(4) The ligand effect was examined in detail in the reaction of 3,4-epoxy-2-pentanone. Other multidentate phosphine ligands, such as bis(diphenylphosphino)propane, (+)-2,3-*O*-isopropylidene-2,3-dihydroxy-1,4-bis(diphenylphosphino)butane (diop), or bis(2-diphenylphosphinoethyl)phenylphosphine (a tridentate ligand), worked much less effectively. In the presence of such ligands, metal precipitation was avoided, but consumption of the starting material was slow. Unidentate ligands, $P(C_6H_5)_3$, $P(C_6H_5)_2CH_3$, $P(CH_3)_2C_6H_5$, $P(n\text{-}C_4H_9)_3$, etc., did not give any satisfactory results either. See also entries 1, 6, 9, and 10 in Table I.
(5) Lick, C.; Schank, K. *Chem. Ber.* **1978**, *111*, 2461, and references cited therein.
(6) (a) Trost, B. M. *Tetrahedron*, **1977**, *33*, 2615. (b) Stille, J. K.; Lau, K. S. Y. *Acc. Chem. Res.* **1977**, *10*, 434. (c) Suzuki, M.; Oda, Y.; Noyori, R. *J. Am. Chem. Soc.* **1979**, *101*, 1623, and references cited therein.
(7) The α position of α,β-epoxy ketones is highly susceptible toward nucleophilic displacement. See Horstmann, H. In "Methoden der organischen Chemie (Houben-Weyl)", Bayer, O., Ed.; Georg Thieme Verlag: Stuttgart, 1977; Vol. VII/2c, Chapter 9, p 2380.
(8) Alternatively the hydrogen migration may occur via an 3-ketoenolate–palladium hydride complex formed by β-elimination in **3**.
(9) The accelerating effect by the added dpe ligand is notable, but the exact reason has not yet been elucidated. For related ligand effects on the reactivity of group 8 metal complexes, see: Yoshida, T.; Yamagata, T.; Tulip, T. H.; Ibers, J. A.; Otsuka, S. *J. Am. Chem. Soc.* **1978**, *100*, 2063. Dedieu, A.; Hoffmann, R. *Ibid.* **1978**, *100*, 2074.

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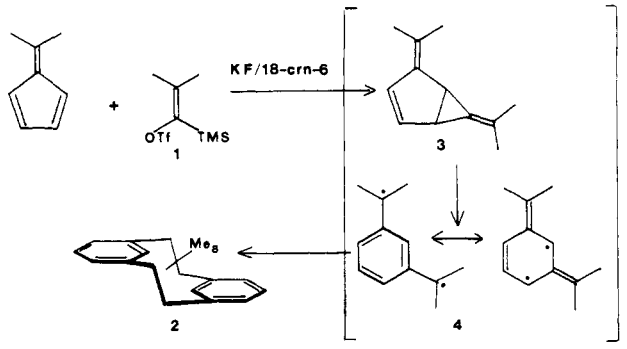
Generation of a *m*-Xylylene Derivative and Formation of a 2,2-Metacyclophane

Sir:

Cross-conjugated π biradicals like trimethylenemethane and 2,2′-bisallyl represent an interesting class of reaction intermediates. Usually derived from opening of small rings with appendaged methylene groups, these species have only $(n/2)-1$ π bonds where n is the number of π electrons. Thus they have been the object of studies to determine their geometry and electron spin state.[1] They are analogous to carbenes in the questions they present to experimentalists and theorists.

m-Xylylene (*m*-quinodimethane) is a member of this group of diradicals, and it too appears to be formed by ring opening of an appropriate precursor. Thus potassium fluoride induced decomposition of the silyl triflate (**1**)[2] in tetrahydrofuran or carbon tetrachloride containing 6,6-dimethylfulvene and 18-crown-6 gives the white crystalline octamethyl-2,2-metacyclophane (**2**) in 20% yield after recrystallization from ethanol. Physical properties of **2**: mp 221–224 °C; *m/e* 320, base peak 161;[3] ^{1}H NMR δ 0.89 (s, 12 H), 1.5 (s, 12 H), 4.9 (s, 2 H), 7.1 (m, 6 H). The characterization follows particularly



from the two-proton singlet which results from the aromatic protons residing over the other aromatic ring in the anti conformation.[4] When the reaction is run in an NMR tube at room temperature, the proton resonances of **2** appear as rapidly as those of fluorotrimethylsilane are formed. Further, the yield according to NMR integrations is 40% based on triflate decomposed. No other products appear in the NMR although a solid deposits on the walls of the tube.

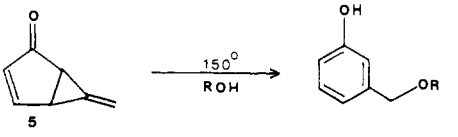
Since electrophilic carbenes like isobutylidene would be expected to add to the internal π bonds of the fulvene on the basis of electronic effects and since steric effects reinforce this expectation,[5] it is not unreasonable that 4,6-diisopropylidenebicyclo[3.1.0]hex-2-ene (**3**) is formed. Ring opening of **3** could lead to the *m*-xylylene (**4**) which dimerizes. Whether triplets are involved in this reaction is not yet clear, although CIDNP signals indicative of triplets are not observed despite the PPP-SCF-CI calculation that triplet *m*-xylylene is 0.34 eV lower in energy than the lowest singlet state of the parent biradical.[6] The assumption that **3** can ring open at room temperature follows from bond-energy considerations which indicate that the *m*-xylylene (**4**) is 20 kcal/mol more stable than its bicyclic precursor, **3**, assuming that each radical site is stabilized to the extent of benzyl radical resonance energy (11 kcal/mol). Thus the bridge bond energy in **3** is roughly −20 kcal/mol!

While it may be surprising that radical recombination is so favorable in this case, it it true that k_{comb}/k_{dis} for cumyl radicals is 20.[7]

Attempts to trap a monomeric species with TCNQ and with di-*tert*-butyl nitroxide at room temperature have led to intractable reaction mixtures. Clearly low-temperature generation of the *m*-xylylene would provide useful information, but we have thus far been unsuccessful in doing so. It will also be instructive to determine if the two *exo*-isopropilidene groups become equivalent in the reaction.

Previous attempts to generate *m*-xylylene include irradiation of *m*-xylene[8] and reductive debromination of α,α'-dibromo-*m*-xylene.[9] In the former case an electronic spectrum was assigned to *m*-xylylene, but no products were obtained. In the latter case no evidence for the biradical was obtained.

Numerous syntheses of 2,2-metacyclophanes have been reported, but most involve bond formation between two previously linked aromatic rings.[10] Only the original synthesis via a Wurtz coupling of α,α'-dibromo-*m*-xylene may involve *m*-xylylene.[11] Thus the route to **2** reported here may be unique and worthy of further exploration. It is also relevant that Berson prepared and isolated 6-methylenebicyclo[3.1.0]hex-3-en-2-one (**5**).[12] This remarkably stable material undergoes ring opening only above 150 °C in alcohol solvents to give the addition product of *m*-quinomethane. The greater stability of **5** compared with **3** may be a result of the greater strength of the CO over the CC double bond. Upon photolysis in an ESR cavity **5** gives a spectrum which appears to be that of the triplet of *m*-quinomethane.



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Total Synthesis of *dl*-Coriolin

Sir:

Coriolin (**1**), a metabolite of *Coriolus consor* is a member of a larger class of microbially derived cis,anti,cis-tricyclo[6.3.0.0^{2,6}] undecanoid sesquiterpenes known as the hirsutanes.[1] The novel ring system of the hirsutanes, embroidered by varied pendant functionality, poses an intrinsic synthetic challenge. Adding to the incentives for the successful realization of this goal are the promising antibacterial and antitumor properties which have been asserted on behalf of several of these compounds.[2] Early and substantive synthetic contributions to this area were provided by Lansbury.[3,4] A major milestone was the total synthesis of hirsutic acid, achieved by Matsumoto[5] and by Trost.[6]

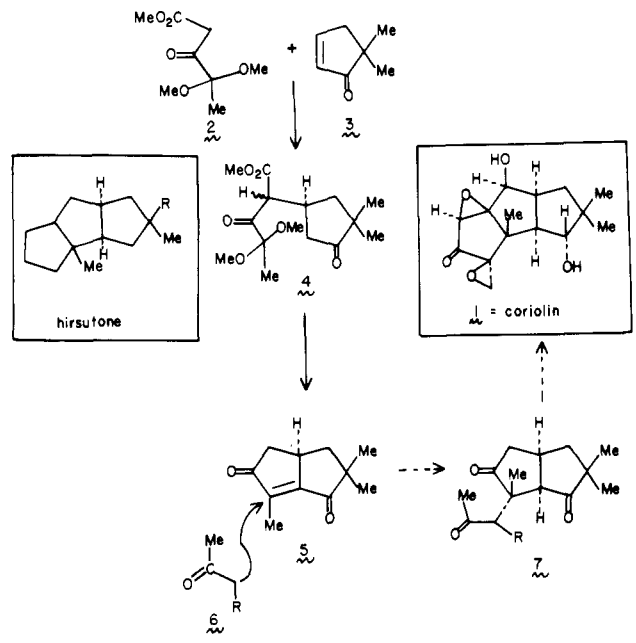
The densely oxygenated coriolin[7] is a particularly attractive target for total synthesis. Its eight centers of chirality arrayed about its six units of unsaturation underscore the need for an orderly approach. Moreover, coriolin and several of its congeners have received rather detailed biological scrutiny vis-à-vis antitumor and antibiotic activity. Indeed, a novel mode of antitumor action, involving the inhibition of uptake of amino acids and potassium ions into tumor cells, has been ascribed to these compounds.[8,9]

Concise and pleasing approaches to the coriolin branch of the hirsutane family have been provided by Tatsuta[10] and by Little.[21] However, for the moment, no fully comprehensive solution has yet been recorded. Below we describe the total synthesis of *dl*-coriolin.

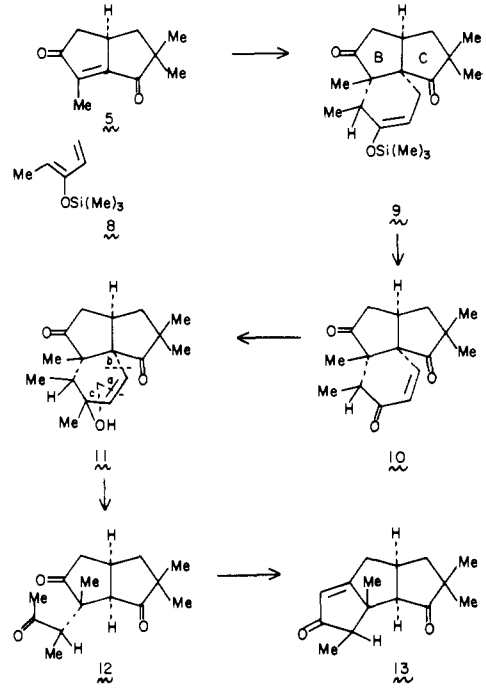
A practical route to enedione **5** was our first subgoal. Michael addition of β-keto ester **2**[11] to cyclopentenone **3**[12] (0.25 equiv of sodium methoxide, methanol, room temperature, 3 days) gave the epimers **4**.[13a] Reaction of **4** with *p*-TsOH in toluene containing 0.2% water, under reflux, provides a 60–65% yield of **5**[13] (Scheme I), mp 54–55 °C, from **4**. We next addressed what we defined to be the central problem of the undertaking, i.e., finding a means for the delivery of an acetonyl fragment **6** (R = H or R = alkyl) to enedione **5** with positional[14] and stereochemical control. The latter issue was complicated by the sheet-like nature of the bicyclic system. Prognoses as to the likely stereochemical sense (α or β) of attack of external reagents at the desired carbon of such an enedione were not convincing.

A more securely based approach is implicit in Scheme II. *It could be predicted that cycloaddition to the double bond would occur in the required α sense, since the alternative and undesired β mode would result, even at the level of the transition state, in an unacceptable trans fusion of the bicyclic BC system.* Reaction of **5** + **8**[15] (3 equiv of **8**, xylene, 120 °C, 11 h) afforded apparently a single product, **9**.[16,17] Treatment of **9** with phenylselenenyl chloride,[15b] followed by oxidation according to Reich and Sharpless,[18] gave the highly crystalline enone **10**, mp 168–169 °C,[13] in 50% overall yield from **5**.

Scheme I



Scheme II



Treatment of **10** with methyllithium (2.5 equiv of MeLi, THF, −78 °C, 1 h) afforded **11**[13,16,19] in 82% yield. The acetonyl group was retrieved from **11** as follows. Ozonolysis followed by Jones oxidation gave, presumably,[20] a hydroxy diacid (cleavage a). Decarboxylation (aqueous barium hydroxide, reflux, 3 h) of the now extraneous bridgehead β-keto acid gave, presumably,[20] a hydroxy monoacid (cleavage b). The next treatment (lead tetraacetate, PhH, room temperature, cleavage c) exposed the required 2-butanon-3-yl residue in the form of the crystalline trione **12**,[13] mp 66–67.5 °C, in 58% yield from **11**. Aldolization-dehydration, according to Stork and Clarke,[21] afforded (70%) **13**.[13,22]

The adjustments of functionality were achieved as shown in Scheme III. Deconjugation, according to Ringold[23] of **13**

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