trary to previous thinking, be used with good advantage in organic synthesis. It is obvious that in order to fully define the utility of the in situ generated RC(O)Li reagents, much more work is required. Chlorosilanes, ketones, aldehydes, and esters are by no means the only types of electrophiles that merit investigation, and broadly based studies are underway to include the many other classes of electrophiles whose nucleophilic acylation would be of synthetic interest. Most of our work in the nucleophilic acylation of chlorosilanes, ketones, aldehydes, and esters has been carried out by using alkyllithium reagents. To be studied yet are the other major types of organolithiums that are known: aryllithiums, vinyllithiums, allyllithiums, alkynyllithiums, and functionally substituted organolithium reagents of diverse kinds. These problems also are receiving our attention.

Note added in proof: Recent results of R. C. Hui in our laboratories have demonstrated that a 1:1 RLi-to-electrophile stoichiometry also is satisfactory. For example, in a *t*-BuLi/Co reaction with 2-methylcyclohexanone, the yield of acyllithium- to alkyllithium-derived products increases from 66% vs. 26% to 92% vs. 8% on going from a 1:2 to a 1:1 ratio of RLi to the ketone. If this is a general trend, it should readily extend the application of the methodology described here.

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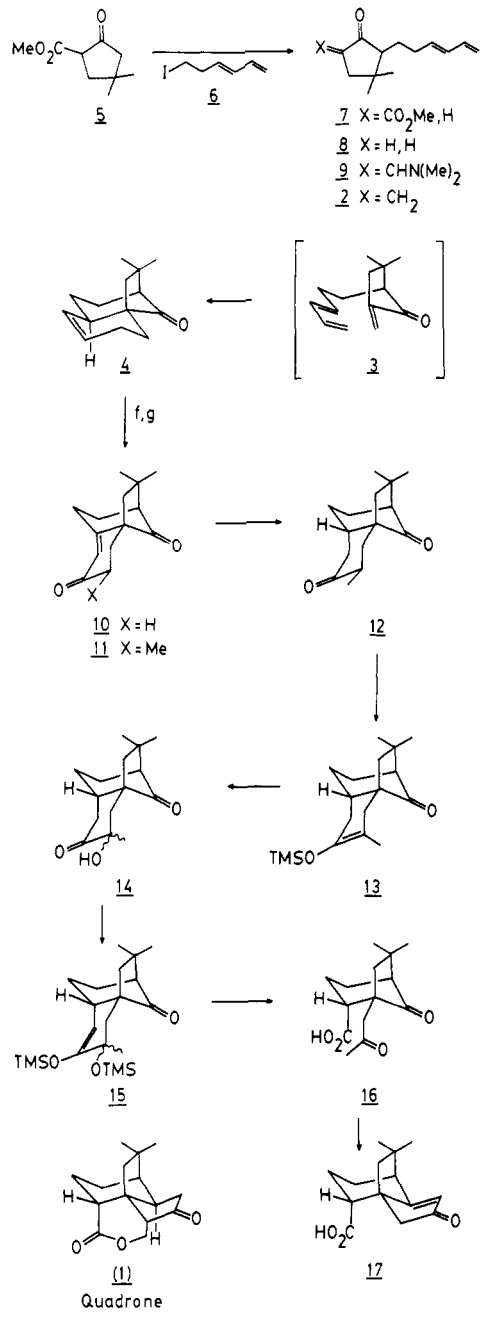
Dietmar Seyferth,* Robert M. Weinstein[1a]
Wei-Liang Wang[1b]
Department of Chemistry
Massachusetts Institute of Technology
Cambridge, Massachusetts 02139
Received January 24, 1983

An Intramolecular Diels–Alder Route to Racemic Quadrone

Summary: A total synthesis of the sesquiterpene quadrone (1) that employs an intramolecular Diels–Alder reaction as the key strategic feature is described.

Sir: The cytotoxic properties and unusual tetracyclic structure of the sesquiterpene quadrone 1[1] have elicited considerable synthetic activity, which has resulted in the development of a number of elegant strategies leading to total syntheses of this natural product.[2] While considering possible routes to quadrone, we were struck with its structural similarity to the kaurane and quassin families of diterpenes[3] and thus attempted to develop a construction of 1 which contained elements that might be applied to the assemblage of these substances.



With respect to quadrone itself, we elected to examine the intramolecular Diels–Alder behavior of the α-methylene cyclopentanone system **2** in the hope of generating a tricyclic system potentially convertible into **1**. The sole literature precedence available at the time we commenced this work suggested that **2** would prefer to undergo cycloaddition via the exo transition state **3**, thus forming the tricycic substance **4**, which possesses trans geometry about the decalin portion of this system.[4] Molecular models of **2** also predicted this result and further indicated that no significant influence on the cycloaddition reaction would be exerted by the *gem*-dimethyl residue present on the cyclopentanone ring of **2**. The alternative endo transition state for reaction of **2** could be ruled out since this geometry requires the developing cyclohexanone ring system to adopt a boat conformation, thereby creating serious non-

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bonded interactions. The anticipated *trans*-decalin ring geometry of **4** is that present in the quassin series, whereas epimerization of this ring junction is required to secure either the kaurane or quadrone systems.

We commenced the synthesis of **1** by alkylating the dianion derived from the β-keto ester **5**[5] with *trans*-1-iodo-3,5-hexadiene (**6**)[6] to obtain **7**, which without purification was decarboxylated into the cyclopentanone **8** by using LiCl in Me_2SO/H_2O.[7] Treatment of **8** with Brederick's reagent,[8] $[(CH_3)_2N]_2CHO$-*t*-Bu, gave the vinylogous amine ketone **9**, which was then reduced with diisobutylaluminum hydride into the α-methylene ketone **2**.[9] Intramolecular Diels–Alder cyclization of **2** in a mixture of toluene and acetonitrile at 120 °C gave the tricyclic ketone **4** as the sole reaction product (oil; 48% overall yield from **5** after chromatography).[10] While the ^{13}C NMR spectrum of **4** indicated it to be only one material, a completely clear assignment of the decalin ring fusion of **4** was not forthcoming from its ^1H NMR spectrum taken at 400 MHz. Furthermore, crystalline derivatives of **4** suitable for X-ray analysis were not easily obtained. Hence, we assumed *trans*-decalin geometry for the adduct and set about developing a means of converting this substance into the synthetic target.

A variety of means to convert **4** into a *cis*-decalin system were investigated, and after considerable experimentation, it was found that allylic oxidation of **4** with a mixture of CrO_3 and 3,5-dimethylpyrazole followed by basic workup gave the enone **10** in 75% yield after chromatography.[11] At this point, several tactics for securing **1** from **10** were examined—the following proved to be the most efficient. Kinetic deprotonation of **10** with LDA and alkylation with iodomethane resulted in production of the methylated enone **11**. Hydrogenation of **11** using 5% palladium on carbon in ethanol containing HCl gave the *cis*-decalin system **12** in 66% yield from **10** after chromatography.[12] Compound **12** was then reacted with trimethylsilyl iodide and hexamethyldisilazane to afford the enol silane **13**.[13] In crude form, this substance was oxidized with a mixture consisting of 4-methylmorpholine 4-oxide containing a catalytic amount of OsO_4 to give the hydroxy ketone **14** in 84% yield from **12**.[14]

Cleavage of the hydroxy ketone **14** was then initiated by deprotonation of the molecule with LDA followed by trapping of the resulting dianion with trimethylsilyl chloride to obtain **15**. Crude **15**, treated with ozone followed by oxidative degradation of the ozonide with $NaIO_4$ and CrO_3, gave the diketo acid **16** (mp 110–113 °C) in 68% yield from **14**.[15] Finally, aldol cyclization of **16** into the cyclopentanone **17** was accomplished in 45% yield by using sodium hydride in refluxing xylene solution.[16] Since **17** has been converted by Danishefsky in excellent yield into quadrone, we terminated our synthetic efforts at this point.[17] Compound **17**, prepared as described above, showed identical spectra, IR, NMR, and mass spectrum, as well as melting point to a sample of **17** kindly supplied to us by Professor Danishefsky.[18] By this route, compound **17** was obtained in 13 steps from **5** in 6% overall yield.

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Registry No. (±)-**1**, 74807-65-1; (±)-**2**, 85083-89-2; (±)-**4**, 85083-90-5; (±)-**5**, 68691-06-5; **6**, 85083-91-6; **7**, 85083-92-7; (±)-**8**, 85083-93-8; (±)-**9**, 85083-94-9; (±)-**10**, 85083-95-0; (±)-**11**, 85083-96-1; (±)-**12**, 85083-97-2; (±)-**13**, 85083-98-3; **14**, 85083-99-4; **15**, 85084-00-0; (±)-**16**, 85084-01-1; (±)-**17**, 78739-64-7.

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(6) Compound **6** was prepared starting from methyl sorbate in the following manner: (a) deprotonation of methyl sorbate followed by kinetic quenching of the resulting enolate as described by Stevens et al. (Stevens, R. V.; Cherpeck, R. E.; Harrison, B. L.; Lai, J.; Lapalme, R. *J. Am. Chem. Soc.* **1976**, *98*, 6317). (b) Reduction of the deconjugated ester with $LiAlH_4$. (c) Mesylation of the homoallylic alcohol with methanesulfonyl chloride in pyridine. (d) Displacement of the mesylate with sodium iodide in acetone.

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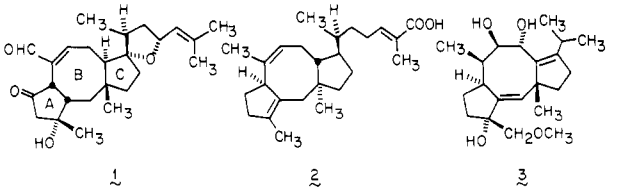
(18) We thank Professor Danishefsky for a generous sample of compound **17**. IR comparison made on a Perkin-Elmer 299B spectrometer, NMR on a Bruker WH-400 spectrometer, and mass spectra on a VG 7035 spectrometer. Melting point of **17** prepared as described, 145–146 °C; lit. 142–146 °C, ref 2a and 2b.

R. H. Schlessinger,* J. L. Wood, A. J. Poss
R. A. Nugent, W. H. Parsons
Department of Chemistry
University of Rochester
Rochester, New York 14627
Received January 7, 1983

Rapid and Efficient Construction of the Ophiobolin Nucleus

Summary: The angularly fused 5-8-5 ring system that comprises the fundamental architectural element of the ophiobolins, ceroplastols, and fusicoccins can be simply produced in two laboratory manipulations. The scheme is general and allows for placement of one or more sites of unsaturation in ring A and positioning of an incipient carbonyl group in ring C. The latter feature should allow in particular for required epimerization of the α proton and proper side-chain installation.

Sir: The assignment of structure and absolute configuration to ophiobolin A (**1**) achieved by Nozoe et al. in 1965[2,3] represents the first definitive characterization of a naturally occurring sesterterpene. Compound **1** has



1 **2** **3**

(1) Author to whom inquiries regarding the X-ray analysis should be directed.

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