BISCYCLOPROPYL TITANOCENE: A NOVEL REAGENT FOR THE SYNTHESIS OF ALKYLIDENE AND VINYL CYCLOPROPANES

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Abstract: Alkylidene cyclopropane derivatives are obtained by reaction of biscyclopropyl titanocene with several types of carbonyl compounds, including aldehydes, ketones and esters. In some cases the isomeric vinyl cyclopropane products are also obtained. Biscyclopropyl titanocene also reacts with alkynes forming, after acidification, the corresponding vinyl cyclopropanes.

The cyclopropyl ring system is characterized by unique chemical reactivity resulting from its high degree of ring strain and its propensity to undergo skeletal rearrangements. Among the most extensively used processess involving this functionality is the rearrangement of vinyl cyclopropanes (1) to the corresponding cyclopentenes (2).¹ The more strained alkylidene derivatives (3) are also synthetically useful,^{2,3} especially for the synthesis of alkylidene cyclopentanes (5), via a thermal⁴ or transition metal-catalyzed^{2,5} [3+2]-cycloaddition with alkenes (4). Although a number of methods for the synthesis of 1 and 3 have been developed, these are often limited to certain substitution patterns or involve multistep routes. For example, while olefination with cyclopropyl yildes,⁶ silanes⁷ or selenides⁷ have been utilized, these reactions do not work with esters or with readily enolizable carbonyls.³ Herein, we report a novel method for the synthesis of alkylidene as well as vinyl cyclopropanes by using biscyclopropyl titanocene (15).



We have recently introduced the dimethyl (8),⁸ dibenzyls (9)⁹ and bistrimethylsilylmethyl (10)¹⁰ titanocenes for the synthesis of alkenes (12) from a variety of carbonyl compounds (11), including aldehydes, ketones, esters, lactones and amides. We have also found that 8-10 initiate the ring-opening metathesis polymerization of norbornene¹¹ and convert alkynes (13) to titanacyclobutenes (14).¹¹ Compounds 8-10 are prepared by the addition of organolithium or organomagnesium reagents (7) to titanocene dichloride (6) and are characterized by ease of preparation, isolation, and handling, and by experimental simplicity. As an extension of this work we report herein the chemistry of biscyclopropyl titanocene (15), a previously unknown compound.



Biscyclopropyl titanocene (15) can be easily prepared from titanocene dichloride and cyclopropyllithium, cleanly generated from cyclopropyl bromide and lithium metal.¹² Although it is thermally unstable at room temperature, turning brown within a few hours, 15 can be stored at -20°C for several months without any significant decomposition.

Despite the possibility for β -hydrogen elimination that may form a highly strained cyclopropene, and although 15 has the potential to undergo isomerization to an allyl system, we have found that this compound exhibits olefinating activity similar to 8-10. Thus, stirring of a toluene solution of 15 (2.5 equiv.) at 50° with carbonyl compounds (11) over 10-15 hrs, afforded the corresponding cyclopropylidenes (16). During isolation, these highly strained alkenes sometimes partially isomerized to the vinyl cyclopropanes (17).

Smooth cyclopropylidenation took place with aldehydes (18, 20) as well as a variety of ketones (21-23, 28, 30), including readily enolizable ones (32).



As with 8-10, titanocene 15 also reacted with esters and lactones forming the corresponding enoi ethers. Thus, butyl formate (34) afforded, after chromatography on alumina in the presence of triethylamine, a 71% yield of 35.¹³ Similarly, lactone 36 gave enoi ether 37 in 67% yield, while dodecyl acetate (38) afforded the cyclopropylidene enoi ether 39 in 65% yield. Compound 39 was readily isomerized to the less strained enoi ether 40, which was identical with the product obtained by the methylenation of the cyclopropyl ester 41. The corresponding deuterated derivatives 42 behaved similarly, although the resulting cyclopropylidene 43 isomerized to 44 to a smaller extent (1-2%). Interestingly, compound 45 could not be detected in this reaction mixture, implying that a mechanism involving addition of the cyclopropyl group to the carbonyl, followed by elimination,^{8a} may not operate in this case.



Vinyl cyclopropanes can be prepared by the reaction of 15 with alkynes. Thermolysis of 15 in the presence of diphenylacetylene (46) formed an adduct, which upon quenching with HCl gave 47 in 80% yield, along with regenerated titanocene dichloride (6). Similarly, phenylacetylene (48) gave a 1:1 mixture of the two possible isomers 49 and 50 in 65% yield.



In summary, we have shown that biscyclopropyl titanocene (15) is readily prepared and serves as a useful reagent for the synthesis of alkylidene cyclopropanes from carbonyl compounds and vinyl cyclopropanes from carbonyl compounds and alkynes. A novel feature of this reagent, not possible with other methods, is its ability to convert esters and lactones to alkoxy cyclopropylidenes (e.g., 35, 37, 39). We are currently investigating the ability of these activated alkylidene cyclopropanes to participate in [3+2] cycloadditions with alkenes and alkynes.

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References and Notes

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- 12. Preparation of 15: To a stirred ice-cooled suspension of lithium (25% dispersion in oil, 1.67g, 60 mmol, prewashed several times with dry ether to remove the oil) in dry ether (25 ml) under argon was added dropwise a solution of cyclopropyl bromide (2.43 ml, 30 mmol) in ether (20 ml). After the addition was completed, the resulting cyclopropyllithium reagent was stirred for an additional 30min and filtered through glass wool (under argon) directly into a stirred suspension of Cp₂TiCl₂ (2.70 g, 10.5 mmol) in ice-cooled dry ether (20 ml). After stirring for 90 min the orange mixture was diluted with ice-water and ether. Separation of the ether layer, drying over MgSO4 and evaporation of the solvent yielded bright orange plates of 15 (2.51 g, 92%). ¹H NMR (250 MHz, CeDe) δ: 5.68 (s, 10H, Cp's), 0.65 (m, 2H), 0.34 (m, 2H), -0.57 (m, 1H); ¹³C NMR (63 MHz, CeDe) δ: 113.4 (Cp), 51.2 (CH₂), 14.2 (CH).
- ¹H NMR (250 MHz, C₆D₆) δ: 6.72 (pentet, 1H, olefinic H), 3.82 (t, 2H, OCH₂), 1.55 (m, 2H), 1.36 (m, 2H), 1.13 (m, 2H), 0.96 (m, 2H), 0.84 (t, 3H); ¹³C NMR (63 MHz, C₆D₆) δ: 136.8 (=CH), 92.9 (=C), 68.5 (OCH₂), 32.0, 19.6, 14.0, 4.9, 0.8.