dd, J_{gem} = 18.9, $J_{5\alpha,3}$ = 2.5 Hz, H5α), 1.85–1.68 (5 H, m), 1.56–1.45 (1 H, m), 1.24–1.15 (1 H, m), 1.08–1.00 (1 H, m), 1.054 (3 H, s, H8′), 0.845 (3 H, s, H9′).

Acknowledgment. We thank the Australian Research Council both for financial support of this work and for the award of a National Research Fellowship to M.D.I.

Supplementary Material Available: IR and MS data for compounds 1, 3–5, 7–10, 12, 15, and 16, 400-MHz ^{1}H NMR spectra of crude mixture of compounds 10 and 11 obtained from oxidation of sulfides 7 and 8, of compound 10, including high-field regions of spectra used for determination of diastereomeric purity of 10 before and after crystallization, of compound 7 and of 1:1 mixture of compounds 7 and 8, of compound 15, and of mixture of compounds 15 and 16, and crystallographic data for compound 10, including an ORTEP plot and tables of positional parameters, bond lengths and angles, and hydrogen atom positional and thermal parameters (22 pages). Ordering information is given on any current masthead page.

The *Cinchona* Alkaloids: A Silicon-Directed Synthesis of Some Advanced Intermediates

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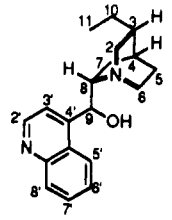
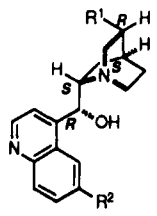
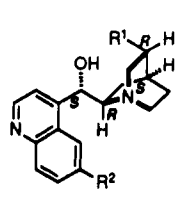
N-Benzylmeroquinene aldehyde (**5b**) was prepared in 10 steps and 21% overall yield from benzylamine. The key transformations involved a stereoselective Lewis acid catalyzed Diels–Alder reaction to produce bicyclic amide **18**, which in turn underwent a regioselective Baeyer–Villager oxidation to produce lactone **20**. Acid-catalyzed ring opening with concomitant Peterson olefination afforded the meroquinene skeleton, which was converted in high yield to meroquinene aldehyde via a reduction/oxidation sequence. Treatment of this aldehyde with anions derived from 4-methylquinoline smoothly generated alcohols **23a,b**, which on acetylation yielded the advanced *Cinchona* alkaloid intermediates **24a,b**.

Introduction

Historically, the *Cinchona* alkaloids have proven to be important therapeutic agents.[1] Today, quinine (**1a**), perhaps the most noted member of this family and best known for its use in the treatment of malaria, is more commonly used for the treatment of leg cramps and quinidine (**2a**) is used to treat cardiac arrhythmias.[2]







Substituents:	1	2
a. R^1 = -C_2H_3; R^2 = -OCH_3	Quinine	Quinidine
b. R^1 = -C_2H_3; R^2 = -H	Cinchonidine	Cinchonine
c. R^1 = -C_2H_5; R^2 = -OCH_3	Dihydroquinine	Dihydroquinidine
d. R^1 = -C_2H_5; R^2 = -H	Dihydrocinchonidine	Dihydrocinchonine

In the early 1900s Rabe pioneered the structure elucidation of these alkaloids by converting degradation products to the naturally occurring material.[3] However, the first total synthesis of quinine did not appear in the literature until Woodward and Doering published their classic synthesis some thirty years later.[4] Despite its elegance, this synthesis was not particularly well-suited for large-scale production of either the natural compounds or new analogues, and researchers at Hoffmann-La Roche therefore reinvestigated the total synthesis of these alkaloids. Their efforts culminated in a series of new syntheses,[5] all of which are based on derivatives of 6-methoxyquinoline and analogues of meroquinene. Since the appearance of these papers, several total syntheses,[6a,b] including a chiral formal synthesis,[6c] and a multitude of meroquinene syntheses have been reported.[6d]

Our initial interest in the key synthetic intermediate meroquinene stemmed from our previous work on the application of ceric ammonium nitrate (CAN) to natural product synthesis.[7a,b] Since it is known that 3-(trimethylsilyl)cyclohexanol (**3**) undergoes oxidation with CAN to give 5-hexenal (eq 1), we anticipated that an appropriately substituted octahydroisoquinoline (**4**) should

(1) Cordell, G. *An Introduction to Alkaloids: A Biogenetic Approach*; Wiley: New York, 1981; p 708.
(2) *Drug Information for the Health Care Professional*; U.S. Pharmacopeial Convention: Maryland, 1988; pp 1866 and 1870.
(3) Rabe, P. *Ber. Dtsch. Chem. Ges.* **1911**, *44*, 2088. Rabe, P.; Kindler, K. *Ber. Dtsch. Chem. Ges.* **1918**, *51*, 466. Rabe, P.; Huntenburg, W.; Schultze, A.; Volger, G. *Chem. Ber.* **1931**, *64*, 2487.
(4) Woodward, R. B.; Doering, W. E. *J. Am. Chem. Soc.* **1944**, *66*, 849. Woodward, R. B.; Doering, W. E. *J. Am. Chem. Soc.* **1945**, *67*, 860. For an improvement on Woodward's approach, see: Grethe, G.; Gutzwiller, J.; Lee, H. L.; Uskokovic, M. R. *Helv. Chim. Acta* **1972**, *55*, 1044.
(5) (a) Uskokovic, M. R.; Henderson, T.; Reese, C.; Lee, H. L.; Grethe, G.; Gutzwiller, J. *J. Am. Chem. Soc.* **1978**, *100*, 571. (b) Gutzwiller, J.; Uskokovic, M. R. *J. Am. Chem. Soc.* **1978**, *100*, 576. (c) Grethe, G.; Lee, H. L.; Mitt, T.; Uskokovic, M. R. *J. Am. Chem. Soc.* **1978**, *100*, 581. (d) Grethe, G.; Lee, H. L.; Mitt, T.; Uskokovic, M. R. *J. Am. Chem. Soc.* **1978**, *100*, 589.
(6) (a) Gates, M.; Sugavanam, B.; Schreiber, W. L. *J. Am. Chem. Soc.* **1970**, *92*, 205. (b) Taylor, E. C.; Martin, S. F. *J. Am. Chem. Soc.* **1972**, *94*, 6218. (c) Hirai, Y.; Terada, T.; Yamazaki, T. *J. Am. Chem. Soc.* **1988**, *110*, 958. (d) Hanessian, S.; Faucher, A.-M.; Léger, S. *Tetrahedron* **1990**, *46*, 231. Funk, R. L.; Munger, J. D. *J. Org. Chem.* **1984**, *49*, 4319. Takano, S.; Takahashi, M.; Hatekeyama, S.; Ogasawara, K. *J. Chem. Soc., Chem. Commun.* **1979**, 556. Brown, R. T.; Leonard, J. *J. Chem. Soc., Chem. Commun.* **1978**, 725. Augustine, R. L.; Koletar, G. *Synth. Commun.* **1974**, *4*, 161.
(7) (a) Wilson, S. R.; Zucker, P. A.; Kim, C. K.; Villa, C. A. *Tetrahedron Lett.* **1985**, *26*, 1969. (b) For CAN oxidations of hydroxyallylsilanes, see: Wilson, S. R.; Augelli-Szafran, C. E. *Tetrahedron* **1988**, *44*, 3983.

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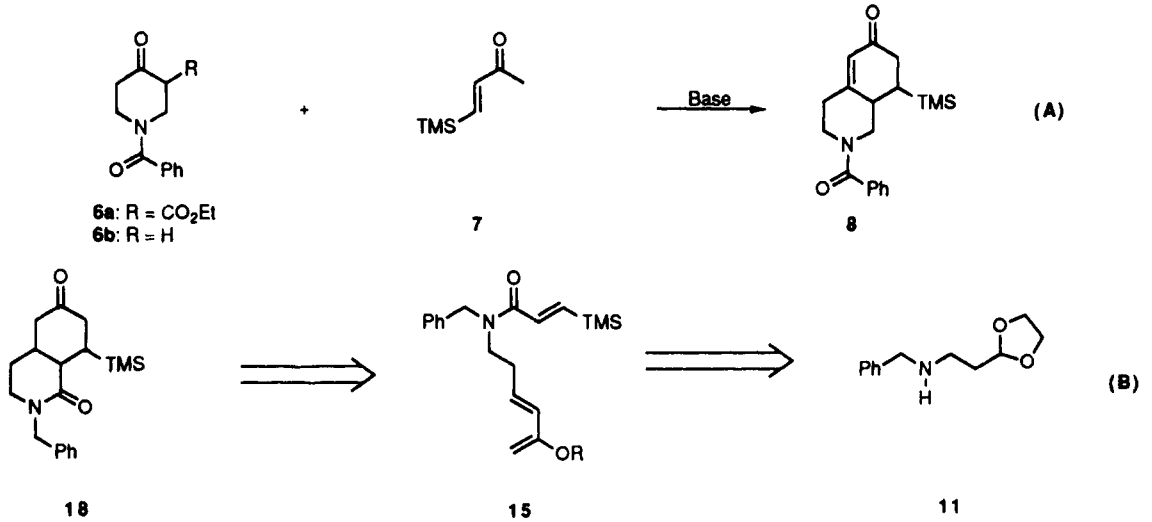
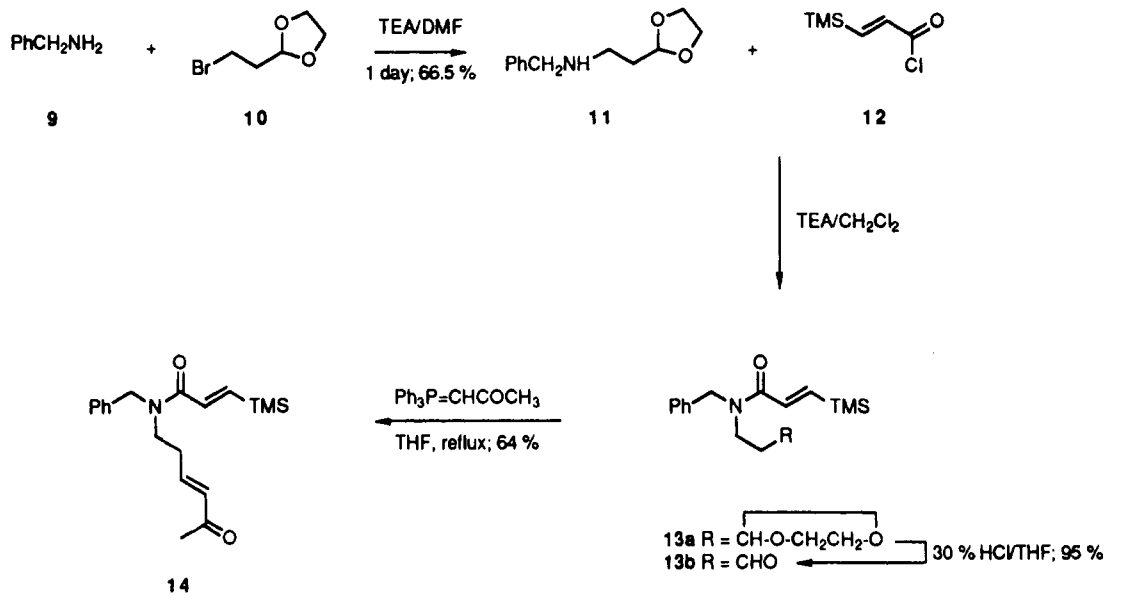
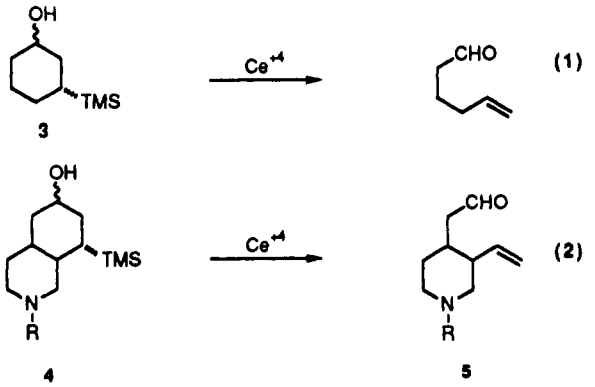
Scheme I



Scheme II



undergo similar oxidative fragmentation to meroquinene aldehyde (5, see eq 2).



Results and Discussion

Our first approach (Scheme I, eq A) into the desired framework was based on a modification of a Marshall paper.[8] However, despite the fact that Fleming[9] was able to add cuprates to 4-(trimethylsilyl)-3-buten-2-one (7; TMS-MVK), treatment of the anion of piperidone 6a or its descarbethoxy analogue 6b with TMS-MVK under a variety of conditions failed to produce any Michael adducts.

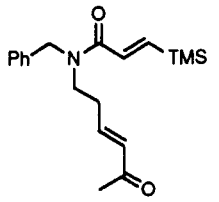
A second approach was based on an intramolecular Diels–Alder reaction (see Scheme I, eq B). The synthesis of the requisite enamide precursor to diene 15 is shown in Scheme II. Alkylation of benzylamine with 0.5 equiv of bromodioxolane 10, based on a modification of Wattanasin's procedure,[10] gave amine 11 in 66.5% yield after a simple vacuum distillation. It was later discovered that the crude product, a mixture of benzylamine and monoalkylated (major) and dialkylated amines, could be used directly. While this complicated purification later on, the benefit was a higher overall yield of 14: 61% vs 36%. Acylation with 3-(trimethylsilyl)-2-propenoyl chloride[11]

(8) Marshall, J. A.; Warne, T. M. *J. Org. Chem.* 1971, *36*, 178.
(9) Fleming, I.; Perry, D. A. *Tetrahedron* 1981, *37*, 4027.

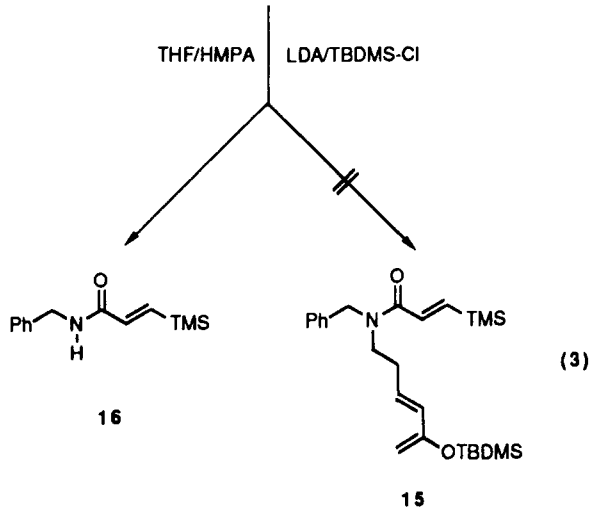
(10) Wattanasin, S.; Kathawala, F. G.; Boeckman, R. K. *J. Org. Chem.* 1985, *50*, 3810.
(11) Acid chloride 12 was prepared from the corresponding acid by treatment with oxalyl chloride; this acid was synthesized by two routes: (1) methyl acrylate was treated with trimethylsilane in the presence of $Co_2(CO)_8$ in benzene, to generate methyl 3-(trimethylsilyl)-2-propenoate, which was then saponified to the acid, or (2) 3-(trimethylsilyl)-2-propyn-1-ol was reduced with $LiAlH_4$ to the allyl alcohol, which was then oxidized to the acid with Jones reagent.

(12) in the presence of triethylamine in methylene chloride gave amide **13a**. After hydrolysis of the dioxolane group (30% aqueous HCl/THF, 95%), Wittig reaction between the commercially available 1-(triphenylphosphoranylidene)-2-propanone and aldehyde **13a** gave the all trans enone **14** in 64% purified yield.

The proposed Diels–Alder reaction required that we generate the kinetic enolate of enone **14**. Since it was anticipated that even under kinetic conditions the reaction mixture would be comprised of both enolates, a bulky silyl protecting group, one stable to chromatography, was required. To that end, the enolate of **14** was quenched at −78 °C with *tert*-butyldimethylsilyl chloride (TBDMS-Cl) in HMPA (eq 3). To our surprise, the product isolated



14

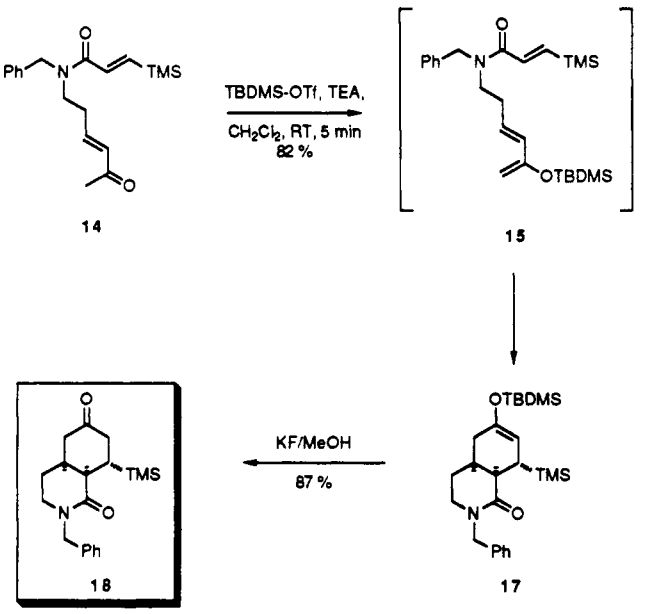


16 **15** (3)

from this reaction was not the desired cross diene enol ether **15** but rather enamide **16**! Apparently, even under kinetic conditions, deprotonation at the γ-position was favored. This may be due to a directing effect of the amide group, as the LDA may be complexing to the amide carbonyl prior to deprotonation. However, the elimination of the enone side chain did not occur until the HPMA was added—if this solvent was omitted, only starting material was recovered.[12]

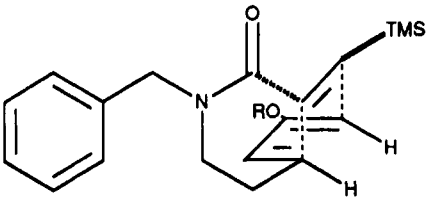
Amide **17** was eventually secured through the use of TBDMS-triflate according to the procedure of Ihara[13] as shown in Scheme III. Thus, treatment of enone **14** with 1.1 equiv of TBDMS-triflate and 1.5 equiv of triethylamine in dichloromethane at rt for 5 min gave the cis-fused enol ether **17** as the sole product. Desilylation was effected with potassium fluoride in refluxing methanol to give *cis*-keto amide **18** in 77% overall yield from **14**. This ketone was crystalline, and the stereochemistry shown was confirmed through single-crystal X-ray analysis.[14]

Scheme III



14 **15** **18** **17**

We propose the following transition state (A) to explain the stereochemical outcome of the Diels–Alder reaction. Secondary orbital overlap and the steric requirements of the TMS group on the dienophile appear to be critical to the observed stereoselectivity. Furthermore, we anticipated that the desired cis ring fused product would be more stable than the trans bicyclic material, a conclusion confirmed both experimentally and through the use of computer modeling. Epimerization of *cis*-**18** with a 20-fold excess of NaOMe in refluxing methanol produced approximately a 3:2 cis:trans equilibrium mixture.[15] Presumably the TMS group is dictating this equilibrium as in the trans compound the silyl group must rotate into an axial position.



A

***cis* 18** ***trans* 18**

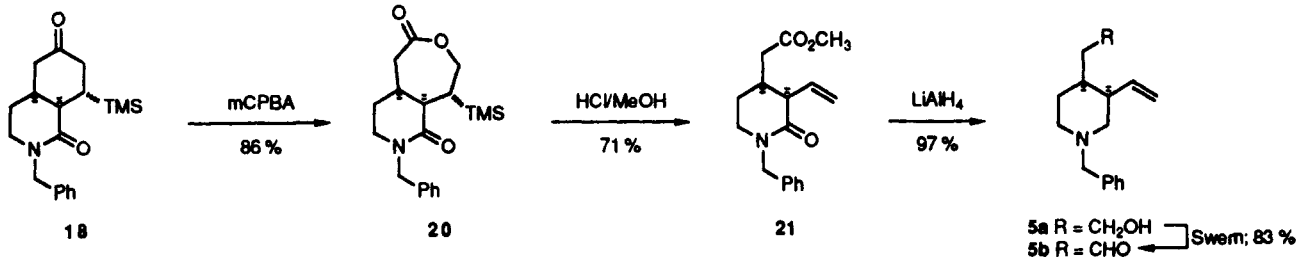
(12) Several other experiments established the sensitivity of this system. Treatment of **19** with LTMP followed by TBDSM-Cl/HMPA also gave enamide **22** as did enamine formation with pyrrolidine/cat. TsOH.

(13) Ihara, M.; Ishida, Y.; Fukumoto, K.; Kametani, T. *Chem. Pharm. Bull.* **1985**, *33*, 4105.

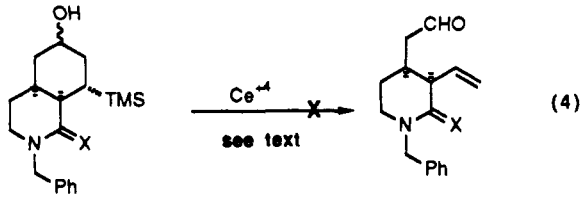
(14) We are grateful to John C. Huffman and Indiana University's Molecular Structure Center for the X-ray crystal analysis.

(15) *trans*-**18** can potentially be converted into *trans*-meroquinene aldehyde which has been used in the syntheses of alkaloids from both the *Corynanthe* and *Rauwolfia* families. For (±)-corynantheidol syntheses, see: Imanishi, T.; Inoue, M.; Wada, Y.; Hanaoka, M. *Chem. Pharm. Bull.* **1983**, *31*, 1551. Imanishi, T.; Inoue, M.; Wada, Y.; Hanaoka, M. *Chem. Pharm. Bull.* **1982**, *30*, 1925. Takano, S.; Masuda, K.; Ogasawara, K. *J. Chem. Soc., Chem. Commun.* **1980**, 887. For (±)-dihydrocorynantheol and (±)-dihydrocorynantheal syntheses, see: Danieli, B.; Lesma, G.; Palmisano, G.; Tollari, S. *J. Chem. Soc., Perkin Trans. 1*, **1984**, 1237. Brown, R. T.; Jones, M. F.; Wingfield, M. *J. Chem. Soc., Chem. Commun.* **1984**, 847. Kametani, T.; Kanaya, N.; Hino, H.; Huang, S.; Ihara, M. *J. Chem. Soc. Perkin Trans. 1* **1981**, 3168. Aimi, N.; Yamanaka, E.; Endo, J.; Sakai, S.; Haginiwa, J. *Tetrahedron* **1973**, 2015. Aimi, N.; Yamanaka, E.; Endo, J.; Sakai, S.; Haginiwa, J. *Tetrahedron Lett.* **1972**, 1081.

Scheme IV



The first attempt at the CAN-induced oxidative fragmentation was on the fully reduced amino alcohols **19a**, available in high yield from **18** through lithium aluminum hydride reduction. The HBr salt of hydroxy amine **19a** was dissolved in aqueous acetonitrile and treated with a 1 M aqueous CAN solution (eq 4). Although GC analysis



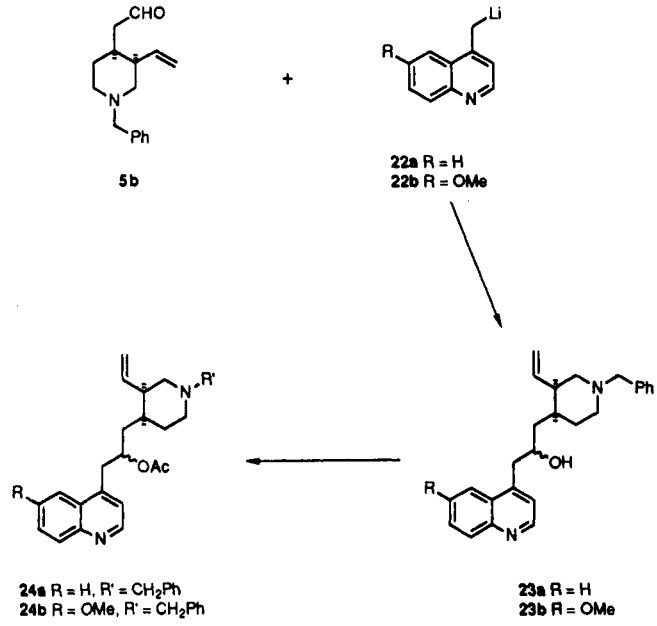
(4)

19a X = H_2
19b X = O

of a worked up aliquot showed a complex mixture and the absence of starting material, the desired product was not detected. It is possible that instead of abstracting the hydroxyl hydrogen atom, CAN is oxidizing the ammonium salt to the corresponding aminium radical. Further oxidation by a second equivalent of Ce^{4+} would generate an imine, which is subsequently hydrolyzed to the free amine in the acidic aqueous media. Since the protonated amine proved unstable to the reaction conditions, keto amide **18** was reduced with sodium borohydride to give hydroxy amides **19b**. Treatment of these compounds with excess CAN reagent yielded only starting material. The apparent failure of this reaction is not easily explained. While this oxidation, in principle, could be sluggish, stirring **19b** in the presence of 10 equiv of CAN at rt for 1 week failed to produce any product. One might also propose that perhaps these substrates lack the proper orbital overlap to fragment. However, two pieces of evidence suggest otherwise. First, the hydroxy amides **19b** are diastereomeric at the hydroxyl position and neither isomer reacted under these conditions as indicated by NMR. Secondly, the work of Wilson[7a] and Hwu[16] has shown this fragmentation to follow a stepwise mechanism, which implies that orbital overlap is not critical for this reaction.

The desired transformation was eventually realized through the use of a silicon-directed Baeyer–Villager oxidation.[17] Keto amide **18** was oxidized with buffered *m*-CPBA in dichloromethane to give lactam–lactone **20** as a single regio- and stereoisomer (Scheme IV). Unexpectedly, this seven-membered lactone resisted opening with methoxide. Although examination of models revealed one side of the carbonyl to be relatively accessible to nucleophilic attack, the formation of a tetrahedral intermediate may be energetically unfavorable as in order to accommodate a new sp^3 center, the trimethylsilyl group

Scheme V



would have to rotate into a sterically encumbered pseudoaxial position. Fortunately, treatment of cis lactone **20** with methanolic HCl cleanly produced vinyl ester **21**, which was subsequently reduced with $LiAlH_4$ and then oxidized under Swern conditions to give *N*-benzylmeroquinene aldehyde (**5b**). Now having fulfilled our goal of synthesizing meroquinene derivatives via silicon-directed reactions, we decided to carry this intermediate further and our plan was to convert aldehyde **5b** to alcohols **23**.

Lepidine or 6-methoxy-4-methylquinoline, prepared by modification of Campbell and Schaffner's protocol from 4-methoxyaniline,[19] was treated with LDA at −78 °C to generate anions **22a** or **22b**. Aldehyde **5b** was then added dropwise to a cooled solution of either anion, and the resulting alcohols were then acetylated with acetic anhydride[20] to give acetates **24a,b**. Intermediates related to **24** (i.e., R′ = H) have been previously converted to the *Cinchona* alkaloids.[5]

Experimental Section

General. High-field ^1H NMR (300 MHz) and ^{13}C NMR (75 MHz) were recorded in deuteriochloroform ($CDCl_3$) as the solvent on either a General Electric QE-300 or GN-300 spectrometer. GC/MS were recorded on a Hewlett-Packard Model 5992B GC/MS system equipped with a 25M capillary OV-100 fused silica column. Exact mass determinations were obtained from either Hoffmann-La Roche, Nutley, NJ, or the NIH Rockefeller Mass Spectrometry Biotechnology Resource at Rockefeller University,

(16) Hwu, J. R.; Gilbert, B. A. *J. Organomet. Chem.* **1987**, *332*, 53.
(17) Hudrlik, P. F.; Hudrlik, A. M.; Nagendrappa, G.; Yimenu, T.; Zellers, E. T.; Chin, E. *J. Am. Chem. Soc.* **1980**, *102*, 6894.
(18) Mancuso, A. J.; Huang, S. L.; Swern, D. *J. Org. Chem.* **1978**, *43*, 2480.
(19) Campbell, K.; Schaffner, I. *J. Am. Chem. Soc.* **1945**, *67*, 86.
(20) Steglich, W.; Höfle, G. *Angew. Chem., Ind. Ed. Engl.* **1969**, *8*, 981. See also: Höfle, G.; Steglich, W.; Vorbrüggen, H. *Angew. Chem., Int. Ed. Engl.* **1978**, *17*, 569.

New York, NY. Elemental analyses were performed by Schwarzkopf Microanalytical Laboratory, New York. Infrared (IR) spectra were recorded on a Mattson Instruments Polaris FT-IR spectrometer, DTGS (deuterated triglycine sulfate) detector. Analytical thin-layer chromatography (TLC) was performed on Baker-Flex silica gel 1B-F sheets or Merck Kieselgel 60 F_{254} glass plates. Preparative TLC was performed using Merck Kieselgel 60 F_{254} glass plates (thickness: 0.5, 1.0, or 2.0 mm as specified). Flash chromatography was performed according to the procedure of Still with EM Science silica gel 60 (particle size 0.040–0.063 mm; 230–400 mesh). Radial chromatography was carried out on a Chromatotron Model 7942T from Harrison Research using 1, 2, or 4 mm silica plates as specified.

Dry tetrahydrofuran and ethyl ether were distilled from sodium/benzophenone ketyl under N_2 immediately prior to use. Dry benzene was obtained by azeotropic distillation followed by distillation from sodium/benzophenone ketyl and storage over Na metal. Dry methylene chloride was distilled from P_2O_5 protected from the atmosphere via a drying tube. Dry methanol was obtained by distillation from Mg/I_2. Diisopropylamine and triethylamine were distilled from CaH_2 and stored over 4-Å sieves. Oxalyl chloride was distilled atmospherically prior to use. Organometallic reagents (nBuLi) were periodically titrated according to the procedures of Gilman and D'Hollander. All other reagents used were of commercial (Aldrich) purity unless otherwise specified. All reactions were carried out in flame-dried glassware under an atmosphere of N_2 unless stated otherwise.

Synthesis of Amine 11. Triethylamine (11.6 g, 0.115 mol), benzylamine (12.2 g, 0.114 mol), and 2-(2-bromoethyl)-1,3-dioxolane (9.8 g, 0.055 mol) were dissolved in DMF (100 mL) and stirred for 23.5 h at rt under N_2. The turbid mixture was poured into a separatory funnel and distilled with saturated $NaHCO_3$ (250 mL). This was extracted with ether (3 × 250 mL, 1 × 100 mL), and the combined ethereals were successively treated with H_2O (3 × 200 mL) and brine (1 × 100 mL). After being dried over $MgSO_4$, the solution was filtered and concentrated in vacuo to yield a pale yellow syrup. The crude product, a mixture of benzylamine and mono- and dialkylated amines (10.15 g, 90%) that decomposed on exposure to silica gel, was purified by vacuum distillation (0.25 mmHg; bp 97–103 °C) to give 7.51 g of amine **11** (66.5%): ^{1}H NMR (ppm): 1.88–1.94 (dt, 2 H, CH_2CH_2CH, J = 4.5, 6.6 Hz), 2.76–2.81 (t, 2 H, NCH_2CH_2), 3.80 (s, 2 H, $ArCH_2N$), 3.81–3.99 (m, 4 H, OCH_2CH_2O), 4.92–4.96 (t, 1 H, CH_2CH), 7.32–7.33 (m, 5 H); GC/MS (relative abundance) 207.0 (M^+, 1.7), 120.0 (24.5), 107.0 (45.9), 106.0 (48.9), 91.0 (100.0), 73.0 (14.9).

Synthesis of 3-(Trimethylsilyl)-2(*E*)-propenoyl Chloride (12). To a solution of 3-(trimethylsilyl)-2(*E*)-propenoic acid (7.0 g, 49 mmol) in CH_2Cl_2 (150 mL) was added oxalyl chloride (87 g, 69 mmol). The mixture was stirred at reflux for 2 h, at which time, the reaction was cooled to rt and concentrated in vacuo. The residue was concentrated two more times in the presence of CCl_4 (to ensure removal of all the oxalyl chloride) before being distilled at aspirator pressure (~20 mmHg) to give pure acid chloride **12** as a clear, colorless oil (bp 110–115 °C; 5.78 g, 73%). This product was not characterized and was used immediately in the next step.

Synthesis of Amide 13a. Distilled 3-(trimethylsilyl)-2(*E*)-propenoyl chloride (0.85 g, 5.2 mmol) was dissolved in CH_2Cl_2 (4 mL) at 0 °C under N_2. To this was added triethylamine (0.55 g, 5.4 mmol), which caused the reaction mixture to become dark yellow. After 5 min at 0 °C, distilled amine **11** (0.83 g, 4.0 mmol) in CH_2Cl_2 (6 mL) was added. The ice bath was removed, and the reaction mixture was allowed to warm to rt. Thin-layer chromatography indicated no starting material after 5 min. Water (75 mL) was added, and the mixture was extracted with ether (3 × 100 mL). The combined ethereals were washed with H_2O (3 × 50 mL) and brine (1 × 50 mL), dried ($MgSO_4$), filtered, and concentrated in vacuo to give a light brown oil. Chromatography (6 in × 50 mm silica gel column eluting with EtOAc/Hex, 4:6) gave pure enamide **13a**: R_f = 0.27 (silica gel, EtOAc/Hex, 3:7); IR (cm^{-1}, $CDCl_3$) 1630, 1250; ^{1}H NMR (ppm) 0.064, 0.17 (s, 9 H, $Si(CH_3)_3$), 1.90–2.06 (m, 2 H, CH_2CH_2CH), 3.47–3.60 (t, 2 H, NCH_2CH_2), 3.82–3.98 (m, 4 H, OCH_2CH_2O), 4.65, 4.68 (s, 2 H, $ArCH_2N$), 4.85–4.94 (t, 1 H, CH_2CH), 6.59–6.65 (d, 1 H, COH-C=CH, J = 18 Hz), 6.81–6.87 (d, 1 H, COHC=CH, J = 18 Hz), 7.17–7.36 (m, 5 H, Ar); GC/MS (relative abundance) 333.2 (M^+, 2.1), 318.1 (2.9), 260.2 (100.0), 172.1 (59.9), 127.1 (28.5), 91.1 (44.3), 73.1 (47.7); exact mass (CI$^+$): calcd for $C_{18}H_{27}NO_3Si$ 333.1760, found 334.1866.

Synthesis of Aldehyde 13b. Crude dioxolane **13a** (contaminated with amide **16**, formed during the acylation of crude **11**; 5.50 g, 16.5 mmol) was dissolved in THF (150 mL) and added to a flask containing 30% HCl (100 mL). This homogeneous mixture was stirred at rt for 42 h. At this point thin-layer chromatography showed no starting material and a new lower R_f spot. The acid was neutralized with saturated $NaHCO_3$ and concentrated in vacuo. After the resulting aqueous solution was extracted with ether (3 × 150 mL), the organic layers were combined, washed with H_2O (1 × 50 mL), dried with $MgSO_4$, filtered, and concentrated in vacuo to a pale yellow syrup (4.40 g, 95%; still contaminated with amide **16**): R_f = 0.19 (silica gel, EtOAc/Hex, 3.7); IR (cm^{-1}, $CDCl_3$) 1715, 1625; ^{1}H NMR (ppm) 0.077, 0.16 (s, 9 H, $Si(CH_3)_3$), 2.69–2.72, 2.79–2.83 (t, 2 H, CH_2CHO), 3.68–3.72 (t, 2 H), 4.69 (s, 2 H, $ArCH_2N$), 6.61–6.67 (d, 1 H, COCH=C(TMS)*H*, J = 18.3 Hz), 7.19–7.41 (m, 6 H, aromatic and α-vinyl proton), 9.74, 9.79 (s, 1 H, *CH*O); GC/MS (relative abundance) 289.1 (M^+, 1.3), 274.1 (10.3), 216.0 (79.2), 172.0 (56.1), 127.0 (26.7), 91.1 (100.0), 73.0 (52.7).

Synthesis of 14. To a flame-dried flask containing 1-(triphenylphosphoranylidene)-2-propanone (6.41 g, 20.1 mmol) in THF (75 mL) was added crude aldehyde **13b** (4.40 g, 15.2 mmol) in THF (25 mL). The reaction mixture was heated to reflux and stirred at that temperature for 14 h. The reaction mixture was cooled to rt and concentrated in vacuo to yield a solid yellow mass. This was partitioned between EtOAc (200 mL) and water (75 mL). The aqueous phase was extracted two more times with EtOAc (200 mL each), and the combined organics were washed with water (2 × 50 mL) and brine (1 × 50 mL), dried ($MgSO_4$), filtered, and concentrated in vacuo to give a brown residue that solidified on standing. Chromatography (6 in × 35 mm silica gel column, eluting with EtOAc/Hex, 4:6) gave 3.19 g of pure enone **14** (64%; 60.5% overall from bromodioxolane **10**): R_f = 0.30 (silica gel, EtOAc/Hex, 4:6); IR (cm^{-1}, $CDCl_3$) 1675, 1625; ^{1}H NMR (ppm) 0.09, 0.16 (s, 9 H, $Si(CH_3)_3$), 2.23, 2.24 (s, 3 H, $COCH_3$), 2.42–2.56 (m, 2 H, NCH_2CH_2), 3.48–3.60 (t, 2 H, NCH_2CH_2), 4.62, 4.70 (s, 2 H, $ArCH_2N$), 6.04–6.10 (d, 2 H, J = 15.9 Hz), 6.61–6.82 (m, 2 H), 7.19–7.41 (m, 6 H, aromatic protons and one vinyl proton); GC/MS (relative abundance) 329.3 (M^+, 25.4), 314.2 (62.7), 286.3 (69.4), 246.3 (29.1), 91.1 (100.0), 73.2 (53.7); exact mass (NCI$^-$) calcd for $C_{19}H_{27}NOSi$ 329.1811, found 328.1720.

Reaction of Enone 14 with LDA and TBDMS-Cl in HMPA. Diisopropylamine (0.021 g, 0.21 mmol) was dissolved in THF (1 mL), cooled to −78 °C, and treated with *n*-BuLi (0.09 mL, 2.5 M in hexanes; 0.22 mmol). The reaction mixture was stirred at −78 °C for 0.25 h, warmed to 0 °C, stirred for 0.5 h, and finally cooled back down to −78 °C at which time enone **14** (0.062 g, 0.19 mmol) was then added dropwise as a THF solution (2 mL). The reaction was quenched at −78 °C with *tert*-butyldimethylsilyl chloride (0.031 g, 0.21 mmol) in HMPA (0.6 mL) after 0.5 h. The mixture was immediately diluted with pentane (15 mL) and washed with H_2O (2 × 10 mL). The organic layer was collected over $MgSO_4$, filtered, and concentrated in vacuo. NMR and GC/MS indicated the sole product to be enamide **16** and not the desired cross diene enol ether: R_f = 0.50 (silica gel, EtOAc/Hex, 4:6); ^{1}H NMR (ppm) 0.14 (s, 9 H, $Si(CH_3)_3$), 4.53–4.55 (d, 2 H, $ArCH_2N$), 5.93 (broad, 1 H, CON*H*), 6.20–6.26 (d, 1 H, COC-*H*=CH, J = 18.7 Hz), 7.10–7.16 (d, 1 H, COCH=C*H*, J = 18.7 Hz), 7.30–7.37 (m, 5 H, Ar); GC/MS (relative abundance) 233.1 (M^+, 21.4), 218.0 (31.8), 217.0 (86.5), 216 (52.3), 160.0 (base peak, $M^+ - Si(CH_3)_3$, 100.0), 91.1 (68.4), 73.0 (34.4).

Synthesis of Enol Ether 17. A 25-mL, two-neck round-bottom flask was charged with dry CH_2Cl_2 (5 mL), dry triethylamine (0.49 g, 4.8 mmol), and *tert*-butyldimethylsilyl triflate (0.93 g, 3.5 mmol). After the mixture was stirred at rt for 5 min, enone **14** (1.06 g, 3.2 mmol) was added fairly rapidly as a CH_2Cl_2 solution (15 mL). During this addition, the mixture turned from pale yellow to deep orange. The reaction was quenched with water (5 mL) after 5 min and extracted with pentane (1 × 50, 1 × 25 mL), and the organics were pooled over $MgSO_4$. This was repeated two more times on this scale so that after concentration in vacuo a total of 4.47 g of crude enol ether **17** were collected. Chroma-

tography on a 6 in. × 90 mm silica gel column, eluting with EtOAc/Hex, 3:7, gave 3.51 g (82%) of pure **17**: R_f = 0.46 (silica gel, EtOAc/Hex, 3:7); ^{1}H NMR (ppm) 0.32, 0.34, 0.37 (s, 15 H, $SiCH_3$), 1.19 (s, 9 H, $C(CH_3)_3$), 1.90–2.60 (m, 5 H), 2.80–3.05 (m, 2 H), 3.30–3.40 (m, 1 H), 3.45–3.54 (dt, 1 H, J = 3, 15 Hz), 4.71–4.76 (d, 1 H, J = 14.7 Hz, $ArCH_2N$), 4.93–4.98 (d, 1 H, J = 14.7 Hz, $ArCH_2N$), 4.85 (s, 1 H, enol proton).

Synthesis of Ketoamide 18. Pure enol ether **17** (3.51 g, 7.9 mmol) was dissolved in dry methanol (40 mL), and $KF{\cdot}2H_2O$ (0.9 g, 10 mmol) was added. This mixture was brought to reflux and stirred at this temperature for 2 h. At this point thin-layer chromatography indicated the absence of starting material, so the reaction was cooled to rt and concentrated in vacuo. The resulting solid residue was partitioned between EtOAc (30 mL) and H_2O (10 mL), and the aqueous phase was extracted with a second portion of EtOAc (30 mL). The organics were combined, washed successively with H_2O (1 × 10 mL) and brine (1 × 10 mL), dried over $MgSO_4$, filtered, and concentrated in vacuo. This gave 2.26 g (87%) of crystalline **18**, pure by NMR. The overall yield for this bicyclic compound from the starting bromodioxolane **10** was 43% after six steps. A sample was evaporatively recrystallized for X-ray analysis (mp 114–115 °C): R_f = 0.19 (silica gel, EtOAc/Hex, 3:7); IR (cm^{-1}, neat) 1640, 1725; ^{1}H NMR (ppm) 0.045 (s, 9 H, $Si(CH_3)_3$), 1.66–1.76 (dq, 1 H, C*H*TMS), 1.94–2.06 (m, 1 H), 2.13–2.34 (m, 4 H), 2.41–2.57 (m, 2 H), 2.70–2.73 (t, 1 H, NCOC*H*, J = 4.5 Hz), 3.24–3.29 (m, 2 H, $CONCH_2C$), 4.52–4.57 (d, 1 H, $ArCH_2N$, J = 14.4 Hz), 4.63–4.68 (d, 1 H, $ArCH_2N$, J = 14.4 Hz), 7.22–7.30 (m, 5 H, Ar); ^{13}C NMR (ppm) −1.77, 24.16, 26.52, 34.57, 39.90, 43.05, 43.28, 44.23, 50.95, 127.83, 128.39, 128.98, 137.40, 171.12, 211.45; GC/MS (relative abundance) 329.2 (M^+, 13.2), 260.0 (49.0), 180.0 (10.6), 91.1 (100.0), 73.0 (39.7); exact mass (EI^+) calcd for $C_{19}H_{27}NO_2Si$ 329.1811, found 329.1882. Anal. Calcd for $C_{19}H_{27}NO_2Si$: C, 69.26; H, 8.27. Found: C, 69.13; H, 8.32.

Synthesis of Lactone 20. Keto amide **18** (0.99 g, 3.0 mmol) was dissolved in CH_2Cl_2 (30 mL), diluted with 4.5 mL of aqueous 0.7 M Na_2HPO_4 (3.03 mmol), and treated with *m*-CPBA (0.78 g, 4.5 mmol). Vigorous stirring was maintained at rt for ~39 h, at which time the reaction was diluted with H_2O (20 mL) and extracted with ether (2 × 100 mL). The combined ethereals were washed with saturated $NaHCO_3$ (1 × 30 mL) and brine (1 × 30 mL), dried ($MgSO_4$), filtered, and concentrated in vacuo. The crude product (1.11 g, 107%) was chromatographed on a 6 in. × 50 mm silica gel column, eluting with EtOAc/Hex, 3:7 to give 0.90 g (86%) pure lactone **20** as a white solid: R_f = 0.19 (silica gel, EtOAc/Hex, 3:7; 2 elutions); IR (cm^{-1}, $CDCl_3$): 1250, 1625, 1725; ^{1}H NMR (ppm) 0.16 (s, 9 H, $Si(CH_3)_3$), 1.78–1.86 (m, 1 H, C*H*TMS), 2.05–2.18 (m, 1 H), 2.37–2.57 (m, 4 H, CH_2COOR and CH_2CH_2N), 2.73–2.81 (t, 1 H, NCOC*H*, J = 12.9 Hz), 3.18–3.29 (m, 2 H, NCH_2), 4.34–4.54, (m, 2 H, CH_2OCO), 4.56–4.60 (d, 1 H, $ArCH_2N$, J = 14.1 Hz), 4.66–4.71 (d, 1 H, $ArCH_2N$, J = 14.1 Hz), 7.28–7.35 (m, 5 H, Ar); GC/MS (relative abundance) 345.1 (M^+, 10.7), 330.2 (26.2), 317.1 (17.9), 286.3 (17.9), 188.2 (20.2), 91.0 (100.0), 73.0 (26.2).

Synthesis of Methyl Ester 21. The purified lactone **20** (0.2 g, 0.6 mmol) was dissolved in dry methanol (7 mL), and one drop of concentrated HCl was added. The reaction was stirred at rt for 24 h, neutralized with saturated $NaHCO_3$, and concentrated in vacuo. The residue was suspended in H_2O (10 mL) and extracted with EtOAc (2 × 25 mL). The combined organics were washed with brine (1 × 10 mL), dried over $MgSO_4$, filtered, and concentrated in vacuo. The product, pure by NMR, was recovered in greater than 100% yield (0.17 g, 101%). Chromatography (6 in. × 25 mm silica gel column, eluting with EtOAc/Hex, 6:4) gave pure **21** (0.118 g, 71%): R_f = 0.28 (silica gel, EtOAc/Hex, 6:4); ^{1}H NMR (ppm) 1.68–1.77 (m, 2 H, CH_2CH_2N), 2.14–2.50 (m, 3 H, $CHCH_2COOCH_3$), 3.20–3.29 (m, 3 H, CH_2NCO, $NCOCHCH{=}CH_2$), 3.64 (s, 3 H, $COOCH_3$), 4.46–4.51 (d, 1 H, $ArCH_2N$, J = 14.7 Hz), 4.65–4.70 (d, 1 H, $ArCH_2N$, J = 14.7 Hz), 5.24–5.30 (m, 2 H, $CH{=}CH_2$), 5.74–5.86 (m, 1 H, $CH{=}CH_2$), 7.21–7.32 (m, 5 H, Ar); GC/MS (relative abundance) 287.2 (M^+, 41.3), 256.1 (8.9), 214.1 (36.4), 186.2 (12.2), 91.1 (100.0).

Synthesis of *N*-Benzylmeroquinene Alcohol 5a. After lithium aluminum hydride (0.16 g, 4.2 mmol) was suspended in dry THF (40 mL) at 0 °C, ester **21** (0.40 g, 1.4 mmol) in THF (10 mL) was added cautiously. The ice bath was removed, and the reaction mixture was brought to reflux. After the mixture was heated for 2 h, thin-layer chromatography indicated the absence of starting material. The reaction mixture was cooled (0 °C) and quenched with saturated NH_4Cl. The clear supernatant was decanted, and the salts were washed with ether (2 × 25 mL, total volume). Saturated NH_4Cl was then added to the salts to generate a slurry, which was diluted with ether (50 mL) and treated with sufficient $MgSO_4$ to cause the slurry to clump into rocks. This heterogeneous mixture was passed through a fritted-glass funnel, and the filtrate was combined with the first organic layer. After drying ($MgSO_4$), filtration and concentration in vacuo gave **5a** as a colorless oil (0.33 g, 97% crude): R_f = 0.15 (silica gel, EtOAc/Hex, 4:6); IR (cm^{-1}, neat) 3600–3000 (broad); ^{1}H NMR (ppm) 1.38–1.70 (m, 5 H, NCH_2CH_2CH, CH_2CH_2OH), 2.04–2.12 (m, 1 H, $NCH_2CHHC{=}CH_2$), 2.22–2.32 (m, 2 H, NCH_2CH_2), 2.72–2.75 (broad d, 1 H, $NCH_2CHHC{=}CH_2$), 2.98–2.83 (broad d, 1 H, $NCH_2CHHC{=}CH_2$), 3.40–3.45 (d, 1 H, $ArCH_2N$, J = 13.5 Hz), 3.48–3.52 (d, 1 H, $ArCH_2N$, J = 13.5 Hz), 3.64–3.68 (t, 2 H, CH_2OH), 5.00–5.09 (m, 2 H, $CH{=}CH_2$), 6.14–6.26 (m, 1 H, $CH{=}CH_2$), 7.22–7.31 (m, 5 H, Ar); GC/MS (relative abundance) 245.2 (M^+, 7.2), 244.2 (9.0), 228.1 (5.2), 200.2 (12.6), 172.1 (11.8), 154.1 (19.1), 146.1 (13.0), 134.1 (22.0), 91.1 (100.0).

Synthesis of *N*-Benzylmeroquinene Aldehyde 5b. Oxalyl chloride (0.090 g, 0.71 mmol) and dimethyl sulfoxide (stored over 4-Å sieves; 0.11 g, 1.4 mmol) were dissolved in CH_2Cl_2 (3 mL) under a blanket of N_2 at −63 °C (dry ice/chloroform). To this was added crude meroquinene alcohol (**5a**; 0.14 g, 0.56 mmol) in CH_2Cl_2 (3 mL) dropwise over 5 min. The reaction mixture was stirred at −63 °C for 30 min, when triethylamine (0.33 g, 3.2 mmol) was added rapidly. After the mixture was warmed to rt, water was added (5 mL) and the product was extracted into $CHCl_3$ (2 × 20 mL). The combined organics were washed with water (1 × 10 mL), dried over $MgSO_4$, filtered, and concentrated in vacuo. Thin-layer chromatography indicated some alcohol was still present, so the crude mixture was reacted under the same conditions as above to give aldehyde **5b**, pure by NMR, in 83% yield: R_f = 0.50 (silica gel, EtOAc/Hex, 4:6); ^{1}H NMR (ppm) 1.52–1.59 (quintet, 2 H, CH_2CH_2CH), 2.12–2.50 (m, 6 H, NCH_2CH_2, $HCCH$, CH_2CHO), 2.70–2.81 (broad dd, 2 H, NCH_2CH), 3.43–3.48 (d, 1 H, $ArCH_2N$, J = 13.2 Hz), 3.50–3.54 (d, 1 H, $ArCH_2N$, J = 13.2 Hz), 4.98–5.14 (ddd, 2 H, $CH{=}CH_2$, J = 2.1, 10.2, 17.4 Hz), 6.12–6.25 (m, 1 H, $CH{=}CH_2$), 7.25–7.33 (m, 5 H, Ar), 9.77 (s, 1 H, C*H*O); GC/MS (relative abundance) 243.2 (M^+, 6.5), 242.2 (4.9), 215.1 (17.5), 214.1 (29.7), 200.2 (21.9), 134.1 (21.4), 124.1 (20.8), 120.1 (10.6), 91.1 (100.0).

Synthesis of 6-Methoxy-4-methylquinoline. To a flask containing $ZnCl_2$ (0.65 g, 4.7 mmol) was added 4-methoxyaniline (4.64 g, 37.7 mmol) in ethanol (12 mL), followed by the addition of $FeCl_3{\cdot}6H_2O$ (16 g, 60 mmol). After this black slurry was heated to 80 °C via a constant heat bath, methyl vinyl ketone (fractionally distilled after drying with $CaCl_2/K_2CO_3$; 2.1 g, 30 mmol) was added dropwise as an ethanol solution (21 mL) over a 1-h period. Once the addition was complete, the bath was replaced by a heating mantle and the blue-black viscous solution was heated to reflux for 2 h.

After being cooled to rt, the black solution was diluted with 25% NaOH (100 mL) and then passed through a Florisil plug (washed with EtOAc). The plug was continually washed until the filtrate was essentially colorless. The two-phase solution was combined with brine and transferred to a separatory funnel, and the aqueous layer was drawn off. The organic layer was collected over $MgSO_4$, filtered, and concentrated in vacuo to a solid black mass. This residue was taken into THF (250 mL) and reacted with triethylamine (4.6 g, 4.5 mmol), DMAP (0.15 g, 1.23 mmol), and acetic anhydride (6.4 g, 6.4 mmol) at rt for 2 h.

At this point, the reaction mixture was concentrated in vacuo and partitioned between EtOAc and H_2O (100 mL each); the aqueous phase was extracted with a second portion of EtOAc (100 mL), and the combined organics were washed with 10% HCl (3 × 100 mL). These acid extracts were pooled and neutralized with solid Na_2CO_3. Extraction with EtOAc (2 × 100 mL) was followed by drying of the organic phases ($MgSO_4$), filtration, and concentration in vacuo. Further purification by flash chromatography (3 in. × 50 mm, eluting with EtOAc/Hex, 6:4) yielded 0.91 g of 6-methoxy-4-methylquinoline (17.5%): R_f = 0.25 (silica gel, EtOAc/Hex, 6:4); ^{1}H NMR (ppm) 2.65 (s, 3 H, $ArCH_3$), 3.95 (s,

3 H, ArOCH_3), 7.16-7.20 (m, 2 H, $H_{5,7}$), 7.35-7.39 (dd, 1 H, H_3, J = 2.7, 9 Hz), 7.99-8.02 (d, 1 H, H_8, J = 9 Hz), 8.63-8.65 (d, 1 H, H_2, J = 4.2 Hz); GC/MS (relative abundance) 173.1 (M^+, 100.0), 158.0 (14.4), 130.1 (67.3), 103.1 (10.9), 77.0 (13.1).

Synthesis of Alcohols 23b. Distilled diisopropylamine (0.060 g, 0.06 mmol) was dissolved in THF (1 mL), cooled to -78 °C, and treated with *n*-BuLi (0.24 mL, 2.3 M in hexanes; 0.55 mmol). The reaction mixture was stirred at this temperature for 0.25 h and then warmed to 0 °C for 0.5 h. After the mixture was cooled to -78 °C, 6-methoxy-4-methylquinoline (0.082 g, 0.47 mmol) was added dropwise as a THF solution (1.5 mL). Once again the reaction mixture was warmed to 0 °C and stirred for 0.5 h. The resulting red solution of anion **22b** was cooled one last time to -78 °C and treated dropwise via syringe with a THF (2 mL) solution aldehyde **5b** (0.10 g, 0.41 mmol). The cold bath was replaced with a large, well-packed ice bath, and the reaction mixture was allowed to gradually warm to rt overnight. The mixture was quenched with H_2O (2 mL) and concentrated in vacuo. The dark brown residue was suspended in H_2O (15 mL) and extracted with EtOAc (2 × 30 mL). The organics were collected over $MgSO_4$, filtered, and concentrated in vacuo. Purification was achieved by eluting a 1-mm chromatotron plate with MeOH/CH_2Cl_2, 1:19 (0.099 g, 58.2%): R_f = 0.42 (silica gel, MeOH/CH_2Cl_2, 1:9); IR (cm^{-1}, neat) 3100-3600, 1100, 1250; ^1H NMR (ppm) 3.41-3.53 (m, 2 H, NCH_2Ph), 3.95 (s, 3 H, ArOCH_3), 4.08-4.18 (m, 1 H, C*H*(OH)), 4.87-5.12 (m, 2 H, HC=CH_2), 6.16-6.30 (m, 1 H, *H*C=CH$_2$), 7.21-7.39 (m, 8 H, Ph and $H_{3,5,7}$ from quinoline ring), 7.98-8.00 (d, 1 H, H_8), 8.60-8.62 (two overlapping d, 1 H each, isomeric H_2); mass spectrum 416 (M^+), 401, 398, 398, 325, 307, 173, 91; exact mass (EI^+) calcd for $C_{27}H_{32}N_2O_2$ 416.2464, found 416.2461.

Synthesis of Acetates 24b. The purified alcohols (0.09 g, 0.22 mmol) were dissolved in THF (4.4 mL) and treated with triethylamine (0.033 g, 0.33 mmol), DMAP (catalytic amount), and acetic anhydride (0.048 g, 0.46 mmol). After the mixture was stirred at rt for 19.5 h, the solvent was removed in vacuo. The resulting residue was suspended in H_2O (15 mL) and extracted with EtOAc (2 × 30 mL). The organics were combined over $MgSO_4$, filtered, and concentrated in vacuo to give crude **24b**, pure by TLC and NMR: R_f = 0.22 (silica gel; EtOAC/Hex, 6:4); IR (cm^{-1}, neat) 1730, 1245; ^1H NMR (ppm) 2.04, 2.08 (s, 3 H, OCOCH_3), 4.02, 4.03 (s, 3 H, ArOCH_3), 4.26-4.46, 4.98-5.06 (m, 2 H, HC=CH_2), 5.29-5.36 (m, 1 H, C*H*(OAc)), 5.79-5.92, 6.03-6.16 (m, 1 H, *H*C=CH$_2$), 7.15-7.39 (m, 8 H), 7.57-7.63 (d, 1 H), 7.99-8.03 (d, 1 H), 8.66-8.68 (d, 1 H); mass spectrum 458 (M^+), 443 415, 399, 367, 91; exact mass (EI^+) calcd for $C_{29}H_{34}N_2O_3$ 458.2569, found 458.2568.

Synthesis of Acetates 24a. Reaction of distilled lepidine with aldehyde **5b** under similar conditions used to synthesize alcohols **23b** gave the corresponding des-6-methoxy alcohols. These alcohols (**23b**) were not purified, but rather acetylated, as in the synthesis of **24b**, directly to the corresponding des-6-methoxy acetates **24a** in 62.3% overall purified yield: R_f = 0.03 (silica gel, EtOAc/Hex, 4:6; alcohols); R_f = 0.18 (silica gel, EtOAc/Hex, 4:6; acetates); ^1H NMR (ppm, acetates) 1.93, 1.99 (s, 3 H, OCOCH_3), 3.03-3.19 (dd, 2 H, ArCH_2CH(OAc), J = 7.2, 13.5 Hz), 3.35-3.49 (m, 2 H, NCH_2Ar), 4.47-4.65, 4.99-5.12 (m, 2 H, HC=CH_2), 5.29-5.36 (m, 1 H, C*H*(OAc), 5.90-6.22 (m, 1 H, *H*C=CH$_2$), 7.21-7.27 (m, 6 H, Ph, H_3), 7.58-7.63 (t, 1 H, H_6), 7.69-7.74 (t, 1 H, H_7), 8.11-8.23 (m, 2 H, $H_{5,8}$), 8.81-8.82 (d, 1 H, H_2).

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Registry No. (±)-**5a**, 134261-48-6; (±)-**5b**, 134261-60-2; **11**, 134261-49-7; **12**, 88946-48-9; **13a**, 134261-50-0; **13b**, 134261-59-9; **14**, 134261-51-1; **16**, 134261-52-2; (±)-**17**, 134261-53-3; (±)-**18**, 134261-54-4; (±)-**20**, 134261-55-5; (±)-**21**, 134261-56-6; (±)-**23a** (isomer 1), 134261-65-7; (±)-**23a** (isomer 2), 134261-66-8; (±)-**23b** (isomer 1), 134261-57-7; (±)-**23b** (isomer 2), 134261-61-3; (±)-**24a** (isomer 1), 134261-58-8; (±)-**24a** (isomer 2), 134261-64-6; (±)-**24b** (isomer 1), 134261-62-4; (±)-**24b** (isomer 2), 134261-63-5; Ph_3P=CHCOCH$_3$, 1439-36-7; $CH_3COCH=CH_2$, 78-94-4; 6-methoxy-4-methylquinoline, 41037-26-7; 4-methoxyaniline, 104-94-9; lepidine, 491-35-0.

Supplementary Material Available: NMR spectra of each compound that appears in the Experimental Section and X-ray crystallography data for *cis*-**18** (37 pages). Ordering information is given on any current masthead page.

Electronic and Steric Effects in the Addition of Electrophilic 1,3-Dicarbonylalkyl Radicals to Styrenes

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The addition reactions of 1,3-dicarbonylalkyl radicals to ring-substituted styrenes have been kinetically investigated in MeOH and/or MeCN. It has been observed that the rate effect of ring substituents is nearly identical in the reactions of MeCOĊHCOMe (**1**), MeOCOĊHCOMe (**2**) and MeOCOĊHCOOMe (**4**), the ρ value, in MeOH being -0.96, -1.01 and -1.06, respectively. Since the three radicals are relatively strong oxidants and have similar reduction potentials, an important contribution of the charge transfer structure RCOCHCOR$^-$ $CH_2CHAr^{\bullet+}$ to the addition transition state is suggested. It has also be found that in the reactions of **1** and **4** with α-alkyl-substituted styrenes the rate of addition is strongly influenced by the nature of the alkyl group, decreasing in the order: Me > Et > ^{i}Pr > ^{t}Bu. The observed effects are much larger than those reported for the corresponding reactions of the nucleophilic cyclohexyl radical. It is suggested that the α-alkyl substituents exert an effect of steric inhibition of resonance thereby ring delocalization of the charge and/or unpaired electron in the transition state is significantly reduced. Delocalization may be more important in the reactions of **1** and **4** than in those of the cyclohexyl radical since it is possible that the former utilizes a transition state occurring later along the reaction coordinate and/or characterized by a larger extent of charge transfer.

In the last two decades, the addition reactions of carbon-centered radicals to alkenes have been intensively investigated both from the theoretical and the practical point of view.[1-5] Most of the research has however been

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