Carbon dioxide fixation by $Cp_2(\eta^3$-allyl)Ti complexes generated from various dienes

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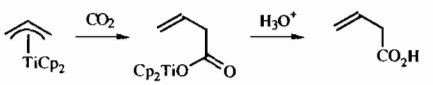
Abstract

$Cp_2(\eta^3$-allyl)Ti complexes having a variety of substituents on their allyl moieties were prepared from corresponding dienes, Cp_2TiCl_2, and Grignard reagents and were subjected to reaction with carbon dioxide. The reaction of CO_2 took place in a highly regioselective manner to give a single β,γ-unsaturated carboxylic acid of a few possible regioisomeric products after hydrolytic workup of the titanium carboxylates. For example, 2-alkylbutadienes selectively yielded $Cp_2(\eta^3$-1-methyl-2-alkylallyl)Ti complexes which were found to react with CO_2 again in a highly regioselective manner to give 2-methyl-3-methylenealkanoic acids as the sole product. A few substituents or their functional groups on the allyl ligand blocked the formation of carboxylic acid, which was discussed in terms of steric and electronic factors. Asymmetric, carbon dioxide insertion reactions were also demonstrated with chiral (neomenthyl-Cp)$_2(\eta^3$-allyl)Ti complexes and provided the carboxylic acids in up to 19% optical purity.

Key words: Carbon dioxide fixation; Titanium complexes; Cyclopentadienyl complexes; Allyl complexes

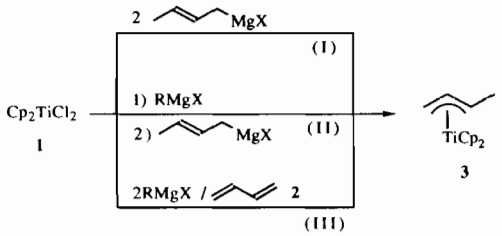
Introduction

In 1981 we [1] and another group [2] reported the first reaction of η^3-allyltitanium complexes [3] of the type $Cp_2(\eta^3$-allyl)Ti with carbon dioxide to afford carboxylic acids according to eqn. (1).



(1)

Scheme 1 shows a few methods, I [4], II [5], and III [4], for the preparation of the requisite η^3-allylTi complexes. Of these three methods, it seemed to us that III would be most attractive, because a variety of



Scheme 1. Methods for the generation of **3**.

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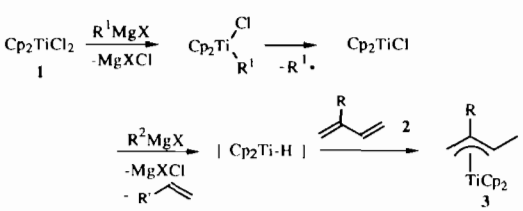
$Cp_2(\eta^3$-allyl)Ti complexes having a functional group(s) and/or a substituent(s) on the allyl moiety could be readily prepared from the corresponding dienes (**2**). This method, which involves the reduction of Cp_2TiCl_2 (**1**) with (at least) 2 equiv. of an alkyl Grignard reagent in the presence of diene (**2**), is known to proceed in the following stepwise manner (eqn. (2)) [4].



(2)

The first equivalent of RMgX (referred to as R^1MgX) reacts with Cp_2TiCl_2 to generate Cp_2TiR^1Cl, which may be isolated under proper conditions [6], but in ethereal solvents collapses to Cp_2TiCl with extrusion of alkyl radical. The resultant Cp_2TiCl is further reduced with the second equivalent of RMgX (shown as R^2MgX) to furnish a Cp_2TiH species [7], that has not been isolated nor characterized in the present system. The Cp_2TiH species then readily adds across the diene bond to form the η^3-allyltitanium complex (**3**).

Usually β,γ-unsaturated acids are prepared by deconjugative protonation or alkylation of the preformed

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α,β-unsaturated acids [8, 9] or, alternatively, by carboxylation of allylmetal reagents prepared by the action of magnesium or zinc to the corresponding allyl halides [10, 11]. The present method taking advantage of hydrotitanation as shown in eqn. (1) is another one which enables the direct preparation of β,γ-unsaturated carboxylic acids from dienes in a highly selective manner and thus complements the above methods. In conjunction with the recent interest in efficient methods of carbon dioxide fixation, we report herein our observation on the reactivity of various $Cp_2(\eta^3\text{-allyl})Ti$ species toward carbon dioxide with full experimental details.

Experimental

General

All reactions were carried out under argon atmosphere to exclude moisture, oxygen and nitrogen. Ether and THF (tetrahydrofuran) were distilled from sodium/benzophenone ketyl prior to use. Hexane and methylene chloride were distilled over calcium hydride before use. Proton NMR spectra were recorded at 90 MHz on a Hitachi R-40 instrument (tetramethylsilane as internal standard and CCl_4 as solvent) or at 300 MHz on a Varian GEMINI-300 spectrometer (tetramethylsilane as internal standard and $CDCl_3$ as solvent) unless otherwise noted. ^{13}C NMR spectra were taken at 75 MHz on a Varian GEMINI-300 spectrometer with $CDCl_3$ as solvent and the middle peak of the solvent as internal standard ($\delta = 77.00$ ppm). IR spectra were recorded on a Jasco A-100 spectrometer. Specific rotation values ($[\alpha]_D$) were measured on a Jasco DIP-370 polarimeter in a 2-ml cell with 10-cm path length. Liquid chromatography refers to flash chromatography on silica gel [12]. Cp_2TiCl_2 was commercially available from Aldrich Chemical Co. and was used without any treatment. All chemicals, unless otherwise cited, were purchased from Tokyo Kasei Kogyo Co. Ltd. (Japan) or Aldrich Chemical Co. and were dried and/or purified in a standard manner [13] if necessary.

Materials

Grignard reagents were prepared from the corresponding alkyl halides and magnesium in a standard manner. Et_2Zn, Et_2AlCl and $EtAlCl_2$ are commercially available as a hexane solution and were used as received. EtZnI was prepared by a reported method [14].

Reaction of $Cp_2(\eta^3$-allyl)Ti complexes (3) with carbon dioxide

General procedure for isolation of $Cp_2(\eta^3$-allyl)Ti complexes [4]. Bis(η^5-cyclopentadienyl)(η^3-methylallyl)titanium (3a)

To a stirred suspension of Cp_2TiCl_2 (2.0 g, 8.0 mmol) and butadiene (**2a**) (0.86 g, 15.9 mmol) in Et_2O (40 ml) was added a solution of n-PrMgBr (1.0 M in Et_2O, 16 ml, 16.0 mmol) over 5 min at 0 °C. After stirring for 30 min at room temperature, the solvent and the excess butadiene were removed thoroughly *in vacuo*. To the residue was added pentane (120 ml). The mixture was stirred for 45 min at room temperature and filtered under argon. The filtrate was cooled slowly to −78 °C, at which point the η^3-allylic complex of titanium (**3a**) crystallized. Purple needles (m.p. 96.5–97.0 °C, lit. 96.5–97 °C (dec.) [4]) of the title titanium complex were obtained in 71% yield by filtration.

Bis(η^5-cyclopentadienyl)(η^3-1,2-dimethylallyl)titanium (3b) (from isoprene (2b))

Yield 71%. M.p. 69–73 °C (lit. 70.5–71 °C (dec.) [4]).

General procedure for the reaction of isolated $Cp_2(\eta^3$-allyl)Ti complexes (3) with carbon dioxide. 2-Methyl-3-butenoic acid (4a) (from 3a)

The isolated complex (**3a**) (1.5 g, 6.4 mmol) was dissolved in Et_2O (30 ml) under argon and gaseous carbon dioxide was passed through the solution for 1 h. After hydrolysis with aq. 4 N HCl (30 ml), air was bubbled into the reaction mixture for 15 min. The precipitated red crystals were collected by filtration to give Cp_2TiCl_2 in 85% recovery. The filtrate was made basic with aq. NaOH and the organic layer was separated and discarded. The aqueous layer was extracted three times with ether and the combined ethereal layers were discarded. The aqueous layer was acidified by the addition of concentrated HCl and extracted with ether. The combined ethereal layers were dried over $MgSO_4$ and concentrated *in vacuo*. The crude product was purified by trap-to-trap distillation to afford the known title compound in 82% yield. ^1H NMR (90 MHz, δ (ppm)): 1.4 (d, 3H), 3.0–3.3 (m, 1H), 5.0–5.3 (m, 2H), 5.8–6.2 (m, 1H), 10.0 (s, 1H).

2,3-Dimethyl-3-butenoic acid (4b) (from 3b)

Obtained in 83% yield along with recovered Cp_2TiCl_2 in 90% yield. ^1H NMR (90 MHz, δ (ppm)): 1.25 (d, 3H), 1.8 (s, 3H), 3.0–3.3 (m, 1H), 5.0 (s, 2H), 11.3 (s, 1H), identical with the reported data [15].

General procedure for the reaction of carbon dioxide with $Cp_2(\eta^3$-allyl)Ti complexes (3) prepared in situ. 2-Methyl-3-butenoic acid (4a)

To a stirred suspension of Cp_2TiCl_2 (2.1 g, 8.4 mmol) and butadiene (**2a**) (0.86 g, 15.9 mmol) in Et_2O (40

ml) was added a solution of n-PrMgBr (1.0 M in Et_2O, 16.6 ml, 16.6 mmol) over 5 min at 0 °C and the resulting solution was subsequently stirred for 30 min at room temperature. Gaseous carbon dioxide was bubbled through the solution for 1 h at room temperature. After this time, the reaction mixture was hydrolyzed by the addition of 30 ml of 4 N HCl, and air was passed into the heterogeneous mixture for 15 min. The workup was performed as described above. The title compound was obtained in 85% yield and Cp_2TiCl_2 was recovered in 93% yield.

*2,3-Dimethyl-3-butenoic acid (**4b**) (from isoprene (**2b**))*

This was obtained in 81% yield and Cp_2TiCl_2 was recovered in 87% yield.

Applicability to 1,3-alkadienes having a functional group

Materials

Myrcene (**2d**) was commercially available. Other dienes (**2c, e–h**) were prepared via standard transformations as shown below.

*3-Methylene-1-dodecene (**2c**)*

Bis-lithiation of methallyl alcohol with n-BuLi and TMEDA (tetramethylethylenediamine) followed by alkylation with $C_8H_{17}Br$ afforded 2-methylene-1-undecanol [16], which was oxidized (DMSO (dimethylsulfoxide)-SO_3-pyridine/NEt_3) [17] and methylenated ($Ph_3P{=}CH_2$) [18]. ^{1}H NMR (300 MHz, δ (ppm)): 0.88 (t, J=6.8 Hz, 3H), 1.28 (br s, 12H), 1.38–1.57 (m, 2H), 2.20 (t, J=7.6 Hz, 2H), 4.97 (s, 1H), 4.99 (s, 1H), 5.04 (d, J=11.3 Hz, 1H), 5.23 (d, J=17.5 Hz, 1H), 6.37 (dd, J_1=17.5, J_2=11.3 Hz, 1H). IR (neat, ν (cm^{-1})): 2925, 2855, 1590, 1460, 990, 890. The spectral properties of this sample were identical with the reported ones [19].

*2-(Trimethylsilylmethyl)butadiene (**2e**)*

Bis-lithiation of methallyl alcohol with n-BuLi and TMEDA followed by silylation with Me_3SiCl afforded 2-(trimethylsilylmethyl)-2-propenol [16], which was oxidized (DMSO-SO_3-pyridine/NEt_3) [17] and methylenated ($Ph_3P{=}CH_2$) [18]. The ^{1}H NMR and IR spectra of this sample were identical with the reported data [20].

*3-Methylene-4-methoxy-1-tridecene (**2f**)*

Lithiation of 2-bromo-2-propenol with t-BuLi followed by the addition of nonanal gave 2-methylene-1,3-dodecanediol [21], which was converted to the title compound via (i) protection of the primary hydroxyl with t-$BuMe_2SiCl$/imidazole, (ii) methylation of the secondary hydroxyl with MeI/NaH, (iii) deprotection of the primary hydroxyl with Bu_4NF, and (iv) oxidation and methylenation as above. ^{1}H NMR (300 MHz, δ (ppm)): 0.85 (t, J=6.8 Hz, 3H), 1.25 (br s, 14H), 1.56 (m, 2H), 3.24 (s, 3H), 3.80 (t, J=6.5 Hz, 1H), 5.08 (d, J=11.3 Hz, 1H), 5.10 (d, J=0.7 Hz, 1H), 5.20 (d, J=0.7 Hz, 1H), 5.41 (dd, J_1=17.5, J_2=1.3 Hz, 1H), 6.31 (dd, J_1=17.5, J_2=11.3 Hz, 1H). IR (neat, ν (cm^{-1})): 2925, 2860, 1590, 1460, 1100, 905.

*3-Methylene-5-methoxy-1-undecene (**2g**)*

This was prepared according to the procedure of **2f** except that 1,2-epoxyoctane was used in place of nonanal. ^{1}H NMR (300 MHz, δ (ppm)): 0.85 (t, J=6.8 Hz, 3H), 1.26 (br s, 8H), 1.37–1.51 (m, 2H), 2.21–2.33 (m, 1H), 2.44–2.57 (m, 1H), 3.28–3.39 (m, 1H), 3.35 (s, 3H), 5.06 (s, 1H), 5.08 (d, J=11.3 Hz, 1H), 5.09 (s, 1H), 5.25 (dd, J_1=17.5, J_2=0.7 Hz, 1H), 6.38 (dd, J_1=17.5, J_2=11.3 Hz, 1H). IR (neat, ν (cm^{-1})): 2925, 2860, 1590, 1460, 1435, 1095, 895.

*3-Methylene-6-methoxy-1-dodecene (**2h**)*

Bis-lithiation of methallyl alcohol with n-BuLi and TMEDA followed by alkylation with 1,2-epoxyoctane afforded 2-methylene-1,5-dodecanediol [16], which was converted to the title compound in an analogous manner to that described for the preparation of **2f**. ^{1}H NMR (300 MHz, δ (ppm)): 0.82 (t, J=6.8 Hz, 3H), 1.22 (br s, 8H), 1.30–1.50 (m, 2H), 1.50–1.64 (m, 2H), 2.08–2.30 (m, 2H), 3.05–3.15 (m, 1H), 3.25 (s, 3H), 4.94 (s, 1H), 4.96 (s, 1H), 4.99 (d, J=11.2 Hz, 1H), 5.17 (d, J=17.5 Hz, 1H), 6.31 (dd, J_1=17.5, J_2=11.2 Hz, 1H). IR (neat, ν (cm^{-1})): 2925, 2860, 1590, 1460, 1100, 895.

*General procedure for the reaction of $Cp_2(\eta^3$-allyl)Ti complexes derived from functionalized dienes (**2c–h**) with carbon dioxide. 3-Methylene-2-methyldodecanoic acid (**4c**)*

A solution of i-PrMgCl (0.82 M in Et_2O, 0.39 ml, 0.32 mmol) was added to a suspension of Cp_2TiCl_2 (40 mg, 0.16 mmol) and **2c** (26 mg, 0.15 mmol) in ether (2 ml) over 5 min at 0 °C with stirring. After stirring for 30 min at the same temperature the generation of the $Cp_2(\eta^3$-allyl)Ti complex was complete. The reaction mixture was rapidly added to dry ice in a minimum volume of ether by syringe. The resulting mixture was gradually allowed to warm to room temperature. After the addition of aq. HCl (4 N, 1.5 ml), the heterogeneous mixture was stirred for 15 min in air. The precipitated Cp_2TiCl_2 was removed by filtration and the organic layer was separated. The aqueous layer was further acidified with concentrated HCl and extracted three times with ether. The combined organic layers were dried over $MgSO_4$ and concentrated *in vacuo*. To the residue was added a 1:1 mixture of ether and hexane to precipitate any remaining Cp_2TiCl_2. After removal of the Cp_2TiCl_2 by filtration and evaporation of the

solvent the crude product was purified by column chromatography (silica gel, ether/hexane) to give 22 mg of the title compound (66% yield). ^{1}H NMR (300 MHz, δ (ppm)): 0.88 (t, J=6.8 Hz, 3H), 1.27 (br s, 12H), 1.29 (d, J=7.6 Hz, 3H), 1.40–1.50 (m, 2H), 2.08 (t, J=7.6 Hz, 2H), 3.13 (q, J=6.8 Hz, 1H), 4.93 (s, 1H), 4.97 (s, 1H), 8.85 (br s, 1H). ^{13}C NMR (75 MHz, δ (ppm)): 14.07, 16.12, 22.86, 27.68, 29.33 (two peaks), 29.54 (two peaks), 31.90, 34.85, 45.44, 111.15, 147.84, 181.31. IR (neat, ν (cm^{-1})): 3000 (br), 2920, 2850, 1700, 1630, 1450, 1405, 1230, 1070, 890, 795.

*3-Methylene-2,7-dimethyl-6-octenoic acid (**4d**)*

^{1}H NMR (300 MHz, δ (ppm)): 1.31 (d, J=7.6 Hz, 3H), 1.62 (s, 3H), 1.68 (s, 3H), 2.14 (m, 4H), 3.18 (q, J=6.8 Hz, 1H), 4.96 (s, 1H), 5.00 (s, 1H), 5.12 (m, 1H), 8.85 (br s, 1H). ^{13}C NMR (75 MHz, δ (ppm)): 16.00, 17.58, 25.56, 26.29, 34.62, 45.56, 111.39, 123.65, 131.80, 147.39, 181.12. IR (neat, ν (cm^{-1})): 3000 (br), 2925, 1698, 1445, 1410, 1220, 895. *Anal.* Calc. for $C_{11}H_{18}O_2$: C, 72.49; H, 9.95. Found: C, 72.10; H, 9.97%.

*3-Methylene-2-methyl-4-(trimethylsilyl)butanoic acid (**4e**)*

^{1}H NMR (300 MHz, δ (ppm)): 0.00 (s, 9H), 1.29 (d, J=7.6 Hz, 3H), 1.63 (s, 2H), 3.02 (q, J=7.2 Hz, 1H), 4.75 (s, 1H), 4.86 (s, 1H), 8.85 (br s, 1H). IR (neat, ν (cm^{-1})): 3000 (br), 2960, 1705, 1415, 1250, 855.

*3-Methylene-2-methyl-6-methoxydodecanoic acid (**4h**) (a 1:1 mixture of diastereoisomers)*

^{1}H NMR (300 MHz, δ (ppm)): 0.88 (t, J=6.8 Hz, 3H), 1.28 (br s, 8H), 1.30 (d, J=7.6 Hz, 3H), 1.40–1.56 (m, 2H), 1.56–1.78 (m, 2H), 2.03–2.24 (m, 2H), 3.09–3.22 (m, 2H), 3.32 (s, 3H), 4.95 (s, 1H), 4.99 (s, 1H), 8.85 (br s, 1H). No separation of any peaks was observed by ^{1}H NMR due to the similarity of both isomers. ^{13}C NMR (75 MHz, δ (ppm)): a pair of peaks for both isomers are in parentheses; 14.09, 16.24, 22.63, 25.19, 29.52, (30.37, 30.62), 31.52, 31.83, 33.29, (45.37, 45.47), 56.31, 80.49, 111.34, 147.79, (179.82, 179.97). IR (neat, ν (cm^{-1})): 3000 (br), 2925, 2850, 1695, 1450, 1085, 890.

Applicability to cyclic dienes

Materials

Cyclopentadiene (**2i**) was prepared by pyrolysis of commercial cyclopentadiene dimer before use.

*1-Vinylcyclohexene (**2k**)*

This known diene was prepared by dehydration of 1-vinyl-1-cyclohexanol with phosphoric oxychloride in pyridine. B.p. 88–91 °C/125 mmHg. ^{1}H NMR (300 MHz, δ (ppm)): 1.52–1.74 (m, 4H), 2.13 (m, 4H), 4.89 (d, J=11.3 Hz, 1H), 5.06 (d, J=17.5 Hz, 1H), 5.75 (d, J=2.5 Hz, 1H), 6.34 (dd, J_1=17.5, J_2=11.3 Hz, 1H). IR (neat, ν (cm^{-1})): 2970, 2900, 1655, 1625, 1455, 1010, 905, 870.

*2-Cyclopentene-1-carboxylic acid (**4i**)*

To a stirred suspension of Cp_2TiCl_2 (300 mg, 1.20 mmol) in THF (7.5 ml) was added a solution of i-BuMgCl (0.69 M in THF, 1.76 ml, 1.20 mmol) at room temperature. After the addition of the Grignard reagent, the resulting solution was immediately cooled to −40 °C and cyclopentadiene (0.085 ml, 1.09 mmol) was added, followed by another equivalent of i-BuMgCl (0.69 M in THF, 1.76 ml, 1.20 mmol) at −40 °C. After being stirred for an additional 10 min, the reaction mixture was cooled to −78 °C and dry ice was added to this cold solution. The resulting mixture was gradually allowed to warm to room temperature. The workup as described in the above general procedure and purification on silica gel afforded the known title compound (71 mg, 58%) as an oil. ^{1}H NMR (300 MHz, δ (ppm)): 2.11–2.25 (m, 2H), 2.30–2.45 (m, 1H), 2.45–2.58 (m, 1H), 3.60 (m, 1H), 5.72–5.76 (m, 1H), 5.92–5.96 (m, 1H), 8.89 (br s, 1H). IR (neat, ν (cm^{-1})): 3000 (br), 2940, 1705, 1420, 1225, 920.

Applicability to asymmetric carbon dioxide fixation (neo-MenthylCp)$_2$TiCl$_2$((NMCp)$_2$TiCl$_2$)

This was synthesized by the literature method reported by Cesarotti and Kagan [22].

Reaction of the (NMCp)$_2$(η^3-1-methylallyl)Ti complex with carbon dioxide. S-(+)-2-Methyl-3-butenoic acid

To a suspension of $(NMCp)_2TiCl_2$ (5.3 g, 10.1 mmol) and butadiene (1.1 g, 20.3 mmol) in Et_2O (60 ml) was added dropwise a solution of n-PrMgBr (1.0 M in Et_2O, 19.0 ml, 19.0 mmol) over 10 min at 0 °C. Then the solution was stirred for 2 h at room temperature, CO_2 gas was bubbled into the solution for 2 h and the resulting mixture was hydrolyzed with aq. HCl (4 N, 40 ml). After the heterogeneous solution had been stirred at r.t. for 30 min, air was blown into the mixture for 20 min while the $(NMCp)_2TiCl_2$ appeared as a red precipitate. When the most of ether was removed by evaporation under vacuum, pentane (40 ml) was added and the $(NMCp)_2TiCl_2$ was recovered by filtration in 84% yield. The heterogeneous filtrate was made basic with aqueous K_2CO_3 and the organic layer was separated. The aqueous layer was extracted three times with ether and the ethereal extracts were discarded. The aqueous layer was carefully acidified with concentrated HCl and was extracted with ether. The combined organic layers were dried over $MgSO_4$ and concentrated *in vacuo*. The crude product was purified by trap-to-trap distillation, and the above title compound

was obtained in 70% yield. $[\alpha]_D$ +7.23° (neat). The ^1H NMR spectrum of this sample was identical with that of the racemic one reported above.

In order to establish the absolute stereochemistry of the product, this sample was hydrogenated (1 atm of H_2) with PtO_2 catalyst in ethanol at room temperature. The reduction product had an $[\alpha]_D$ of +3.4° (neat) and was identified to be *S*-(+)-2-methyl-3-butanoic acid of 18.9% op (optical purity) by comparison with the reported data [23].

Reaction of the (NMCp)$_2$(η^3-1,2-dimethylallyl)Ti complex with carbon dioxide. R-(−)-2,3-Dimethyl-3-butenoic acid

The reaction was carried out according to the above procedure by using isoprene in place of butadiene. 2,3-Dimethyl-3-butenoic acid was obtained in 86% yield and had an $[\alpha]_D$ of −7.32° (neat) (lit. $[\alpha]_D$ −27° (c = 0.73, $CHCl_3$) for a 71% e.e. sample of the *R* enantiomer [15]). Thus this sample should be 19% op. Further structural confirmation was made as follows. After hydrogenation of this sample as above, the saturated product had an $[\alpha]_D$ valuc of −2.20° (neat) and, accordingly, was identified to be *R*-(−)-2,3-dimethyl-3-butanoic acid of 11.3% op by comparison with the reported data [24].

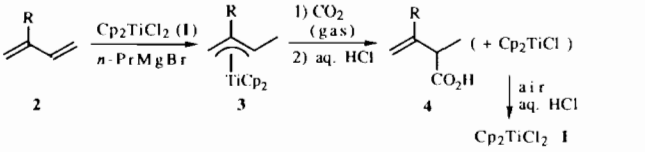
Results and discussion

Reaction of Cp$_2$(η^3-allyl)Ti complexes (3) with carbon dioxide

We initiated the investigation on carbon dioxide fixation by this titanium complex, particularly focussing our attention on the following points: (i) regiochemical control in the formation of carboxylic acid, (ii) comparison of the reactivities of carbon dioxide with other electrophiles such as aldehydes and acid chlorides, (iii) the possibility of extension of the reaction to a variety of functionalized Cp$_2$(η^3-allyl)Ti complexes, and (iv) application to asymmetric carbon dioxide fixation with chiral Cp$_2$(η^3-allyl)Ti complexes. Cp$_2$(η^3-allyl)Ti complexes prepared from two simple dienes, Cp_2TiCl_2, and a Grignard reagent were isolated according to the literature [4] and were allowed to react with gaseous CO_2. Alternatively, these complexes were generated from the same starting materials *in situ* and were exposed to CO_2 as such. The results are summarized in Table 1.

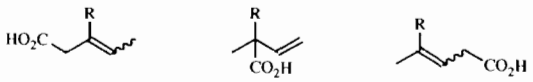
Isolated Cp$_2$(η^3-allyl)Ti complexes (**3**) and those prepared *in situ* showed no significant difference in both the product distribution and yields. The complex with structure **3** always formed with high regioselectivity. In addition, the new carbon–carbon bond formation always took place at the more substituted allylic terminus of

TABLE 1. Reaction of the Cp$_2$(η^3-allyl)Ti complex (**3**) with CO_2



Entry	R	2	Sample of 3[a]	Yield of 4[b] (%)	Recovery of 1[c] (%)
1	H	**a**	isolated	82[d]	85
2	H	**a**	*in situ*	85[e]	93
3	Me	**b**	isolated	83[d]	90
4	Me	**b**	*in situ*	81[e]	87

[a]Isolated: isolated sample, *in situ*: sample prepared *in situ*. [b]No other isomers of **4** shown below were isolated. [c]After aerial oxidation of Cp_2TiCl. [d]Based on **3**. [e]Based on **2**.



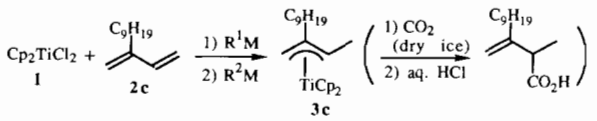
3 in a highly regioselective manner to give β,γ-unsaturated carboxylic acids **4** as the sole regioisomer. The same regioselection has been also documented in the reactions with aldehydes [25] and acid chlorides [26]. The present reaction cleanly stopped at the carboxylate stage so that the formation of ketones or tertiary alcohols was not observed in contrast to the reaction of **3** with acid chlorides [26]. It should be also noted that the starting titanium complex **1** could be recovered in good yields after aqueous workup and subsequent aerial oxidation.

Applicability to 1,3-alkadiene having a functional group

As all the previous work on carbon dioxide fixation had been limited to very simple substrates such as **3a** or **b** [1, 2, 27], we investigated other more complex dienes in order to broaden the applicability of this method. Although a few Grignard reagents such as n-Pr, i-Bu and i-PrMgX are usually used for the generation of Cp$_2$(η^3-allyl)Ti species from simple dienes [4, 25–28], the one which allows the mildest reaction conditions (e.g. a low temperature) may be preferable for the reactions with dienes having a functional group. Since study on the difference in reactivity between these reducing reagents is somewhat limited, we briefly investigated the feasibility of using other reducing agents which were not limited to Grignard reagents. The efficiency of these reducing agents was evaluated in carbon dioxide fixation utilizing 3-methylene-1-dodecene (**2c**) as the diene counterpart as summarized in Table 2.

Ethyl Grignard reagent (2 equiv.) was found to effect the conversion of **2c** to **3c** in 49% at r.t. (entry 2) while the prior derivatization of Cp_2TiCl_2 to Cp_2TiCl with 1

TABLE 2. Effect of reducing agents in the generation of the $Cp_2(\eta^3\text{-allyl})Ti$ complex



Entry	R^1M/R^2M[a]	Method of addition R^1M/R^2M[b]	Reaction conditions **1**→**3c**	Conversion of **2c** (%)
1	EtMgBr	A	0 °C, 30 min; Et_2O–THF	no reaction
2	EtMgBr	A	r.t., 20 min; Et_2O–THF	49
3	i-BuMgCl/EtMgBr	B	r.t., 20 min; Et_2O–THF	45
4	n-PrMgCl	A	0 °C, 30 min; Et_2O	30
5	n-PrMgCl	A	r.t., 20 min; Et_2O	100
6	i-BuMgCl	A	0 °C, 30 min; Et_2O	100
7	i-PrMgCl	A	0 °C, 30 min; Et_2O	100
8	i-BuMgCl/Et_2Zn	B	r.t., 2 h; Et_2O	no reaction
9	EtZnI	A	r.t., 2 h; THF	no reaction
10	Et_2AlCl	A	r.t., 2 h; Et_2O	no reaction
11	$EtAlCl_2$	A	r.t., 2 h; Et_2O	no reaction

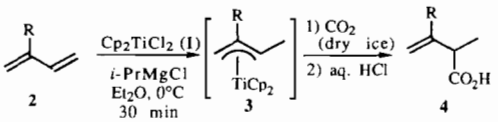
[a]Indication of only one reagent refers to both R^1M and R^2M. [b]Method A: to a mixture of **1** (1 equiv.) and **2c** (0.9 equiv.) was added organometallic reagent (2 equiv.); B: to **1** (1 equiv.) was added R^1M (1 equiv.) to effect the conversion of **1** to Cp_2TiCl, and then diene (0.9 equiv.) and R^2M (1 equiv.) were added.

equiv. of i-BuMgCl [4, 28] (see entry 6 for the clean conversion of **1** to Cp_2TiCl to **3** by 2 equiv. of this Grignard reagent) followed by the addition of the diene **2c** and 1 equiv. of EtMgBr effected the conversion of **2c** again in a comparable degree (45%) (entry 3) to the former case (entry 2). This clearly indicates that the reduction of Cp_2TiCl_2 to Cp_2TiCl with ethyl Grignard reagent is as smooth as the reaction with other frequently used Grignard reagents like i-BuMgCl, but the generation of reactive Cp_2TiH species from the intermediate Cp_2TiCl was not complete with EtMgBr. n-PrMgCl is apparently less reactive than both i-BuMgCl and i-PrMgCl at 0 °C (cf. entries 4, 6 and 7), but the former effects satisfactory conversion at r.t. (entry 5). Other organometallics such as Et_2Zn, EtZnI, Et_2AlCl and $EtAlCl_2$ were totally ineffective (entries 8–11). Even though some difference in the reactivity was demonstrated with respect to the type of Grignard reagents, it has been confirmed that, in general, these are the reagents of choice.

Using the Grignard reagent which effects the smooth conversion of Cp_2TiCl_2 and 3-methylene-1-dodecene to the intermediate $Cp_2(\eta^3\text{-allyl})Ti$ complex at low temperature (0 °C), several other dienes (**2**) having a longer alkyl side chain and/or a functional group were successfully transformed to the titanium complex **3** *in situ* which, in turn, were carboxylated. The results are shown in Table 3, in which dry ice was used as a convenient CO_2 source in place of gaseous carbon dioxide.

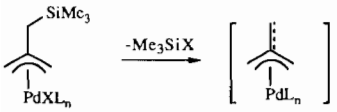
As previously demonstrated, 2-alkyl-1,3-butadiene (**2c**) participated in this reaction to give the β,γ-unsaturated carboxylic acid in good yield (entry 1). Although some isolated olefinic substituents in a diene had been reported to isomerize to a more stable position during $Cp_2(\eta^3\text{-allyl})Ti$ complex formation [26], the remote double bond found in myrcene (**2d**) did not isomerize to other positions nor inhibit the reaction (entry 2). The allylic trimethylsilyl group was not desilylated and the expected carboxylic acid was isolated in good yield (entry 3). This presents a contrast to a case of the corresponding η^3-allylpalladium complex which is known to give trimethylenemethane-palladium species via spontaneous elimination of the Me_3Si group (eqn. (3)) [29].

TABLE 3. Carbon dioxide fixation with **3** derived from functionalized dienes



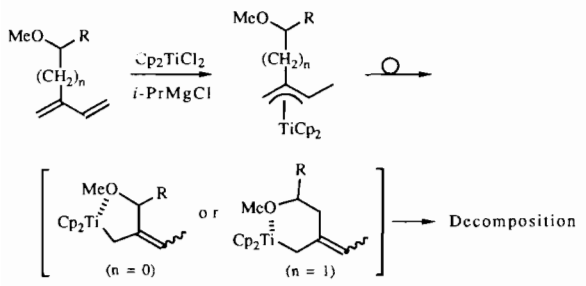
Entry	**2**	R in **2**	Yield (%) of **4**[a,b]
1	**c**	C_9H_{19}–	72 (66)
2	**d**	$Me_2C{=}CH(CH_2)_2$–	81 (71)
3	**e**	Me_3SiCH_2–	77 (65)
4	**f**	$C_9H_{19}CH(OMe)$–	0[c]
5	**g**	$C_6H_{13}CH(OMe)CH_2$–	0[c]
6	**h**	$C_6H_{13}CH(OMe)CH_2CH_2$–	81 (66)[d]

[a]Determined by ^1H NMR. Isolated yields in parentheses. All yields are based on **2**. [b]No other isomers of **4** were seen in a crude reaction mixture. [c]No diene **2** was recovered. [d]A 1:1 mixture of diastereomers.



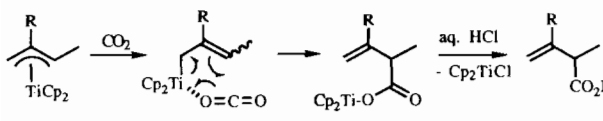
(3)

We envisaged that additional chelation of an oxygen functionality to the titanium center might control the diastereoselectivity of the reaction. A few dienes having a methoxy group at an appropriate position were prepared and subjected to the reaction (entries 4–6). The substrate with a methoxy group at allylic (**2f**) and homo-allylic positions (**2g**) did not give any of the carboxylic acids (entries 4 and 5), but that having the bis-homo-allylic methoxy group (**2h**) did give the desired carboxylic acid (entry 6). In the first two cases, the coordination of the methoxy group to the titanium via a five- or six-membered ring would generate a σ-allylTi complex as depicted in eqn. (4). This species should be so reactive and thus unstable that decomposition of the complex occurs to give a mixture of messy products after usual workup. However, in the last case (entry 6), the seven-membered chelation seems to be negligible so that the carboxylic acid was, in fact, produced as usual, yet no stereochemical control by the methoxy group was observed as the product was a 1:1 mixture of the two diastereoisomers.



(4)

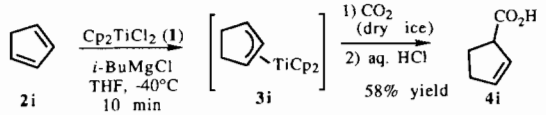
These observations suggest that a highly reactive σ-allylTi complex is produced by the coordination of an oxygen nucleophile. Analogous coordination of the C=O group of carbon dioxide to the titanium center would also result in a reactive σ-allyl complex as above, in which the titanium occupies the less substituted, allylic terminus. This σ-allyl intermediate should readily collapse, as illustrated in eqn. (5), via a six-membered transition state involving the C=O bond to give the β,γ-unsaturated carboxylic acid with the observed regiochemistry.



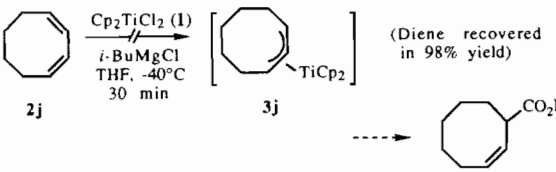
(5)

Applicability to cyclic dienes

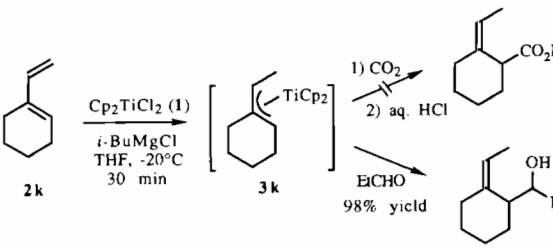
Although the $Cp_2(\eta^3$-allyl)Ti complex **3i** generated from cyclopentadiene (**2i**), Cp_2TiCl_2 and i-BuMgCl [28] reacted with carbon dioxide to give 2-cyclopentene-1-carboxylic acid (**4i**) in good yield (eqn. (6)), a homologous cyclooctadiene (**2j**) did not afford the corresponding $Cp_2(\eta^3$-allyl)Ti species **3j** under a variety of reaction conditions, resulting in a complete recovery of the diene (eqn. (7)). The latter observation was consistent with the earlier one reported by Martin and Jellinek [4]. The difference in reactivity between these two dienes may be attributable to the steric accessibility of the Cp_2TiH species to the diene plane.



(6)



(7)



(8)

1-Vinyl-1-cyclohexene (**2k**) did produce the intermediate $Cp_2(\eta^3$-allyl)Ti complex **3k** as evidenced by the fact that it gave the corresponding homo-allyl alcohol after the reaction with propionaldehyde [28], but it did not react with carbon dioxide even under forcing reaction conditions (eqn. (8)). Since other $Cp_2(\eta^3$-allyl)Ti complexes such as **3a, b** and **i** have been reported to react with aldehydes equally well [25, 28], this stark difference in reactivity between CO_2 and an aldehyde noted in this particular complex deserves comment. Though the sterically demanding allyl ligand of **3k** generally inhibits the coordination of a C=O group to the titanium center, the more electron-rich aldehyde oxygen could still coordinate to titanium, but the electron poorer oxygen of CO_2 may not for electronic reasons, but not steric, as the aldehyde is obviously more sterically demanding than CO_2. This observation is consistent with the interpretation that the reaction is triggered by coordination of the C=O group to the titanium centre as discussed in eqn. (5). Table 4 summarizes some aspects on the feasibility of the carbon dioxide fixation with respect to the starting dienes.

Application to asymmetric carbon dioxide fixation

Replacement of the achiral Cp ligands of Cp_2TiCl_2 with chiral ones could enable asymmetric carbon dioxide

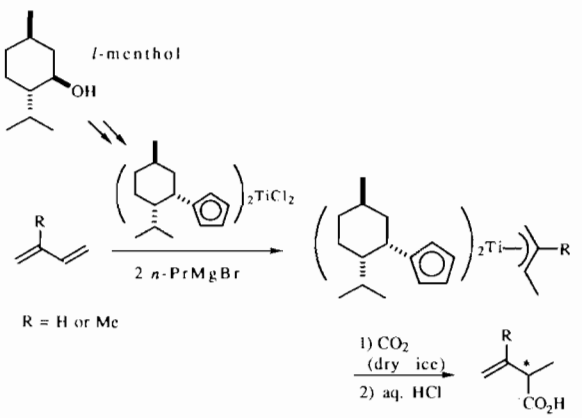
TABLE 4. Summary of the reactivity of some typical dienes

	Butadiene[a]	Cyclopentadiene	1-Vinyl-1-cyclohexene	Cyclooctadiene
Formation of $Cp_2(\eta^3\text{-allyl})Ti$ (**3**)	+	+	+	–
Reaction of **3** with RCHO	+	+	+	
Reaction of **3** with CO_2	+	+	–	

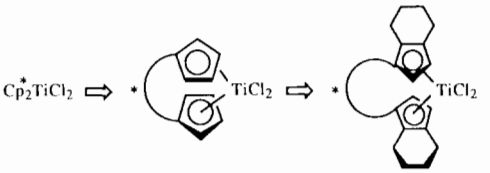
[a]This represents most 2-alkylbutadienes.

fixation. This idea was first realized by us with an optically active complex ($Cp^*_2TiCl_2$; an asterisk (*) stands for a chiral element), which has two neomenthyl-η^5-cyclopentadienyl (NMCp) groups as Cp* and was easily prepared from *l*-menthol according to Kagan's procedure [22]. The $(NMCp)_2(\eta^3\text{-allyl})Ti$ species successfully generated from $(NMCp)_2TiCl_2$ and butadiene or isoprene by the standard method as described above actually underwent the asymmetric carbon dioxide fixation (Scheme 2) [1]. The resultant β,γ-unsaturated carboxylic acids, 2-methyl-3-butenoic acid (from butadiene) and 2,3-dimethyl-3-butenoic acid (isoprene), have the following absolute stereochemistries and optical purities, respectively: the former: *S*, 18.9% op; the latter: *R*, 11.3% op determined after hydrogenation to the known, optically active carboxylic acids [23, 24] (see 'Experimental' for details).

The low optical purities of these carboxylic acids might be improved by switching the Cp* moiety from a monodentate ligand to a bidentate one, i.e. a bis-cyclopentadienyl ligand having C_2 symmetry. Switching a bis-cyclopentadienyl ligand to bis-tetrahydroindenyl ligand which is more sterically demanding (thus producing a more efficient chiral environment) than the former may further increase the efficiency of the chiral induction (Scheme 3). A study along this line [5, 30] to improve the optical purities of the products is now actively underway.



Scheme 2. Asymmetric carbon dioxide fixation with $Cp^*_2TiCl_2$.



Scheme 3. Notion aiming at more efficient $Cp^*_2TiCl_2$.

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