Titanium-Mediated Carboxylation of Alkynes With Carbon Dioxide

Yvan Six[a]

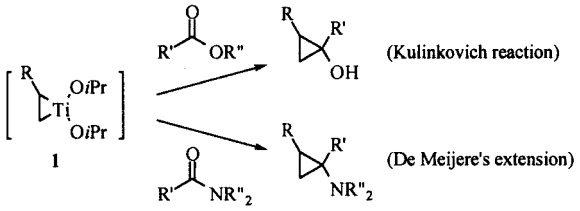
Dedicated to Professor William B. Motherwell

Keywords: Carbon dioxide / Carbonylation / Lactones / Metallacycles / Titanium

The regioselective carboxylation of nonactivated internal alkynes can be performed with carbon dioxide under atmospheric pressure using a simple procedure based on the chemistry of Sato-type diisopropyloxytitanacyclopropenes. Various polysubstituted vinylcarboxylic acids and butenolides can be prepared in this way. In addition, this paper describes an experimental protocol for the preparation of solutions of (η^2-cyclopentene)diisopropyloxytitanium. This complex also reacts with carbon dioxide, and mediates pinacol coupling of acetophenone.

Introduction

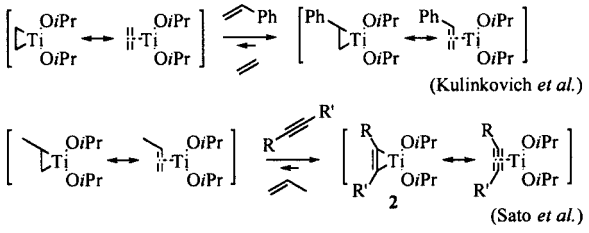
The Kulinkovich reaction provides a general route to cyclopropanols from carboxylic esters in a simple one-step procedure.[1−4] In an extension discovered by de Meijere et al., carboxylic amides can be used as substrates leading to cyclopropylamines.[3,5] In both cases, the commonly accepted mechanism operates through dialkoxytitanacyclopropane intermediates **1** (Scheme 1).



Scheme 1

These complexes have been shown to undergo ligand exchange with olefins[6−8] and alkynes,[9] leading to new dialkoxytitanacyclopropanes and dialkoxytitanacyclopropenes **2**, respectively (Scheme 2).

Complexes **1** and **2** behave as 1,2-dicarbanion equivalents. Several synthetically useful transformations have been developed based on their rich chemistry.[3,10−15] To the best of our knowledge, however, their reaction with carbon dioxide has not been investigated so far, although examples involving bis(cyclopentadienyl)titanacyclopropenes are known.[16−19]



Scheme 2

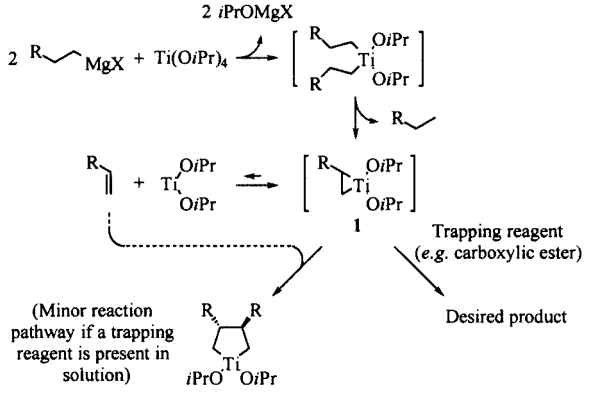
Titanacyclopropanes **1** are prepared most conveniently from titanium alkoxides[20] and Grignard reagents, but since they are prone to decomposition according to the pathway shown, they are normally generated in the presence of the substrate to be transformed (Scheme 3).[20,21] Using CO_2 as a substrate means that this standard procedure cannot be applied, however, because of its well-known reaction with Grignard reagents,[22] and so a preformed solution of titanacyclopropane is required.

Results and Discussion

Preparation of (η^2-Cyclopentene)diisopropyloxytitanium and Its Reaction with Carbon Dioxide

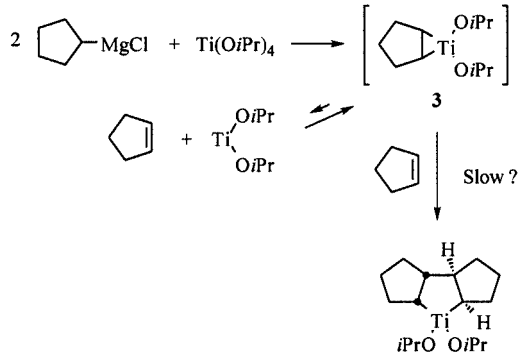
Marek et al. have reported the successful preparation of diisopropyloxy(η^2-propene)titanium in diethyl ether at −50 °C, albeit with unsatisfactory reproducibility.[21] This result encouraged us to try to work with the cyclopentylmagnesium chloride/titanium tetraisopropoxide system[23] because we expected the 1,2-insertion side reaction might be slower in this case (Scheme 4). (η^2-Cyclopentene)-

[a] Institut de Chimie des Substances Naturelles, UPR 2301 du CNRS,
Avenue de la Terrasse, 91198 Gif-sur-Yvette, France
Fax: (internat.) + 33-1/69077247
E-mail: Yvan.Six@icsn.cnrs-gif.fr



Scheme 3

diisopropyloxytitanium (**3**) is also advantageous because it is particularly suitable for ligand-exchange reactions.[23,24]



Scheme 4

We warmed a diethyl ether solution of cyclopentylmagnesium chloride (3 equiv.) and titanium tetraisopropoxide (1 equiv.) from −70 °C to −40 °C over 5 min, then maintained the solution at that temperature for additional 5 min. After addition of CO_2 gas under atmospheric pressure, and then treatment with deuterium oxide, a classical workup procedure allowed us to isolate the resulting carboxylic acids (see Exp. Sect.). The crude product contained cyclopentanecarboxylic acid only, which was partially deuterated in the β-position as revealed by ^{13}C NMR spectroscopy (Figure 1, a and b). In spite of poor resolution, the relative amount (*r*) of deuterated acid **4**-*d* could be evaluated approximately by measuring the relative intensities at the C-1 and C-3 peaks. Thus, this experiment not only demonstrates that complex **3** reacts with carbon dioxide, presumably via titanalactone **5** (Scheme 5), but also provides an indirect means to assess roughly the amount of **3** formed. The presence of non-deuterated cyclopentanecarboxylic acid presumably stems from the reaction of carbon dioxide with residual cyclopentylmagnesium chloride.

This experiment was repeated several times under various conditions. The results are presented in Table 1. The data for the reaction conducted at −30 °C with 3.0 equiv. of Grignard reagent (Entries 5−8) clearly show that the amount of complex **3**, estimated according to the yield of

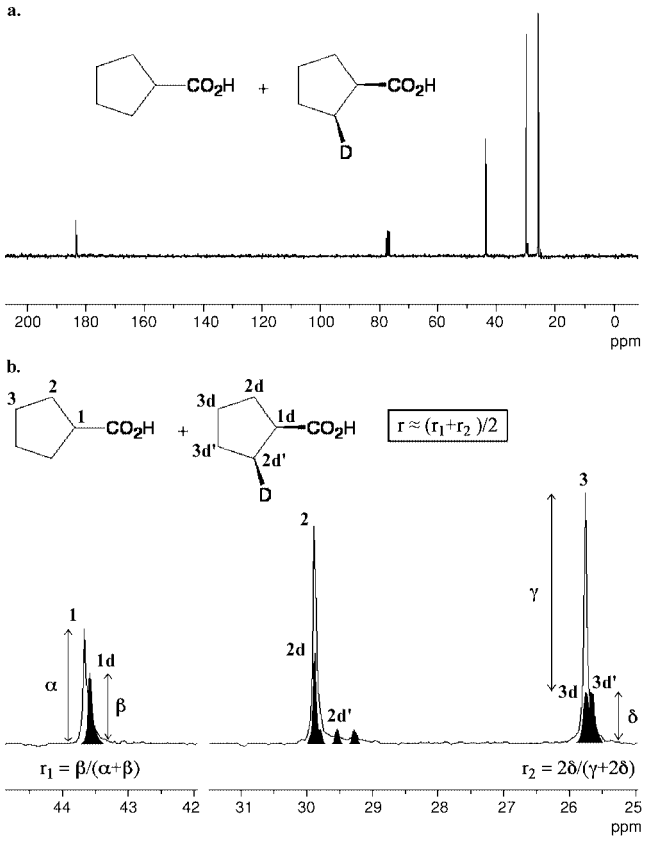
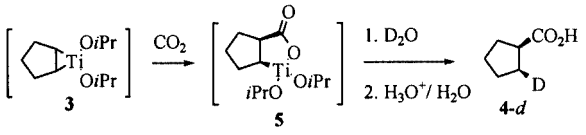


Figure 1. ^{13}C NMR spectrum of the crude product obtained when preformed complex **3** is trapped with CO_2 and then D_2O



Scheme 5

4-*d*, decreases with time. This situation was also observed at −40 °C (Entries 1−4) after a few minutes.

The use of an excess of Grignard reagent was beneficial. Although good results were still obtained with 2.4 equiv. of Grignard reagent, reducing this amount further led to lower yields (Entries 9−11). A possible explanation is that excess Grignard reagent ensures that the rate of formation of **3** remains high until all the titanium precursor has been consumed. Since the formation and decomposition of complex **3** occur simultaneously, this process would explain why the amount of **3** in the reaction mixture only decreases slowly with time and is almost steady for several minutes, while the amount of the remaining Grignard reagent decreases more rapidly.

We also tried working with diisopropyl ether and THF as solvents (Entries 12−13). The results were less satisfactory with the former and no reaction was detected in THF at −40 °C, which is consistent with earlier observations made by the group of Cha.[23]

Table 1. The reaction of complex **3** with carbon dioxide, followed by trapping with D_2O; in each case, a solution of $Ti(OiPr)_4$ and cC_5H_9MgCl at −70 °C was warmed to temperature *T* over 5 min, then maintained at that temperature for *t* min before the addition of CO_2

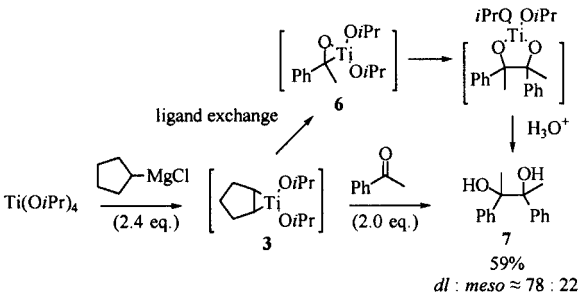
Entry	Solvent	Grignard reagent [equiv.]	*T* [°C]	*t* [min]	Yield in **4**-*d* [%]	Unreacted Grignard reagent[a] [equiv.]
1	Et_2O	3.0	–40	0	42	1.1
2				5	52	0.93
3				15	49	0.62
4				30	46	0.23
5	Et_2O	3.0	–30	0	53	0.94
6				2.5	51	0.68
7				15	48	0.34
8				30	39	0.18
9	Et_2O	2.4	–30	0	54	0.39
10		2.2			49	0.30
11		2.0			39	0.14
12	iPr_2O	2.2	–30	0	12	0.15
13	THF	3.0	–40	30	0	2.0
14	See note for conditions[b]				44	0.24

[a] Estimated according to the yield of non-deuterated acid **4**. [b] Same conditions as in Entry 9, except that the reaction mixture was kept at −70 °C for 1 h before the addition of CO_2.

In summary, the most simple and convenient procedure we have found for the preparation of complex **3** is the following: fast (5 min) warming from −70 °C to −30 °C of a diethyl ether solution of $Ti(OiPr)_4$ (1.0 equiv.) and cyclopentylmagnesium chloride (2.4 equiv.). The complex should preferably be used immediately, but may be kept at −70 °C for 1 h without too much decomposition (Entry 14).

Application to the Pinacol Coupling of Acetophenone

Preparing solutions of (η^2-cyclopentene)diisopropyloxytitanium **3** not only enables the study of its reaction with carbon dioxide, but also with any reagent that is not compatible with Grignard reagents or titanium tetraisopropoxide. To illustrate this concept, acetophenone was added to a preformed solution of complex **3** (Scheme 6). The pinacol coupling product **7** was isolated in satisfactory yield (59%). In contrast, generating **3** in the presence of acetophenone resulted in a much lower yield (15%), the major product being 1-phenylethanol stemming from the reaction of acetophenone with cyclopentylmagnesium chloride.[25]

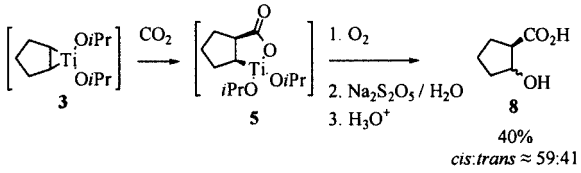


Scheme 6

Formation of **7** can be explained by [1,2] insertion of the carbonyl group of acetophenone into the C−Ti bond of the intermediate oxatitanacylopropane **6**. Direct addition of **3** to the carbonyl group is evidently slower than the ligand exchange yielding **6**. Similar results have been obtained by Eisch et al. using a different method.[14]

Extending the Scope of the Reaction of Titanacyclopropanes with Carbon Dioxide

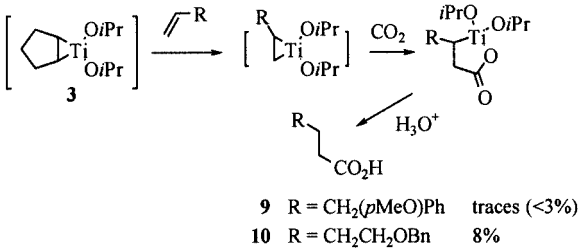
As we have seen previously, trapping of intermediate **5** with deuterium oxide yields deuterated acid **4**-*d*. It was interesting to us to investigate the use of other trapping reagents, and so oxygen[26] was tested, leading to the formation of β-hydroxy acid **8** as a mixture of the two possible diastereoisomers (Scheme 7). Radical intermediates may account for the loss of stereochemical integrity.



Scheme 7

Quenching with aldehydes was also investigated, but without success. When using benzaldehyde and isobutyraldehyde, the expected products were not detected and only unsubstituted cyclopentanecarboxylic acid, simple Grignard addition adducts, and diols arising from pinacol coupling, were observed.

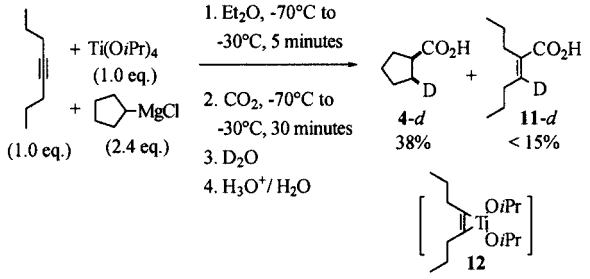
From a synthetic point of view, it would obviously be extremely useful to extend the reaction with carbon dioxide to titanacyclopropanes other than **3**. A few studies concerning ligand exchange with olefins prior to CO_2 addition were undertaken, but the results were extremely modest (Scheme 8) since only small amounts of the expected acids **9** and **10** were formed. Further work is needed to develop this potentially useful transformation.



Scheme 8

The Reaction of Titanacyclopropenes with Carbon Dioxide

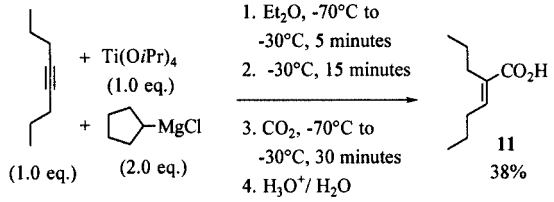
The best conditions (Table 1, Entry 9) found for the formation of deuterated cyclopentanecarboxylic acid **4**-*d* were used for the reaction repeated in the presence of 4-octyne. Acid **4**-*d* was still the major product, but deuterated acid **11**-*d* was also isolated, albeit in low yield and purity (Scheme 9).



Scheme 9

Two conclusions can be drawn from this early experiment. First, the titanacyclopropene **12** generated by ligand exchange with the alkyne reacts with carbon dioxide and deuterium oxide to give the corresponding acid **11**-*d*. Secondly, the yield of **4**-*d* indicates that a large amount of complex **3** was still present in solution when the CO_2 was added, showing that ligand exchange with the alkyne is a relatively slow process at −30 °C.

According to this observation, the carboxylation of 4-octyne was improved by maintaining the temperature at −30 °C for 15 min before the addition of CO_2 (Scheme 10). It was also found that the purity of the crude product was greatly enhanced by using 2.0 equiv. of Grignard reagent instead of 2.4 (Figure 2). The ligand-exchange reaction transforms complex **3** into the more stable titanacyclopropene **12**, and decomposition of **3** becomes a less significant pathway. In contrast to the situation where no alkyne is present, using excess Grignard reagent is not required; it actually seems that it becomes a problem.



Scheme 10

We optimised the reaction one step further by using a deficiency of alkyne, which led to higher conversions. The results of reactions with several different alkynes are presented in Table 2.

The reaction appears to be fairly general, as a diverse range of substituted alkynes leads to the expected alkenecarboxylic acids. Nonetheless, some limitations have been discovered. The expected acid was not isolated from the reaction of 1,4-diphenylbuta-1,3-diyne (Entry 9); only triple-bond reduction products were observed, the major one being enyne **20**. 1,4-Bis(trimethylsilyl)buta-1,3-diyne and methyl octynoate were also unsuitable substrates, giving only complex mixtures of unidentified compounds. Terminal alkynes led to conjugated dienes **21** and **22** (Scheme 11). Since monosubstituted titanacyclopropenes should be very reactive towards carbon dioxide, the observed dimerisation already reported by Sato et al.[27] must be a fast process. The resulting titanacyclopentadienes appear to be unreactive towards carbon dioxide under our experimental conditions, probably because of their reduced ring strain as compared with titanacyclopropenes.

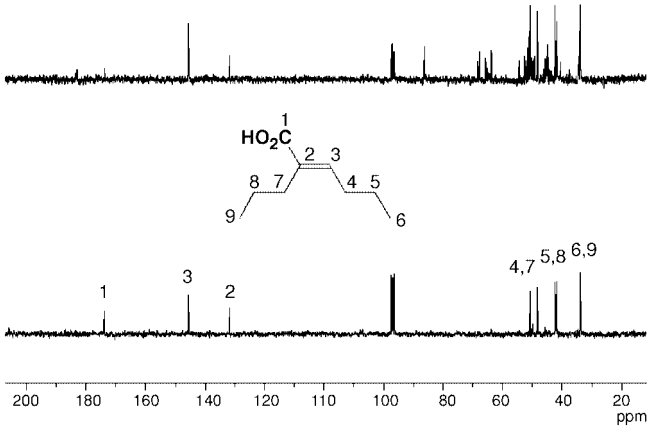
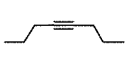
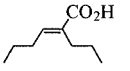
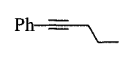
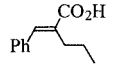
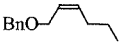
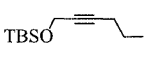
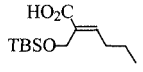
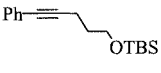
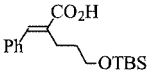
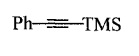
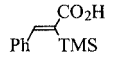
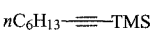
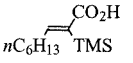
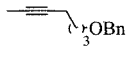
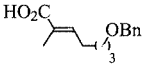
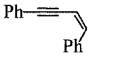
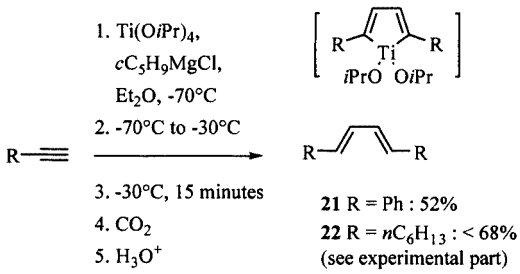


Figure 2. ^{13}C NMR spectra of the crude products of the reaction displayed in Scheme 10 with 2.4 (top) and 2.0 (bottom) equiv. of Grignard reagent

Table 2. The reaction of titanacyclopropenes, generated from alkynes, with carbon dioxide

Entry	Starting alkyne	Product	Yield	Regioselectivity
1			**11** 83%[a,e]	–
2			**13** 43%[a,f]	86 : 14
3			**14** 87%[a,e]	–
4			**15** 42%[c,e]	80 : 20
5			**16** 74%[b,e]	85 : 15
6			**17** 50%[d,e]	81 : 19
7			**18** 53%[b,e]	58 : 42
8			**19** 41%[a,e]	67 : 33
9			**20** 30%[a,e]	–

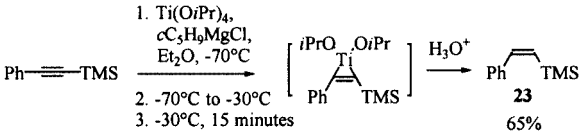
[a] CO_2 was added while warming from −70 °C to −30 °C over 30 min. [b] CO_2 was added at −30 °C over 30 min. [c] CO_2 was added at −30 °C over 1 h. [d] 1.0 equiv. of alkyne was used, CO_2 was added at 0 °C over 2 h, and the yield was calculated on the basis of recovered starting material. [e] Isolated by column chromatography. [f] Isolated by crystallisation.



Scheme 11

1-Benzyloxyhex-2-yne did not give the expected vinylcarboxylic acid, but was converted instead into the corresponding (*Z*)-disubstituted alkene **14** in good yield (Entry 3). We believe that in this case, the intermediate titanacyclopropene is stabilised strongly by coordination with the oxygen atom of the ether group, thus making the reaction with carbon dioxide more difficult. This is supported by the observation that replacing the benzyl group with a *tert*-butyldimethylsilyl group solves the problem (Entry 4).

In a preliminary account of this work, we reported low yields in a few cases where the starting alkynes were sterically encumbered.[28] For instance, vinylic acid **17** had been isolated in only 19% yield from 1-phenyl-2-(trimethylsilyl)acetylene. We found that hydrolysing the titanacyclopropene intermediate without adding CO_2 led, after purification, to analytically pure (*Z*)-alkene **23** in 65% yield (Scheme 12). This observation demonstrated that the problem was due mainly to the carbon dioxide addition step: simply performing these additions at higher temperatures and for longer times improved the results for all of the less-reactive substrates (Entries 4−6).



Scheme 12

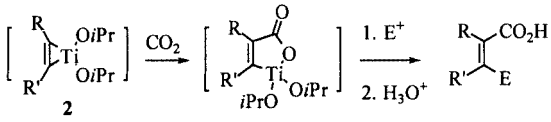
Selectivity Issues

The present method for the carboxylation of alkynes appears to be completely stereoselective, and poorly (Table 2, Entry 7) to highly (Entry 2) regioselective. It is obvious from the results that the observed regioselectivities do not stem from steric factors alone. In the case of 1-(*tert*-butyldimethylsilyloxy)hex-2-yne (Entry 4), carboxylation occurs preferentially at the carbon atom bearing the bulkiest group, whereas in the case of 7-benzyloxyhept-2-yne (Entry 8), carboxylation at the least-hindered carbon atom is favoured. In view of our results, a tentative classification for the directing power of substituents in carboxylations at the carbon atoms that bear them is the following: $CH_2OTBS > CH_3 > TMS \approx CH_2$-alkyl > Ph.

The strong directing effect of CH_2OR groups has been reported previously for the reaction of titanacyclopropenes with aldehydes and ketones, and is probably due to their electronic character.[29] Most of the selectivities we have observed, however, differ sharply from those reported for reactions with aldehydes, ketones and imines.[9,30] For instance, the reactions of the complex derived from 1-trimethylsilyloct-1-yne with these compounds display higher and opposite regioselectivities to those found in our reaction of the same complex with carbon dioxide (Table 2, Entry 7).[9,30] This observation could be due in part to the small size of carbon dioxide, making it less sensitive to steric effects, and also possibly to differences in the reaction mechanisms. Further synthetic and molecular modelling studies would be helpful to get a better insight into these problems.

Substitution at the Second Carbon Atom of the Triple Bond

As we have seen earlier with the formation of **11**-*d* (Scheme 9), and in light of previously reported related work,[31,32] we hoped that the intermediate titanalactone generated after the addition of carbon dioxide could be treated with a variety of electrophiles (Scheme 13). This idea proved to be correct and thus tetrasubstituted carboxylated olefins were obtained (Table 3).



Scheme 13

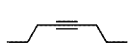
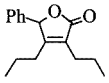
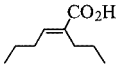
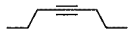
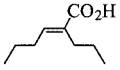
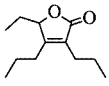
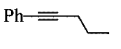
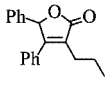
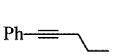
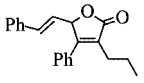
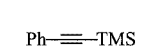
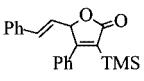
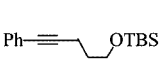
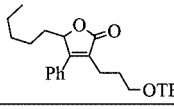
Table 3. The reaction of titanacyclopropenes, generated from alkynes, with carbon dioxide and an electrophilic reagent; in each case, CO_2 was added while warming from −70 °C to −30 °C over 30 min

Entry	Starting alkyne	Electrophile	Product	Yield
1	Ph—≡—	D_2O	D, CO_2H, Ph	**13**-*d* 41%[a]
2	—≡—	Br_2	Br, CO_2H	**24** 26%[b]
3	—≡—	NBS	Br, CO_2H	**24** 43%[b]
4	—≡—	I_2	I, CO_2H	**25** 44%[b]
5	—≡—	NIS	I, CO_2H	**25** 43%[b]
6	—≡—	F_3C, NBn, H	CO_2H	**11** 56%[b]
7	—≡—	Ph, H, O	Ph, O, O	**26** 50%[b]

[a] Isolated by crystallisation. [b] Isolated by column chromatography.

N-Bromosuccinimide (NBS) appeared to be superior to bromine for the preparation of bromoalkenes (Entries 2 and 3), whereas iodine and *N*-iodosuccinimide gave similar results (Entries 4 and 5). When benzaldehyde was used, the corresponding lactone was isolated (Entry 7). In contrast, *N*-(2,2,2-trifluoroethylidene)benzylamine was poorly reactive and only acid **11** was isolated. Further examples of the lactone formation were then studied because of their potential value as a synthetic method. The results are displayed in Table 4.

Table 4. The reaction of titanacyclopropenes, generated from alkynes, with carbon dioxide and a carbonyl compound

Entry	Starting alkyne	Carbonyl compound	Product	Yield (regioselectivity)
1				**26** 50%[a,d]
2				**11** 44%[a,d]
3				**11** [a,e]
4				**27** 41%[b,d]
5				**28** 46%[b,f] (78 : 22)
6				**29** 58%[b,d] (88 : 12)
7				**30** 8%[c,d] (not determined)
8				**31** 52%[b,d] (85 : 15)

[a] CO_2 was added while warming from −70 °C to −30 °C over 30 min. [b] CO_2 was added at −30 °C over 30 min. [c] CO_2 was added at 0 °C over 2 h. [d] Isolated by column chromatography. [e] Although the yield was not determined, this compound was the major product as shown by NMR spectroscopy. [f] Isolated by recrystallisation.

Since isobutyraldehyde and acetophenone failed to lead to the corresponding butenolides (Entries 2 and 3), the method seems to be limited just to nonbulky aldehydes. It is, nonetheless, a fairly general procedure that benefits from the good regioselectivity of the carbon dioxide addition.

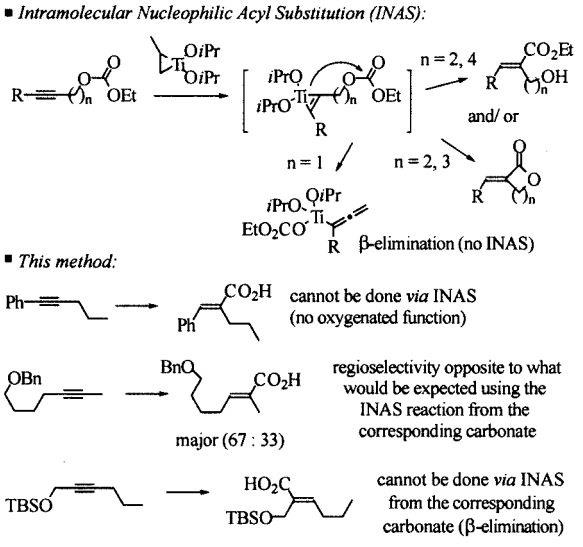
Comparison with Other Methods: Advantages and Drawbacks

The present carboxylation reaction has interesting potential because of its great complementarity with the other existing methods that do not require carbon monoxide.

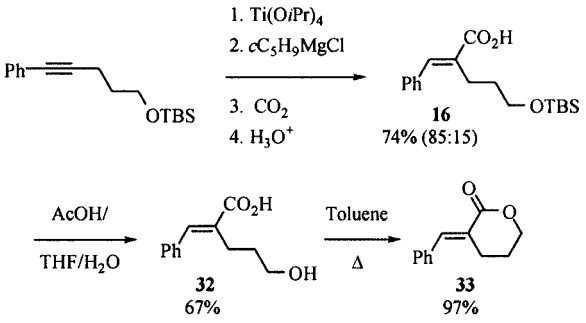
For instance, electroreductive carboxylation of alkynes using $[Ni(bpy)_3](BF_4)_2$ requires a catalytic amount of nickel complex and accepts a wider range of substrates, but is far more limited in its functionalising of the second carbon atom of the triple bond.[33] Also worthy of note is a recently reported nickel-promoted alkylative carboxylation of alkynes.[34] This reaction allows the formation of two carbon−carbon bonds, but is limited to terminal alkynes, which in turn cannot be used with our presently described procedure.

In principle, trisubstituted vinylcarboxylic acids may be obtained from alkynes by $[Cp_2TiCl_2]$-catalysed hydromagnesiation.[35] The regioselectivity pattern of this method, which has been applied in a total synthesis,[36] appears to be very different from our own.

Our method is also complementary to Sato's intramolecular nucleophilic acyl substitution (INAS), in which titanacyclopropene intermediates are involved as well.[31,32] The INAS reaction requires an oxygenated function at a definite distance from the triple bond. This condition is not necessary with the carboxylation described herein, whose scope, therefore, is wider (Scheme 14). Although INAS reaction products can be accessed using our method (Scheme 15), the INAS reaction should be preferred when it is applicable because of its complete regioselectivity.



Scheme 14



Scheme 15

Conclusions

A simple procedure based on the chemistry of titanacyclopropenes enables the carboxylation of nonactivated internal alkynes. The method is fairly general, and satisfactorily regioselective. The source of the carboxyl group is carbon dioxide under atmospheric pressure. Moreover, the second carbon atom of the triple bond may also be substituted, leading to tetrasubstituted olefins of well-defined stereochemistry.

In the course of this work, an experimental protocol was found to prepare solutions of (η^2-cyclopentene)diisopropyloxytitanium (**3**) in diethyl ether, which may then be used in ligand-exchange reactions where the presence of Grignard reagents must be avoided.

Experimental Section

General Remarks: NMR spectra were recorded with AC250 (^{1}H spectra at 250 MHz, ^{13}C spectra at 62.9 MHz) and AM300 Bruker spectrometers (^{1}H spectra at 300 MHz, ^{13}C spectra at 75.5 MHz). Chemical shifts are given in ppm, referenced to the peak of tetramethylsilane, defined at $\delta = 0.00$ ppm (^{1}H NMR), or the solvent peak of $CDCl_3$, defined at $\delta = 7.26$ ppm (^{1}H NMR) or $\delta = 77.0$ ppm (^{13}C NMR). Infrared spectra were recorded with a Perkin−Elmer BX FT-IR spectrometer neat. Mass spectra (MS) were obtained with Hewlett-Packard HP 5989B (chemical ionisation, CI), Thermo Finnigan Automass (electronic impact, EI, 70 eV) and Micromass LCT (electrospray, ES^+) spectrometers. Melting points were determined using a Büchi BS540 apparatus and were not corrected. Flash column chromatography was performed on SDS Chromagel silica gel 60 (35−70 μm). All reactions were carried out under argon unless otherwise stated. The temperatures mentioned are the temperatures of the cold baths or the oil baths used. Analytical grade diethyl ether, DMF and toluene were purchased from SDS and used as such. THF was distilled from sodium/benzophenone under argon. Carbon dioxide gas was obtained by sublimation of dry ice, placed in separate flasks, and was passed through calcium chloride before being bubbled through the reaction mixtures. 7-Benzyloxyhept-2-yne and some of the 5-phenylpent-4-yn-1-ol that we used were gifts from Mr. A. Parenty. Some 5-phenylpent-4-yn-1-ol was prepared also by us according to a literature procedure.[37] 1-Trimethylsilyloct-1-yne was prepared by treating the lithium salt of 1-octyne with chlorotrimethylsilane.[38] 1,4-Diphenylbuta-1,3-diyne was prepared by the Eglinton reaction of phenylacetylene.[39] Cyclopentylmagnesium chloride (2.0 M solution in diethyl ether) was purchased from Aldrich or Fluka and titrated using the following method: The solution (1.0 mL) was added at 0 °C to *p*-anisaldehyde (4.0 mmol) in diethyl ether (10 mL) under argon. After 15 min of stirring at room temperature, 0.3 N HCl aqueous solution (20 mL) and diethyl ether (10 mL) were added. Stirring was continued until complete dissolution of the precipitate occurred. The organic layer was separated and the aqueous layer extracted with diethyl ether (20 mL). The combined organic layers were dried with magnesium sulfate and most of the solvent was evaporated under vacuum. ^{1}H NMR spectroscopy of the crude product revealed the formation of two alcohols, (*p*-methoxyphenyl)-cyclopentylmethyl alcohol and (*p*-methoxyphenyl)methyl alcohol. Integration of the aromatic and methoxy signals allowed the ratio of products/unchanged aldehyde to be determined. The concentration of the Grignard reagent was calculated accordingly, a 50:50 ratio corresponding to a concentration of 2.0 M.

Deuterated Acid 4-*d*: Cyclopentylmagnesium chloride (2.0 M in diethyl ether, *n* equiv.) was added dropwise at −70 °C to a solution of titanium tetraisopropoxide (1.0 equiv., 1.0 mmol, 0.30 mL) in diethyl ether (10 mL). The resulting yellow mixture was warmed to *T* °C over 5 min (when *T* was −30 °C, the mixture turned black). After *t* min at *T* °C, the mixture was cooled down to −70 °C again, and carbon dioxide was added for 30 min while the bath was warmed to −30 °C. Deuterium oxide (0.5 mL) was added, the cold bath was removed, and stirring was continued for 25 min. Aqueous 0.3 N HCl (20 mL) and diethyl ether (10 mL) were added. The organic layer was separated, and the aqueous phase extracted with diethyl ether (2 × 20 mL). The combined organic layers were extracted with 1 N aqueous NaOH solution (25 mL). The aqueous phase was then washed with diethyl ether (25 mL), acidified using concentrated aqueous HCl solution, and extracted with diethyl ether (3 × 20 mL). These last three organic phases were combined, dried with magnesium sulfate, filtered, and concentrated, to yield a colourless oil. ^{13}C NMR spectroscopic analysis showed that the product contained only cyclopentanecarboxylic acid and β-deuterated cyclopentanecarboxylic acid **4**-*d*, and allowed an estimation of the amount of each. The results are gathered in Table 1. With $n = 2.4$, $T = -30$, and $t = 0$, 0.11 g of crude product was obtained, and cyclopentanecarboxylic acid was estimated to contain 58% deuterium. The amount of non-deuterated acid was thus approximately 0.39 mmol, and the yield of **4**-*d* was estimated to be 54%.

4-*d*: ^{13}C NMR: δ = 25.7, 25.8, 29.6 (t, $^1J = 20.5$ Hz), 29.9, 43.6, 183.5 ppm.

2,3-Diphenylbutane-2,3-diol (7): Cyclopentylmagnesium chloride (2.0 M in diethyl ether, 2.4 equiv., 4.8 mmol, 2.4 mL) was added dropwise at −70 °C to a solution of titanium tetraisopropoxide (1.0 equiv., 2.0 mmol, 0.59 mL) in diethyl ether (20 mL). The resulting yellow mixture was warmed to −30 °C over 5 min, at which point it turned black. The mixture was then immediately cooled down to −70 °C, and acetophenone (2.0 equiv., 4.0 mmol, 0.47 mL) was added. The cold bath was removed, stirring was continued for 2 h at 25 °C, and the red-brown mixture became orange. Aqueous 0.3 N HCl (40 mL) and diethyl ether (20 mL) were added. The aqueous layer was saturated with sodium chloride, and the organic layer was separated. The aqueous phase was extracted with diethyl ether (4 × 30 mL). The combined organic layers were dried with magnesium sulfate, filtered and concentrated to afford a colourless oil (0.51 g), which later crystallised. Recrystallisation (cyclohexane) yielded analytically pure (*dl*)-**7** (0.15 g). Flash chromatography of the mother liquor (ethyl acetate/heptane, gradient from 0 to 30%) led to the isolation of a mixture of (*dl*)-**7**, (*meso*)-**7**, and 1-phenylethanol (0.18 g; ratio 35:28:37 estimated by integration of the ^{1}H NMR spectrum). Estimated yields are thus: (*dl*)-**7** (0.92 mmol, 46%), (*meso*)-**7** (0.25 mmol, 13%), and 1-phenylethanol (0.33 mmol, 8%).

(*dl*)-7: [40,41] Colourless crystals (needles), m.p. 122.0−123.4 °C (ref.[40] 125−126 °C). $C_{16}H_{18}O_2$ (242.32): calcd. C 79.31, H 7.49; found C 79.36, H 7.63. IR: $\tilde{\nu}$ = 3490, 3401, 1445, 1139, 1062, 1026 cm^{-1}. ^{1}H NMR: δ = 1.51 (s, 6 H), 2.55 (br. s, 2 H, OH), 7.17−7.26 (m, 10 H, Ph) ppm. ^{13}C NMR: δ = 25.0, 78.8, 127.0, 127.1, 127.3, 143.4 ppm.

(*meso*)-7: [41] Main differences: ^{1}H NMR: δ = 1.57 (s, 6 H), 2.34 (br. s, 2 H, OH) ppm. ^{13}C NMR: δ = 25.1, 78.6 ppm.

1-Phenylethanol:[42] ^{1}H NMR: δ = 1.45 (d, *J* = 6.5 Hz, 3 H), 2.29 (br. s, 1 H, OH), 4.83 (q, *J* = 6.5 Hz, 1 H), 7.20−7.38 (m, 5 H, Ph) ppm. ^{13}C NMR: δ = 25.1, 70.3, 125.3, 127.3, 128.4, 145.8 ppm.

β-Hydroxycarboxylic Acid 8: Cylopentylmagnesium chloride (2.0 M in diethyl ether, 2.4 equiv., 4.8 mmol, 2.4 mL) was added dropwise at −70 °C to a solution of titanium tetraisopropoxide (1.0 equiv., 2.0 mmol, 0.59 mL) in diethyl ether (20 mL). The resulting yellow mixture was warmed to −30 °C over 5 min, at which point it turned black. The mixture was then cooled down to −70 °C again, and carbon dioxide was added for 30 min while the bath was warmed to −30 °C. The red-brown solution was cooled down to −70 °C again, and oxygen was added for 30 min while the temperature was raised to −30 °C, then kept at −30 °C for 30 min more. Saturated aqueous $Na_2S_2O_5$ solution (10 mL) was added. After 5 min of stirring, 1 N aqueous HCl solution (30 mL) and diethyl ether (20 mL) were added, and the aqueous layer was saturated with sodium chloride. The organic phase was separated and the aqueous phase was extracted with diethyl ether (5 × 40 mL). The combined organic layers were dried with magnesium sulfate, filtered and concentrated to afford a colourless oil (0.28 g). Purification by flash column chromatography (diethyl ether/cyclohexane, gradient from 0 to 100%) yielded pure **8** (0.10 g, 0.79 mmol, 40%) as a mixture of the two possible diastereoisomers (*cis*/*trans* ≈ 55:45). ^{1}H NMR spectroscopic analysis revealed that the *cis*/*trans* ratio was about 59:41 in the crude product.

8:[43,44] A mixture of the two isomers: colourless liquid. MS (EI): *m*/*z* = 112 [$M^{+\cdot} - H_2O$], 102, 73, 58, 55. IR: $\tilde{\nu}$ = 3397, 2961, 2879, 1709, 1414, 1346, 1305, 1210 cm^{-1}. ^{1}H NMR: δ = 1.55−2.15 (m, 6 H), 2.66−2.81 (m, 1 H), 4.42 (q, *J* = 6.5 Hz, 0.45 H, *trans* isomer), 4.50 (q, *J* = 4.0 Hz, 0.55 H, *cis* isomer), 7.13 (br. s, 2 H, OH and CO_2H) ppm. ***cis*-8:** ^{13}C NMR: δ = 21.9, 25.9, 33.9, 49.7, 73.9, 178.8 ppm. ***trans*-8:** ^{13}C NMR: δ = 22.0, 27.3, 33.9, 52.3, 76.3, 179.9 ppm.

Carboxylic Acid 9: Titanium tetraisopropoxide (1.0 equiv., 1.0 mmol, 0.30 mL) was added at −70 °C to a solution of *p*-allylanisole (1.0 equiv., 1.0 mmol, 0.15 mL) in diethyl ether (10 mL). Cylopentylmagnesium chloride (2.0 M in diethyl ether, 2.4 equiv., 2.4 mmol, 1.2 mL) was then added dropwise. The resulting yellow mixture was warmed to −30 °C over 5 min, at which point it became red-brown. After cooling back to −70 °C, carbon dioxide was added over 30 min, during which time the bath was warmed to −30 °C. The solution became red. Aqueous 0.3 N HCl (20 mL) and diethyl ether (10 mL) were then added. The organic layer was separated and the aqueous extracted with diethyl ether (2 × 20 mL). The combined organic layers were extracted with 1 N aqueous NaOH solution (25 mL). The aqueous phase was washed with diethyl ether (25 mL), acidified using concentrated aqueous HCl solution, and then extracted with diethyl ether (3 × 20 mL). These last three organic phases were combined, dried with magnesium sulfate, filtered and concentrated to afford a crude product (57 mg). ^{1}H NMR spectroscopic analysis indicated that the product contained mostly cyclopentylcarboxylic acid. It revealed the presence also of acid **9**, which is a known compound.[45] Integration of the signals indicated that the yield of **9** was not more than 3%.

9:[45] ^{1}H NMR: δ = 2.36 (t, *J* = 7.5 Hz, 2 H), 2.61 (t, *J* = 7.5 Hz, 2 H), 3.79 (s, 3 H), 6.83 (d, *J* = 8.5 Hz, 2 H), 7.10 (t, *J* = 8.5 Hz, 2 H) ppm; other signals were concealed by those of cyclopentanecarboxylic acid. ^{13}C NMR: δ = 55.2, 113.8, 129.4 ppm; other chemical shifts could not be determined because of the small amount of compound obtained.

Carboxylic Acid 10. Preparation of the Starting Alkene: Sodium hydride (60% in oil, 1.1 equiv., 44 mmol, 1.8 g) was added in portions to a solution of 3-butene-1-ol (1.0 equiv., 40 mmol, 3.4 mL) in THF (40 mL) at 0 °C. Tetrabutylammonium iodide (0.01 equiv., 0.40 mmol, 0.15 g) was added, followed by the dropwise addition of benzyl bromide (1.1 equiv., 44 mmol, 5.2 mL). After stirring at 20 °C for 130 min, the mixture, which had become white, was diluted with diethyl ether (100 mL), washed with 0.3 N aqueous HCl (100 mL), dried with magnesium sulfate, filtered and concentrated to afford a yellow liquid (8.1 g). Purification by flash column chromatography (ethyl acetate/heptane, gradient from 0 to 10%) yielded pure 4-benzyloxybut-1-ene (5.6 g, 35 mmol, 87%).

4-Benzyloxybut-1-ene:[46] Colourless oil. ^{1}H NMR: δ = 2.38 (qt, *J* = 7.0, 1.0 Hz, 2 H), 3.53 (t, *J* = 7.0 Hz, 2 H), 4.52 (s, 2 H), 5.01−5.16 (m, 2 H), 5.84 (m, 1 H), 7.21−7.38 (m, 5 H) ppm. ^{13}C NMR: δ = 34.2, 69.6, 72.9, 116.3, 127.5, 127.6, 128.3, 135.2, 138.4 ppm.

Carboxylation: Using the same procedure as that for obtaining **9**, and starting from 4-benzyloxybut-1-ene (1.0 mmol), the crude product (0.15 g) was obtained as a colourless oil containing mostly cyclopentanecarboxylic acid, as shown by ^{1}H NMR spectroscopic analysis. The signals corresponding to acid **10** were also apparent, and the yield was estimated by integration to be ca. 6%. Note: Several other attempts were performed. The best result (8% yield) was obtained with 0.6 equiv. of alkene, 1.0 equiv. of titanium tetraisopropoxide and 2.0 equiv. of Grignard reagent, and with the reaction temperature being maintained at −30 °C for 15 min before the addition of CO_2. No significant improvement was observed when the alkene was added to preformed titanacyclopropane complex **3**.

10:[47] ^{1}H NMR: δ = 2.38 (t, *J* = 7.0 Hz, 2 H), 3.49 (t, *J* = 6.0 Hz, 2 H), 4.50 (s, 2 H), 7.21−7.40 (m, 5 H) ppm; other signals were concealed by those of cyclopentanecarboxylic acid. ^{13}C NMR: δ = 21.5, 29.0, 33.7, 69.7, 72.9, 127.6, 127.6, 128.4 ppm; other chemical shifts could not be determined because of the small amount of compound obtained.

General Procedure for the Hydrocarboxylation of Alkynes: Titanium tetraisopropoxide (2.0 equiv., 2.0 mmol, 0.59 mL) was added at −70 °C to a solution of alkyne (1.0 equiv., 1.0 mmol) in diethyl ether (20 mL). Cylopentylmagnesium chloride (2.0 M in diethyl ether, 4.0 equiv., 4.0 mmol, 2.0 mL) was then added dropwise. The resulting yellow mixture was warmed to −30 °C over 5 min and then maintained at −30 °C for 15 min, by which time it had turned black. The mixture was cooled down to −70 °C again, and carbon dioxide was added, either for 30 min while the bath was warmed to −30 °C (variation A), for 30 min at −30 °C (variation B), or for 1 h at −30 °C (variation C). Aqueous 0.3 N HCl (40 mL) and diethyl ether (20 mL) were then added. The organic layer was separated and the aqueous one extracted with diethyl ether (2 × 30 mL). The combined organic layers were extracted with 1 N aqueous NaOH solution (50 mL). The aqueous phase was washed with diethyl ether (50 mL), acidified using concentrated aqueous HCl solution, and then extracted with diethyl ether (3 × 30 mL). These last three organic phases were combined, dried with magnesium sulfate, filtered and concentrated to afford the crude product, which was then purified either by flash column chromatography or recrystallisation.

Note: When the isolation of nonacidic reaction products was desired, all the organic layers that had been obtained before the acidification of the aqueous phase with concentrated aqueous HCl solution were combined, dried with magnesium sulfate, filtered and concentrated. The resulting "nonacidic" crude product was then purified either by flash column chromatography or recrystallisation.

Carboxylic Acid 11: Preparation according to the General Procedure for the hydrocarboxylation of alkynes, starting from 4-octyne, and applying variation A. The crude product (0.16 g) was purified by flash column chromatography (ethyl acetate/heptane, gradient from 0 to 20%) to afford pure **11** (0.13 g, 0.83 mmol, 83%).

11:[48] Colourless liquid. MS (CI, NH_3): *m*/*z* = 175, 174 [MH^+ + NH_3], 157 [MH^+], 139. IR: $\tilde{\nu}$ = 3401, 2962, 2933, 2873, 1686, 1638, 1289, 1113, 1069 cm^{-1}. ^1H NMR: δ = 0.92 (t, *J* = 7.5 Hz, 3 H), 0.95 (t, *J* = 7.5 Hz, 3 H), 1.38−1.55 (m, 4 H), 2.19 (q, *J* = 7.5 Hz, 2 H), 2.27 (dd, *J* = 8.0, 7.5 Hz, 2 H), 6.92 (t, *J* = 7.5 Hz, 1 H), 11.11 (br. s, 1 H, CO_2H) ppm. ^{13}C NMR: δ = 13.9, 13.9, 22.0, 22.4, 28.4, 30.8, 131.8; 145.5, 173.8 ppm.

Carboxylic Acid 13: Preparation according to the General Procedure for the hydrocarboxylation of alkynes, starting from 1-phenyl-1-pentyne, and applying variation A. The crude product (0.18 g) was purified by flash column chromatography (ethyl acetate/heptane, gradient from 0 to 30%) and recrystallisation (heptane) to afford pure **13** (82 mg, 0.43 mmol, 43%). During the purification process, a small amount of the other regioisomer was also isolated, albeit as a mixture with an unidentified compound. ^1H NMR spectroscopic analysis of the crude product revealed that the regioselectivity of the reaction was about 86:14 in favour of **13**.

13:[49,50] Colourless crystals; m.p. 82.3−83.3 °C (ref. m.p. 82 °C[49]; 90−91 °C[50]). MS (CI, NH_3): *m*/*z* = 208 [MH^+ + NH_3], 191 [MH^+], 173. IR: $\tilde{\nu}$ = 2958, 2929, 1667, 1449, 1423, 1283, 1235, 914 cm^{-1}. ^1H NMR: δ = 0.99 (t, *J* = 7.5 Hz, 3 H), 1.63 (m, 2 H), 2.52 (m, 2 H), 7.29−7.45 (m, 5 H), 7.81 (s, 1 H), 11.90 (br. s, 1 H, CO_2H) ppm. ^{13}C NMR: δ = 14.2, 22.5, 29.3, 128.5, 128.7, 129.4, 132.7, 135.5, 141.1, 174.5 ppm.

Regioisomer of 13:[49] ^1H NMR: δ = 0.88 (t, *J* = 7.5 Hz, 3 H), 1.45 (sext, *J* = 7.5 Hz, 2 H), 2.09 (q, *J* = 7.5 Hz, 2 H), 7.17−7.40 (m, 6 H) ppm. The signal for the CO_2H group could not be identified precisely.

Deuterated Carboxylic Acid 13-*d*: Titanium tetraisopropoxide (2.0 equiv., 2.0 mmol, 0.59 mL) was added at −70 °C to a solution of 1-phenyl-1-pentyne (1.0 equiv., 1.0 mmol, 0.16 mL) in diethyl ether (20 mL). Cylopentylmagnesium chloride (1.8 M in diethyl ether, 4.0 equiv., 4.0 mmol, 2.2 mL) was then added dropwise. The resulting yellow mixture was warmed to −30 °C over 5 min, then was maintained at −30 °C for 15 min, by which time it had turned black. The mixture was cooled down to −70 °C again, and carbon dioxide was added over 30 min, during which time the bath was warmed to −30 °C. Deuterium oxide (1.0 mL) was added. The temperature was increased slowly to 20 °C, and the mixture was stirred for 17 h. Aqueous 0.3 N HCl (40 mL) and diethyl ether (20 mL) were added. The organic layer was separated and the aqueous phase extracted with diethyl ether (2 × 30 mL). The combined organic layers were extracted with 1 N aqueous NaOH solution (50 mL). The aqueous phase was washed with diethyl ether (50 mL), acidified by using concentrated aqueous HCl solution, and then extracted with diethyl ether (3 × 30 mL). These last three organic phases were combined, dried with magnesium sulfate, filtered and concentrated to afford a mixture of colourless crystals and liquid (0.18 g), which was purified by recrystallisation from heptane. A second crop of crystals was obtained by sequential flash column chromatography (ethyl acetate/heptane, gradient from 0 to 20%) and recrystallisation (heptane) of the mother liquor. Carboxylic acid **13**-*d* was obtained (79 mg, 0.41 mmol, 41%). The extent of deuterium incorporation was estimated to be 86% by ^1H NMR spectroscopic analysis.

13-*d*: Colourless crystals; m.p. 82.2−83.5 °C. MS (CI, NH_3): *m*/*z* = 209 [MH^+ + NH_3], 208 [MH^+ + NH_3] (residual non-deuterated), 192 [MH^+], 174. IR: $\tilde{\nu}$ = 2959, 2930, 1669, 1447, 1423, 1321, 1285, 1230, 916 cm^{-1}. ^1H NMR: δ = 0.98 (t, *J* = 7.5 Hz, 3 H), 1.62 (sext, *J* = 7.5, 2 H), 2.52 (m, 2 H), 7.10−7.45 (m, 5 H), 7.81 (s, 0.14 H, residual non-deuterated), 11.09 (br. s, 1 H, CO_2H) ppm. ^{13}C NMR: δ = 14.2, 22.5, 29.2, 128.5, 128.7, 129.4, 132.6, 135.4, 141.1 (no C−D coupling was observed in the spectrum, but the intensity of this peak was much lower than that of non-deuterated **13**), 174.4 ppm.

(*Z*)-Alkene 14. Preparation of the Starting Alkyne: Sodium hydride (60% in oil, 1.1 equiv., 4.4 mmol, 0.18 g) was added to a solution of 2-hexyn-1-ol (1.0 equiv., 4.0 mmol, 0.44 mL) in THF (4.0 mL) at 0 °C. Tetrabutylammonium iodide (0.01 equiv., 40 μmol, 15 mg) was added, followed by the dropwise addition of benzyl bromide (1.1 equiv., 4.4 mmol, 0.52 mL). After stirring at 0 °C for 90 min, the mixture was diluted with diethyl ether (50 mL), washed with 0.3 N aqueous HCl (50 mL) and water (50 mL), dried with magnesium sulfate, filtered and concentrated to afford a yellow oil (0.97 g). Purification by flash column chromatography (ethyl acetate/heptane, gradient from 0 to 10%) yielded pure 1-benzyloxy-hex-2-yne (0.51 g, 2.7 mmol, 67%).

1-Benzyloxyhex-2-yne: Colourless oil. MS (CI, NH_3): *m*/*z* = 207, 206 [MH^+ + NH_3], 189 [MH^+], 171, 145, 108. IR: $\tilde{\nu}$ = 2962, 2932, 2869, 1455, 1259, 1134, 1074 cm^{-1}. ^1H NMR: δ = 0.99 (t, *J* = 7.5 Hz, 3 H), 1.55 (sext, *J* = 7.5 Hz, 2 H), 2.21 (tt, *J* = 7.5, 2.0 Hz, 2 H), 4.15 (t, *J* = 2.0 Hz, 2 H), 4.58 (s, 2 H), 7.24−7.38 (m, 5 H) ppm. ^{13}C NMR: δ = 13.5, 20.7, 22.1, 57.7, 71.3, 75.9, 87.1, 127.7, 128.0, 128.3, 137.6 ppm.

Attempted Carboxylation: The general procedure for the hydrocarboxylation of alkynes was applied, starting from 1-benzyloxy-hex-2-yne, and applying variation A. The crude product (26 mg) contained mostly cyclopentylcarboxylic acid as shown by NMR spectroscopy. Purification, however, of the "nonacidic" crude product (0.20 g, yellow oil) by flash column chromatography (ethyl acetate/heptane, gradient from 0 to 5%) afforded pure (*Z*)-alkene **14** (0.17 g, 0.87 mmol, 87%).

14:[51] Colourless oil. MS (CI, NH_3): *m*/*z* = 209, 208 [MH^+ + NH_3], 191 [MH^+], 173, 108. IR: $\tilde{\nu}$ = 2958, 2928, 2861, 1452, 1095, 1074, 1028 cm^{-1}. ^1H NMR: δ = 0.89 (t, *J* = 7.5 Hz, 3 H), 1.38 (sext, *J* = 7.5 Hz, 2 H), 2.01 (m, 2 H), 4.07 (m, 2 H), 4.50 (s, 2 H), 5.54−5.67 (m, 2 H), 7.22−7.39 (m, 5 H) ppm. ^{13}C NMR: δ = 13.6, 22.7, 29.6, 65.7, 72.0, 126.1, 127.5, 127.7, 128.3, 133.6, 138.4 ppm.

Carboxylic Acid 15. Preparation of the Starting Alkyne:[52] Chloro-*tert*-butyldimethylsilane (1.2 equiv., 4.8 mmol, 0.72 g) was added to a solution of 2-hexyn-1-ol (1.0 equiv., 4.0 mmol, 0.44 mL) and imidazole (2.5 equiv., 10 mmol, 0.68 g) in DMF (1.0 mL) at 0 °C. After 15 min of stirring at 20 °C, the mixture was diluted with diethyl ether (50 mL), washed with 0.1 N aqueous HCl (50 mL) and water (50 mL), dried with magnesium sulfate, filtered and concentrated to afford a yellow oil (0.91 g). Purification by flash column chromatography (ethyl acetate/heptane, gradient from 0 to 5%) yielded pure 1-(*tert*-butyldimethylsilyloxy)hex-2-yne (0.70 g, 3.3 mmol, 83%).

1-(*tert*-Butyldimethylsilyloxy)hex-2-yne: Colourless liquid. MS (CI, NH_3): *m*/*z* = 231, 230 ($MH^{+\cdot}$ + NH_3), 214, 213 [MH^+], 208, 206, 132. IR: $\tilde{\nu}$ = 2959, 2931, 2858, 1472, 1462, 1254, 1140, 1080, 837 cm^{-1}. ^1H NMR: δ = 0.12 (s, 6 H), 0.91 (s, 9 H), 0.97 (t, *J* = 7.0 Hz, 3 H), 1.53 (sext, *J* = 7.0 Hz, 2 H), 2.18 (tt, *J* = 7.0, 2.0 Hz, 2 H),

4.30 (t, J = 2.0 Hz, 2 H) ppm. ^{13}C NMR: δ = −5.1, 13.5, 18.3, 20.8, 22.0, 25.9, 52.0, 78.8, 85.3 ppm.

Carboxylation: The General Procedure for the hydrocarboxylation of alkynes was applied on half the scale, starting from 1-(*tert*-butyldimethylsilyloxy)hex-2-yne (0.50 mmol, 106 mg), and applying variation C. The workup, which differed from the general procedure, was carried out as follows: Aqueous 0.3 N HCl (40 mL) and heptane (20 mL) were added. The organic layer was separated, and the aqueous phase extracted with heptane (2 × 30 mL). The combined organic layers were dried with magnesium sulfate, filtered and concentrated to afford a colourless oil (97 mg). ^{1}H NMR analysis revealed that the regioselectivity of the reaction was about 80:20 in favour of **15**. Purification by flash column chromatography (ethyl acetate/heptane, gradient from 0 to 10%) afforded an analytically pure mixture of **15** and its regioisomer (ratio ca. 81:19, 55 mg, 0.21 mmol, 42%).

Note: When variation A was applied, and with the General Procedure workup, the yield of **15** was only 19%. The (*Z*)-alkene corresponding to simple reduction of the triple bond was isolated in 29% yield.

15: Colourless oil (solid at −7 °C). $C_{13}H_{26}O_3Si$ (258.44): calcd. C 60.42, H 10.14; found C 60.55, H 9.99. MS (CI, NH_3): m/z = 276 [$MH^+ + NH_3$], 260, 259 [MH^+], 241, 179. IR: $\tilde{\nu}$ = 2958, 2930, 2857, 1691, 1256, 1084, 837 cm^{-1}. ^{1}H NMR: δ = 0.09 (s, 6 H), 0.89 (s, 9 H), 0.95 (t, J = 7.5 Hz, 3 H), 1.51 (sext, J = 7.5 Hz, 2 H), 2.30 (q, J = 7.5 Hz, 2 H), 4.41 (s, 2 H), 7.03 (t, J = 7.5 Hz, 1 H), 11.22 (br. s, 1 H, CO_2H) ppm. ^{13}C NMR: δ = −5.3, 13.9, 18.3, 21.9, 25.9, 30.7, 57.1, 130.7, 148.8, 172.2 ppm.

Regioisomer of 15. Main Differences: ^{1}H NMR: δ = 0.91 (s, 9 H), 2.24 (t, J = 8.0 Hz, 2 H), 4.38 (d, J = 5.5 Hz, 2 H), 6.93 (t, J = 5.5 Hz, 1 H) ppm. ^{13}C NMR: δ = 22.2, 28.8, 60.3, 131.2, 144.4 ppm.

(*Z*)-1-*tert*-(Butyldimethylsilyloxy)hex-2-ene: Colourless liquid. MS (CI, NH_3): m/z = 232 [$MH^+ + NH_3$], 215 [MH^+], 165, 132, 100. IR: $\tilde{\nu}$ = 2957, 2929, 2857, 1463, 1253, 1089, 836 cm^{-1}. ^{1}H NMR: δ = 0.07 (s, 6 H), 0.91 (s, 9 H), 0.90 (t, J = 7.5 Hz, 3 H), 1.38 (sext, J = 7.5 Hz, 2 H), 2.01 (q, J = 7.5 Hz, 2 H), 4.23 (d, J = 7.0 Hz, 1 H), 5.37−5.57 (m, 2 H) ppm. ^{13}C NMR: δ = −5.1, 13.7, 18.4, 22.8, 26.0, 29.6, 59.5, 129.7, 130.7 ppm.

Carboxylic Acid 16. Preparation of the Starting Alkyne:[52] Chloro-*tert*-butyldimethylsilane (1.2 equiv., 1.6 mmol, 0.24 g) was added to a solution of 5-phenylpent-4-yn-1-ol (1.0 equiv., 1.3 mmol, 0.21 g) and imidazole (2.5 equiv., 3.3 mmol, 0.23 g) in DMF (0.50 mL) at 0 °C. After 20 min of stirring at 0 °C and then 15 min at 20 °C, the mixture was diluted with diethyl ether (25 mL), washed with 0.1 N aqueous HCl (25 mL) and water (25 mL), dried with magnesium sulfate, filtered and concentrated to afford a colourless oil (0.39 g). Purification by flash column chromatography (ethyl acetate/heptane, gradient from 0 to 5%) yielded pure 1-phenyl-5-(*tert*-butyldimethylsilyloxy)pent-1-yne (0.35 g, 1.3 mmol, 97%).

5-(*tert*-Butyldimethylsilyloxy)-1-phenylpent-1-yne: Colourless liquid. $C_{17}H_{26}OSi$ (274.48): calcd. C 74.39, H 9.55; found C 74.11, H 9.77. MS (CI, NH_3): m/z = 276, 275 [MH^+], 132, 117. IR: $\tilde{\nu}$ = 2953, 2928, 2856, 1490, 1471, 1462, 1256, 1105, 1070, 835 cm^{-1}. ^{1}H NMR: δ = 0.08 (s, 6 H), 0.91 (s, 9 H), 1.80 (tt, J = 7.0, 6.0 Hz, 2 H), 2.49 (t, J = 7.0 Hz, 2 H), 3.76 (t, J = 6.0 Hz, 2 H), 7.24−7.30 (m, 3 H), 7.35−7.41 (m, 2 H) ppm. ^{13}C NMR: δ = −5.3, 15.8, 18.4, 26.0, 31.8, 61.6, 80.7, 89.9, 124.0, 127.5, 128.2, 131.5 ppm.

Carboxylation: The General Procedure for the hydrocarboxylation of alkynes was applied starting from 5-(*tert*-butyldimethylsilyloxy)-1-phenylpent-1-yne, and applying variation B. The workup, which differed from the General Procedure, was carried out as follows: Aqueous 0.3 N HCl (40 mL) and diethyl ether (20 mL) were added. The organic layer was separated, and the aqueous phase extracted with diethyl ether (2 × 30 mL). The combined organic layers were dried with magnesium sulfate, filtered and concentrated to afford of a mixture of colourless solid and oil (0.38 g). ^{1}H NMR spectroscopic analysis revealed that the regioselectivity of the reaction was about 85:15 in favour of **16**. Purification by flash column chromatography (ethyl acetate/heptane, gradient from 0 to 50%) afforded the (*Z*)-alkene corresponding to simple reduction of the triple bond (70 mg, 0.25 mmol, 25%), pure **16** (0.19 g) and a mixture of **16** and its regioisomer (ratio ca. 25:75, 47 mg). The yield of carboxylated products was thus 0.24 g (0.74 mmol, 74%).

Note: When variation A was applied, and with the general procedure's workup, **16** was found in the "nonacidic" crude product, and the yield was only 38%. It seems that the carboxylate salt of **16** dissolves well in diethyl ether.

16: Colourless crystals, m.p. 83.2−83.8 °C. $C_{18}H_{28}O_3Si$ (320.51): calcd. C 67.46, H 8.81; found C 67.51, H 8.79. MS (CI, NH_3): m/z = 323, 322, 321 [MH^+], 304, 303. IR: $\tilde{\nu}$ = 2926, 2850, 1686, 1678, 1674, 1668, 1418, 1270, 1096, 959 cm^{-1}. ^{1}H NMR: δ = 0.03 (s, 6 H), 0.88 (s, 9 H), 1.80 (m, 2 H), 2.62 (m, 2 H), 3.68 (t, J = 6.0 Hz, 2 H), 7.30−7.40 (m, 3 H), 7.42−7.48 (m, 2 H), 7.77 (s, 1 H), 11.21 (br. s, 1 H, CO_2H) ppm. ^{13}C NMR: δ = −5.3, 18.3, 24.1, 26.0, 32.1, 63.0, 128.6, 128.8, 129.7, 132.1, 135.3, 141.2, 174.2 ppm.

Regioisomer of 16: Colourless oil. ^{1}H NMR: δ = −0.01 (s, 6 H), 0.83 (s, 9 H), 1.63 (tt, J = 7.5, 6.0 Hz, 2 H), 2.18 (q, J = 7.5 Hz, 2 H), 3.56 (t, J = 6.0 Hz, 2 H), 7.15−7.40 (m, 6 H), 9.73 (br. s, 1 H, CO_2H) ppm. ^{13}C NMR: δ = −5.4, 18.2, 25.9, 26.4, 31.8, 62.3, 127.6, 128.0, 129.7, 134.6, 147.5, 172.5 ppm.

(*Z*)-5-(*tert*-Butyldimethylsilyloxy)-1-phenylpent-1-ene: Colourless liquid. MS (CI, NH_3): m/z = 294 [$MH^+ + NH_3$], 293, 279, 278, 277 [MH^+], 236, 162, 133, 132. IR: $\tilde{\nu}$ = 2954, 2928, 2856, 1471, 1255, 1104, 835, 774 cm^{-1}. ^{1}H NMR: δ = 0.01 (s, 6 H), 0.86 (s, 9 H), 1.66 (tt, J = 7.5, 6.5 Hz, 2 H), 2.38 (qd, J = 7.5, 1.5 Hz, 2 H), 3.62 (t, J = 6.5 Hz, 2 H), 5.65 (dt, J = 11.5, 7.5 Hz, 1 H), 6.40 (dt, J = 11.5, 1.5 Hz, 1 H), 7.14−7.35 (m, 5 H) ppm. ^{13}C NMR: δ = −5.3, 18.3, 25.1, 25.9, 33.1, 62.6, 126.5, 128.1, 128.7, 129.1, 132.5, 137.6 ppm.

Carboxylic Acid 17: Titanium tetraisopropoxide (1.0 equiv., 2.0 mmol, 0.59 mL) was added at −70 °C to a solution of 1-phenyl-2-(trimethylsilyl)acetylene (1.0 equiv., 2.0 mmol, 0.39 mL) in diethyl ether (20 mL). Cyclopentylmagnesium chloride (2.1 M in diethyl ether, 2.0 equiv., 4.0 mmol, 1.9 mL) was then added dropwise. The resulting yellow mixture was warmed to −30 °C over 5 min, then was maintained at −30 °C for 15 min, by which time it had turned black. Carbon dioxide was added at 0 °C over 2 h [after 1 h, diethyl ether (15 mL) was added to compensate for evaporation]. Aqueous 0.3 N HCl (40 mL) and diethyl ether (30 mL) were then added. The organic layer was separated, and the aqueous phase extracted with diethyl ether (2 × 30 mL). The combined organic layers were extracted with 1 N aqueous NaOH solution (50 mL). The aqueous phase was washed with diethyl ether (50 mL), and the combined organic phases were dried with magnesium sulfate, filtered and concentrated to afford a colourless oil (0.24 g). Purification by flash column chromatography (heptane) led to the isolation of starting 1-phenyl-2-trimethylsilylacetylene (0.19 g, 1.1 mmol, 54%). The aqueous phase was acidified using concentrated HCl

aqueous solution, and extracted with diethyl ether (3 × 30 mL). These last three organic phases were combined, dried with magnesium sulfate, filtered and concentrated to afford colourless crystals (0.15 g). ^{1}H and ^{13}C NMR spectroscopic analyses revealed that the regioselectivity of the reaction was about 81:19 in favour of **17**. Purification by flash column chromatography (ethyl acetate/heptane, gradient from 0 to 20%) afforded pure **17** (99 mg, 0.45 mmol, 23%, i.e., 50% based on recovered starting material).

Note: When variation A of the general procedure was applied, **17** was isolated in only 19% yield; (*Z*)-alkene **23** was the major product, isolated in 46% yield.

17:[53] Colourless crystals (needles), m.p. 104.4−105.7 °C. $C_{12}H_{16}O_2Si$ (290.35): calcd. C 65.41, H 7.32; found C 65.39, H 7.46. MS (EI): *m*/*z* = 220 [$M^{+\cdot}$], 206, 205, 204, 131, 102, 75. IR: $\tilde{\nu}$ = 2954, 1664, 1411, 1286, 1272, 1259, 1249, 842 cm^{-1}. ^{1}H NMR: δ = 0.08 (s, 9 H), 7.24−7.37 (m, 5 H), 8.34 (s, 1 H), 11.30 (br. s, 1 H, CO_2H) ppm. ^{13}C NMR: δ = 0.4, 128.0, 128.5, 128.6, 136.6, 137.6, 155.2, 177.4 ppm.

Carboxylic Acid 18: Preparation by using the General Procedure for the hydrocarboxylation of alkynes, starting from 1-trimethylsilyloct-1-yne, and applying variation B. The crude product (79 mg, colourless oil) contained the expected acid **18**, and the "nonacidic" crude product (0.20 g, colourless oil) contained the carboxylate salt of **18**. Both crude products were combined, dissolved in heptane (100 mL), and then washed with 0.3 N aqueous HCl (50 mL). A new crude product (0.23 g) was obtained as a colourless oil after filtration and concentration under reduced pressure. ^{1}H NMR spectroscopic analysis revealed that the regioselectivity of the reaction was about 58:42 in favour of **18**. Purification by flash column chromatography (ethyl acetate/heptane, gradient from 0 to 10%) afforded a 59:41 mixture of **18** and its regioisomer (0.12 g, 0.53 mmol, 53%).

Mixture of 18 and Its Regioisomer (59:41): Colourless liquid. MS (ES^+): *m*/*z* = 283, 279, 267 [M + K^+], 251 [M + Na^+], 246, 229 [MH^+], 213, 211. HRMS (ES^+): calcd. for $C_{12}H_{23}Na_2O_2Si$ [M − H^+ + 2Na^+] 273.1263, found 273.1242. IR: $\tilde{\nu}$ = 2957, 2928, 2858, 1682, 1251, 842 cm^{-1}. ^{1}H NMR: δ = 0.18 (s, 9 H, regioisomer), 0.25 (s, 9 H, **18**), 0.89 (t, *J* = 6.5 Hz, 3 H), 1.15−1.55 (m, 8 H), 2.30 (q, *J* = 7.5 Hz, 2 H, **18**), 2.37 (t, *J* = 7.5 Hz, 2 H, regioisomer), 6.97 (s, 1 H, regioisomer), 7.35 (t, *J* = 7.5 Hz, 1 H, **18**), 11.73 (br. s, 1 H, CO_2H) ppm. ^{13}C NMR: δ = −0.4, 0.7, 14.1, 22.6, 29.1, 29.6, 30.2, 31.7, 31.9, 133.1, 143.7, 147.3, 160.2, 173.0, 177.3 ppm.

Carboxylic Acid 19: Preparation obtained according to the General Procedure for the hydrocarboxylation of alkynes, starting from 7-benzyloxyhept-2-yne, and applying variation A. ^{1}H NMR analysis of the crude product (0.16 g, colourless oil) revealed that the regioselectivity of the reaction was about 67:33 in favour of **19**. Purification by flash column chromatography (ethyl acetate/heptane, gradient from 2 to 20%) afforded a 63:37 mixture of **19** and the other regioisomer (0.10 g, 0.41 mmol, 41%). Flash column chromatography (ethyl acetate/heptane, gradient from 0 to 10%) of the "nonacidic" crude product (0.11 g, colourless oil) led to the isolation of pure (*Z*)-7-benzyloxyhept-2-ene (33 mg, 0.16 mmol, 16%), the simple reduction product.

Mixture of 19 and Its Regioisomer (63:37): Colourless liquid. MS (CI, NH_3): *m*/*z* = 268, 267, 266 [MH^+ + NH_3], 251, 249 [MH^+], 248, 231. HRMS (ES^+): calcd. for $C_{15}H_{20}NaO_3$ [MNa^+] 271.1310, found 271.1307. IR: $\tilde{\nu}$ = 2940, 2862, 1700, 1695, 1684, 1453, 1102 cm^{-1}. ^{1}H NMR: δ = 1.30−1.90 (m, 7 H), 2.21 (q, *J* = 7.5 Hz, 2 H, **19**), 2.32 (t, *J* = 7.5 Hz, 2 H, regioisomer), 3.45 (t, *J* = 6.0 Hz, 2 H, regioisomer), 3.47 (t, *J* = 6.0 Hz, 2 H, **19**), 4.50 (s, 2 H), 6.90 (t, *J* = 7.5 Hz, 1 H, **19**), 7.00 (q, *J* = 7.0 Hz, 1 H, regioisomer), 7.21−7.38 (m, 5 H), 10.48 (br. s, 1 H, CO_2H) ppm. ^{13}C NMR: δ = 11.9, 14.5, 25.1, 28.6, 29.4, 29.5, 69.9, 70.2, 72.9, 127.3, 127.4, 127.5, 127.6, 128.3, 132.6, 138.4, 138.5, 140.3, 144.8, 173.3, 173.6 ppm.

(*Z*)-7-Benzyloxyhept-2-ene: Colourless liquid. MS (CI, NH_3): *m*/*z* = 222 [MH^+ + NH_3], 220, 205 [MH^+], 203, 108, 102. IR: $\tilde{\nu}$ = 2930, 2856, 1453, 1103 cm^{-1}. ^{1}H NMR: δ = 1.44 (quint, *J* = 7.0 Hz, 2 H), 1.59 (d, *J* = 6.0 Hz, 3 H), 1.55−1.70 (m, 2 H), 2.05 (q, *J* = 7.0 Hz, 2 H), 3.47 (t, *J* = 6.5 Hz, 2 H), 4.50 (s, 2 H), 5.31−5.55 (m, 2 H), 7.21−7.38 (m, 5 H) ppm. ^{13}C NMR: δ = 12.8, 26.1, 26.6, 29.4, 70.3, 72.9, 124.0, 127.4, 127.6, 128.3, 130.4, 138.7 ppm.

Enyne 20: This compound was obtained when the General Procedure for the hydrocarboxylation of alkynes was applied, starting from 1,4-diphenylbuta-1,3-diyne, and applying variation A. The crude product (55 mg) contained a complex mixture of compounds, as shown by NMR spectroscopy. Therefore, the "nonacidic" crude product (0.18 g, brown oil) was purified by several flash column chromatographies (ethyl acetate/heptane, gradient from 0 to 5%). Enyne **20** (62 mg, 0.30 mmol, 30%) and (*Z*,*Z*)-1,4-diphenylbuta-1,3-diene (11 mg, 52 μmol, 5%) were isolated. 1,4-Diphenylbut-1-yne and 1,4-diphenylbut-2-yne were also observed, although we were not able to obtain them in pure form. We find their formation difficult to explain.

20:[54,55] Yellow oil. ^{1}H NMR: δ = 5.91 (d, *J* = 12.0 Hz, 1 H), 6.68 (d, *J* = 12.0 Hz, 1 H), 7.14−7.40 (m, 8 H), 7.48 (m, 1 H), 7.91 (d, *J* = 7.0 Hz, 1 H) ppm. ^{13}C NMR: δ = 88.3, 95.8, 107.4, 123.4, 128.3, 128.3, 128.4, 128.5, 128.7, 131.4, 136.5, 138.7 ppm.

(*Z*,*Z*)-1,4-Diphenylbuta-1,3-diene:[56] Pale yellow oil. ^{1}H NMR: δ = 6.65 (AB, Δ*ν* = 41 Hz, J_{AB} = 8.0 Hz, 4 H), 7.22−7.45 (m, 10 H) ppm. ^{13}C NMR: δ = 126.6, 127.3, 128.3, 129.2, 132.0, 137.3 ppm.

1,4-Diphenylbut-1-yne:[57] ^{1}H NMR: δ = 2.69 (t, *J* = 7.5 Hz, 2 H), 2.92 (t, *J* = 7.5 Hz, 2 H) ppm. ^{13}C NMR: δ = 21.7, 35.2 ppm; because of insufficient purity, the signals for the triple bond and phenyl groups could not be assigned.

1,4-Diphenylbut-2-yne:[58] ^{1}H NMR: δ = 3.65 (s, 4 H) ppm. ^{13}C NMR: δ = 25.2, 80.0 ppm; because of insufficient purity, the signals for the phenyl groups could not be assigned.

Diene 21: Compound **21** was obtained according to the General Procedure for the hydrocarboxylation of alkynes, starting from phenylacetylene, and applying variation A. The crude product (55 mg) contained mostly cyclopentanecarboxylic acid, as shown by NMR spectroscopy. Purification, however, of the "nonacidic" crude product (0.14 g, yellow crystals) by several recrystallisations (diethyl ether or heptane) led to pure **21** (54 mg, 0.26 mmol, 52%).

21:[59] Colourless crystals; m.p. 152.7−153.0 °C (ref.[59] m.p. 153 °C). ^{1}H NMR: δ = 6.66 (m, 2 H), 6.94 (m, 2 H), 7.22 (m, 2 H), 7.32 (t, *J* = 7.5 Hz, 4 H), 7.43 (m, 4 H) ppm. ^{13}C NMR: δ = 126.4, 127.5, 128.6, 129.2, 132.8, 137.3 ppm.

Diene 22: Compound **22** was obtained according to the General Procedure for the hydrocarboxylation of alkynes, starting from 1-octyne, and applying variation A. The crude product (63 mg) contained essentially cyclopentylcarboxylic acid, as shown by NMR spectroscopy. Purification, however, of the "nonacidic" crude product (0.17 g, yellow oil) by flash column chromatography (heptane) led to a colourless liquid (75 mg), which proved to be a mixture of

bis(cyclopentane) and **22**. We were not able to separate them. Had **22** been pure, its yield would have been 68%.

22:[60,61] ^{1}H NMR: δ = 0.88 (t, *J* = 6.5 Hz, 6 H), 1.20−1.50 (m, 16 H), 2.04 (q, *J* = 7.0 Hz, 4 H), 5.56 (m, 2 H), 5.99 (m, 2 H) ppm. ^{13}C NMR: δ = 14.1, 22.7, 29.0, 29.5, 31.9, 32.7, 130.4, 132.4 ppm.

(*Z*)-Alkene 23: Titanium tetraisopropoxide (2.0 equiv., 2.0 mmol, 0.59 mL) was added at −70 °C to a solution of 1-phenyl-2-trimethylsilylacteylene (1.0 equiv., 1.0 mmol, 0.20 mL) in diethyl ether (20 mL). Cyclopentylmagnesium chloride (2.1 M in diethyl ether, 4.0 equiv., 4.0 mmol, 1.9 mL) was then added dropwise. The resulting yellow mixture was warmed to −30 °C over 5 min, then maintained at −30 °C for 15 min. Aqueous 0.3 N HCl (40 mL) and heptane (20 mL) were added. The organic layer was separated, and the aqueous phase extracted with heptane (2 × 30 mL). The combined organic layers were dried with magnesium sulfate, filtered and concentrated to afford a colourless oil (0.17 g). Purification by flash column chromatography (heptane) afforded analytically pure **23** (0.12 g, 0.65 mmol, 65%).

23:[62] Colourless liquid. $C_{11}H_{16}Si$ (176.34): calcd. C 74.93, H 9.15; found C 75.11, H 9.33. MS (EI): *m*/*z* = 247, 246, 245, 73. IR: $\tilde{\nu}$ = 2958, 2898, 1593, 1571, 1492, 1247, 840 cm^{-1}. ^{1}H NMR: δ = 0.04 (s, 9 H), 5.82 (d, *J* = 15.0 Hz, 1 H), 7.20−7.30 (m, 5 H), 7.36 (d, *J* = 15.0 Hz, 1 H) ppm. ^{13}C NMR: δ = 0.2, 127.3, 127.9, 128.1, 132.8, 140.1, 146.6 ppm.

General Procedure for the Halocarboxylation of 4-Octyne: Titanium tetraisopropoxide (2.0 equiv., 2.0 mmol, 0.59 mL) was added at −70 °C to a solution of 4-octyne (1.0 equiv., 1.0 mmol, 0.15 mL) in diethyl ether (20 mL). Cyclopentylmagnesium chloride (2.0 M in diethyl ether, 4.0 equiv., 4.0 mmol, 2.0 mL) was then added dropwise. The resulting yellow mixture was warmed to −30 °C over 5 min, then was maintained at −30 °C for 15 min, by which time it had turned black. The mixture was cooled down to −70 °C again, and carbon dioxide was added for 30 min while the bath was warmed to −30 °C. The halogenating reagent (2.0 equiv., 2.0 mmol) was then added, and the mixture was stirred at 20 °C for 2 h. Saturated aqueous sodium bisulfite ($Na_2S_2O_5$) solution (20 mL) was added. After a few min of stirring, diethyl ether (20 mL) and 1 N aqueous HCl (20 mL) were added. The organic layer was separated, and the aqueous phase extracted with diethyl ether (2 × 30 mL). The combined organic layers were extracted with 1 N aqueous NaOH solution (50 mL). The aqueous phase was washed with diethyl ether (50 mL), acidified using concentrated HCl aqueous solution, and then extracted with diethyl ether (3 × 30 mL). These last three organic phases were combined, dried with magnesium sulfate, filtered and concentrated to afford the crude product, which was then purified by flash column chromatography.

Bromocarboxylic Acid 24: Compound **24** was obtained according to the General Procedure for the halocarboxylation of 4-octyne, using either bromine or *N*-bromosuccinimide as the halogenating reagent. Using bromine, the crude product (0.15 g) was obtained as a colourless oil. Flash column chromatography (ethyl acetate/heptane, gradient from 0 to 20%) afforded **24** (62 mg, 0.26 mmol, 26%). With *N*-bromosuccinimide, the crude product (0.18 g) was obtained as a colourless oil. Flash column chromatography yielded **24** (0.10 g, 0.43 mmol, 43%).

24: Colourless liquid. MS (CI, NH_3): *m*/*z* = 254 ([$MH^+ + NH_3$], ^{81}Br), 253, 252 ([$MH^+ + NH_3$], ^{79}Br), 237 ([MH^+], ^{81}Br), 235 ([MH^+], ^{79}Br), 219, 217, 208. IR: $\tilde{\nu}$ = 2964, 2933, 2874, 1700, 1290 cm^{-1}. ^{1}H NMR: δ = 0.95 (t, *J* = 7.5 Hz, 3 H), 0.96 (t, *J* = 7.5 Hz, 3 H), 1.52 (sext, *J* = 7.5 Hz, 2 H), 1.66 (sext, *J* = 7.5 Hz, 2 H), 2.36 (t, *J* = 7.5 Hz, 2 H), 2.54 (t, *J* = 7.5 Hz, 2 H), 10.79 (br. s, 1 H, CO_2H) ppm. ^{13}C NMR: δ = 13.2, 13.7, 21.4, 21.8, 33.3, 39.3, 128.5; 133.9, 174.2 ppm.

Iodocarboxylic Acid 25: Compound **25** was obtained according to the General Procedure for the halocarboxylation of 4-octyne, using either iodine or *N*-iodosuccinimide as the halogenating reagent. Using iodine, the crude product (0.19 g) was obtained as a colourless oil. Flash column chromatography (ethyl acetate/heptane, gradient from 2 to 20%) afforded **25** (0.12 g, 0.44 mmol, 44%). With *N*-iodosuccinimide, the crude product (0.22 g) was obtained as a colourless oil. Flash column chromatography yielded **25** (0.12 g, 0.43 mmol, 43%).

25: Colourless liquid. IR: $\tilde{\nu}$ = 2962, 2932, 2872, 1697, 1288 cm^{-1}. ^{1}H NMR: δ = 0.94 (t, *J* = 7.5 Hz, 3 H), 0.96 (t, *J* = 7.5 Hz, 3 H), 1.52 (sext, *J* = 7.5 Hz, 2 H), 1.61 (sext, *J* = 7.5 Hz, 2 H), 2.39 (t, *J* = 7.5 Hz, 2 H), 2.60 (t, *J* = 7.5 Hz, 2 H), 11.50 (br. s, 1 H, CO_2H) ppm. ^{13}C NMR: δ = 13.0, 13.7, 21.9, 22.6, 33.4, 43.2, 107.3; 140.1, 175.0 ppm.

General Procedure for the Synthesis of Lactones from Alkynes: Titanium tetraisopropoxide (2.0 equiv., 2.0 mmol, 0.59 mL) was added at −70 °C to a solution of alkyne (1.0 equiv., 1.0 mmol) in diethyl ether (20 mL). Cyclopentylmagnesium chloride (2.0 M in diethyl ether, 4.0 equiv., 4.0 mmol, 2.0 mL) was then added dropwise. The resulting yellow mixture was warmed to −30 °C over 5 min, then was maintained at −30 °C for 15 min, by which time it had turned black. The mixture was cooled down to −70 °C again, and carbon dioxide was added, either for 30 min while the bath was warmed to −30 °C (variation A), for 30 min at −30 °C (variation B), or for 2 h at 0 °C (variation C). The carbonyl compound (2.0 equiv., 2.0 mmol) was then added, and the mixture was stirred at 20 °C for 2 h. Aqueous 0.3 N HCl (40 mL) and diethyl ether (20 mL) were then added. The organic layer was separated, and the aqueous phase extracted with diethyl ether (2 × 30 mL). The combined organic layers were washed with 1 N aqueous NaOH solution (50 mL). The aqueous phase was extracted with diethyl ether (50 mL). The combined organic phases were dried with magnesium sulfate, filtered and concentrated to afford the crude product, which was purified by flash column chromatography.

Note: When the isolation of the acidic reaction products was desired, the last (basic) aqueous layer was acidified using concentrated HCl aqueous solution, and extracted with diethyl ether (3 × 30 mL). The combined organic phases were dried with magnesium sulfate, filtered and concentrated. The resulting "acidic" crude product was then purified by flash column chromatography.

Butenolide 26: Compound **26** was obtained according to the General Procedure for the synthesis of lactones, starting from 4-octyne, applying variation A, and using benzaldehyde. Flash column chromatography (ethyl acetate/heptane, gradient from 0 to 10%) of the crude product (0.32 g) afforded pure **26** (0.12 g, 0.50 mmol, 50%).

26:[63] Viscous colourless oil. IR: $\tilde{\nu}$ = 2961, 2934, 2872, 1756, 1455, 1106, 1004 cm^{-1}. ^{1}H NMR: δ = 0.88 (t, *J* = 7.5 Hz, 3 H), 0.96 (t, *J* = 7.5 Hz, 3 H), 1.35 (m, 1 H), 1.45 (m, 1 H), 1.61 (sext, *J* = 7.5, 2 H), 1.96 (ddd, *J* = 14.0, 9.0, 5.5 Hz, 1 H), 2.30 (t, *J* = 7.5 Hz, 2 H), 2.33 (ddd, *J* = 14.0, 9.5, 7.0 Hz, 1 H), 5.67 (s, 1 H), 7.18 (m, 2 H), 7.36 (m, 3 H) ppm. ^{13}C NMR: δ = 13.8, 13.9, 21.2, 21.5, 25.5, 28.4, 83.6, 126.8, 128.8, 129.1, 135.0, 163.2, 174.5 ppm.

Butenolide 27: Compound **27** was obtained according to the General Procedure for the synthesis of lactones, starting from 4-octyne, applying variation B, and using propanal. Flash column chromato-

graphy (ethyl acetate/heptane, gradient from 0 to 10%) of the crude product (0.20 g) afforded analytically pure **27** (80 mg, 0.41 mmol, 41%).

27: Colourless oil. $C_{12}H_{20}O_2$ (196.29): calcd. C 73.43, H 10.27; found C 73.21, H 10.53. MS (EI): *m*/*z* = 196 [$M^{+\cdot}$], 181, 139, 81, 69. IR: $\tilde{\nu}$ = 2963, 2935, 2874, 1752, 1462, 1120, 1074, 978 cm^{-1}. ^1H NMR: δ = 0.92 (t, *J* = 7.5 Hz, 3 H), 0.98 (t, *J* = 7.5 Hz, 3 H), 1.35−1.65 (m, 5 H), 1.99 (dqd, *J* = 14.5, 7.5, 3.5 Hz, 1 H), 2.19 (ddd, *J* = 14.0, 9.0, 5.5 Hz, 1 H), 2.23 (m, 2 H), 2.46 (ddd, *J* = 14.0, 9.0, 7.0 Hz, 1 H), 4.80 (dd, *J* = 7.0, 3.5 Hz, 1 H) ppm. ^{13}C NMR: δ = 8.3, 13.8, 14.0, 21.3, 21.5, 25.0, 25.5, 28.4, 82.3, 127.8, 162.8, 174.4 ppm.

Butenolide 28: Compound **28** was obtained according to the General Procedure for the synthesis of lactones, starting from 1-phenyl-1-pentyne, applying variation B, and using benzaldehyde. Flash column chromatography (ethyl acetate/heptane, gradient from 0 to 10%) of the crude product (0.31 g), followed by recrystallisation (heptane), afforded a mixture of **28** and of the other possible regioisomer (ratio ca. 78:22 in favour of **28**, 0.13 g, 0.46 mmol, 46%). The ratio of the two products was about the same in the crude product as shown by ^1H NMR analysis. A second recrystallisation led to the isolation of analytically pure **28** as a single regioisomer (92 mg, 0.33 mmol, 33%).

28: Colourless crystals, m.p. 79.5−80.7 °C. $C_{19}H_{18}O_2$ (278.35): calcd. C 81.99, H 6.52; found C 81.86, H 6.49. IR: $\tilde{\nu}$ = 2962, 2932, 1753, 1455, 1094, 1006 cm^{-1}. ^1H NMR: δ = 0.98 (t, *J* = 7.5 Hz, 3 H), 1.69 (m, 2 H), 2.48 (m, 2 H), 6.14 (s, 1 H), 7.13−7.23 (m, 4 H), 7.24−7.37 (m, 6 H) ppm. ^{13}C NMR: δ = 14.0, 21.5, 26.2, 83.6, 127.2, 127.7, 128.7, 129.0, 129.4, 131.4, 134.9, 159.1, 174.0 ppm.

Regioisomer of 28. Main Differences: ^1H NMR: δ = 0.84 (t, *J* = 7.5 Hz, 3 H), 1.30−1.58 (m, 2 H), 2.08 (ddd, *J* = 14.5, 9.5, 5.5 Hz, 1 H), 2.57 (ddd, *J* = 14.5, 10.0, 7.0 Hz, 1 H), 5.85 (s, 1 H) ppm. ^{13}C NMR: δ = 21.2, 29.0, 134.7, 164.4 ppm.

Butenolide 29: Compound **29** was obtained according to the General Procedure for the synthesis of lactones, starting from 1-phenyl-1-pentyne, applying variation B, and using *trans*-cinnamaldehyde. Flash column chromatography (ethyl acetate/heptane, gradient from 0 to 20%) of the crude product (0.40 g) afforded a mixture of **29** and of the other possible regioisomer (ratio ca. 81:19 in favour of **29**, 0.18 g, 0.58 mmol, 58%). The ratio of the two products was about 88:12 in the crude product as shown by ^1H NMR analysis.

Mixture of 29 and Its Regioisomer (81:19): Pale yellow oil. MS (ES^+): *m*/*z* = 306, 305 [MH^+], 261, 185, 161, 117. HRMS (ES^+): calcd. for $C_{21}H_{20}NaO_2$ [M + Na^+] 327.1361, found 327.1350. IR: $\tilde{\nu}$ = 2961, 1752, 1448, 1112, 1086, 1068, 1001, 967 cm^{-1}.

29: ^1H NMR: δ = 0.95 (t, *J* = 7.5 Hz, 3 H), 1.63 (m, 2 H), 2.44 (m, 2 H), 5.80 (d, *J* = 7.5 Hz, 1 H), 5.92 (dd, *J* = 16.0, 7.5 Hz, 1 H), 6.74 (d, *J* = 16.0 Hz, 1 H), 7.15−7.50 (m, 10 H) ppm. ^{13}C NMR: δ = 14.1, 21.4, 26.4, 82.3, 123.2, 126.7, 128.7, 128.3, 128.5, 128.9, 129.7, 135.1, 158.5, 173.8 ppm.

Regioisomer of 29. Main Differences: ^1H NMR: δ = 0.93 (t, *J* = 7.5 Hz, 3 H), 2.65 (ddd, *J* = 14.0, 9.5, 7.0 Hz, 1 H), 5.49 (d, *J* = 8.5 Hz, 1 H), 6.01 (dd, *J* = 16.0, 8.5 Hz, 1 H), 6.86 (d, *J* = 16.0 Hz, 1 H) ppm. ^{13}C NMR: δ = 21.2, 29.0, 82.8, 123.0, 136.0 ppm.

Butenolide 30: Compound **30** was obtained according to the General Procedure for the synthesis of lactones, starting from 1-phenyl-2-trimethylsilylacetylene, applying variation C, and using *trans*-cinnamaldehyde. Several sequential flash column chromatographies (ethyl acetate/heptane, gradient from 0 to 10%) of the crude product (0.41 g) afforded a 50:50 mixture of **30** and *trans*-cinnamaldehyde (orange oil, 36 mg). Accordingly, the yield of **30** was estimated to be ca. 8%.

30: ^1H NMR: δ = 0.11 (s, 9 H), 5.66 (dd, *J* = 7.5, 1.0 Hz, 1 H), 5.90 (dd, *J* = 15.5, 7.0 Hz, 1 H), 6.65 (dd, *J* = 15.5, 1.0 Hz, 1 H), 7.19−7.44 (m, 10 H) ppm. ^{13}C NMR: δ = −1.0, 85.4, 122.7, 126.7, 128.4, 129.6, 134.6, 175.8 ppm; not all signals could be assigned because of the presence of *trans*-cinnamaldehyde on the spectrum.

Butenolide 31: Compound **31** was obtained according to the General Procedure for the synthesis of lactones, on a 2.2-mmol scale, starting from 5-*tert*-butyldimethylsilyloxy-1-phenylpent-1-yne, applying variation B, and using hexanal. Two sequential flash column chromatographies (ethyl acetate/heptane, gradient from 0 to 20%) of the crude product (1.2 g) afforded pure **31** (0.18 g) and a mixture of **31** and the other possible regioisomer (0.28 g) as colourless oils. The total amount of lactones was thus 0.46 g (1.1 mmol, 52%). The ratio of the two products was about 85:15 after the first column chromatography, as shown by ^1H NMR analysis.

31: Colourless oil. MS (EI): *m*/*z* = 346, 345, 115, 91, 75, 73, 57. HRMS (ES^+): calcd. for $C_{24}H_{38}NaO_3Si$ [MNa^+] 425.2488, found 425.2469. IR: $\tilde{\nu}$ = 2955, 2929, 2858, 1754, 1255, 1099, 835, 775 cm^{-1}. ^1H NMR: δ = 0.00 (s, 3 H), 0.02 (s, 3 H), 0.82 (m, 3 H), 0.86 (s, 9 H), 1.10−1.48 (m, 7 H), 1.65−1.90 (m, 3 H), 2.51 (m, 2 H), 3.63 (m, 2 H), 5.31 (m, 1 H), 7.30−7.50 (m, 5 H) ppm. ^{13}C NMR: δ = −5.4, 13.9, 18.3, 21.0, 22.4, 24.0, 25.9, 31.1, 31.3, 32.8, 62.5, 81.8, 127.7, 127.7, 129.0, 129.6, 131.6, 159.8, 174.2 ppm.

Regioisomer of 31. Main Differences: ^1H NMR: δ = 2.00 (m, 1 H), 2.45 (m, 1 H), 2.84 (m, 1 H), 3.55−3.70 (m, 2 H), 5.00 (dd, *J* = 7.0, 3.0 Hz, 1 H), 7.25−7.45 (m, 5 H) ppm. ^{13}C NMR: δ = 14.0, 32.2, 62.1, 81.6, 128.4 ppm.

δ-Hydroxy Acid 32: This compound was obtained by removing the TBS group of acid **16** according to a literature procedure.[64] Water (1.0 mL) and acetic acid (3.0 mL) were added to a solution of silyl ether **16** (1.0 equiv., 0.59 mmol, 0.19 g) in THF (1.0 mL). The mixture was stirred for 200 min at 20 °C, then concentrated under vacuum (heptane was used as an azeotrope to remove acetic acid thoroughly) to give a viscous colourless oil (0.13 g) that later crystallised. Recrystallisation (heptane/ethyl acetate) afforded analytically pure **32** (82 mg, 0.40 mmol, 67%).

32: Colourless crystals; m.p. 98.5−99.5 °C. $C_{12}H_{14}O_3$ (206.24): calcd. C 69.89, H 6.84; found C 70.01, H 6.86; MS (EI): *m*/*z* = 206 [$M^{+\cdot}$], 188, 187, 160, 143, 142, 129, 128, 116, 115, 91. IR: $\tilde{\nu}$ = 3330, 2925, 1672, 1421, 1036 cm^{-1}. ^1H NMR: δ = 1.87 (dd, *J* = 7.5, 6.0 Hz, 2 H), 2.66 (t, *J* = 7.5 Hz, 2 H), 3.70 (t, *J* = 6.0 Hz, 2 H), 7.20−7.50 (m, 7 H), 7.84 (s, 1 H) ppm. ^{13}C NMR: δ = 23.3, 31.9, 62.0, 128.6, 128.9, 129.4, 131.7, 135.2, 141.7, 173.5 ppm.

Lactone 33: A solution of δ-hydroxy acid **32** (1.0 equiv. 0.36 mmol, 75 mg) in toluene (5.0 mL) was stirred under reflux for 6 h. After cooling, the solvent was evaporated under vacuum to afford a colourless liquid (69 mg). Purification by flash column chromatography (ethyl acetate/heptane, gradient from 5 to 30%) yielded pure **33** (66 mg, 0.35 mmol, 97%).

33: Colourless oil. MS (EI): *m*/*z* = 188 [$M^{+\cdot}$], 187, 129, 128, 118, 115, 102, 91. IR: $\tilde{\nu}$ = 1708, 1612, 1447, 1260, 1172, 1121, 1071,

978, 772 cm^{-1}. ^1H NMR: δ = 1.97 (tt, *J* = 6.5, 5.0 Hz, 2 H), 2.88 (td, *J* = 6.5, 2.0 Hz, 2 H), 4.39 (t, *J* = 5.0 Hz, 2 H), 7.30−7.50 (m, 5 H), 7.91 (t, *J* = 2.0 Hz, 1 H) ppm. ^{13}C NMR: δ = 22.9, 25.8, 68.6, 125.7, 128.5, 129.1, 130.1, 134.8, 141.4, 166.9 ppm.

Acknowledgments

This work was funded by the Centre National de la Recherche Scientifique (C.N.R.S.). We wish to thank Professor Samir Z. Zard, Mr. Arnaud Parenty, Dr. Jean-Marc Campagne and Dr. Benoît Crousse for the gifts of several reagents and starting compounds. We are also grateful to the people who carried out the elemental analyses and the mass spectra of our compounds.

[1] O. G. Kulinkovich, S. V. Sviridov, D. A. Vasilevskii, T. S. Pritytskaya, *J. Org. Chem. USSR (Engl. Trans.)* **1989**, *25*, 2027−2028.
[2] O. G. Kulinkovich, S. V. Sviridov, D. A. Vasilevski, *Synthesis* **1991**, 234.
[3] Review: O. G. Kulinkovich, A. de Meijere, *Chem. Rev.* **2000**, *100*, 2789−2834.
[4] Theoretical study: Y.-D. Wu, Z.-X. Yu, *J. Am. Chem. Soc.* **2001**, *123*, 5777−5786.
[5] V. Chaplinski, A. de Meijere, *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 413−414.
[6] O. G. Kulinkovich, A. I. Savchenko, S. V. Sviridov, D. A. Vasilevski, *Mendeleev Commun.* **1993**, 230−231.
[7] A. Kasatkin, T. Nakagawa, S. Okamoto, F. Sato, *J. Am. Chem. Soc.* **1995**, *117*, 3881−3882.
[8] J. Lee, C. H. Kang, H. Kim, J. K. Cha, *J. Am. Chem. Soc.* **1996**, *118*, 291−292.
[9] K. Harada, H. Urabe, F. Sato, *Tetrahedron Lett.* **1995**, *36*, 3203−2306.
[10] F. Sato, H. Urabe, S. Okamoto, *Synlett* **2000**, 753−775.
[11] F. Sato, H. Urabe, S. Okamoto, *Chem. Rev.* **2000**, *100*, 2835−2886.
[12] F. Sato, S. Okamoto, *Adv. Synth. Catal.* **2001**, *343*, 759−784.
[13] J. J. Eisch, *J. Organomet. Chem.* **2001**, *617−618*, 148−157.
[14] J. J. Eisch, J. N. Gitua, P. O. Otieno, X. Shi, *J. Organomet. Chem.* **2001**, *624*, 229−238.
[15] F. Sato, H. Urabe in *Titanium and Zirconium in Organic Synthesis* (Ed.: I. Marek), Wiley-VCH, Weinheim, **2002**, pp. 319−354.
[16] I. S. Kolomnikov, T. S. Lobeeva, V. V. Gorbachevskaya, G. G. Aleksandrov, Y. T. Struchkov, M. E. Vol'pin, *J. Chem. Soc., Chem. Commun.* **1971**, 972−973.
[17] B. Demerseman, R. Mahé, P. H. Dixneuf, *J. Chem. Soc., Chem. Commun.* **1984**, 1394−1396.
[18] H. G. Alt, G. S. Herrmann, M. D. Rausch, D. T. Mallin, *J. Organomet. Chem.* **1988**, *356*, C53−C56.
[19] V. V. Burlakov, U. Rosenthal, A. I. Yanovskii, Y. T. Struchkov, O. G. Ellert, V. B. Shur, M. E. Vol'pin, *Organomet. Chem. USSR* **1989**, *2*, 633.
[20] For an evaluation of the titanium partner in the Kulinkovich reaction, see: J. C. Lee, M. J. Sung, J. K. Cha, *Tetrahedron Lett.* **2001**, *42*, 2059−2061.
[21] C. Averbuj, J. Kaftanov, I. Marek, *Synlett* **1999**, 1939−1941.
[22] M. B. Smith, J. March, *Advanced Organic Chemistry: Reactions, Mechanisms, and Structure*, 5th ed., Wiley-Interscience, New York, **2001**, p. 1215.
[23] J. Lee, Y. G. Kim, J. G. Bae, J. K. Cha, *J. Org. Chem.* **1996**, *61*, 4878−4879.
[24] Sato and co-workers have described the successful synthesis of silylated (diisopropyloxy)titanacyclopropanes, but these compounds are not suitable for further ligand exchange with alkynes: R. Mizojiri, H. Urabe, F. Sato, *J. Org. Chem.* **2000**, *65*, 6217−6222. More recently, Eisch et al. have reported the preparation of solutions of (diisopropyloxy)titanacyclopropanes, using a novel method, see ref.[14]
[25] When cyclopentylmagnesium chloride (1.2 equiv.) was added to acetophenone (1.0 equiv.) in diethyl ether under the same temperature and time conditions as for the preparation of diol **7**, 1-phenylethanol was isolated in 62% yield.
[26] M. B. Smith, J. March, *Advanced Organic Chemistry: Reactions, Mechanisms, and Structure*, 5th ed., Wiley-Interscience, New York, **2001**, p. 795−796.
[27] S. Yamaguchi, R.-Z. Jin, K. Tamao, F. Sato, *J. Org. Chem.* **1998**, *63*, 10060−10062.
[28] Y. Six, *J. Chem. Soc., Perkin Trans. 1* **2002**, 1159−1160.
[29] K. Yamashita, F. Sato, *Tetrahedron Lett.* **1996**, *37*, 7275−7278.
[30] Y. Gao, K. Harada, F. Sato, *Tetrahedron Lett.* **1995**, *36*, 5913−5916.
[31] A. Kasatkin, S. Okamoto, F. Sato, *Tetrahedron Lett.* **1995**, *36*, 6075−6078.
[32] S. Okamoto, A. Kasatkin, P. K. Zubaidha, F. Sato, *J. Am. Chem. Soc.* **1996**, *118*, 2208−2216.
[33] S. Dérien, E. Duñach, J. Périchon, *J. Am. Chem. Soc.* **1991**, *113*, 8447−8454.
[34] M. Takimoto, K. Shimizu, M. Mori, *Org. Lett.* **2001**, *3*, 3345−3347.
[35] F. Sato, H. Ishikawa, M. Sato, *Tetrahedron Lett.* **1981**, *22*, 85−88.
[36] P. J. Kocienski, C. J. Love, R. J. Whitby, G. Costello, D. A. Roberts, *Tetrahedron* **1989**, *45*, 3839−3848.
[37] M. Yamagushi, Y. Nobayashi, I. Hirao, *Tetrahedron* **1984**, *40*, 4261−4266.
[38] E. Valentí, M. A. Pericàs, F. Serratosa, *J. Org. Chem.* **1990**, *55*, 395−397.
[39] I. D. Campbell, G. Eglinton, *Org. Synth., Coll. Vol.* **1973**, *5*, 517−520.
[40] J. H. Stocker, R. M. Jenevein, *J. Org. Chem.* **1968**, *33*, 294−297.
[41] K. Mashima, T. Oshiki, K. Tani, *J. Org. Chem.* **1998**, *63*, 7114−7116.
[42] D. Guijarro, M. Yus, *Tetrahedron* **1994**, *50*, 3447−3452.
[43] H. Baumann, N. C. Franklin, H. Möhrle, *Tetrahedron* **1967**, *23*, 4331−4336.
[44] B. Herradón, D. Seebach, *Helv. Chim. Acta* **1989**, *72*, 690−714.
[45] H. M. Chang, K. P. Cheng, T. F. Choang, H. F. Chow, K. Y. Chui, P. M. Hon, F. W. L. Tan, Y. Yang, Z. P. Zhong, C. M. Lee, H. L. Sham, C. F. Chan, Y. X. Cui, H. N. C. Wong, *J. Org. Chem.* **1990**, *55*, 3537−3543.
[46] H. Kohn, M. B. Bean, C. von Rohrscheidt, M. R. Willcott, III, E. W. Warnhoff, *Tetrahedron* **1981**, *37*, 3195−3201.
[47] L. Börjesson, I. Csöregh, C. J. Welch, *J. Org. Chem.* **1995**, *60*, 2989−2999.
[48] D. R. Brittelli, *J. Org. Chem.* **1981**, *46*, 2514−2520.
[49] P. Coutrot, A. Ghribi, *Synthesis* **1986**, 790−792.
[50] M.-P. Teulade, P. Savignac, E. About-Jaudet, N. Collignon, *Synth. Commun.* **1989**, *19*, 71−81.
[51] M. Chini, P. Crotti, C. Gardelli, E. Giovani, F. Macchia, M. Pineschi, *J. Org. Chem.* **1993**, *58*, 1221−1227.
[52] E. J. Corey, A. Venkateswarlu, *J. Am. Chem. Soc.* **1972**, *94*, 6190−6191.
[53] C. Lefeber, A. Ohff, A. Tillack, W. Baumann, R. Kempe, V. V. Burlakov, U. Rosenthal, H. Görls, *J. Organomet. Chem.* **1995**, *501*, 179−188.
[54] M. Kosugi, T. Kimura, H. Oda, T. Migita, *Bull. Chem. Soc. Jpn.* **1993**, *66*, 3522−3524.
[55] R. A. Aitken, C. Boeters, J. J. Morrison, *J. Chem. Soc., Perkin Trans. 1* **1994**, 2473−2480.
[56] C. Cannes, S. Condon, M. Durandetti, J. Périchon, J.-Y. Nédélec, *J. Org. Chem.* **2000**, *65*, 4575−4583.
[57] S. Ma, L. Wang, *J. Org. Chem.* **1998**, *63*, 3497−3498.
[58] I. U. Khand, G. R. Knox, P. L. Pauson, W. E. Watts, *J. Organomet. Chem.* **1974**, *73*, 383−388.

[59] K. Sasaki, K. Nakao, Y. Kobayashi, M. Sakai, N. Uchino, Y. Sakakibara, K. Takagi, *Bull. Chem. Soc. Jpn.* **1993**, *66*, 2446−2448.
[60] N. Satyanarayana, M. Periasamy, *Tetrahedron Lett.* **1986**, *27*, 6253−6256.
[61] T. Chou, M. You, *J. Org. Chem.* **1987**, *52*, 2224−2226.
[62] J. J. Eisch, M. W. Foxton, *J. Org. Chem.* **1971**, *36*, 3520−3526.
[63] C. Copéret, T. Sugihara, G. Wu, I. Shimoyama, E. Negishi, *J. Am. Chem. Soc.* **1995**, *117*, 3422−3431.
[64] W. R. Li, W. R. Ewing, B. D. Harris, M. M. Joullié, *J. Am. Chem. Soc.* **1990**, *112*, 7659−7672.
[65] A. W. Murray, R. G. Reid, *Synthesis* **1985**, 35−38.
Received October 25, 2002
[O02595]