followed by the removal of the THP ether to give des-mosterol (1, 78%).[22] The 20R configuration of 1 was confirmed by spectroscopic comparisons with the authentic desmosterol. Desmosterol has been converted into cholesterol and 24,25-epoxy- and 24,25-dihydroxycholesterols (the precursors to the active vitamin D metabolites).[3a]

The approach described herein provides a novel, efficient and totally stereocontrolled steroid side-chain synthesis and can be applied to the steroids with various 24,25-branched side chains from the intermediate olefin 11.

Note Added in Proof. Since submission of the manuscript, Dr. M. Tanabe of Stanford Research Institute kindly provided us with a preprint of studies on his new approach to the synthesis of sterol side chains: Tanabe, M.; Hayashi, K. J. Am. Chem. Soc. 1980, 102, 862.

(22) Dasgupta, S. K.; Crump, D. R.; Gut, M. J. Org. Chem. 1974, 39, 1658.

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Diels–Alder Reactions Using In Situ Generated Quinones

Summary: High-yield syntheses of Diels–Alder adducts involving dienes and unstable quinones can be effected by generating the quinone in the presence of the diene with silver oxide.

Sir: Synthetic studies directed toward the synthesis of antitumor compounds required an efficient preparation of substituted benzoquinones 1a–c for use in Diels–Alder reactions. A literature search revealed that the sole synthetic method involved silver oxide oxidation of the corresponding hydroquinone.[1] The quinones isolated in low
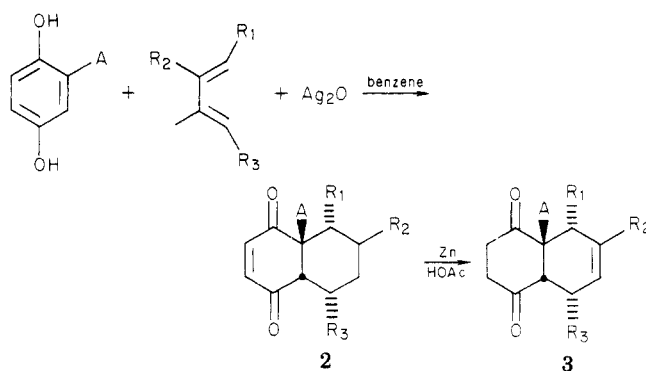
performed with 1a,[3] no Diels–Alder reactions of aldehyde 1b or ketone 1c have been reported. We wish to communicate a significant modification which permits the high-yield syntheses of Diels–Alder adducts with 1a–c. It utilizes a one-pot technique wherein the diene, silver oxide, and the requisite hydroquinone are stirred in the absence of light to afford adducts 2a–g in high yield.[4] The resultant adducts can be reduced with zinc and acetic acid to produce diketone 3. Epimerization of adducts from (carbomethoxy)benzoquinone can simply be effected by chromatography on alumina.[5] Attempted epimerization of adduct 3e on alumina led to deformylation. However, epimerization of 3e could be accomplished with concurrent acetal formation using triethyl orthoformate and p-toluenesulfonic acid with a few drops of ethanol. The entries in Table I illustrate the versatility of our procedure. The reaction also works well for naphthoquinones as evidenced by the 77% isolated yield of 7 from ketohydroquinone 5 and diene 6.
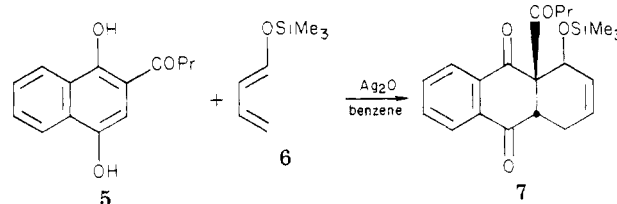

In a typical experiment, 5 mmol of isoprene, 5 mmol of methyl gentisate, and 10 mL of benzene were placed in a dry, wide-mouth, amber bottle. After the mixture was cooled to ca. 10 °C in an ice bath, 10 mmol of Ag_2O was added at once to the stirred solution. The ice bath was

Table I. Diels–Alder Reactions of 1^a

A	R_1	R_3	compd	% yield^b	compd	% yield^b	mp, °C
CO_2CH_3	$OSiMe_3$	CH_3	2a	96	3a	98	
CO_2CH_3	$CH_2CH_2OCH_2Ph$	H	2b	95	3b	96	75–76
CO_2CH_3	H	H	2c	100^c	3c	100	88–95
CO_2CH_3	CH_2CO_2Et	H	2d	98	3d	96	
CHO	CH_2CO_2Et	H	2e	94	3e	90	
CHO	$CH_2CH_2OCH_2Ph$	H	2f	97	3f	91	94
COCH₃	$CH_2CH_2OCH_2Ph$	H	2g	100	3g	93	117

^{a} R_2 = CH_3 for all cases. ^{b} Isolated yield. Adducts were characterized by IR, NMR, ^{13}C NMR, and high-resolution mass spectroscopy and by combustion analysis. ^{c} Mixture of regioisomers (ratio of expected/unexpected = 70–30).

yield by this procedure are rather unstable to both air and water.[2] Although some Diels–Alder reactions had been

removed and the reaction allowed to stir overnight at room temperature. The reaction was diluted with Et_2O and
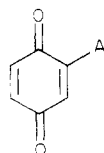
1a, A = CO_2CH_3 b, A = CHO   c, A = C(O)CH₃

(1) For 1a, see: Brunner, K. Monatsh. Chem. 1913, 34, 913. For 1b, see: Bruce, J. M.; Creed, D. J. Chem. Soc. C 1970, 649. For 1c, see: Kloetzel, M. C.; Dayton, R. P.; Abadir, B. Y. J. Org. Chem. 1955, 20, 38.

(2) Cason, J. Org. React. 1948, 4, 354.

(3) Ansell, M. F.; Culling, G. C.; Nash, B. W.; Wilson, D. A. Proc. Chem. Soc., London 1960, 405. Ansell, M. F.; Lown, J. W.; Turner, D. W.; Wilson, D. A. J. Chem. Soc. 1963, 3036. Ansell, M. F.; Clements, A. H. J. Chem. Soc. C 1971, 269. Goldsmith, D. J.; Srouji, G.; Kwong, C. J. Org. Chem. 1978, 43, 3182.

(4) While this work was in progress a brief report of similar methodology for o-quinone synthesis was reported: Al-Hamdany, R.; Ali, B. J. Chem. Soc., Chem. Commun. 1978, 397.

(5) Ansell, M. F.; Lown, J. W.; Turner, D. W.; Wilson, D. A. J. Chem. Soc. 1963, 3036.

filtered. Concentration of organic solution yielded 1.17 g (5 mmol, 100% yield) of the Diels–Alder product.

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(6) Fellow of the Alfred P. Sloan Foundation, 1979–1981.

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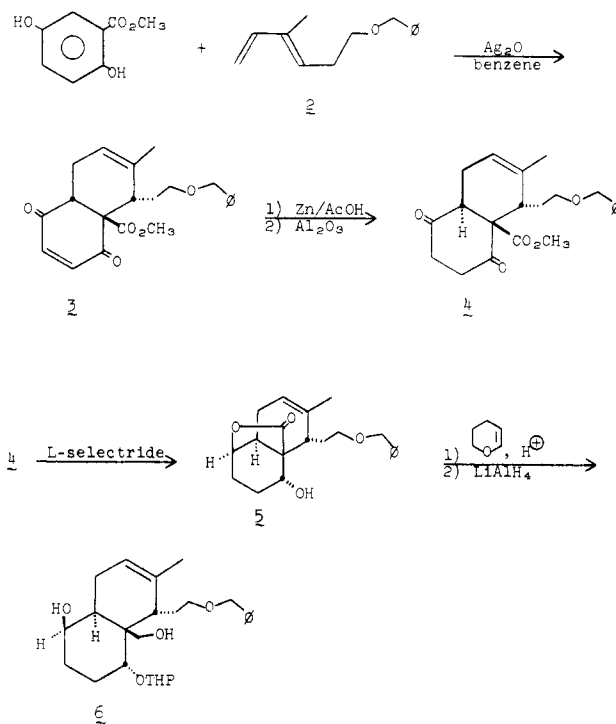## Model Studies for the Synthesis of Quassinoids. 1. Construction of the BCE Ring System

Summary: A tricyclic intermediate for the synthesis of quasimarin has been synthesized in 14 steps.

Sir: The structures of quasimarin (**1a**) and bruceantin (**1b**) were determined by Kupchan and co-workers.[1] Both their
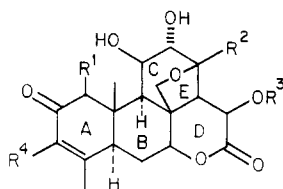

1a, $R^1 = OH$; $R^2 = CH_3$;
  $R^3 = COC(OAc)(CH_3)Et$; $R^4 = H$
b, $R^1 = H$; $R^2 = CO_2CH_3$;
  $R^3 = COCH=C(CH_3)(i\text{-Pr})$; $R^4 = OH$

cytotoxic activity and their challenging structures have prompted considerable synthetic interest.[2] Our approach has centered around the initial construction of a BC unit on which the A, D, and E rings can sequentially be appended. The requisite BC building block is efficiently assembled by the use of novel Diels–Alder reaction conditions described previously.[3] Diene **2**[4] is reacted with methyl gentisate in the presence of silver oxide to produce **3** in 95% yield. Reduction (Zn/HOAc) and epimerization (alumina chromatography)[6] afford diketone **4**[7] in 65–70% overall yield. L-Selectride reduction of **4** (THF, −78 °C, −25 °C for 12 h) provides lactone **5**,[8] whose structure is supported by IR absorptions at 3450 and 1770 cm^{-1} and the absence of ketone resonances in the ^{13}C NMR spec-

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(1) Bruceantin: Kupchan, S. M.; Britton, R. W.; Ziegler, M. F.; Siegel, C. W. *J. Org. Chem.* **1973**, *38*, 178. Quasimarin: Kupchan, S. M.; Streelman, D. R. *J. Org. Chem.* **1976**, *41*, 3481.

(2) Dias, J. R.; Ramachandra, R. *Tetrahedron Lett.* **1976**, 3685; *J. Org. Chem.* **1977**, *42*, 1613; *Synth. Commun.* **1977**, 293; *J. Org. Chem.*, **1977**, *42*, 3584. Snitman, D. L.; Tsai, M.-Y.; Watt, D. S. *Synth. Commun.* **1978**, 195.

(3) Kraus, G. A.; Taschner, M. J. *J. Org. Chem.*, previous paper in this issue.

(4) Diene **2** is prepared by deconjugation[5] of methyl 4-methyl-2,4-hexadienoate with lithium diisopropylamide, reduction with LiAlH$_4$, and protection of the alcohol with benzyl bromide.

(5) Torssell, K. *Tetrahedron Lett.* **1974**, 623.

(6) Ansell, M. F.; Lown, J. W.; Turner, D. W.; Wilson, D. A. *J. Chem. Soc.* **1963**, 3036.

(7) ^1H NMR δ 1.71 (3 H, br s), 2.6–3.5 (12 H, m), 3.70 (3 H, s), 4.42 (2 H, s), 5.28 (1 H, m), 7.33 (5 H, s); IR (film) 1740, 1720, 1215, 1090, 730, 690 cm^{-1}; mp 75–76 °C.

(8) ^1H NMR δ 1.72 (3 H, m), 3.56 (2 H, t, $J = 5.5$ Hz), 4.28 (1 H, d, $J = 4$ Hz), 4.52 (2 H, s), 5.26 (1 H, m), 7.3 (5 H, s); mp 105–106 °C.

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trum. The presence of only 19 ^{13}C NMR resonances presents strong evidence that hydroxy lactone **5** is stereochemically homogeneous. Protection of the hydroxyl group in **5** as the tetrahydropyranyl ether (THP) in quantitative yield by the method of Grieco[9] followed by lithium aluminum hydride reduction (1 equiv of LAH, Et$_2$O, 0 °C) affords diol **6** in 99% yield from **5**. Protection of the alcohol was necessary to avoid base-catalyzed fragmentation during the reduction. Ring E can now be introduced by the selenocyclization method developed by Nicolaou.[10]
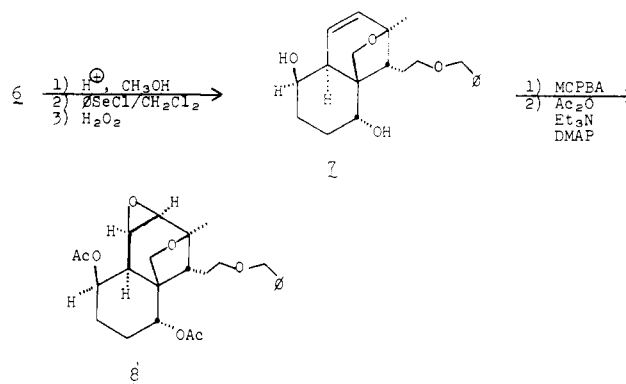
We initially planned to construct the trans diaxial diol group in ring C by epoxide opening. Although this reaction is well precedented for simple unhindered systems, all attempts to open epoxide **8**[11] by external nucleophiles (H$_2$O, KO$_2$; PhCH$_2$(N(CH$_3$)$_3$)OCHO; AcOH/Al$_2$O$_3$) were unsuccessful. However, the sequence involving hydrogenolysis (H$_2$/Pd/C, MeOH), oxidation, and internal epoxide opening (CF$_3$CO$_2$H, CH$_2$Cl$_2$, 25 °C) to afford **9** provides an attractive solution to this difficulty. Infrared

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(9) Miyashita, N.; Yoshikoshi, A.; Grieco, P. A. *J. Org. Chem.* **1977**, *42*, 3772.

(10) Nicolaou, K. C.; Lysenko, Z. *J. Am. Chem. Soc.* **1977**, *99*, 3185.

(11) ^1H NMR δ 1.48 (3 H, s), 2.00 (3 H, s), 2.20 (3 H, s), 2.90 (1 H, d, $J = 4$ Hz), 3.30 (1 H, dd), 3.61 (2 H, t, $J = 5.7$ Hz), 3.96 (1 H, d, $J = 8$ Hz), 4.61 (2 H, s), 4.61 (1 H, d, $J = 8$ Hz), 7.5 (5 H, s).

(12) Corey, E. J.; Suggs, J. W. *Tetrahedron Lett.* **1975**, 2647.

(13) Lindgren, B. O.; Nilsson, T. *Acta Chem. Scand.* **1973**, *27*, 888. Our modification used 2-methyl-2-butene as the chlorine scavenger.