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A SYNTHESIS OF INSIDE-INSIDE BICYCLICS.

A ONE STEP SYNTHESIS OF [10] PARACYCLOPHANES.

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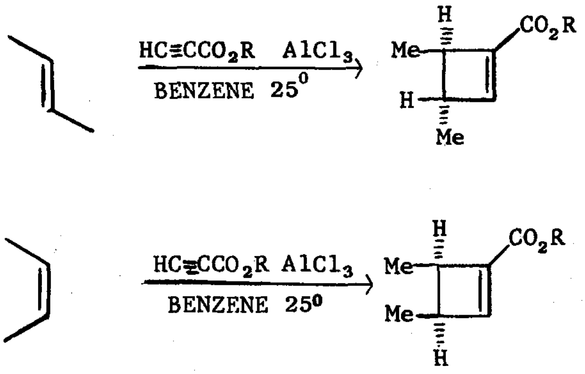
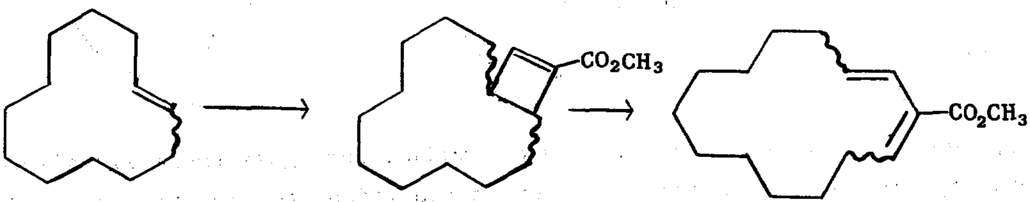
We have recently described the aluminum chloride catalyzed 2+2 cycloaddition reaction of propiolate esters with mono- and 1,2-disubstituted alkenes. Stirring methyl propiolate and 0.5 equiv. of aluminum chloride with a slight excess (1.2-2 equiv.) of alkene in benzene for several days at 25° results in stereospecific cycloaddition in good yield (equation 1).[1]



(1)

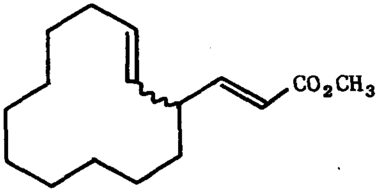
A similar reaction of methyl propiolate with cyclododecene is of special interest since the resulting cycloadduct should undergo facile thermal ring opening to give a methyl cyclotetradecadienecarboxylate (equation 2).[2] This is of interest as an example of a general 2-carbon ring expansion reaction,



(2)

especially applicable to medium and large rings, which in this case can lead to a simple synthesis of muscone.[3] The diene derived from the *trans*-fused cyclobutene is also of special interest since Diels-Alder reactions of cyclic *trans*, *trans*-1,3-dienes are constrained to give inside-inside bicyclic compounds, a class of compounds of considerable interest.[4]

Treatment of methyl propiolate (30 mmole) and aluminum chloride (24 mmole) in toluene with cyclododecene (60 mmole, cis and trans mixture) for seven days at 25° gives the ene adduct 1 in 13% yield and the cis fused cyclobutene adduct 2 in 6% yield. None of the *trans*-fused cyclobutene adduct 3 is obtained. However the two 2:1 adducts 4 and 5 are obtained in 28% and 32% yield respectively, based on methyl propiolate.



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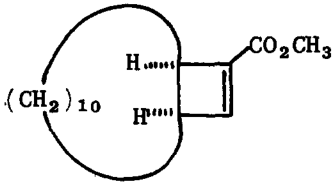

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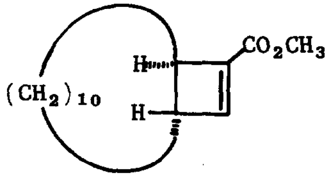

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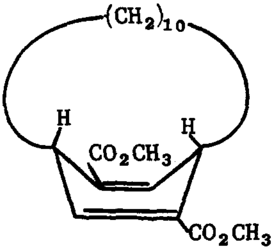

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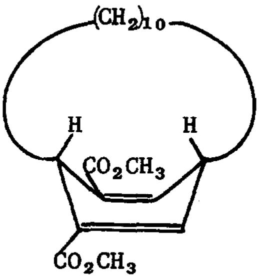

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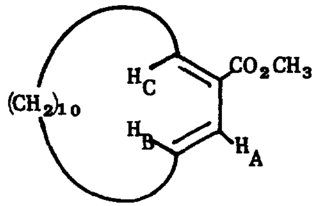

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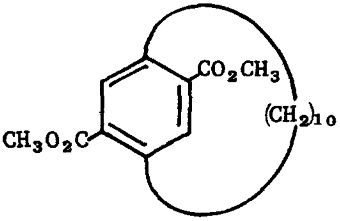

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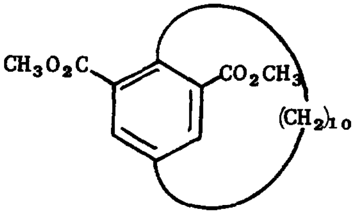

8[8]

Apparently the trans fused cyclobutene adduct undergoes thermally allowed conrotatory ring opening under the reaction conditions to give the expected methyl *trans*, *trans*-1,3-cyclotetradecadiene-2-carboxylate (6).[2] This then undergoes an aluminum chloride catalyzed Diels-Alder reaction to give a mixture of the two inside-inside bicyclo[10,2,2] hexadecadienes 4 and 5.[4a-5] The inside-inside assignment is based on both the mechanistic requirement for a Diels-Alder reaction of a cyclic *trans*-*trans*-diene and on the fact that the inside bridgehead hydrogen protons are shielded relative to the outside protons of model compounds.[4a,8]

Heating either 4 or 5 in carbon tetrachloride for 3 days at reflux in air results in dehydrogenation to give the dimethyl [10] paracyclophanedicarboxylates 7 and 8 in virtually quantitative yield. These compounds are identified by the characteristic aromatic resonance at 7.8 δ and the absorptions of the shielded methylene protons between 0 and 1 δ in the nmr spectra. These compounds are easily distinguished since the benzylic protons of 7 appear as the A and M parts of an AMXX′ multiplet at 2.6 and 3.6 δ. The benzylic protons of 8 appear as the AA′ parts of two AA′XX′ multiplets at 3.4 and 2.7 δ each identical in shape to the benzylic protons of unsubstituted [10] paracyclophane.[6]

It is somewhat surprising that an unstrained cyclobutene such as 3 should undergo ring opening at 25°. It was therefore of interest to isolate 3 and determine how readily it undergoes ring opening to give 6. By lowering the temperature of the cycloaddition to 4° one obtains, after 15 days, 8% of the ene adduct 1, 4% of 4 and 5% of 5 in addition to 22% of a 15:85 mixture of cyclobutenes 2 and 3. A solution of 3 in deuteriochloroform or benzene undergoes complete ring opening in less than one hour at 80°. The cis fused cyclobutene is stable for twelve hours at 80°. This order of reactivity has been observed with cis and trans 3,4-dimethyl-cyclobutene.[8] Given the longer time and possible aluminum chloride catalysis it is not surprising that 3 undergoes ring opening under cycloaddition conditions at 25°. The stereochemistry of diene 6 is clear from an examination of the nmr spectrum; J_{H_A,H_B} = 16 Hz, and H_C absorbs at 6.08 δ indicating that the proton is not strongly deshielded by a cis carbomethoxy group.

The syntheses we have described indicate the preparative value of the aluminum chloride catalyzed reaction of propiolate esters with alkenes in obtaining compounds not easily available by other methods.

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