employing diene carboxylates.

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Registry No. **1**, 86669-09-2; **2** (R = Et), 76200-27-6; **3** (R = Et), 86688-50-8; **4** (R = Et), 86709-23-1; **5**, 86668-91-9; **5** methyl ester, 32775-94-3; **5** free acid, 32775-95-4; **5**·NH_3, 86669-10-5; **6**, 86668-96-4; **6** free acid, 75283-35-1; **6**-Li, 86669-12-7; **7**, 86668-92-0; **7**-d_5, 86669-11-6; *cis*-**7**, 86708-66-9; **8**, 86668-93-1; **9**, 30982-08-2; **10** (R = Me), 86668-94-2; **11** (R = Me), 86668-95-3; H_2, 1333-74-0; MeOCOC≡CCOOMe, 762-42-5; 2,6-dimethylbenzoquinone, 527-61-7; 2,5-dimethylbenzoquinone, 137-18-8; methyl 7-oxabicyclo[2.2.1]hept-2-ene-3-carboxalate, 86708-65-8; acrolein, 107-02-8; methacrolein, 78-85-3; 2-nitropropene, 4749-28-4; 2-methoxy-6-methylbenzoquinone, 611-68-7; 2-methoxy-5-methylbenzoquinone, 614-13-1; (1α,4α,4aβ,5β,8aβ)-1,2,3,4,4a,5,8,8a-octahydro-4a-(methoxycarbonyl)-1,4-epoxynaphthalene-5-propanoic acid, 86668-97-5; *trans*-6-formyl-2-cyclohexene-1-propanoic acid methyl ester, 86668-98-6; *cis*-6-formyl-2-cyclohexene-1-propanoic acid methyl ester, 86668-99-7; *trans*-6-formyl-6-methyl-2-cyclohexene-1-propanoic acid methyl ester, 86669-00-3; *cis*-6-formyl-6-methyl-2-cyclohexene-1-propanoic acid methyl ester, 86669-01-4; *trans*-6-methyl-6-nitro-2-cyclohexene-1-propanoic acid methyl ester, 86669-02-5; *cis*-6-methyl-6-nitro-2-cyclohexene-1-propanoic acid methyl ester, 86669-03-6; 3-(3-methoxy-3-oxopropyl)-1,4-cyclohexadiene-1,2-dicarboxylic acid dimethyl ester, 86669-04-7; (1α,4aα,8aβ)-7,8a-dimethyl-5,8-dioxo-1,4,4a,8a-tetrahydronaphthalene-1-propanoic acid methyl ester, 86669-05-8; (1α,4aα,8aβ)-6,8a-dimethyl-5,8-dioxo-1,4,4a,8a-tetrahydronaphthalene-1-propanoic acid methyl ester, 86669-06-9; (1α,4aβ,8aβ)-7-methoxy-8a-methyl-5,8-dioxo-1,4,4a,8a-tetrahydronaphthalene-1-propanoic acid methyl ester, 86669-07-0; (1α,4aβ,8aα)-7-methoxy-4a-methyl-5,8-dioxo-1,4,4a,8a-tetrahydronaphthalene-1-propanoic acid methyl ester, 86669-08-1.

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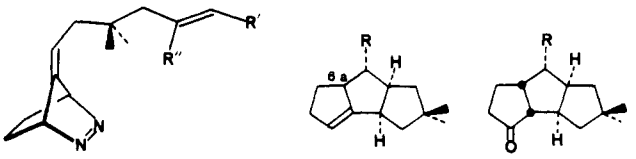
Consequences of Intramolecular Diyl Trapping Reactions Using Unactivated Diylophiles. A Short, Convergent Synthesis of Hirsutene

Summary: The consequences of utilizing an unactivated diylophile in an intramolecular diyl trapping reaction were examined. While the diyls derived from diazenes **6** and **7** both have unactivated diylophile π bonds, their chemistries differ substantially. Thus, while diyl dimerization and a reverse regiochemical mode of trapping are observed when starting with **7**, no dimer and only the normal mode of trapping leading to the linearly fused tricyclopentanoids **8** and **9** in a 5:1 ratio are observed when starting with **6**. The major product, **8**, was converted to ketone **5**, thereby completing a short, efficient, and convergent synthesis of the mold metabolite hirsutene.

Sir: The diyl trapping reaction can be characterized as one that involves a cycloaddition, either inter- or intramolecular, between a 2-alkylidenecyclopentane-1,3-diyl and a diylophile.[1-3] In general, those olefins that are reactive Diels–Alder dienophiles are also reactive diylophiles.[1] For the intermolecular process, diyl dimerization and diyl trapping are competitive. It was for this reason that our published route to racemic hirsutene was a deliberately cautious one that utilized a diylophile activated by an electron-withdrawing group, despite the fact that the trapping reaction was to be intra- rather than intermolecular.[2] Thus, starting with diazene **1**, the cis,anti and cis,syn tricyclopentanoids **2** and **3** were isolated in high



1, R' = CO_2CH_3, R'' = H
6, R' = R'' = H
2, R = CO_2CH_3, C_{6a} β-H
3, R = CO_2CH_3, C_{6a} α-H
8, R = H, C_{6a} β-H
9, R = H, C_{6a} α-H
4, R = CHO
5, R = H

yield (>85%) in a ratio of 9:1. The ring-fusion stereoselectivity was attributed to the lower energy of the extended pseudochair transition-state representation leading to the cis,anti product in comparison with that of the folded pseudochair representation leading to the cis,syn product. Two factors of unequal importance were suggested to contribute to the energy difference: namely, a dominant conformational factor favoring the extended conformation in preference to the folded and the existence of two weakly bonding secondary orbital interactions that can exist in the extended but not in the folded formulation.[1b,2] A natural consequence of the cautious approach outlined above was the requirement that the carbomethoxy activating group be removed at a later stage in the hirsutene synthesis. Thus, after functional group manipulation, a $(Ph_3P)_3RhCl$-induced decarbonylation of keto aldehyde **4** was utilized to achieve this objective. Obviously, the synthesis could have been shortened considerably and the costly decarbonylation step avoided if an unactivated diylophile would have been utilized.

Objectives. With the factors outlined above in mind, diazene **6** was selected for study (1) to determine whether diyl dimerization is competitive with the intramolecular diyl trapping reaction when an unactivated diylophile is present; (2) to determine the cis,anti to cis,syn product ratio for a system wherein the bonding secondary orbital interactions referred to above cannot be operable; (3) to devise a short, efficient synthesis of hirsutene that does not require the removal of the diylophile activating group; and, finally, (4) to compare the regiochemical outcome of the trapping reaction of the diyl derived from diazene **6** with that observed beginning with diazene **7**, which is also devoid of diylophile activation.[3]

Results and Discussion. Compound **6** was conveniently and simply prepared starting with 3,3-dimethylglutaric anhydride.[2] Analysis of the reaction mixture that resulted from simply refluxing a 0.1 M solution of diazene **6** in THF clearly indicated the presence of the cis,anti and

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(2) Little, R. D.; Muller, G. W. *J. Am. Chem. Soc.* **1981**, *103*, 2744–2749.
(3) (a) Little, R. D.; Carroll, G. L. *Tetrahedron Lett.* **1981**, *22*, 4389–4392. (b) Little, R. D.; Carroll, G. L.; Petersen, J. L. *J. Chem. Soc.* **1983**, *105*, 928–932.

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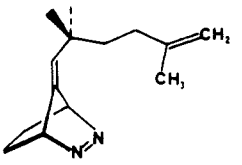
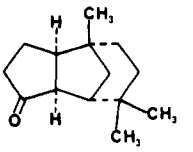
cis,syn ring-fused tricyclopentanoids **8** and **9** in a ratio of 5:1 (76%, not optimized) as well as the absence of detectable amounts of diyl dimer (determined by using 300-MHz proton NMR and capilary column GC/MS). Tricyclopentanoid **8** was readily converted into ketone **5** by using a standard hydroboration–oxidation sequence (61%, not optimized), thereby culminating a much shortened convergent synthesis of racemic hirsutene.[2]

The decrease in the ring-fusion stereoselectivity from 9:1 using the diyl derived from **1** to 5:1 using the diyl derived from **6** is of significance since at least, in principle, it reflects a decrease due to the absence of the transition-state energy-lowering secondary orbital interactions. It is amusing to note that the observed product ratio is so very close to the value of 5.2:1, which one would have predicted on the basis of the use of our previously published estimate of the energy associated with the secondary interactions.[4]

The second observation clearly illustrates that in the present instance, diyl dimerization does not compete with the intramolecular diyl trapping reaction even though an unactivated diylophile is utilized. This result is in marked contrast with the result of trapping experiments using the diyl generated from diazene **7**.[3b] Thus, while in both instances unactivated diylophiles are involved, the only way to minimize competitive dimerization starting from **7** was to use syringe pump techniques. Furthermore, the



7



10

major product obtained once the dimerization was controlled and after hydroboration–oxidation corresponded to the tricyclic ketone **10** (reverse regiochemical mode of trapping) and not to the usually observed linearly fused tricyclopentanoid ring system. These differences in behavior point to the need for exercising caution in attempting to utilize the conclusion drawn from experiments involving diazene **6** to other systems bearing unactivated diylophiles but with differing substitution patterns on the acyclic chain and on the diylophile π bond.

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(4) As is indicated in ref 1b, the calculated order of magnitude of the secondary orbital interactions is but a fraction of a kcal/mol. Since this number is so small, it may in fact be meaningless. Obviously then, one must exercise extreme interpretive caution when noting that the calculated and observed product ratios are so close to one another.

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