy-1-keto-3-methoxy-8$\beta$-methoxymethyl-7-methyl-1,4,4a$\alpha$,5,8,8a-hexahydronaphthalene-8a$\alpha$-carboxylate, as a syrup. IR $\nu_{max}^{liq.}$ cm$^{-1}$: 3450, 1734, 1668, 1616. NMR ($CDCl_3$) $\delta$ ppm: 1.79 (3H, m), 3.22 (3H, s), 3.74 (3H, s), 3.79 (3H, s), 5.45 (1H, s), 5.55 (1H, m). UV $\lambda_{max}^{EtOH}$ 252 m$\mu$ ($\varepsilon$ 11000).

The crude **24d** thereby obtained was dissolved in 25 ml of pyridine and 10 ml of $Ac_2O$ was added. The mixture was warmed for 1.5 hr on a steam bath and, after cooling, diluted with ice-water. The mixture was extracted with ether and the extract was washed with dil. aq. $NaHCO_3$, dil. HCl, and $H_2O$ successively. The extract was dried and evaporated *in vacuo*, leaving a syrup which was recrystallized from AcOEt–hexane, giving 6.11 g of an acetate of **24d**, mp 151.5—153°. Further, concentration of the recrystallization mother liquor gave 0.54 g of a second crop of the acetate, mp 145—150°. IR $\nu_{max}^{Nujol}$ cm$^{-1}$: 1745, 1725, 1675, 1620. UV $\lambda_{max}^{EtOH}$ 247 m$\mu$ ($\varepsilon$ 12000). *Anal.* Calcd. for $C_{18}H_{24}O_7$: C, 61.35; H, 6.86. Found: C, 61.20; H, 6.89.

**$NaBH_4$ Reduction of the *trans* Adduct (20d)**——The *trans* adduct (**20d**) (188 mg) was treated with 30 mg of $NaBH_4$ in 2 ml of MeOH as described earlier, giving 46 mg of the monohydroxy compound (**22d**), methyl 4$\alpha$-hydroxy-1-keto-3-methoxy-8$\beta$-methoxymethyl-7-methyl-1,4,4a$\beta$,5,8,8a-hexahydronaphthalene-8a$\alpha$-carboxylate, mp 141—142.5° (from AcOEt–hexane). IR $\nu_{max}^{Nujol}$ cm$^{-1}$: 3410, 1698, 1651, 1616. UV $\lambda_{max}^{EtOH}$ 255 m$\mu$ (15000). *Anal.* Calcd for $C_{16}H_{22}O_6$: C, 61.92; H, 7.15. Found: C, 61.88; H, 7.37.