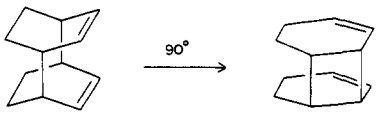
ficient regeneration of **9**. The ultraviolet spectrum of **12**, no maximum >190 nm, gives no clear evidence for an interaction between the neighboring, but nonconjugated, π systems. Photoelectron spectroscopy will provide a better probe of this important possibility.

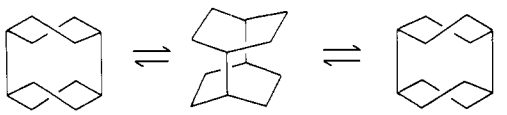
Diene **12** is not thermally stable. At 90 °C, Cope rearrangement to **13** occurred quantitatively over a 2-day period.[11,12] Apparently, the trans-skeletal interactions in **12**, probably of simple steric origin, are of sufficient magnitude (and therein remarkable) to destabilize **12** relative to the all-cis tetrasubstituted cyclobutane **13**.



12 13

Catalytic hydrogenation of **12** gave **1**, perhydro[0.0]paracyclophane: IR ν 2920, 1480, 1460 cm^{-1}. The high symmetry of **1** on the NMR time scale is apparent from its two line proton-decoupled ^{13}C NMR spectrum: δ 30.2 (4 C, d, J = 130 Hz) and 24.6 ppm (8 C, t, J = 126 Hz). The ^1H NMR spectrum shows a significant downfield shift for the endo protons, presumably a result of steric compression:[13] δ 2.03 (8 H, br d, J = 9 Hz), 1.95 (4 H, br s), 1.48 ppm (8 H, br d, J = 9 Hz).

Although more conveniently drawn in the symmetric, double boat conformation **1a**, **1** is better represented as the lower energy, double twist boat **1b** and its mirror image **1c**. It is interesting to speculate whether passage from **1b** to **1c** is by way of the high energy D_{2h} conformer **1a**.



1b 1a 1c

Application of our synthetic scheme to somewhat modified intermediates should permit us access to hexaprismane (**14**) and, via rhodium(I) induced opening of **14**, to tetrahydro[0.0]paracyclophane (**15**), *p*-dibenzene. We shall report our progress with these systems in due course.

14 15

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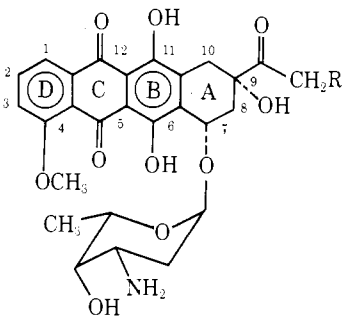
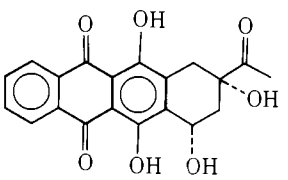
A Novel Synthesis of (±)-4-Demethoxydaunomycinone

Sir:

The anthracyclines daunorubicin (**1**) and adriamycin (**2**) are of current interest in view of their activity against various experimental tumors as well as some types of human cancer.[1]



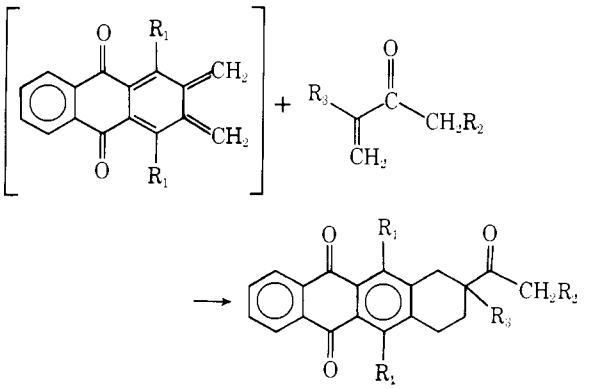
1, R = H
2, R = OH



3

The activity of these compounds can be improved by structural modification, as shown by the recent report that 4-demethoxydaunorubicin is four to eight times more active than daunorubicin itself.[2] We now wish to report a basically new, simple, and efficient synthesis of the dimethyl ether of the corresponding aglycone 4-demethoxydaunomycinone (**3**).

Our synthetic strategy centers on the construction of ring



(1)

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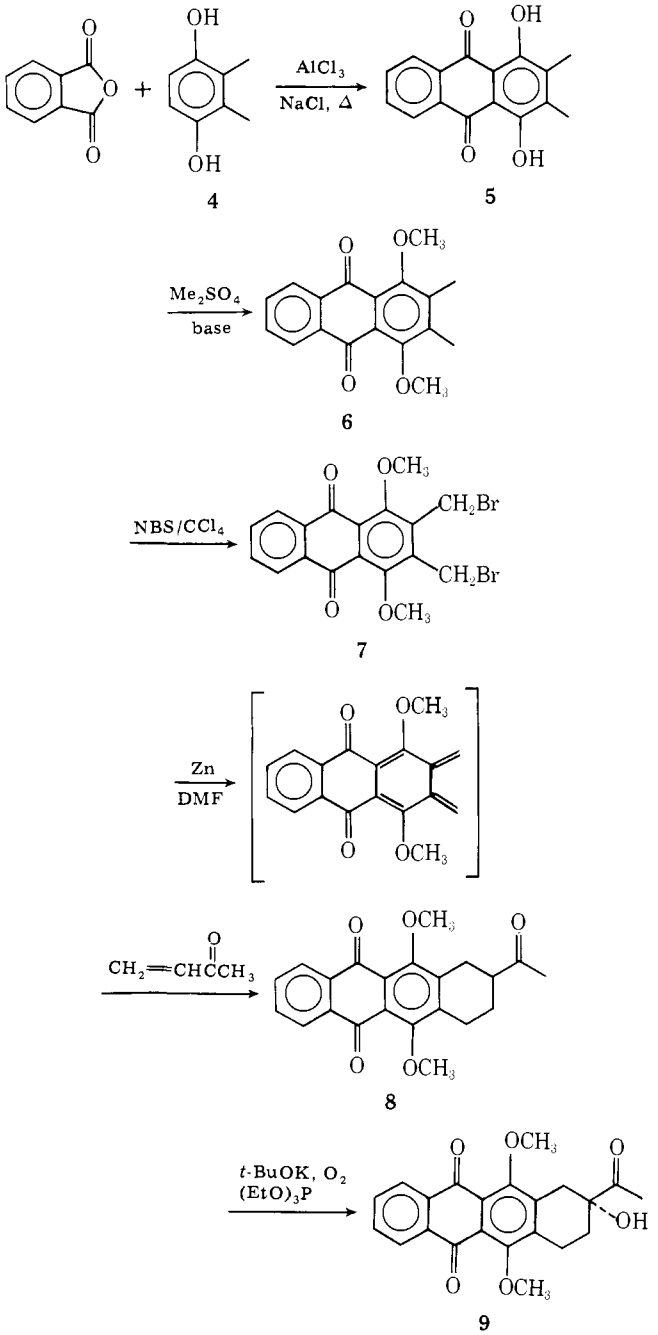
A by the Diels–Alder addition of a reactive *o*-quinodimethane intermediate to the olefinic portion of an α,β-unsaturated ketone as shown in eq 1.[3] The generation of an *o*-quinodimethane from an *o*-xylene derivative and its trapping by a dienophile has ample precedence in the literature.[4]

Phthalic anhydride was condensed with the readily prepared 2,3-dimethylhydroquinone (**4**)[5] ($AlCl_3$/NaCl, 190 °C, 2 min) to give, after heating with dilute hydrochloric acid, 2,3-dimethyl-1,4-dihydroxyanthraquinone (**5**) (81%, mp 252–253 °C).[6,7] Methylation of **5** (Me_2SO_4/K_2CO_3, refluxing 2-butanone, 12 h) afforded the dimethoxy compound **6** (95%, mp 159–160 °C) which was brominated photochemically (NBS/CCl_4, reflux, 8 h) to give the key dibromide **7** (95%, mp 171–173 °C). Reaction of dibromide **7** (Zn dust, DMF, 25 °C, 6 h) in the presence of excess methyl vinyl ketone gave, after aqueous workup, the tetracyclic ketone **8** (52%, mp 145–147 °C). Oxidation of ketone **8** (KO-*t*-Bu/O_2, DMF, −20 °C, 1 h) followed by reduction ($(EtO)_3P$, DMF, −20 °C, 1 h)[8] gave, after mild acid hydrolysis, the hydroxy ketone **9** (55%, mp 184–186 °C).[9]



4 5 6 7 8 9

Since the conversion of **9** to 4-demethoxydaunomycinone (**3**) has already been described,[2,9,10] our synthesis of **9** also constitutes a new synthesis of **3**.

We are currently studying variations of this *o*-quinodimethane approach, in particular the use of oxy derivatives of methyl vinyl ketone in order to provide a direct route to tetracyclic ketones containing an oxygenated side chain.

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A General, Selective, and Facile Method for Ketone Synthesis from Acid Chlorides and Organotin Compounds Catalyzed by Palladium

Sir:

Transition metal catalyzed coupling reactions of organic halides with Grignard reagents or organolithium compounds generally are not applicable for ketone synthesis via the acid chlorides, since the organometallics react with the product ketone.[1] Alkylrhodium complexes, prepared from a rhodium complex and organolithium or Grignard reagents, however, may be used for alkylation of acid chlorides, giving alkyl ketones.[2,3] Unfortunately, in addition to being a two-stage synthesis, this reaction is stoichiometric with respect to rhodium and will not tolerate a number of other functional groups on the acid chloride.

We have found that organotin compounds readily undergo a palladium catalyzed coupling with acid chlorides, thereby providing a general and simple method for preparation of ketones (eq 1).[4] The reaction is general both with respect to the organotin compound and the acid chloride (Table I).

$$\mathrm{RCOCl} + \mathrm{R'_4Sn} \xrightarrow[\text{HMPA}]{\mathrm{PhCH_2Pd(PPh_3)_2Cl\ (1)}} \mathrm{RCOR'} + \mathrm{R'_3SnCl} \quad (1)$$

The following features make this method synthetically attractive. (1) The yields are high, and in many cases virtually quantitative. (2) The reaction can be carried out in the presence

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