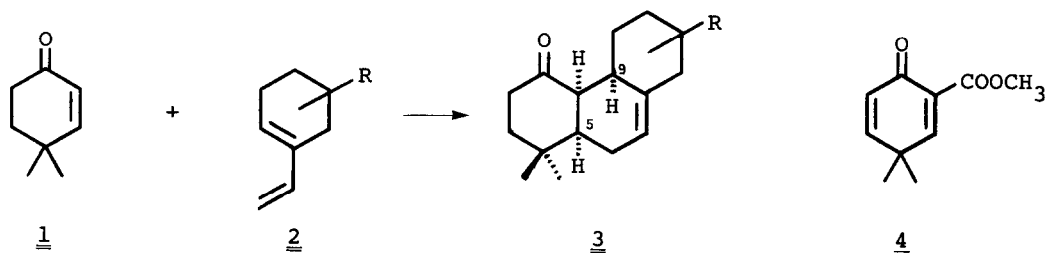


2-CARBOMETHOXY-4,4-DIMETHYL-2,5-CYCLOHEXADIEN-1-ONE
 AS A DIENOPHILE. A CONVENIENT APPROACH TO THE
 4,4-DIMETHYL-1-DECALONE SYSTEM

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In approaches to the total synthesis of polycyclic di- and triterpenoids¹, the cycloaddition of 4,4-dimethyl-2-cyclohexen-1-one (1)² to a suitably functionalized vinylcyclohexene 2 represents an especially attractive general approach. As shown in Scheme 1, such a process not only facilitates the formation of the *gem*-dimethyl containing tricycle 3 (common to a vast number of higher terpenoids¹) with suitable functionalities for further elaboration, it also predetermines the relative stereochemistry of two critical chiral centers C-5 and C-9³ in the desired orientation. Obviously, the feasibility of this approach relies on the reactivity of 1 as a dienophile. In this connection, the Diels-Alder reactions of 1 with isoprene and 1,3-butadiene were examined under a variety of conditions. In no instance however, did the attempted reaction give rise to more than a trace (<5% yield) of the desirable adduct. As a consequence of these findings, several derivatives of 1 were subjected to further investigation.


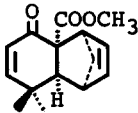

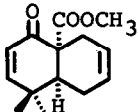

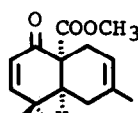

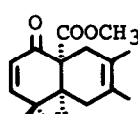


Scheme 1

In sharp contrast to the lack of dienophilicity observed for its parent compound 1, the titled dienone ester 4⁴ was found to be a powerful dienophile⁵. In the presence of boron trifluoride, the cycloaddition of 4 to the four dienes studied (see Table 1) proceeded smoothly and cleanly under mild reaction conditions similar to those given below for cyclopentadiene.

A solution of 4 (297 mg; 1.65 mmol) and boron trifluoride etherate (116 mg; 0.85 mmol) in ether (20 ml) was stirred at room temperature for 20 min. Cyclopentadiene (2.17 g; 33 mmol)⁶ was added as a solution in ether (5 ml). The resulting solution, after stirring for 3 hr, was made basic with aqueous sodium bicarbonate and extracted with methylene chloride. The organic solution, after work-up in the usual manner gave an oil which was chromatographed on silica gel. Elution with a solution of 5% ether in hexane afforded 284 mg of 5: ir (neat) 1738, 1662, 1379 and 1366 cm^{-1} ; nmr (CCl_4) δ 1.17, 1.27 (both s, 3H each, $-\text{C}(\text{CH}_3)_2$), 1.41 (ddd, $J = 9$, $J' = J'' = 2$ Hz, 1H, $-\text{CHH}-$), 1.60 (d, $J = 9$ Hz, 1H, $-\text{CHH}-$), 2.49 (dd, $J = 2.5$, $J' = 1.5$ Hz, 1H, $(\text{CH}_3)_2\text{CCH}-$), 3.00, 3.45 (both m, 1H each, $-\text{CHCH}_2\text{CH}-$), 3.65 (s, 3H, $-\text{OCH}_3$), 5.60 (d, $J = 10$ Hz, 1H, $-\text{COCH}=\text{C}$), 5.75 6.05 (both dd, $J = 6$, $J' = 2.5$ Hz, 1H each, $-\text{CH}=\text{CH}-$), and 6.31 (dd, $J = 10$, $J' = 1.5$ Hz, 1H, $-\text{COCH}=\text{CH}-$); ms M^+ 246.1253 (calcd. for $\text{C}_{15}\text{H}_{18}\text{O}_3 = 246.1256$).

Table 1. Cycloaddition of 4 to 1,3-dienes

Diene	Time (hr)	Product ⁷	Isolated % yield
	3		70
	6		70
	4		90
	96		63

While 4 possesses two double bonds, both theoretically subject to diene attack, the cycloaddition reactions were shown to be completely regioselective. Without exception, the compounds listed in Table 1 were obtained as the only adducts. The exclusive participation of the more substituted double bond is apparently due to enhancement of its reactivity by the electron-withdrawing ester group.⁹

The foregoing report illustrates the first examples of the direct formation of synthetically very useful 4,4-dimethyl-1-decalone derivatives using a Diels-Alder approach. This method for the construction of the gem-dimethyl substituted decalin system compares favorably to those existing¹¹ in terms of both simplicity and efficiency. It is also noteworthy that this method permits direct functionalization of the aforementioned system at C-1, a salient feature which would otherwise be difficult to achieve. Its extension to terpenoid synthesis is in progress.

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References and Footnotes

1. T. K. Devon and A. I. Scott, "Handbook of Naturally Occurring Compounds," Vol. II, Academic Press, New York, N.Y., 1972.
2. R. L. N. Harris, F. Komitsky, Jr., and C. Djerassi, J. Amer. Chem. Soc., 89, 4765 (1967).
3. Steroidal numbering is used throughout for all the compounds possessing two or more rings.
4. Prepared in 53% yield from 1 in two steps: Carbomethoxylation [NaH and CO(OCH₃)₂ in refluxing 1,2-dimethoxyethane] and oxidation [SeO₂ in refluxing t-BuOH-HoAc (19:1)].
5. It was also found that 4,4-dimethyl-2,5-cyclohexadien-1-one underwent cycloadditions with dienes but at a much slower rate. Its addition to 1,3-butadiene, for example, gave 18% yield of the desirable adduct with 32% of the starting material recovered after three weeks when the reaction was carried out under the conditions similar to those cited for 4 and cyclopentadiene (vide infra).
6. In the case of 1,3-butadiene, the ether solution was saturated with the diene throughout the reaction.
7. The stereochemistry follows from the cis and endo rules⁸ governing the Diels-Alder reaction and is confirmed by nmr data.
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9. A similar observation has been made previously on quinones possessing a strongly electron-withdrawing substituent¹⁰.
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