temperature appears to be almost the same for mono- and bifunctional Pt compounds. Already in the first platination step the duplex is destabilized, whereafter chelation can take place to form a "kinked" structure, apparently without further major helix destabilization. The details of the helix distortion studied with CD and NMR is the subject of future investigations.

Acknowledgment. We acknowledge EEC support (Grant No. ST2J-0462-C), allowing regular scientific exchange with the group of Prof. Dr J.-C. Chottard, and Johnson and Matthey Ltd. (Reading, UK) for their loan of K_2PtCl_4.

Elaboration of Fused *gem*-Dimethylcyclopropane Systems via Cyclopropene Cycloaddition. A Stereocomplementary Approach

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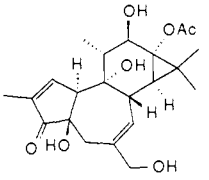
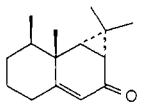
A *gem*-dimethylcyclopropane unit fused to a six-membered carbocycle is a commonly displayed architectural feature characteristic of natural products as structurally diverse as the tumor-promoting diterpene, phorbol (**1**),[1] and the sesquiterpene, aristolone (**2**).[2]



1

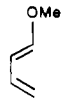
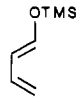


2

To date, access into the bicyclo[4.1.0]heptane carbon skeleton has most often employed dihalocarbene insertion–organocopper substitution technology, which often provides the target in only modest overall yields.[3,4] We wish to report a highly stereoselective, general protocol based on cyclopropene cycloaddition chemistry as an alternative method for the elaboration of fused *gem*-dimethylcyclopropane species. A noteworthy aspect of this methodology is the capability of assembling systems with complementary stereoselection by minor reaction sequence modification.

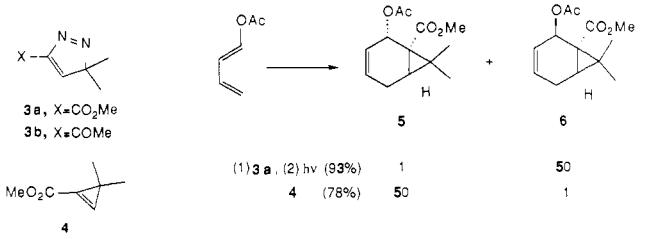
While several substituted cyclopropene species have displayed dienophilic behavior in simple systems,[5] *gem*-dimethylcyclopropene itself is a notoriously poor participant in the Diels–Alder reaction.[6] We were, however, intrigued with the notion of exploiting the cycloaddition chemistry of the carbonyl-activated dimethylcyclopropene series as an attractive entry into the CD rings of phorbol (**1**) and related diterpenes.

Table I. Cycloadditions of Cyclopropane and Pyrazole Addends with Dienes

entry	diene	dienophile	pressure (kbar)	exo:endo	% yield of cyclopropane[a]
1		**3a**	10	1:22	92[b,c]
2		**3a**	10	1:5	89[b,c]
3		**3b**	10	1:19	98[b,c]
4		**3b**	10	1:50	92[b,c]
5		**4**	10	50:1	81[c]
6		**4**	10	50:1	78[c]

[a] All new compounds reported herein exhibited satisfactory spectral (IR, ^1H NMR, ^{13}C NMR), analytical, and/or high resolution mass spectral characteristics. [b] Overall yield for cycloaddition and quantitative photochemical nitrogen extrusion. [c] Yield of isolated, purified products.

The requisite addends **3a**,**b** and **4** were readily prepared by cycloaddition of 2-diazopropane to the appropriately functionalized acetylenes followed, in the case of **4**, by photochemically induced nitrogen extrusion.[7] Typically, thermal cycloaddition reactions (CH_2Cl_2, 50 °C, 96 h) of these reagents required massive excesses of diene to assure adequate yields of adducts. However, performing the additions at high pressure (CH_2Cl_2, 8–10 kbar, 18 h) provided excellent yields of products employing essentially 1:1 diene–dienophile stoichiometry. The results of the reaction of **3a** and **4** with (*E*)-1-acetoxy-1,3-butadiene are illustrative.



Exposure of this diene to cyclopropene **4** (CH_2Cl_2, 10 kbar, 18 h) provided adducts **5** (exo) and **6** (endo) in 78% yield with an exo:endo ratio of 50:1[8,9] paralleling the established proclivity for exo addition exhibited by hindered cyclopropenes.[5a] *In marked contrast, pyrazole* ***3a*** *gave, after cycloaddition* (CH_2Cl_2, *10 kbar, 18 h) and quantitative photochemical nitrogen extrusion (3500 Å, 2.5 h) from the bicyclic pyrazoline intermediate, a 93% overall yield of a mixture of* ***5*** *and* ***6*** *in which the endo diastereomer* ***6*** *prevailed in a ratio of 50:1.*[10] Thus, effective complementary

(1) For synthetic studies on the phorbol system, see: Wender, P. A.; Keenan, R. M.; Lee, H. Y. *J. Am. Chem. Soc.* **1987**, *109*, 4390 and references cited therein.

(2) For recent synthetic studies on aristolone, see: Prasad, C. V. C.; Chan, T. H. *J. Org. Chem.* **1987**, *52*, 120 and references cited therein.

(3) (a) Taylor, M. D.; Minaskanian, G.; Winzenberg, K. N.; Santone, P.; Smith, A. B. *J. Org. Chem.* **1982**, *47*, 3960. (b) Marshall, J. A.; Ruth, J. A. *Ibid.* **1974**, *39*, 1971.

(4) Higher order cuprates can provide some improvement in the alkylation step: Harayama, T.; Fukushi, H.; Ogawa, K.; Yoneda, I. *Chem. Pharm. Bull.* **1985**, *33*, 3564.

(5) For examples of other *gem*-disubstituted cyclopropenes as dienophiles, see: (a) Apeloig, Y.; Arad, D.; Kapon, M.; Wallerstein, M. *Tetrahedron Lett.* **1987**, *28*, 5917. (b) Boger, D. L.; Brotherton, C. E. *Tetrahedron* **1986**, *42*, 2777. For previous studies on the cycloaddition of carbonyl activated *gem*-dimethylcyclopropenes and pyrazoles, see: (c) Dietrich-Buchecker, C.; Martina, D.; Franck-Neumann, M. *J. Chem. Res. (S)* **1978**, 78; *J. Chem. Res. (M)* **1978**, 1014. (d) Huisgen, R.; Reissig, H.-U. *J. Chem. Soc., Chem. Commun.* **1979**, 568. (e) Huisgen, R.; Reissig, H.-U. *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 330.

(6) Closs, G. L.; Closs, L. E.; Boell, W. A. *J. Am. Chem. Soc.* **1963**, *85*, 3796.

(7) Padwa, A. *1,3-Dipolar Cycloaddition Chemistry*; John Wiley & Sons: New York, 1987; Vol. 1, pp 393–558. The photochemistry of **3b** was not well-behaved, and the corresponding cyclopropene was not readily available for cycloaddition studies: Dietrich-Buchecker, C.; Franck-Neumann, M. *Tetrahedron* **1977**, *33*, 751.

(8) The exo/endo designation is relative to the *gem*-dimethylcyclopropane moiety.

(9) The corresponding *Z*-dienes do not react to any appreciable extent under these conditions as evidenced by the total absence of reactivity of (*Z*)-1-acetoxy-1,3-butadiene toward **3a** and **4**.

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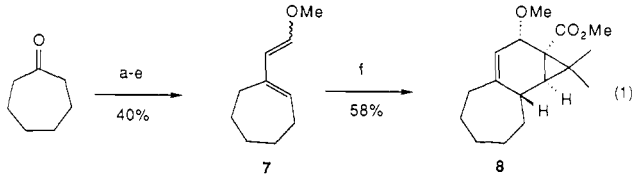
Scheme I[a]



[a] (a) Tf_2O, $(t\text{-}Bu)_2MeC_5H_5N$;[13] (b) CO, MeOH, $Pd(OAc)_2$, Et_3N, Ph_3P;[14] (c) Dibal; (d) Swern oxidation; (e) $Ph_3P^+CH_2OMe\ Cl^-$, *n*-BuLi; (f) **4**, 6 kbar.

diastereoselectivity can be achieved merely by proper selection of dienophile.[11] Additional examples of this process are delineated in Table I.

It is interesting to note that when similar cycloadditions are performed at ambient pressure, the dominant isomer is the same as that produced in the high-pressure experiments although the magnitude of the selectivity was diminished.[12] For example, (*E*)-1-(trimethylsilyloxy)-1,3-butadiene gave a 1:3 (exo:endo) mixture of cycloadducts when warmed with pyrazole **3a** at 50 °C, while **4** gave a 5:1 (exo:endo) mixture under the same conditions (cf. entries 2 and 6, Table I). This observation is suggestive that factors in addition to pressure effects are influencing the complementary stereoselectivity displayed by the two dienophiles. The stereochemical result in entry 4, Table I renders it unlikely that a purely steric argument can be advanced to rationalize the stereocomplementarity of **3a** and **4** since in most cases the most hindered dienophile substituent assumes an endo orientation in cycloadditions with cyclic dienes.[5a,b] Thus, in the absence of other factors, the pyrazole moiety is presumed to be more hindered than the carbomethoxy group. It is tempting to speculate that an unusual competitive secondary orbital interaction may be operative in these reactions. To the best of our knowledge this type of competition is without precedent. This phenomenon, if general, could be profitably exploited in numerous situations as a powerful stereochemical control element in organic synthesis.

To illustrate the synthetic utility of our methodology, a rapid, stereoselective assembly of a model for the BCD ring component of phorbol has been achieved. Readily available dienol ether **7** (2:1 [*E*:*Z*] mixture of geometrical isomers) was reacted with cyclopropene **4** (1 equiv, CH_2Cl_2, 6 kbar, 18 h) to provide tricycle **8** as a single diastereomer in 58% yield.[15] None of the minor *Z*-diene was observed to engage in cycloaddition in this case. This overall process efficiently controls the relative stereochemistry of four contiguous stereogenic centers (three have the correct phorbol orientation) while simultaneously elaborating three of the four rings comprising the tigliane carbon skeleton in a single operation. Application of this methodology to the total synthesis of phorbol and further examination of the unique stereochemical features of this chemistry are underway in our laboratory.

Acknowledgment. We thank the National Institutes of Health (CA-36543) for their generous financial support of this project and Dr. M. J. Heeg, W.S.U., for obtaining the X-ray of the pyrazole adduct of (*E*)-1-((3,5-dinitrobenzoyl)oxy)-1,3-butadiene.

Supplementary Material Available: IR, NMR, and MS data for the compounds discussed (4 pages). Ordering information is given on any current masthead page.

(10) For recent examples of cycloadditions in which a single reagent adds with reversal of diastereoselectivity at high pressure; see: (a) Padwa, A.; Kline, D. N.; Norman, B. H. *Tetrahedron Lett.* **1988**, *29*, 265. (b) Bell, S. I.; Weinreb, S. M. *Ibid.* **1988**, *29*, 4233.

(11) The "endo" nature of the pyrazole adducts was established by single-crystal X-ray analysis of the pyrazole cycloadduct of (*E*)-1-((3,5-dinitrobenzoyl)oxy)-1,3-butadiene. Full details of this crystallographic analysis will appear in a separate publication.

(12) For a discussion of pressure-induced diastereoselectivity in the Diels-Alder reaction, see: Tietze, L. F.; Huebsch, T.; Voss, E.; Buback, M.; Tost, W. *J. Am. Chem. Soc.* **1988**, *110*, 4065 and references cited therein.

(13) Stang, P. J.; Treptow, W. *Synthesis* **1980**, 283.

(14) Ortar, G.; Cacchi, S.; Morera, E. *Tetrahedron Lett.* **1985**, *26*, 1109.

(15) All new compounds in this sequence display satisfactory spectral (IR, ^1H NMR, ^{13}C NMR) and high resolution mass spectral data.

The Palladium-Catalyzed Directed Aldol Reaction of Aldehydes with Ketone Enolates Generated by the Decarboxylation of Allyl β-Keto Carboxylates under Neutral Conditions

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During the last decade new methods have been developed for the directed aldol reaction to produce a desired cross aldol.[1] The success of these methods depends on how to generate enolates regioselectively. Regioselective formation of various metal enolates is now known. The generation of organotransition-metal enolates and their use in directed aldol reaction are attracting increasing interests. Particularly, in situ formation of Ti[2] and Zr[3] enolates and their reactions with aldehydes are well-known. However, stoichiometric amounts of these organometallic compounds are required. Recently aldol reactions catalyzed by Rh complexes involving Rh enolates have been reported.[4] In this communication, we wish to report the catalytic and directed cross aldol reaction based on the generation of the palladium enolates by the decarboxylation of allyl β-keto carboxylates under mild conditions. Concerning the chemistry of palladium enolates, formation of (oxo-π-allyl)palladium intermediates, which can be regarded as palladium enolates, by the reaction of silyl enol ethers with $Pd(OAc)_2$ was proposed.[5] Also reaction of Pd^0 complexes with α-halo carbonyl compounds affords palladium enolates.[6] But standard enolate reactions such as aldol reaction were not reported with these kinds of palladium enolates. Thus the chemistry of palladium enolates is virtually unexplored. We wish to present in this communication the aldol reaction as the first typical enolate reaction of palladium. The characteristic feature of our new method for aldol via the palladium enolates is that the reaction proceeds with a catalytic amount of palladium complex under neutral condition.

We have reported a series of palladium-catalyzed reactions of allyl β-keto carboxylates under neutral conditions via decarboxylation[7] followed by allylation,[8] dehydrogenation,[9] deacetoxylation,[10] and hydrogenolysis.[11] We assumed that the first step in these reactions is the formation of (π-allyl)palladium enolates [(oxo-π-allyl)(π-allyl)palladium complex **16** in Scheme I]. On the basis of this assumption, we investigated the possibility of aldol reaction of the palladium enolate. We carried out intramolecular reaction of allyl β-keto carboxylates having an aldehyde side chain and discovered a very smooth aldol reaction to give the β-ketols

(1) A recent review: Mukaiyama, T. *Organic Reactions*; John Wiley & Sons, inc.: New York; 1982; Vol. *28*, pp 203.

(2) Stille, J. R.; Grubbs, R. H. *J. Am. Chem. Soc.* **1983**, *105*, 1664-1665.

(3) Evans, D. A.; McGee, L. R. *Tetrahedron Lett.* **1980**, *21*, 3975-3978. Yamamoto, Y.; Maruyama, K. *Ibid.* **1980**, *21*, 4607-4610.

(4) Sato, S.; Matsuda, I.; Izumi, Y. *Chem. Lett.* **1985**, 1875-1878. Sato, S.; Matsuda, I.; Izumi, Y. *Tetrahedron Lett.* **1986**, *27*, 5517-5520; *J. Organomet. Chem.* **1988**, *352*, 223-238. Reetz, M. T.; Vougioukas, A. E. *Tetrahedron Lett.* **1987**, *28*, 793-796.

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(7) For reviews: Tsuji, J.; Minami, I. *Acc. Chem. Res.* **1987**, *20*, 140-157. Tsuji, J. *Tetrahedron* **1986**, *42*, 4361-4401.

(8) Shimizu, I.; Yamada, T.; Tsuji, J. *Tetrahedron Lett.* **1980**, *21*, 3199-3202. Tsuji, J.; Yamada, T.; Minami, I.; Yuhara, M.; Nisar, M.; Shimizu, I. *J. Org. Chem.* **1987**, *52*, 2988-2995. Tsuda, T.; Chujo, Y.; Nishi, S.; Tawara, K.; Saegusa, T. *J. Am. Chem. Soc.* **1980**, *102*, 6381-6384.

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(10) Tsuji, J.; Nisar, M.; Minami, I. *Tetrahedron Lett.* **1986**, *27*, 2483-2486.

(11) Tsuji, J.; Nisar, M.; Shimizu, I. *J. Org. Chem.* **1985**, *50*, 3416-3417.

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