DOI: 10.1002/chem.200903273

The Nickel-Catalyzed Carbonylative Cycloaddition of Allyl Halides and Acetylenes: An Efficient Tool for Cyclopentane Annelation

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This paper is dedicated to Professor Francesc Camps and Professor Pedro Molina

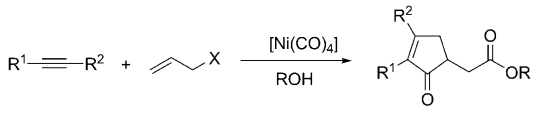
Abstract: From a practical synthetic point of view, the nickel-mediated carbonylative cycloaddition of alkynes and allyl halides is a straightforward method for obtaining the cyclopentane skeleton in high yields and with controlled stereochemistry, especially when considering the efficiency of the intermolecular version of the reaction. The efforts to make the previously stoichiometric process catalytic in nickel, after experimental mechanistic observations, are reported herein. The unexpected intervention of iron as a reductant and the isolation of a final dimeric species that exhibits interesting tautomeric behavior are also presented. An extension of the reaction to new substrates has led to the conclusion that, although the steric and electronic effects of the alkyne substituents are generally irrelevant in relation to the adducts and their yields, those of the allylic counterpart may have a significant influence on the outcome of the reaction. However, the presence of the amine moiety in the alkyne completely inhibited the reaction. The feasibility of a multicentered reaction was verified with a triacetylene in which up to 12 bonds were created at once and in good yield.

Keywords: carbonylation · catalysis · cycloaddition · iron · nickel

Introduction

Multicomponent reactions are recognized as being of the utmost interest in synthetic organic chemistry as a result of their atom economy and the time-saving features in the reaction processes. The vast majority of these reactions require a transition-metal center to activate the substrates to allow unequivocally and sequentially the synthesis of the required linkages to yield the final product.[1] However, much of their practical interest is lost when the metal mediator is involved in the final product or spoiled during the reaction, especially when an expensive metal center or a very sophisticated ligand is involved. The efforts to provide the synthetic chemist with an efficient catalytic Pauson–Khand reaction have been reflected in many recent contributions to the chemical literature, although the most efficient procedures involve the use of expensive metals and apply mainly to the intramolecular version of the reaction.[2]

For two decades, we have studied the carbocyclization reactions of allyl halides and acetylenes mediated by nickel, a reaction formally related to the aforementioned Pauson–Khand process.[3] This reaction was originally reported by Chiusoli and Cassar to give allylacrylic acids[4] and later applied also by Oppolzer et al. to synthesize cyclopentenones.[5] More recently, a similar palladium-catalyzed process with allyl tosylates was reported by Tsukada et al.[6] We initially found that, by using stoichiometric amounts of the hazardous $[Ni(CO)_4]$ as a mediator and disubstituted alkynes as reagents, cyclopentenones were exclusively obtained[3a] (Scheme 1).



Scheme 1. General scheme for the carbonylative cycloaddition reaction of allyl halides and disubstituted alkynes mediated by $[Ni(CO)_4]$.

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Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/chem.200903273.

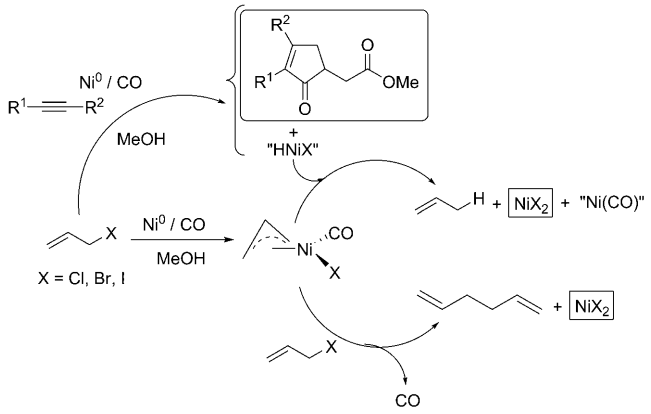
The reaction, which provided adducts in acceptable-to-high yields depending on the substrates, proved to be regioselective in both components and stereoselective when one of them carried a stereogenic center. Moreover, and more importantly when compared with other metal-mediated cycloaddition reactions, the intermolecular version of the reaction was also efficient. Thus, in the next step we tried to replace the dangerous mediator by the less hazardous [Ni(cod)$_2$] under a CO atmosphere. The reactions performed with this mediator proved to be successful and we were able to report a range of new applications.[3d] However, the lability and stoichiometric use of this mediator did not augur well for its practical and large-scale application in organic synthesis. Therefore we directed our efforts towards establishing a process truly catalytic in nickel. Two facts lent support to this proposal: Oppolzer et al.[5] had proved the substoichiometry of the reaction (four cycles, intramolecularly) and we had observed that, starting from 1-halo-1,4-dienes, the carbocyclization proceeded catalytically.[7] This latter observation told us that the step (or steps) responsible for the noncatalytic character of the global reaction was the allylmetallation of the alkyne because beyond this step the same intermediates should be involved. Bearing these facts in mind, we explored new conditions in an effort to make the process catalytic and to find a cheap and stable source of mediator that would allow its practical use. This was achieved by the use of iron in the form of a powder[8] and, three years later, the reaction was applied to strained olefins[9] to construct, in both cases, the cyclopentane skeleton.

In recent years the importance of environmentally benign syntheses has been increasingly recognized and parameters such as the *E* factor,[10] atom efficiency,[1a] and the "12 Principles of Green Chemistry"[11] are often considered as essential driving forces in the quest for sustainable chemical processes. The cycloaddition process reported herein deals with three of the twelve green principles: The reaction is catalytic in nickel, hazardous and cumbersome Ni^0 species have been replaced by available Ni^{II} salts, and up to four bonds are created in one single synthetic operation. Furthermore, in recent work we have shown that the process can take place by using compressed fluids, with an important reduction in the amount of organic solvent used and with an unexpected chemoselectivity.[12] On the other hand, the reaction product, the cyclopentane ring, is often present in natural products of bioactive interest. Thus, aside from steroids and prostaglandins, they are found in iridoids, which display different biological activities, for example, antibiotics (methylenomicin, pentalenolactone), antitumorals (coriolin, quadrone),[13] crop control agents (specionin, strygol), and perfumes (jasmine, vetivone).[14]

We report herein a full account of our research that finally led to the nickel-catalyzed version of the carbonylative cycloaddition reaction between allyl halides and acetylenes and insights into the reaction mechanism. A study of the scope and limitations of this reaction is also reported.

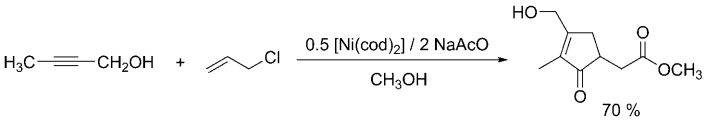
Results and Discussion

When considering the mechanism proposed for the original reaction, one could anticipate that it should display catalytic character because the putative side-product released in the last step, HNiX, would presumably suffer reductive elimination to the corresponding hydrogen halide to regenerate a Ni^0 species. This is not so, and products arising from solvolytic cleavage of the π-allyl complex have previously been found by Chiusoli et al.[15] and ourselves[3a] (reductive substitution) with the concomitant formation of inactive Ni^{II} species. More pernicious than that, however, is the known and very efficient concurrent allyl halide self-coupling reaction, which was the reason for the use of hyperstoichiometric amounts of allyl halides and nickel(0) mediators in our earlier methodology (Scheme 2). Both processes yield inactive nickel dihalide.



Scheme 2. Solvolytic cleavage and allyl halide self-coupling leading to inactive nickel dihalide.

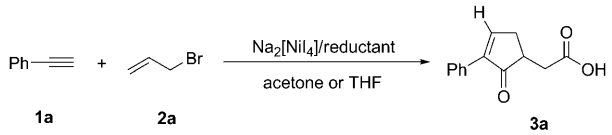
To suppress the reductive substitution of the allyl component we added a compatible base (sodium acetate) to a new system ([Ni(cod)$_2$], CO, 2-butyn-1-ol, allyl chloride, and methanol). In this way we attained slightly more than two cycles (Scheme 3). Although similar results had already



Scheme 3. Carbonylative cycloaddition reaction of 2-butyn-1-ol (3 equiv) and allyl chloride (3 equiv) using [Ni(cod)$_2$] (0.5 equiv) at room temperature with methanol as solvent in the presence of NaAcO.

been reported by Oppolzer et al. by adding a chelating phosphine to avoid catalyst degradation,[5a] our own intermolecular system was now operating catalytically thus proving its feasibility.[16]

From this result it seemed that allyl self-coupling was the main side-reaction responsible for catalyst degradation to inactive Ni^{II} salts. This reaction had previously been studied mechanistically and a Ni^{I} free radical seemed to be the key for the reaction to proceed.[17] In our attempt to establish conditions that are unfavorable to allyl self-coupling, we changed the substrate model and solvent (Scheme 4). Unexpectedly, we concluded that the same Ni^{I} pseudoradical was responsible for both processes and the result depended on the relative kinetics of the reaction of a common Ni^{I} intermediate towards allyl halide or alkyne.[8]



Scheme 4. Model substrates phenylacetylene and allyl bromide used in the cycloaddition reaction to give the cycloadduct **3a**.

We then directed our efforts towards the in situ generation of Ni^{I} species to promote the catalytic cycloaddition reaction. We envisaged that an efficient generation of Ni^{I} species, combined with the absence of any Ni^{II} in the medium, would provide a long catalytic lifetime because the allyl self-coupling reaction seems to require the presence of the two valence states.[17c] In the absence of Ni^{II} species, the Ni^{III}–π-allyl complex generated after oxidative addition would coordinate the acetylene and mediate the carbonylative cycloaddition reaction.[18] The exclusive generation of Ni^{I} species was attempted by the monoelectronic reduction of Ni^{II} salts or by mixing equimolar amounts of Ni^{0} and Ni^{II} complexes under CO to stabilize the Ni^{I} species(Table 1). Although nickel iodide was not considered the best halide in terms of preventing allyl self-coupling,[17c] it was chosen because of its higher solubility.

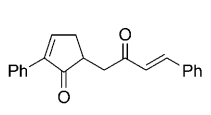
Table 1. Catalytic efficiency of different reducing systems in the nickel-mediated cyclocarbonylation of allyl halides and alkynes.

	System	Subs./ Ni[a]	Conv.[b] [%]	Yield[c] [%]	Turnover[d]
1	$Na_2[NiI_4]$/cat. $C_{10}H_8$/Na/ THF	2	25	15	<1
2	$[Ni(cod)_2]/Na_2[NiI_4]$/ THF	2	32	30	<1
3	$Et_3SiH/Na_2[NiI_4]$/THF	2	46	40	<1
4	$Et_3SnH/Na_2[NiI_4]$/THF	2	48	45	<1
5	$^1/_2$TDAE/$Na_2[NiI_4]$/acetone	4	100	95	3.8
6	$Sn/Na_2[NiI_4]$/acetone	10	64	53	6.4
7	$Fe/Na_2[NiI_4]$/acetone	20	83	85	16

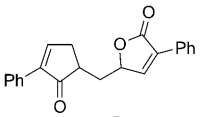
[a] Number of intended catalytic cycles. Substrate mixture: Phenylacetylene/allyl bromide 1:1. [b] Conversion, given as a percentage of the crude product relative to the theoretical value, assuming total conversion into the oxocyclopentenecarboxylic acid. [c] Total yield of 2-oxocyclopent-3-eneacetic acid in the crude, as estimated from the corresponding ^{1}H NMR spectrum. [d] Estimated turnover based on the total product.

Although the results in entries 1–4 of Table 1 were very disappointing, in all cases the major product was, by far, the expected cycloadduct **3**, which confirmed the mediation of Ni^{I} radicals in the whole process. Despite that, the reduced nickel species was easily reoxidized by the excess allyl halide and the turnover was stopped. Tetrakis(diethylamino)ethylene (TDAE)[19] was the first reductant to confer a true catalytic role on the nickel (entry 5). Unfortunately, we could not attain more than four cycles with it.[20] Although excess tin showed an acceptable efficiency, iron was even better, attaining up to 16 cycles (entry 7). In all cases, the CO uptake was about 2 mol of CO per mol of Ni,[21] which approximately corresponds to the theoretical uptake for the full conversion of the substrates into cycloadduct **3**. Unlike tin and iron, zinc and magnesium gave black metallic nickel with no cycloadduct being obtained. Powdered manganese and Cr^{II} salts were also used without success despite the fact that, in the presence of a catalytic amount of quinoline, manganese efficiently reduces Ni^{II} to yield $[Ni(cod)_2]$ by an easy well-known method.[22]

Role of iron in the reaction: Although iron was initially thought to be only the reductant of the Ni^{II} halide, excess iron was used to secure its effect under the heterogeneous conditions of the reaction. The initial brick-red color of the NiI_4^{2-} anion turned to grey in 30 min with a slight uptake of CO. Then the substrate (phenylacetylene/allyl bromide, 1:1) mixture was added dropwise to the rapidly stirred mixture containing the catalyst. Soon gas absorption started and continued until the theoretical 2 mol of CO per mol of substrate were reached. Then the reaction was stopped. By weighing the remaining iron attached to the stirring bar we noted that 0.5 mol of iron per mol of substrate had disappeared, which points to its active participation in the whole reaction. Simple acidic work-up in air and removal of any small amounts of iodine formed with $Na_2S_2O_3$ solution afforded the crude product, which consisted of 85% of the cycloadduct **3a** with the remaining 15% corresponding to two nonpolar adducts identified as **4a** (minor) and **5a** (1:1 mixture of stereoisomers) derived from a further insertion of the alkyne. Similar products have previously been reported in related processes.[6]

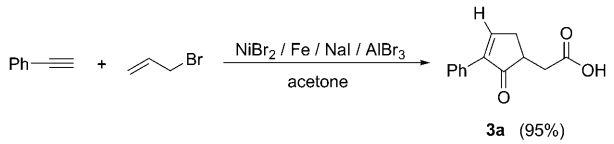


4a



5a

We soon observed that the relative amounts of these side-products decreased with the spontaneous oxidation of the starting nickel iodide. We concluded that the iodine formed in the oxidation of the nickel salt, as a Lewis acid, was beneficial for the selectivity of the reaction and that we could replace the nickel iodide by a mixture of stable $NiBr_2$, NaI (6 mol), and $AlBr_3$, with identical or better results than those obtained with the nickel iodide (Scheme 5).



Scheme 5. Carbonylative cycloaddition using $NiBr_2$ (0.25 mmol) as the catalyst, NaI (1.5 mmol), Fe (5 mmol), and $AlBr_3$ (1 mmol) with phenylacetylene (5 mmol) and allyl bromide (5.8 mmol) as the reagents.

We then directed our efforts towards characterizing the primary reaction adduct and its side-products to determine the role of iron. With this aim, the final mixture was dried under vacuum. From the distillate of the final reaction mixture we isolated significant amounts of mesityl oxide and an insignificant amount of hydrogen bromide with a complete absence of isopropyl alcohol. The IR spectrum of the residue (Figure 1, spectrum a) showed no metal–carbonyl band

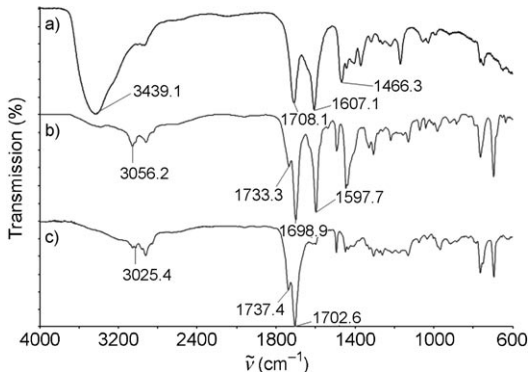


Figure 1. FTIR spectra of a) the crude residue, b) the residue after treatment with pyridine (compound **6**), and c) the crude product after oxidative hydrolysis (compound **3a**).

but strong bands at 3439, 1708, 1607, and 1466 cm^{-1}, absent in the IR spectrum of **3a**, which indicates the presence of hydroxy and extra double bond functionalities. The amount of iron consumed was in agreement with a total abstraction of the halide as $FeBr_2$, which precludes an iron enolate as the final reaction product. The product could not be a carboxylic acid nor an aldehyde nor a mixture of the two because there are no bands assignable to carbonyl functions in the IR spectrum of the crude products other than those of cyclopentenone.

All attempts to derivatize the crude product failed.[23] Because the ketone in the cycle in the final adduct was not enolized (strong band at 1708 cm^{-1}), we concluded that the hydroxy group present in the final mixture must have arisen from self-condensation of the acetone and addition of the resulting water to the final adduct. This was apparently the beneficial role of the Lewis acid (iodine[24] or $AlBr_3$). Our suspicion was confirmed when the addition of small amounts of water to the solvent had the same effect as the Lewis acid, that is, preventing the formation of side-products **4a** and **5a**. It was further found that the addition of small amounts of aliphatic alcohols, either to the solvent or the substrate mixture, had the same beneficial effect as water. However, the effect of the added alcohols was limited compared with the in situ generated water (ranging from 21% of the *tert*-butyl ester when using *t*-butanol to 37% of the methyl ester when using methanol).

Because all the observations indicated that iron was present in the final product as a complexed iron salt, we directed our efforts towards the separation of the metal salts under nonoxidative conditions to allow the characterization of the organic adduct by spectroscopic means. This was achieved by the addition 6 mol of pyridine, which led to the removal of all the iron as the corresponding tetracoordinated complex, which could be readily filtered. The residual iron-free crude oil could now be analyzed spectroscopically. The combination of MS, IR, and ^1H and ^{13}C NMR data evidenced the dimeric nature of the product obtained, $m/z = 410$ being the highest significative peak in the MS. In such a case, owing to the stereogenic center of the α-keto carbon in the cycle, duplicity of signals in the corresponding ^{13}C NMR spectrum was to be expected. However, the spectrum corresponded to a single isomer.

The absence of signals at around 175–180 ppm in the ^{13}C NMR spectrum (Figure 2, spectrum a) and beyond 1700 cm^{-1} in the corresponding IR spectrum (Figure 1, spectrum b) excluded the presence of any α-diketo product[25] or carboxylic functionality. The strong IR band at 1597 cm^{-1} (Figure 1, spectrum b) and the absence of the exocyclic methylene and carboxylate signals and the presence of α-diketo methine as a rudimentary signal in the ^{13}C NMR spectrum (Figure 2, spectrum a) together with a lack of resolution in the corresponding ^1H NMR spectrum only for the protons in the side-chain indicate rapid motion in the system.

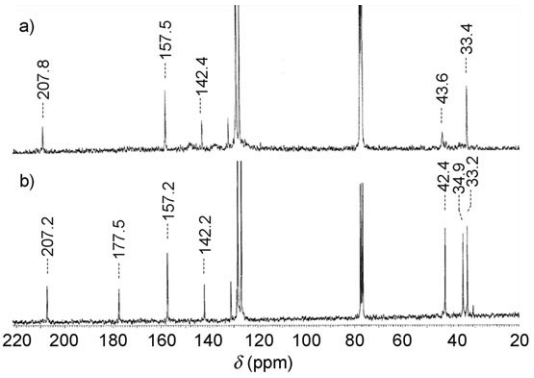
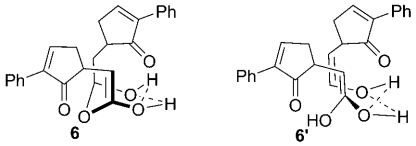


Figure 2. ^{13}C NMR spectra of a) the residue after treatment with pyridine (compound **6**) and b) compound **3a** after oxidative hydrolysis.

Because the crude product was able to undergo an aldolic reaction with paraldehyde[8] we tentatively propose structure **6** as the primary product.[26] This structure contains the originally dehalogenated adducts plus one water moiety in agree-



ment with the methodological requirement of a small amount of water for the reaction to proceed. Because the two enolized forms are degenerate in energy, they should rapidly tautomerize through the dienol form **6′**.[27]

But why do hydroxy groups appear in the IR spectrum of the iron-containing crude? Our explanation is based on the unique and fundamental role of iron. Like Ni^{II}, iron very readily forms hydroxy complexes. Its fundamental role in radical hydroxylation reactions of unsaturated organic substrates, such as the Fenton reaction, is widely recognized and applied. It is based on the easy single-electron oxidation of Fe^{II} to Fe^{III}. In the present case, despite the Mössbauer and EPR spectra of the crude indicating that most of the iron is in a Fe^{II} oxidation state, about 15% of it is present as Fe^{III} (Figure 3).

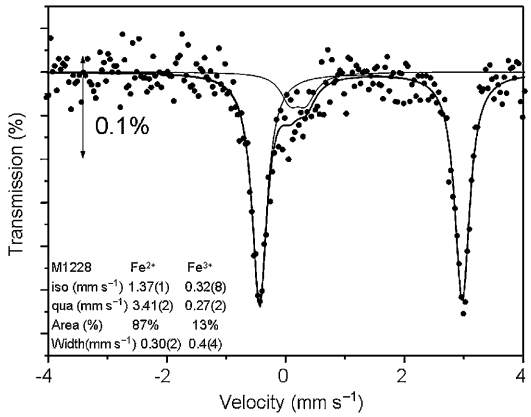
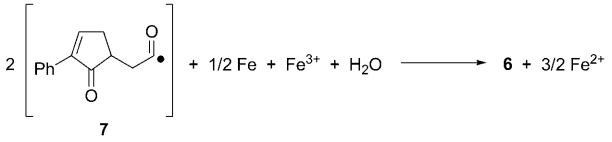


Figure 3. EPR spectrum of the reaction crude.

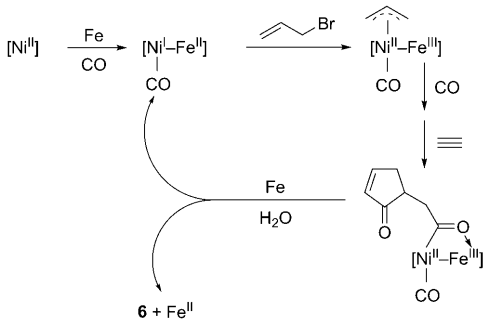
This was unexpected under the strict reductive conditions of the reaction. However, iron has been reported, under noncarbonylative conditions, to be capable of coupling allyl halides to give nonconjugated dienes.[28] Therefore allyl halides are efficient oxidants for iron. From a formal point of view, product **6** can be regarded as the enolized ester of its own reduced (aldehyde) and oxidized counterpart (the carboxylic acid **3a**) arising from single-electron oxidation and reduction of common radical intermediate **7** (Scheme 6).



Scheme 6. Generation of product **6**.

If water is scarce, a portion of the acyl radical might be oxidized by the ferric ion to the corresponding cation to give the Friedel–Crafts-type products **4a** and **5a**.[29]

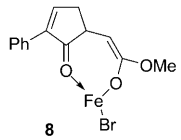
It is plausible that some or all of the electron-transfer reactions can occur on a polynuclear iron–nickel species with the metal centers in different oxidation states.[30] Thus, in the light of our last results, we propose the mechanistic scheme in Scheme 7 as the most plausible with only the iron atom



Scheme 7. Proposed mechanism for the carbonylative cycloaddition reaction.

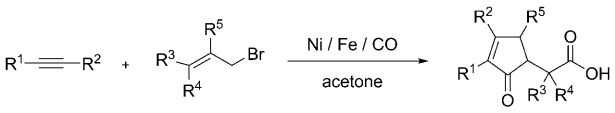
adjacent to the active nickel depicted although an undefined number of them may be integrated into the reacting species.

Unlike the reaction with nonfunctionalized allyl halides, when using methyl 4-bromocrotonate as reagent, all the theoretical iron was consumed (iron/substrate, 1:1) and the reaction, although with an inferior yield, could be performed in THF in the complete absence of water. In this case, the formation of the halo-enolate **8** in complex form as the final reaction product is plausibly assumed.



Study of the reaction scope: Having ascertained the catalytic nature of the reaction and taken into account the good efficiency of the synthetic process, we then directed our efforts towards extending its scope to more sophisticated substrates, occasionally with the presence of different functionalities and/or heteroatoms, either in the acetylenic or allylic component, to encourage the synthetic chemist to apply the reaction to the synthesis of more elaborate targets. We present here the extension of the catalytic reaction to acetylenes with ether, amino, alkene, and alkyne (conjugated and nonconjugated) functionalities and to substituted linear and cyclic allyl halides (Scheme 8).

For this study, we chose 10 different acetylenes (both internal and terminal, including a good variety of functional groups in the structure) and also seven allyl derivatives (mono-, di-, and trisusbtituted and cyclic). The results of



Scheme 8. General scheme for the carbonylative cycloaddition reaction between acetylenes (5 mmol) and allyl halides (5.8 mmol) catalyzed by $NiBr_2$ (0.25 mmol).

these reactions, performed under standard conditions, are shown in Table 2.

The reactions of alkynes **1a** and **1b** have already been reported to give good yields in the presence of an added Lewis acid.[8] The substitution of the Lewis acid by a small amount of water improved the yields (entries 1 and 2). As a general trend, we observe that the reactions under these new conditions take place in good yields with most of the acetylenes.

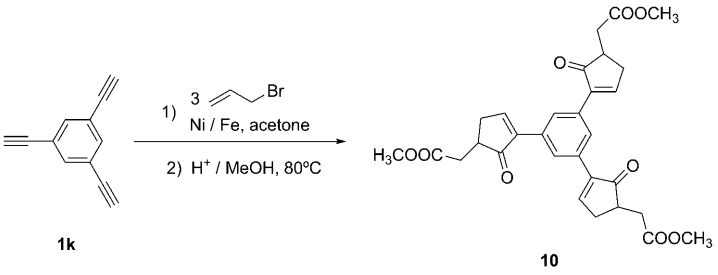
The presence of an alcohol or ether linkage in the alkyne also provided the expected cycloadduct in good yields (entries 3–5). It is surprising that the use of alkyne **1c** led to the exclusive formation of ester **3c** in view of the low yields of ester obtained when noncoordinating alcohols replace the added water, as seen above. The ability of triple bonds to coordinate the active species may account for this result and others reported below.[31] Although oxygen functionalities are completely compatible with this reaction, amines are not (entries 9 and 10). The complete inhibition of the reaction brought about by amines has already been observed in the stoichiometric version of the reaction and also when amines were used as proton scavengers to turn the reaction into a catalytic process. The acetylenic amine was recovered unchanged in these cases. Competition with the alkyne for an active coordination site may explain this result.

Unlike the results obtained in the stoichiometric reaction with conjugated allylic systems,[3b] the enyne **1f** reacted with allyl bromide to give the cycloadduct **3f** in good yield (entry 6). The extraordinary affinity of triple bonds for the activated allyl ligand is evidenced in entries 7 and 8 in which diacetylenes, either conjugated or not, gave excellent yields of dicycloadducts (using 2 equiv of the allyl derivative). These new results, together with those previously reported, led us to the conclusion that only very severe steric hindrance on the alkyne substituents can preclude the reaction taking place in a satisfactory way. In contrast, the reaction is very sensitive to the steric restrictions imposed by the substituents on the allyl system. Although monosubstitution of the allyl functionality still provides a good yield of the cycloadduct (entries 11 and 12), *gem* disubstitution slows down the reaction considerably thereby allowing a further insertion of the alkyne into the unfinished cycloadduct "tail" in a pseudo-Friedel–Crafts coupling reaction (entry 13). Although 1,3-disubstituted 3-bromocyclohexene displays conformational steric constraints leading to results similar to those obtained with *gem*-disubstituted homologues, the more flexible seven- and eight-membered cyclic allyl systems afford the corresponding oxocyclopenteneacetic adducts in high yields (entries 14–16). Particularly remarkable is the complete and opposite stereoselectivity in the resulting ring fusions. All these results parallel those found in the stoichiometric version of the reaction, for which we have given a plausible explanation.[3c]

Because, in a few very slow reactions, we isolated the carbonylative cycloadduct from the reaction of the allyl bromide with itself, we performed the reaction in the absence of acetylene and a good yield of the cycloadduct **9** was obtained (Table 2, entry 17). Although activated olefins like norbornene or norbonadiene are also suitable substrates for the reaction,[9] this is the first case of the reaction of a plain olefin. Presumably, the 1,5-hexadiene is generated independently from the allyl bromide with an excess of iron[32] and subsequently treated with the nickel–allyl active species to give the final compound **9** with high stereoselectivity (only one of the two possible stereoisomers is isolated after the final work-up). Unfortunately, similar reactions did not take place under the standard conditions with more hindered allyl halides and when we performed the cross-reactions with different allyl derivatives only undefined mixtures were obtained. This result again indicates the importance of steric hindrance in the allylic moiety.

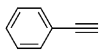
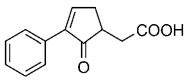
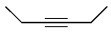
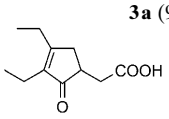
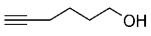
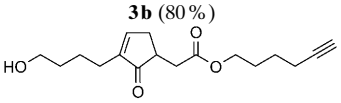
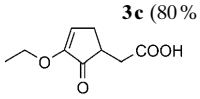
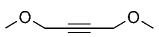
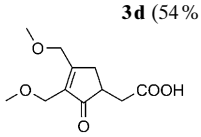
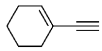
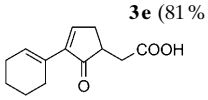
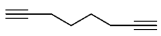
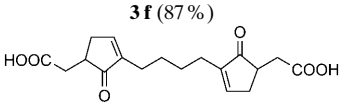
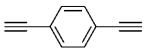
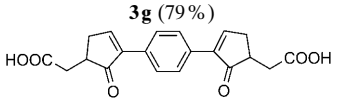
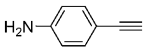
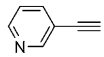
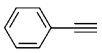
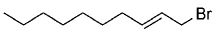
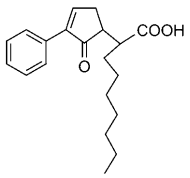
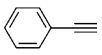
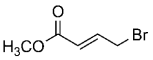
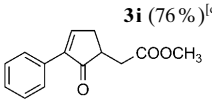
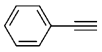
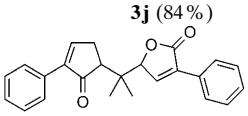
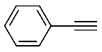
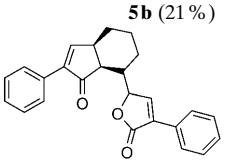
Again, to account for this result we feel obliged to propose the polynuclear model. Because, most probably, the formation of a coordinated 1,5-hexadiene requires two metal centers[32] in close proximity, and because iron does not perform any cyclocarbonylation under these conditions, the collaborative presence of three metal centers turns out to be very plausible. Such a mediator would impose severe steric restrictions on the substrates and products and this would be reflected in the strong stereoselectivity of the reaction. Almost with no exception, only one single diastereoisomer was obtained in each case.

Finally, as an example of the feasibility of the present reaction, we report the reaction of 1,3,5-trialkynylbenzene **1k** in which 12 bonds were formed at once in good yield (Scheme 9), again with a single isomer being observed. However, in this case the tri-acid obtained after the usual work-up was insoluble in the solvents used in the oxidative treatment. After esterification of the crude product in acidic media, the corresponding final product **10** was isolated in a yield of 51%.



Scheme 9. Triple carbonylative cycloaddition between 1,3,5-trialkynylbenzene (5 mmol) and allyl bromide (17.4 mmol) using $NiBr_2$ (0.25 mmol).

Table 2. Products and yields of the carbonylative cycloaddition reactions between different functionalized acetylenes and allyl halides under standard conditions.[a]

	Acetylene	Allyl	Product (Yield [%])
1			
	1a	**2a**	**3a** (95%)
2			
	1b	**2a**	**3b** (80%)
3			
	1c	**2a**	**3c** (80%)[b]
4			
	1d	**2a**	**3d** (54%)[c]
5			
	1e	**2a**	**3e** (81%)
6			
	1f	**2a**	**3f** (87%)
7			
	1g	**2a**	**3g** (79%)
8			
	1h	**2a**	**3h** (55%)
9			
	1i	**2a**	–
10			
	1j	**2a**	–
11			
	1a	**2b**	**3i** (76%)[d]
12			
	1a	**2c**	**3j** (84%)
13			
	1a	**2d**	**5b** (21%)
14			
	1a	**2e**	**5c** (40%)

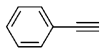
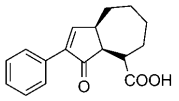
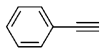
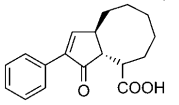
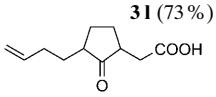
Product **10** displays high reaction versatility: Conjugate additions to activated double bonds, allylic substitutions, ketone condensations, reduction of the carbonyl and carboxy moieties, and, by using a monosubstituted allyl halide, it should be possible to be used in dendrimer chemistry as a multifunctional "core".[33]

Conclusion

Efforts to make the previous stoichiometric metal-mediated carbonylative cycloaddition of allyl halides and alkynes catalytic in nickel, based on experimental mechanistic observations, have been reported herein. Although the active catalytic species was an in situ generated Ni^{I} complex, the unexpected involvement of iron and water generated from the solvent (acetone) in the final release of the organic cycloadduct has been rationalized. Thus, iron acts in all cases as a dehalogenating agent whereas water is required only with nonfunctionalized allyl halides to give an adduct that is stable under the experimental conditions.

The catalytic version of the carbonylative cycloaddition of alkynes and allyl halides using a controlled amount of water instead of a Lewis acid shows a wide tolerance towards functional and steric substitution on the alkyne. Steric factors, however, are much more important in the allylic component, thwarting the termination step and leading to adducts with alkyne polyinsertion. The eagerness of the allyl–nickel intermediate for triple bonds is so great that multicentered reactions with high yields are possible with polyacetylenes.

Table 2. (Continued)

	Acetylene	Allyl	Product (Yield [%])
15			
	1a	**2f**	**3k** (61%)
16			
	1a	**2g**	**3l** (73%)
17			
	–	**2a**	**9** (81%)[d]

[a] Standard conditions: 0.25 mmol $NiBr_2$, 1.5 mmol NaI, 5 mmol Fe, 5 mmol acetylene, 5 mmol allyl halide, and 5 mmol H_2O in acetone as solvent at room temperature under a CO atmosphere (1.0 bar pressure). [b] Two-fold alkyne was used. [c] Estimated from the reaction crude. [d] Only one stereoisomer was detected.

Experimental Section

^{1}H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$ on a Bruker ARX 300 (300 and 75.5 MHz) spectrometer, on a Bruker AC 250, and on a Bruker AC 500. Chemical shifts are given in ppm relative to TMS (^{1}H $\delta = 0.0$ ppm) or $CDCl_3$ (^{13}C $\delta = 77.0$ ppm). IR spectra were recorded on a Perkin Elmer Spectrum One FTIR spectrometer, using CH_2Cl_2 as the solvent. Mass spectra were obtained on an AutoSpec-Q mass spectrometer. Elemental analyses were performed using a Carlo Erba 1106 apparatus. Standard Schlenck techniques were used. Acetone was distilled under Ar just before use. THF was freshly distilled from sodium benzophenone under argon. Iron powder (10μm diameter (reduced by hydrogen)), was provided by Merck-Darmstadt (product no.: 1.03819.0100). Unless otherwise stated, all common reagents and solvents were used as obtained from commercial suppliers without further purification.

General procedure: $NiBr_2$ (55 mg, 0.25 mmol), NaI (225 mg, 1.5 mmol), and iron powder (300 mg) were introduced into a 50 mL three-necked flask, provided with an efficient magnetic stirring bar. The three necks were connected to a gas burette with vaseline oil, a source of CO gas, and a rubber septum (through a stopcock). The internal atmosphere was also filled with CO, the internal pressure set equal to atmospheric pressure. The chosen solvent (usually acetone, 2.0 mL) was introduced into the reaction flask by means of a syringe and the stirrer was set to its maximum speed in such a way that the iron powder keeps turning around, released from the magnetic bar by centrifugal forces. The initial deep-red solution turned pale red or grey.

After 30 min the CO uptake had reached up to 10–12 mL and a solution of the corresponding allyl halide (5.8 mmol) and the corresponding acetylene (5.0 mmol) was added dropwise by means of a syringe pump and a polypropylene cannula through the septum and the stopcock hole over 3 h (if water or an alcohol was used as an additive, the required amount of the additive was added to the reagents together with acetone (1.0 mL) to homogenize the solution). After the addition of a few drops to the flask, the suspension turned turbid red and some gas evolution was observed. Soon after, the uptake of CO restarted. After 1 h, the reaction mixture had become a deep red-brown solution and the uptake increased dramatically, up to nearly 1 mL min^{-1}. At around 200 mL of CO, the rate decreased until a standstill at 220 mL when all the substrate had fully reacted.

After 4–5 h the reaction was over (no more CO uptake, approx. 220 mL of CO). The solvent was removed and the contents of the flask were transferred to a separation funnel, washing the flask (with the remaining iron) with dichloromethane. The reaction mixture darkened deeply on contact with air. The solution was treated with portions of 5 N HCl solution until no further discoloration was observed. After washing the organic phase with water until neutralization, the organic layer was treated with a solution of $Na_2S_2O_3$ (to remove any I_2 produced by oxidation), washed again with water, and dried on $MgSO_4$. After removal of the solvent and flash chromatography (CH_2Cl_2/CH_3OH) the products were obtained.

Compound characterization

3a: ^{1}H NMR (300 MHz, $CDCl_3$): $\delta =$ 2.47 (ddd, J(H,H) = 19, 3, 3 Hz, 1H; CH_2), 2.58 (dd, J(H,H) = 17, 9 Hz, 1H; CH_2), 2.85–2.95 (m, 1H; CH), 2.97 (dd, J(H,H) = 17, 3 Hz, 1H; CH_2), 3.02 (ddd, J(H,H) = 19, 6, 3 Hz, 1H; CH_2), 7.30–7.45 (m, 3H; Ph), 7.65–7.75 (m, 2H; Ph), 7.80 ppm (dd, J(H,H) = 3, 3 Hz, 1H; CH); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 33.2$ (t), 34.9 (t), 42.4 (d), 127.0 (d), 128.5 (d), 128.6 (d), 131.4 (s), 142.2 (s), 157.2 (d), 177.5 (s), 207.2 ppm (s); IR (CH_2Cl_2): $\tilde{\nu} =$ 3600–3000 (O–H), 1737 (C=O), 1703 cm^{-1} (C=O); HRMS (EI): m/z: calcd for $[M]^+$: 216.0783; found: 216.0785.

3b: ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 0.98$ (t, J(H,H) = 8 Hz, 3H; CH_3), 1.14 (t, J(H,H) = 8 Hz, 3H; CH_3), 2.10–2.55 (m, 6H; CH_2), 2.70–2.80 (m, 1H; CH), 2.82–2.92 ppm (m, 2H; CH_2); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta =$ 11.9 (q), 13.2 (q), 16.2 (t), 23.9 (t), 35.3 (t), 35.7 (t), 42.9 (d), 140.1 (s), 174.3 (s), 176.9 (s), 209.9 ppm (s); IR (CH_2Cl_2): $\nu\tilde{}$ = 3600–3000 (O–H), 1727 (C=O), 1705 cm^{-1} (C=O); MS (EI): m/z (%): 195.9 (11) $[M+1]^+$, 194.9 (100) $[M]^+$, 151.0 (4).

3c: ^{1}H NMR (300 MHz, $CDCl_3$): $\delta =$ 1.30–2.00 (m, 10H; CH_2), 2.19 (br s, 2H; CH_2), 2.20–2.50 (m, 3H; CH, CH_2), 2.60–2.70 (m, 1H; CH), 2.74 (dd, J(H,H) = 16, 3 Hz, 1H; CH_2), 2.88 (ddd, J(H,H) = 22, 6, 3 Hz, 1H; CH_2), 3.64 (br s, 2H; CH_2), 4.06 (br s, 2H; CH_2), 7.28 ppm (m, 1H; CH); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 23.8$ (t), 23.9 (t), 24.1 (t), 28.3 (t), 29.6 (t), 32.2 (t), 33.6 (t), 35.2 (t), 41.7 (d), 62.5 (t), 64.4 (t), 68.1 (s), 84.0 (d), 145.3 (s), 156.0 (d), 172.0 (s), 209.5 ppm (s); MS (EI): m/z (%): 293.2 (18) $[M+1]^+$, 292.2 (100) $[M]^+$.

3d: From the reaction crude: ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 1.36$ (t, J-(H,H) = 9 Hz, 3H; CH_3), 2.20–2.60 (m, 2H; CH_2), 2.60–3.00 (m, 3H; CH, CH_2), 3.91 (q, J(H,H) = 9 Hz, 2H; CH_2), 6.32 ppm (dd, J(H,H) = 3, 3 Hz, 1H; CH); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 14.2$ (q), 34.7 (t), 36.4 (t), 41.5 (d), 65.4 (t), 126.3 (d), 155.6 (s), 174.3 (s), 202.8 ppm (s).

3e: ^{1}H NMR (300 MHz, $CDCl_3$): $\delta =$ 2.43 (dd, J(H,H) = 22, 3 Hz, 1H; CH_2), 2.47 (dd, J(H,H) = 19, 10 Hz, 1H; CH_2), 2.74 (dddd, J(H,H) = 10, 7, 5, 3 Hz, 1H; CH), 2.88 (dd, J(H,H) = 19, 5 Hz, 1H; CH_2), 3.01 (dd, J-(H,H) = 22, 7 Hz, 1H; CH_2), 3.31 (s, 3H; CH_3), 3.39 (s, 3H; CH_3), 4.11 (s, 2H; CH_2), 4.43 ppm (s, 2H; CH_2); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta =$ 34.2 (t), 34.4 (t), 40.8 (d), 58.2 (q), 58.7 (q), 63.0 (t), 69.7 (t), 135.4 (s), 173.3 (s), 175.8 (s), 208.1 ppm (s); IR (CH_2Cl_2): $\nu\tilde{}$ = 3600–3000 (O–H), 1730 (C=O), 1705 cm^{-1} (C=O); HRMS (EI): m/z: calcd for $[M]^+$: 228.0993; found: 228.0988.

3f: ^{1}H NMR (300 MHz, $CDCl_3$): $\delta =$ 1.50–1.80 (m, 4H; CH_2), 2.10–2.15 (m, 4H; CH_2), 2.35 (ddd, J(H,H) = 22, 4, 4 Hz, 1H; CH_2), 2.48 (dd, J-(H,H) = 20, 9 Hz, 1H; CH_2), 2.75–2.90 (m, 1H; CH), 2.93 (dd, J(H,H) = 20, 5 Hz, 1H; CH_2), 2.99 (ddd, J(H,H) = 22, 6, 4 Hz, 1H; CH_2), 6.92 (t, J-(H,H) = 4 Hz, 1H; CH), 7.35 ppm (dd, J(H,H) = 4, 4 Hz, 1H; CH); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta =$ 21.7 (t), 22.3 (t), 25.3 (t), 26.2 (t), 32.5 (t), 34.9 (t), 42.6 (d), 128.0 (s), 128.8 (d), 141.9 (s), 153.3 (d), 176.8 (s), 208.1 ppm (s); IR (CH_2Cl_2): $\nu\tilde{}$ = 3600–3000 (O–H), 1730 (C=O), 1703 cm^{-1} (C=O); HRMS (EI): m/z: calcd for $[M]^+$: 220.1095; found: 220.1089.

3g: ^{1}H NMR (300 MHz, $CDCl_3$): $\delta =$ 1.30–1.60 (m, 4H; CH_2), 2.00–2.30 (m, 4H; CH_2), 2.35 (ddd, J(H,H) = 19, 3, 3 Hz, 2H; CH_2), 2.55 (dd, J-(H,H) = 16, 8 Hz, 2H; CH_2), 2.60–2.70 (m, 2H; CH), 2.81 (dd, J(H,H) = 16, 3 Hz, 2H; CH_2), 2.89 (ddd, J(H,H) = 19, 6, 3 Hz, 2H; CH_2), 7.29 ppm

(dd, J(H,H) = 3, 3 Hz, 2H; CH); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 24.6 (t), 27.2 (t), 33.5 (t), 34.9 (t), 41.4 (d), 145.1 (s), 156.8 (d), 176.7 (s), 210.0 ppm (s); IR (CH_2Cl_2): $\nu\tilde{}$ = 3600–3000 (O−H), 1731 (C=O), 1707 cm^{-1} (C=O); HRMS (EI): m/z: calcd for $[M]^+$: 334.1410; found: 334.1403.

3h: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.49 (ddd, J(H,H) = 20, 3, 3 Hz, 2H; CH_2), 2.57 (dd, J(H,H) = 15, 8 Hz, 2H; CH_2), 2.80–2.95 (m, 2H; CH), 2.97 (dd, J(H,H) = 15, 3 Hz, 2H; CH_2), 3.04 (ddd, J(H,H) = 20, 6, 3 Hz, 2H; CH_2), 7.74 (s, 4H; Ph), 7.80 ppm (dd, J(H,H) = 3, 3 Hz, 2H; CH); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 33.3 (t), 34.9 (t), 42.6 (d), 127.0 (d), 132.2 (s), 142.0 (t), 157.3 (d), 176.3 (s), 207.3 ppm (s); IR (CH_2Cl_2): $\nu\tilde{}$ = 3600–3000 (O−H), 1735 (C=O), 1705 cm^{-1} (C=O); HRMS (EI): m/z: calcd for $[M]^+$: 354.1098; found: 354.1107.

3i: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.87 (t, J(H,H) = 7 Hz, 3H; CH_3), 1.15–1.45 (m, 10H; CH_2), 1.65–1.75 (m, 2H; CH_2), 2.66 (ddd, J(H,H) = 19, 2, 2 Hz, 1H; CH_2), 2.87 (ddd, J(H,H) = 19, 6, 2 Hz, 1H; CH_2), 2.95–3.05 (m, 2H; CH), 7.30–7.45 (m, 3H; Ph), 7.65–7.75 (m, 2H; Ph), 7.84 ppm (dd, J(H,H) = 2, 2 Hz, 1H; CH); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.8 (q), 22.4 (t), 27.5 (t), 27.6 (t), 28.8 (t), 29.2 (t), 29.6 (t), 31.5 (t), 45.1 (d), 47.8 (d), 126.7 (d), 128.2 (d), 128.3 (d), 131.1 (s), 142.8 (t), 157.6 (d), 180.8 (s), 206.6 ppm (s); IR (CH_2Cl_2): $\nu\tilde{}$ = 3600–3000 (O−H), 1724 (C=O), 1707 cm^{-1} (C=O); HRMS (EI): m/z: calcd for $[M]^+$: 314.1875; found: 314.1874.

3j: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.48 (ddd, J(H,H) = 19, 3, 3 Hz, 1H; CH_2), 2.56 (dd, J(H,H) = 18, 10 Hz, 1H; CH_2), 2.85–3.00 (m, 1H; CH), 2.96 (dd, J(H,H) = 18, 4 Hz, 1H; CH_2), 3.05 (ddd, J(H,H) = 19, 7, 3 Hz, 1H; CH_2), 3.72 (s, 3H; CH_3), 7.30–7.45 (m, 3H; Ph), 7.65–7.75 (m, 2H; Ph), 7.82 ppm (dd, J(H,H) = 3, 3 Hz, 1H; CH); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 33.1 (t), 34.8 (t), 42.6 (d), 51.7 (q), 126.8 (d), 128.0 (d), 128.2 (d), 131.2 (s), 142.2 (s), 157.1 (d), 172.3 (s), 207.2 ppm (s); IR (CH_2Cl_2): $\nu\tilde{}$ = 1726 (C=O), 1704 cm^{-1} (C=O).

3k: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.1–2.3 (m, 8H; CH_2), 2.40 (dd, J(H,H) = 6, 3 Hz, 1H; CH), 3.08 (m, 1H; CH), 3.38 (ddd, J = 10, 8, 3 Hz, 1H; CH), 7.25–7.50 (m, 3H; Ph), 7.50–7.70 (m, 2H; Ph), 7.74 ppm (d, J(H,H) = 3 Hz, 1H; CH); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 24.8 (t), 30.4 (t), 31.6 (t), 33.3 (t), 41.4 (d), 42.1 (d), 55.6 (d), 127.1 (d), 128.4 (d), 128.5 (d), 132.1 (s), 141.7 (s), 159.9 (d), 180.1 (s), 207.3 ppm (s); IR (CH_2Cl_2): $\nu\tilde{}$ = 3600–3000 (O−H), 1739 (C=O), 1704 cm^{-1} (C=O); HRMS (EI): m/z: calcd for $[M]^+$: 270.1251; found: 270.1255.

3l: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.9–2.3 (m, 10H; CH_2), 2.42 (dd, J(H,H) = 7, 3 Hz, 1H; CH), 3.10 (m, 1H; CH), 3.46 (ddd, J = 12, 9, 3 Hz, 1H; CH), 7.25–7.50 (m, 3H; Ph), 7.50–7.70 (m, 2H; Ph), 7.77 ppm (d, J(H,H) = 3 Hz, 1H; CH); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 24.9 (t), 25.4 (t), 26.3 (t), 26.4 (t), 34.4 (t), 41.6 (d), 43.8 (d), 53.3 (d), 126.9 (d), 128.1 (d), 128.6 (d), 131.9 (s), 140.6 (d), 161.8 (s), 179.5 (s), 207.8 ppm (s); IR (CH_2Cl_2): $\nu\tilde{}$ = 3600–3000 (O−H), 1739 (C=O), 1705 cm^{-1} (C=O); MS (EI): m/z (%): 285.1 (18) $[M+1]^+$, 284.1 (100) $[M]^+$.

4a: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.41 (ddd, J(H,H) = 17, 3, 3 Hz, 1H; CH_2), 2.84 (dd, J(H,H) = 17, 10 Hz, 1H; CH_2), 3.00–3.10 (m, 1H; CH), 3.12 (ddd, J(H,H) = 17, 6, 3 Hz, 1H; CH_2), 3.41 (dd, J(H,H) = 17, 2 Hz, 1H; CH_2), 6.77 (d, J(H,H) = 11 Hz, 1H; CH), 7.30–7.45 (m, 6H; Ph), 7.50–7.80 (m, 4H; Ph), 7.60 (d, J(H,H) = 11 Hz, 1H; CH), 7.83 ppm (dd, J(H,H) = 3, 3 Hz, 1H; CH); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 33.8 (t), 41.9 (t), 42.4 (d), 125.7 (d), 126.9 (d), 128.2 (d), 128.3 (d), 128.9 (d), 130.5 (d), 131.7 (s), 134.2 (s), 142.2 (s), 143.1 (d), 157.5 (d), 197.9 (s), 208.2 ppm (s).

5a (mixture of isomers): Major isomer: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.67 (ddd, J(H,H) = 14, 8, 7 Hz, 1H; CH_2), 2.53 (ddd, J(H,H) = 14, 3, 3 Hz, 1H; CH_2), 2.57 (ddd, J(H,H) = 16, 3, 3 Hz, 1H; CH_2), 2.75–2.90 (m, 1H; CH), 3.08 (ddd, J(H,H) = 16, 7, 3 Hz, 1H; CH_2), 5.41 (ddd, J(H,H) = 7, 3, 2 Hz, 1H; CH), 7.30–8.00 ppm (m, 12H; Ph, CH); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 34.3 (t), 35.6 (t), 44.0 (d), 80.0 (d), 127.0 (d), 128.5 (d), 128.7 (d), 129.4 (d), 131.4 (s), 131.6 (s), 142.3 (s), 147.8 (d), 157.8 (d), 171.5 (s), 208.1 ppm (s). IR (CH_2Cl_2): $\nu\tilde{}$ = 3059 (C=C), 1755 (C=O), 1699 (C=O); minor isomer: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.10 (ddd, J(H,H) = 17, 6, 3 Hz, 1H; CH_2), 2.37 (ddd, J(H,H) = 17, 6, 3 Hz, 1H; CH_2), 2.60–2.80 (m, 1H; CH), 2.62 (ddd, J(H,H) = 15, 3, 3 Hz, 1H; CH_2), 2.99 (ddd, J(H,H) = 15, 5, 3 Hz, 1H; CH_2), 5.29 (ddd, J(H,H) = 4, 3, 2 Hz, 1H; CH), 7.25–8.00 ppm (m, 12H; Ph, CH); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 33.7 (t), 34.5 (t), 42.8 (d), 78.8 (d), 127.0 (d), 128.5 (d), 128.6 (d), 128.7 (d), 129.5 (d), 131.4 (s), 132.2 (s), 142.5 (s), 147.5 (d), 157.7 (d), 171.4 (s), 208.0 ppm (s); IR (CH_2Cl_2): $\nu\tilde{}$ = 3059 (C=C), 1755 (C=O), 1699 (C=O).

5b (mixture of isomers): ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.97 (s, 3H; CH_3), 1.04 (s, 3H; CH_3), 1.10 (s, 3H; CH_3), 1.18 (s, 3H; CH_3), 2.50–3.10 (m, 3H; CH_2), 5.52 (s, 1H; CH), 6.03 (s, 1H; CH), 7.00–8.10 ppm (m, 12H; Ph, CH); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 19.5 (q), 20.2 (q), 20.3 (q), 20.4 (q), 29.8 (t), 40.4 (s), 40.6 (s), 51.2 (d), 52.8 (d), 84.5 (d), 85.6 (d), 127.0 (d), 128.6 (d), 129.3 (d), 131.1 (s), 133.0 (s), 143.7 (s), 146.2 (d), 146.3 (d), 157.1 (d), 157.7 (d), 171.7 (s) 171.8 (s), 207.3 (s), 207.5 ppm (s); IR (CH_2Cl_2): $\nu\tilde{}$ = 1756 (C=O), 1694 cm^{-1} (C=O); HRMS (EI): m/z: calcd for $[M]^+$: 358.1569; found: 358.1565.

5c (mixture of isomers): Major isomer: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.25–2.40 (m, 7H; CH, CH_2), 2.95 (t, J(H,H) = 6 Hz, 1H; CH), 3.09 (brs, 1H; CH), 5.75 (d, J(H,H) = 9 Hz, 1H; CH_2), 7.30–7.90 (m, 10H; Ph), 7.97 ppm (s, 1H; CH); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.2 (t), 25.5 (t), 28.3 (t), 38.9 (d), 43.0 (d), 48.7 (d), 83.0 (d), 126.9 (d), 127.0 (d), 128.5 (d), 128.7 (d), 131.3 (s), 131.5 (s), 141.7 (s), 148.0 (d), 161.9 (d), 171.7 (s), 207.8 ppm (s); IR (CH_2Cl_2): $\nu\tilde{}$ = 1755 (C=O), 1698 cm^{-1} (C=O); HRMS (EI): m/z: calcd for $[M]^+$: 370.1569; found: 370.1595. Minor isomer: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.25–2.10 (m, 7H; CH, CH_2), 3.17 (brs, 2H; CH), 6.04 (d, J(H,H) = 8 Hz, 1H; CH_2), 7.30–7.95 (m, 10H; Ph), 7.72 ppm (s, 1H; CH); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 18.6 (t), 22.5 (t), 27.0 (t), 38.8 (d), 40.9 (d), 47.5 (d), 81.3 (d), 126.9 (d), 127.0 (d), 128.5 (d), 128.7 (d), 131.3 (s), 131.5 (s), 142.4 (s), 148.1 (d), 160.1 (d), 171.6 (s), 207.9 ppm (s); IR (CH_2Cl_2): $\nu\tilde{}$ = 1755 (C=O), 1698 (C=O); HRMS (EI): m/z: calcd for $[M]^+$: 370.1569; found: 370.1595.

6: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.53 (ddd, J(H,H) = 19, 3, 3 Hz, 1H; CH_2), 2.55–2.75 (m, 1H; CH_2), 2.90–3.00 (m, 1H; CH), 2.95–3.05 (m, 1H; CH_2), 3.06 (ddd, J(H,H) = 19, 6, 3 Hz, 1H; CH_2), 7.30–7.45 (m, 3H; Ph), 7.65–7.75 (m, 2H; Ph), 7.82 ppm (dd, J(H,H) = 3, 3 Hz, 1H; CH); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 33.5 (t), 43.6 (d), 127.0 (d), 128.4 (d), 128.5 (d), 131.6 (s), 142.5 (s), 157.5 (d), 207.9 ppm (s); IR (CH_2Cl_2): $\nu\tilde{}$ = 3600–3000 (O−H), 3056 (C=C), 1733 (C=O), 1699 cm^{-1} (C=O); MS (EI): m/z (%): 410.08 (100) $[M]^+$.

9: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.30–1.60 (m, 2H; CH_2), 1.80–1.90 (m, 1H; CH_2), 1.90–2.00 (m, 1H; CH_2), 2.00–2.35 (m, 5H; CH, CH_2), 2.35–2.50 (m, 1H; CH), 2.49 (dd, J(H,H) = 15, 7 Hz, 1H; CH_2), 2.81 (dd, J(H,H) = 15, 2 Hz, 1H; CH_2), 4.98 (d, J(H,H) = 10 Hz, 1H; CH_2), 5.03 (d, J(H,H) = 17 Hz, 1H; CH_2), 5.78 ppm (ddt, J(H,H) = 17, 10, 7 Hz, 1H; CH); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 27.4 (t), 27.6 (t), 29.3 (t), 31.4 (t), 34.0 (t), 45.6 (d), 48.1 (d), 115.2 (t), 137.9 (d), 178.1 (s), 220.0 ppm (s); IR (CH_2Cl_2): $\nu\tilde{}$ = 3600–3000 (O−H), 1732 (C=O), 1714 cm^{-1} (C=O); HRMS (EI): m/z: calcd for $[M]^+$: 196.1095; found: 196.1098.

10: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.45 (ddd, J(H,H) = 19, 3, 3 Hz, 3H; CH_2), 2.56 (dd, J(H,H) = 18, 10 Hz, 3H; CH_2), 2.80–2.95 (m, 3H; CH), 2.94 (dd, J(H,H) = 18, 4 Hz, 3H; CH_2), 3.02 (ddd, J(H,H) = 19, 7, 3 Hz, 3H; CH_2), 3.68 (s, 9H; CH_3), 7.89 (dd, J(H,H) = 3, 3 Hz, 3H; CH), 8.04 ppm (s, 3H; Ph); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 33.0 (t), 34.7 (t), 42.5 (d), 51.6 (q), 125.3 (d), 131.6 (s), 141.6 (s), 157.9 (d), 172.1 (s), 207.0 ppm (s); IR (CH_2Cl_2): $\nu\tilde{}$ = 1725 (C=O), 1705 cm^{-1} (C=O); HRMS (EI): m/z: calcd for $[M]^+$: 534.1881; found: 534.1878.[32]

Acknowledgements

The authors acknowledge Dr. Anna Roig for the Mössbauer spectra and Mrs. Maria Huerta-Fontela for the MS spectra. Also we acknowledge financial support from the Spanish Dirección General de Investigación (DGI) (EMOCIONA project CTQ2006-06333/BQV) and the Consejo Interdepartamental de Investigación e Innovación Tecnológica (CIRIT) (D. del Moral, grant no.: 2007FIC00554).

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Received: November 30, 2009
Revised: April 23, 2010
Published online: June 23, 2010

