CO ligands in the formation of $W_4(OCH_2\text{-}i\text{-}Pr)_{12}(CO)_3$ suppresses the C–O bond cleavage in $W_4(OR)_{12}(CO)$. The two additional π-acceptor CO ligands withdraw electron density that otherwise would have been used to form the carbide and oxide ligands.

Further studies are in progress.[7]

Supplementary Material Available: Table of fractional coordinates and isotropic thermal parameters (4 pages). Ordering information is given on any current masthead page.

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Use of Methylenecyclopropanone Ketals for Cyclopentane Synthesis. A New Efficient Thermal [3 + 2] Cycloaddition

Shigeru Yamago and Eiichi Nakamura*

Department of Chemistry
Tokyo Institute of Technology
Meguro, Tokyo 152, Japan

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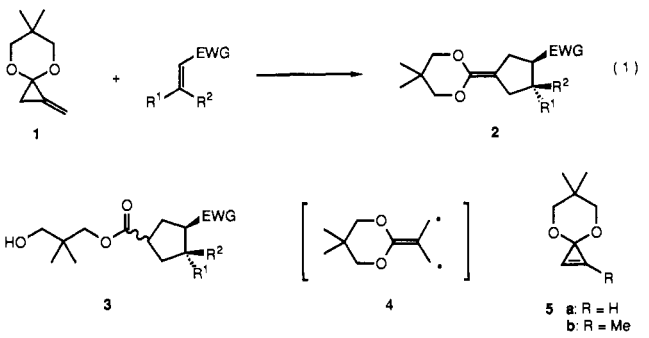
Much interest has recently been focused on reactions that effect direct formation of five-membered carbocycles[1] through [3 + 2] cycloadditions.[2,3] Among these, cycloadditions of trimethylenemethane (TMM)[2] and its organometallic complexes[3] occupy a uniquely important position due to their synthetic as well as theoretical significance. However, except for some intramolecular cases[4] the prototypal thermal reaction of TMM intermediates with olefins have not attained a synthetically useful level of development. We report here that the ketal of methylenecyclopropanone **1** undergoes a highly efficient thermal cycloaddition to electron-deficient olefins which may involve a TMM intermediate (eq 1). An important feature of this reaction is that it is highly regioselective with respect to the three-carbon partner (cf. **4**) and stereoselective with respect to the two-carbon acceptor.



The methylenecyclopropanone ketal **1** has been prepared in two steps from a readily available cyclopropenone ketal **5a**.[5a] Thus, methylation of **5a** (4.21 g, 30 mmol; BuLi, HMPA/THF at −72 °C; then MeI)[5b] followed by isomerization of the product **5b** (*t*-BuOK, 6 mmol, and *t*-BuOH, 9 mmol, in ether at 20 °C)[5c] afforded **1** in 73% overall yield (3.36 g; 70–73 °C/15 mmHg). This compound is a thermally stable, distillable compound, remaining virtually unchanged even after heating for 10 h in CD_3CN (91% recovery). *However, heating **1** with 1 equiv of an electron-deficient olefin leads to a smooth cycloaddition to give a cycloadduct **2** in excellent yield.* Thus, the reaction of **1** (0.77 g, 5.0 mmol) and methyl methacrylate (0.55 g, 5.5 mmol) in 12.5 mL of acetonitrile at 80 °C for 18 h under nitrogen gave the cycloadduct **2** (R^1 = Me, R^2 = H, EWG = COOMe; a single isomer by ^1H and ^{13}C NMR) which was hydrolyzed (with 0.5 mL of H_2O and 100 mg of Amberlyst 15 at room temperature) to the diester **3** and isolated in 91% yield (1.25 g). The reaction is subject to only marginal solvent effects, proceeding several times more slowly as the solvent is changed from CD_3CN to THF-d_8 to C_6D_6, producing in each case the same cycloadduct in excellent yield.

A wide range of electron-deficient olefins bearing ester, nitrile, and ketone functionalities[6] take part in the cycloaddition (Table I). The reaction proceeds cleanly not only with acyclic olefins but also with cyclic ones (e.g., entries 5–9), thus providing a powerful new strategy for the construction of cis-fused bicyclo[3.*n*.0] systems. The reaction, tolerating the use of β,β-disubstituted unsaturated carbonyl compounds, allows the preparation of bridgehead substituted products. For instance, a relatively slow reaction of a 3-methyl-2-butenolide with **1** afforded a bridgehead substituted product in 84% yield after heating for 90 h at 80 °C (entry 5). In line with the well-known effects of pressure upon cycloadditions,[7] we observed a significant rate acceleration under high pressure: the cycloaddition to the methylbutenolide under 13 kbar (in CH_2Cl_2) realized 87% yield only after 16 h at 70 °C (entry 6). The stereospecificity of the cycloaddition is noteworthy. The reaction with *E* and *Z* isomers of methyl 2-heptenoate proceeded with 100% and 98% retention of the stereochemistry of the starting materials (entries 3 and 4, respectively). This stereospecificity as well as the fact that thermolysis of simple methylenecyclopropanes has been considered to generate TMMs[2,8]

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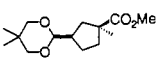
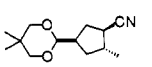
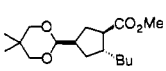
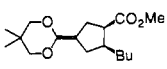
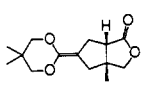
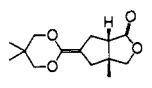
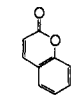
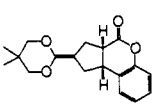
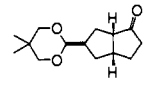
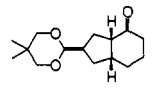
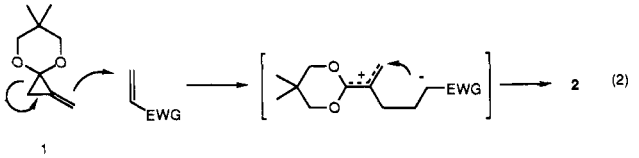
Table I. Cycloaddition of Methylenecyclopropanone Ketal 1 with Electron-Deficient Olefins[a]

entry	olefin	(equiv)	temp (°C)	time (h)	product	% yield[b]
1		(1.1)	80	18		91
2		(1.1)	80	39		85[c]
3		(1.1)	70	26		89
4		(1.1)	70	46		86[d]
5		(0.85)	80	90		84
6		(0.85)	70[e]	16		87
7		(1.1)	80	20		95
8		(1.1)	80	28		88
9		(2.0)	80	28		85

[a] The reaction was carried out in CH_3CN (2.5 mL/mmol except in entries 3 and 4, 0.5 mL/mmol, and in entries 7 and 8, 1.0 mL/mmol). The cycloadduct consisted of a single product (except entries 2 and 4) as determined by capillary GLC and by ^{13}C NMR for the equivalent reaction carried out in CD_3CN. [b] Isolated yield of the ester 3 obtained after hydrolysis of the ketene acetal 2 (Amberlyst 15 in aqueous acetonitrile at room temperature for 30 min). The yields are based on 1 except in entries 5 and 6 wherein they are based on the butenolide. [c] Both the starting olefin and the product were a 88:12 mixture of E and Z isomer. [d] The starting olefin was 100% Z, and the product was 98% Z. [e] The reaction was carried out under high pressure (13 kbar) in CH_2Cl_2.

suggests that the major pathway of the present reaction involves a concerted cycloaddition of a TMM intermediate (e.g., 4).[9] At the present time, however, other possibilities including a step-wise mechanism (eq 2) cannot be rigorously eliminated. Mechanistic studies as well as the synthetic exploration of this new reaction is under active investigation.



(2)

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Supplementary Material Available: Spectral data (IR, ^1H NMR, and ^{13}C NMR) for the new compounds (6 pages). Ordering information is given on any current masthead page.

(8) Curiously, however, there has been reported, to our knowledge, only a single case of *thermal* [3 + 2] cycloaddition of a methylenecyclopropane to olefins (i.e., 2,2-diphenyl derivative added to tetracyanoethylene and related highly reactive olefins, ref 2c).

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Cooperative Site Specific Binding of Oligonucleotides to Duplex DNA

Scott A. Strobel† and Peter B. Dervan*

Arnold and Mabel Beckman Laboratories of Chemical Synthesis, California Institute of Technology Pasadena, California 91125

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Cooperative interactions between DNA binding ligands are critical to their specificity, affinity, and biological activity.[1-4] Triple helix formation by oligonucleotides is the most powerful *chemical* approach to date for the sequence-specific recognition of double helical DNA.[5-9] Hoogsteen hydrogen bonded base triplets, TAT and C+GC, result from pyrimidine oligonucleotides binding site specifically to purine duplex sequences. In the triple helical model, a binding site size of 18 purine base pairs affords 36 discrete sequence-specific hydrogen bonds for recognition of DNA in the major groove. As a possible mechanism for improving the specificity of triple helix formation, we tested whether oligonucleotides could cooperatively bind to a double-stranded DNA template.

We report that two different pyrimidine oligonucleotides, which are nine bases in length, *cooperatively* bind to an 18 base-pair homopurine site in bacteriophage λ genomic DNA by triple helix formation. The purine target sequence 5′-$A_4GA_6GA_4GA$-3′ occurs once in λ DNA[10] (48.5 kilobase pairs) and can be considered as two contiguous unique half-sites, 5′-A_4GA_4-3′ and 5′-A_2GA_4GA-3′.

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