www.elsevier.nl/locate/jorganchem

Journal of Organometallic Chemistry 621 (2001) 284–298

Meta, *para* and *meta*, *ortho* double *exo* nucleophilic additions of trimethylsilylester enolates derived from saturated and unsaturated carboxylic acids to tricarbonylchromium complexes of aryl ethers: dearomatizing cyclization to lactones

Henri Rudler [a,*], Virginie Comte [a], Eva Garrier [a,c], Moncef Bellassoued [c], Evelyne Chelain [c], Jacqueline Vaissermann [b]

[a] *Laboratoire de Synthèse Organique et Organométallique, Université Pierre et Marie Curie, 4 place Jussieu, UMR 7611, T 44-45, 75252 Paris, Cedex 5, France*

[b] *Laboratoire de Chimie Inorganique et Matériaux Moléculaires, Université Pierre et Marie Curie, 4 place Jussieu, ESA 7071, 75252 Paris, Cedex 5, France*

[c] *Laboratoire de Synthèse Organométallique associé au CNRS, Université de Cergy-Pontoise, 5 Mail Gay Lussac, Neuville-sur-Oise, 95031 Cergy-Pontoise, Cedex, France*

Received 2 August 2000; accepted 14 September 2000

Abstract

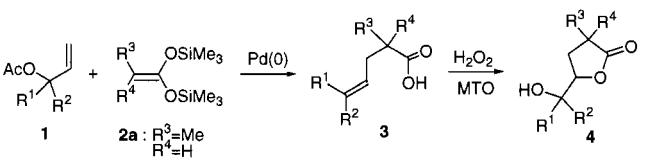
Potassium enolates derived from saturated and unsaturated bis(trimethylsilyl) ketene acetals react with tricarbonylchromium complexes of anisole and diphenylether to give, in addition to α-arylcarboxylic acids, the mono adducts, lactones, arising from a double *exo* nucleophilic addition. The latter were not observed in the case of benzenetricarbonylchromium. The intermediate dienol ethers could be isolated and fully characterized by X-ray crystallography. The influence of the nature of the substituents on the ketene acetals, of the nature of the oxidant, and of the nature of the ester enolates on the course of the reaction has been established and will be discussed.

Keywords: Potassium enolates; Tricarbonylchromium complexes; Aryl ethers; Dearomatization; Dienol

1. Introduction

Cyclofunctionalization reactions are very important for the construction of elaborate molecules [1,2]. Among them, one can cite the formation of lactones by the successive introduction of the RCH_2COOH group on an organic fragment containing a carbon–carbon double bond, followed by a cyclization reaction.

Recently, we described two approaches to lactones involving such reactions [3–5]. First, a two-step catalytic process, involving the interaction of π-allyl complexes of palladium obtained from the allylic acetates **1** with bis(trimethylsilyl) ketene acetals **2** [6], which gave **3** via the formation of a carbon–carbon single bond between an unsaturated fragment and a R^3R^4CH–COOH group. This was followed by a catalytic oxidation–cyclization with H_2O_2/MTO leading to the formation of a carbon–oxygen bond and generating δ-hydroxy-γ-lactones **4** (Eq. (1)).



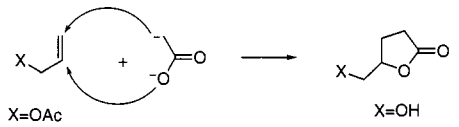
(1)

Overall, and assuming that the first step occurs via an S_N2' reaction, this can be considered as a double nucleophilic addition of a dianion originating from a carboxylic acid to a carbon–carbon double bond (Eq. (2)).

* Corresponding author. Tel.: +331-44-276197; fax: +331-44-277089.

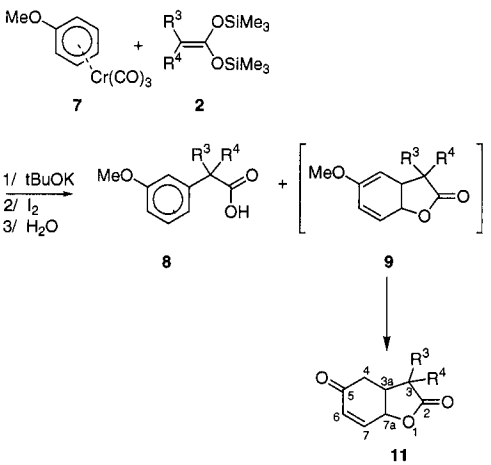
E-mail address: rudler@ccr.jussieu.fr (H. Rudler).

0022-328X/01/$ - see front matter
PII: S0022-328X(00)00848-2



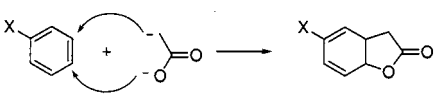
(2)

A one pot, two-step stoichiometric sequence involving arenetricarbonylchromium complexes **7** and enolates of trimethylsilyl esters obtained from **2** and *t*-BuOK also results in lactones. In this case, the first step involved is a well documented, nucleophilic addition of enolates to arenetricarbonylchromium [7–10] and is useful in the synthesis of elaborate organic molecules. In the second step, iodine was used as an oxidizing agent for the demetallation of the organic substrates. Whereas in the case of complexes of non-functionalized aromatic derivatives the expected α-arylcarboxylic acids **6** were obtained in high yield, surprisingly for the anisole complex, the formation of tetrahydrobenzofuran-2,5-diones **11** was observed via a dearomatization reaction, double nucleophilic addition on an aromatic carbon–carbon double bond and subsequent hydrolysis (Eq. (3)).



(3)

Similarly, this methodology can be considered as a double nucleophilic addition of a carboxylic acid dianion, in this case, to a carbon–carbon double bond of an aromatic system with the formation of vicinal carbon–carbon and carbon–oxygen bonds (Eq. (4)).



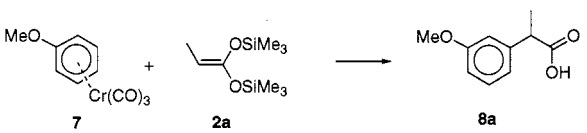
(4)

The purpose of this paper is first to demonstrate that the formation of these lactones takes place via dienol ethers which could be isolated and fully characterized in the case of both anisole and diphenylether [11]. Secondly, to determine the structural features and the conditions which drive the reaction towards the formation of these lactones (structure of the enolates and nature of their substituents, nature of the oxidizing agents) and finally, to examine the behaviour of ketene acetals bearing an extra carbon–carbon double bond towards tricarbonylchromium complexes of benzene, anisole, and diphenylether.

2. Results and discussion

2.1. Isolation and characterization of dienol ethers. The case of anisole

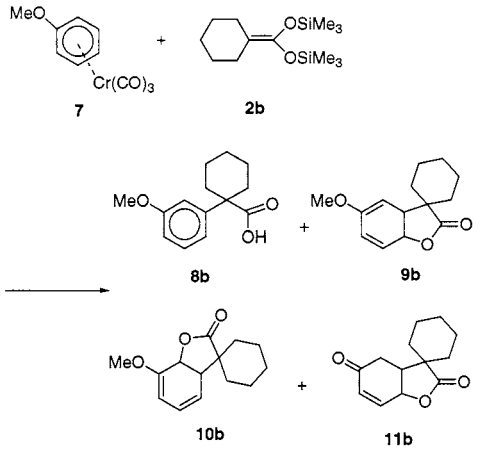
According to preliminary experiments [3,4], it was concluded that success in the formation of lactones was intimately linked to the nature of the substituents on the starting ketene acetals **2**; satisfactory yields of lactones were observed from the acetal derived from cyclohexanecarboxylic acid. Indeed, reduction of the size of the substituents progressively suppressed the formation of the lactones. This was demonstrated and confirmed by the reaction of ketene acetal **2a** bearing only a methyl group with complex **7** which led to a single product, the expected α-arylcarboxylic acid **8a** in 48% yield (Eq. (5)).



(5)

In the case of the formation of the lactones, to confirm that indeed a double addition on the *meta*, *para* positions of this complex took place, we attempted to isolate the dienol ethers **9**, the surmized precursors of the lactones, and proceeded as follows. A THF solution of anisoletricarbonylchromium (**7**) was treated with 1.5 equivalents of bis(trimethylsilyl) ketene acetal (**2b**), derived from cyclohexanecarboxylic acid in the presence of a slight excess of *t*-BuOK (THF solution, 1.1 equivalents/**2b**), and DMF, at −70°C, then at −30°C for 3 h. Addition of an excess of iodine in THF (5 equivalents/**7**) to the cloudy brownish solution, at −70°C, followed by warming to room temperature and stirring overnight gave, after treatment with sodium dithionite to remove the excess of iodine and extraction with diethyl ether, an oil which was chromatographed on silica gel. Elution with P.E.–diethyl ether (98:2) led to a white solid which was recrystallized in hexane–dichloromethane to give the dienol ether **9b** (36%, m.p. 75°C) which could be fully characterized by its ^{1}H- and ^{13}C-NMR data. The ^{1}H-NMR spectrum disclosed signals for the three olefinic protons at δ 5.97(dd), 5.91(dd), 4.50(m), and for the two protons at the ring junction at δ 5.06 and 3.21, together with a signal for the methoxy group at δ 3.55. From the mother liquor, the second minor dienol ether **10b** could be isolated as an oil ($< 1\%$). Its ^{1}H-NMR spectrum confirmed again the presence of three olefinic protons at δ 5.91 (ddd),

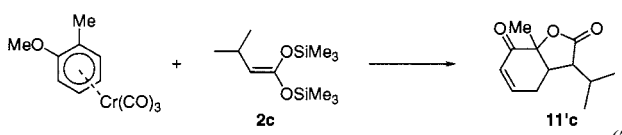
5.30 (dd) and 5.11(d) ppm, of the two protons at the ring junction at δ 4.85 and 3.25 ppm, and the singlet for the methoxy group at δ 3.59. Elution with P.E.–diethyl ether (90/10) gave the acid **8b** (5%) and finally with P.E.–diethyl ether (20/80), the lactone **11b** (8%) (Eq. (6)).



(6)

Two observations have to be made at this point:

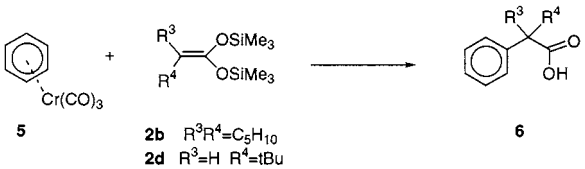
- When the extraction was carried out as above and the ethereal layer washed with dilute HCl, then only the tetrahydrobenzofuran-2,5-dione **11b** was isolated in 51% yield together with 5% of the arylcarboxylic acid **8b**. The NMR data of these compounds were fully consistent with their structures.
- Such behaviour was also observed in the case of the *t*-Bu-substituted ketene acetal **2d**. In the case of the *ortho* methylanisole complex, only the lactone **11′c** arising from the *meta*, *ortho* di-addition of the enolate derived from **2c** was isolated, in low yield, the corresponding dienol ether being unstable under the conditions used for the work up procedure (Eq. (7)).



(7)

2.2. Interaction of benzenetricarbonylchromium complex with enolates derived from crowded ketene acetals ($R_3 = H$, $R_4 = t$-Bu, $R_3R_4 = C_5H_{10}$): exclusive high yield formation of α-arylcarboxylic acids in high yield

We earlier observed that tricarbonylchromium complexes derived from benzene led only to α-arylcarboxylic acids. We have now confirmed that even with the most crowded ketene acetals, no products originating from a double nucleophilic addition were formed. Thus, the ketene acetals **2b** and **2d** derived from cyclohexanecarboxylic and *t*-butylacetic acid gave the expected acids **6b** and **6d** (Eq. (8)).

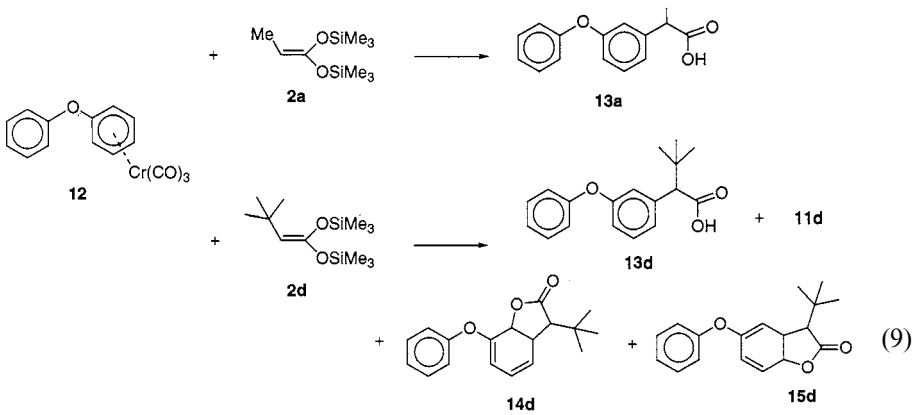


(8)

According to this result, a first prerequisite for the formation of lactones appeared thus to be the presence of an ether linkage in the starting complex.

2.3. Reaction of diphenylether complex with ketene acetals

As already described, the behaviour of the complex of diphenylether **12** paralleled that of the complex of benzene, since even with moderately crowded enolates, only arylcarboxylic acids of the type **13** were obtained. Thus, complex **12** led to **13a**, the well-known non-steroidal anti-inflammatory drug fenoprofen in 79% yield. Similar results were obtained from this complex and a series of other ketene acetals (Eq. (9)).



(9)

However, a careful examination of the reaction mixture obtained upon interaction of this complex with the ketene acetal **2c** ($R^3 = H$, $R^4 = i$-Pr) allowed us to detect small amounts of the lactone **11c** ($< 5\%$). Thus it appeared clearly that even for this arylether, a double nucleophilic addition could take place, albeit to a very low extent, to give upon cleavage of the ether linkage a conjugated ketone.

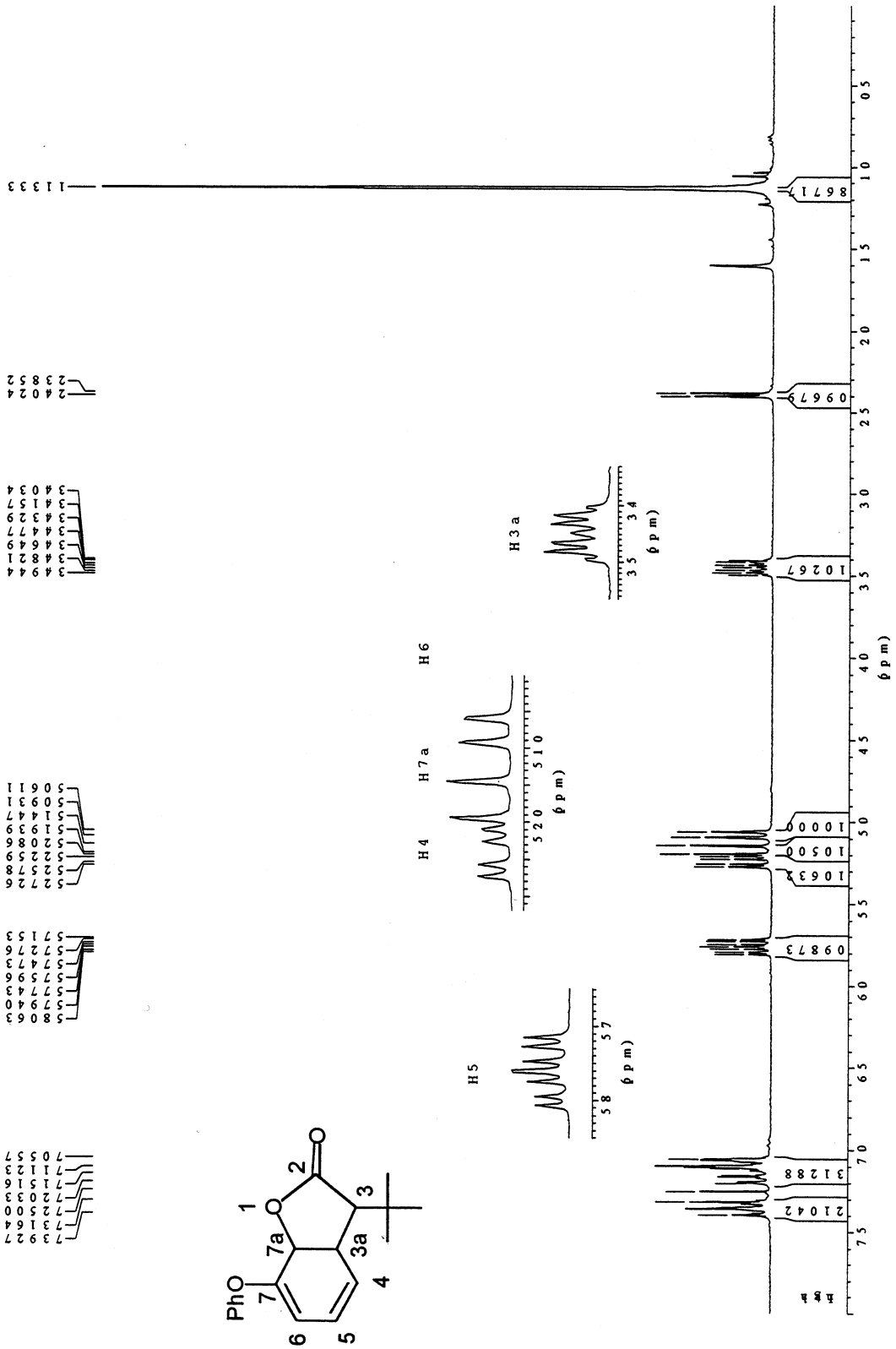


Fig. 1. ^{1}H-NMR spectrum of **14d** ($CDCl_3$, 400 MHz).

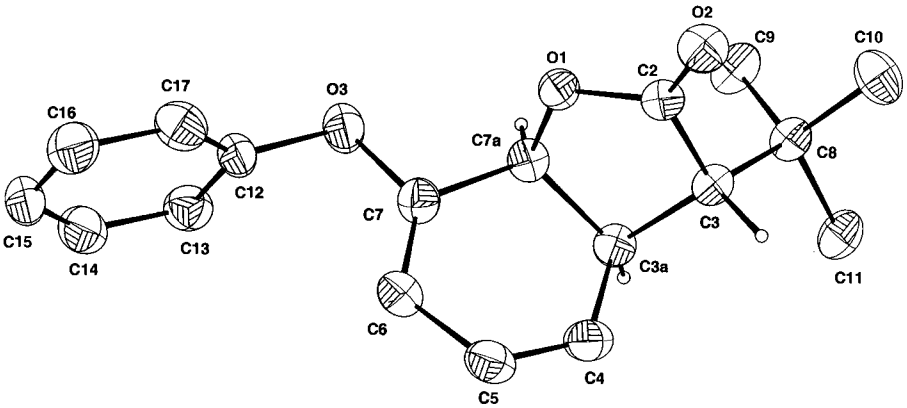


Fig. 2. X-ray structure of **14d**.

This interesting observation prompted us to examine the behaviour of complex **12** towards the more crowded ketene acetals **2d** and **2b**. The interaction of **2d** with complex **12** under the same conditions used for the complex of anisole led surprisingly to four compound after oxidative cleavage, two of moderate polarity, and two of higher polarity.

The two less polar compounds formed, respectively, in 43 and 17% yield could be partially separated by silica gel chromatography. The elemental analysis as well as the NMR data of the less polar products were in agreement with the structures **14d** and **15d**. Extensive ^{1}H- and ^{13}C-NMR spectroscopic techniques allowed the assignment of all the signals. Thus, for the major product **14d**, the ^{1}H-NMR spectrum (Fig. 1) disclosed signals at δ 7.28–7.00 for the five aromatic protons, at δ 5.69 (ddd), 5.18 (dd) and 5.01 (d) for the three protons of the diene, at δ 5.10 (d) and 3.38 (dddd) for the two protons at the ring junction and at δ 2.32 for the proton on the carbon bearing the *t*-butyl group.

Crystals of this compound suitable for an X-ray analysis could be grown from hexane–dichloromethane. The molecular structure shown in Fig. 2, confirmed the NMR data and thus the double *meta*, *ortho* addition of the enolate with formation of a γ-lactone and a dienol ether. The X-ray data can be found in Table 1.

The slightly more polar compound was assigned as **15d** according to its NMR data. The ^{1}H-NMR spectrum disclosed signals, in addition to those for the aromatic protons, at δ 5.95 (dd), 5.83 (dd), and 4.74 (m) for the three protons of the diene, at δ 5.13 (ddd) and 3.23 (ddd) for the protons at the ring junction (Fig. 3).

This product thus originates from a *meta*, *para* double nucleophilic addition to the aromatic ring. The third product, isolated in 17% yield as white crystals, corresponds to the expected α-arylcarboxylic acid **13d** resulting from a single nucleophilic addition of the enolate of *t*-Butyl acetic acid on the chromium complex. Finally, the most polar compound, obtained as a white solid in 11% yield, could be identified by its physical data to the previously isolated lactone **11d** and results from the hydrolysis of the dienol ether **15d.**

Table 1
X-ray data for **14d** ($C_{17}H_{16}O_3$)

Formula weight	268.3
Crystal system	Monoclinic
Space group	$P2_1/n$
Unit cell dimensions	
a (Å)	5.409(3)
b (Å)	42.493(13)
c (Å)	6.643(4)
α (°)	90
β (°)	107.91(4)
γ (°)	90
V (Å^3)	1450(1)
Z	4
Linear absorption coefficient μ (cm^{-1})	0.78
Density ρ (g cm^{-3})	1.23
Diffractometer	CAD4 Enraf–Nonius
Radiation	Mo–K$_\alpha$ ($\lambda = 0.71069$ Å)
Scan type	$\omega/2\theta$
Scan range (°)	$0.8 + 0.345$ tgθ
θ Limits (°)	1–28
Temperature of measurement	295 K
Octants collected	0, 7; 0, 55; −8, 8
Number of data collected	3907
Number of unique data collected	3488 ($R_{int} = 0.03$)
Number of unique data used for refinement	1648 $(F_o)^2 > 3\sigma(F_o)^2$
$R = \Sigma\|\|F_o\| - \|F_c\|\|/\Sigma\|F_o\|$	0.0544
$Rw^* = [\Sigma w(\|F_o\| - \|F_c\|)^2/\Sigma wF_o^2]^{1/2}$ [a]	0.0674
S	1.00
Extinction parameter	142
Number of variables	183
$\Delta\rho$ min (e Å^{-3})	−0.16
$\Delta\rho$ max (e Å^{-3})	0.18

[a] $*w = w'[1 - ((\|\|F_o\| - \|F_c\|\|)/6\sigma(F_o))^2]^2$ with $w' = 1/\Sigma_r A_r T_r(X)$ with 3 coefficients 8.48, 2.40 and 6.62 for a Chebyshev Series, for which X is F_c/F_c(max).

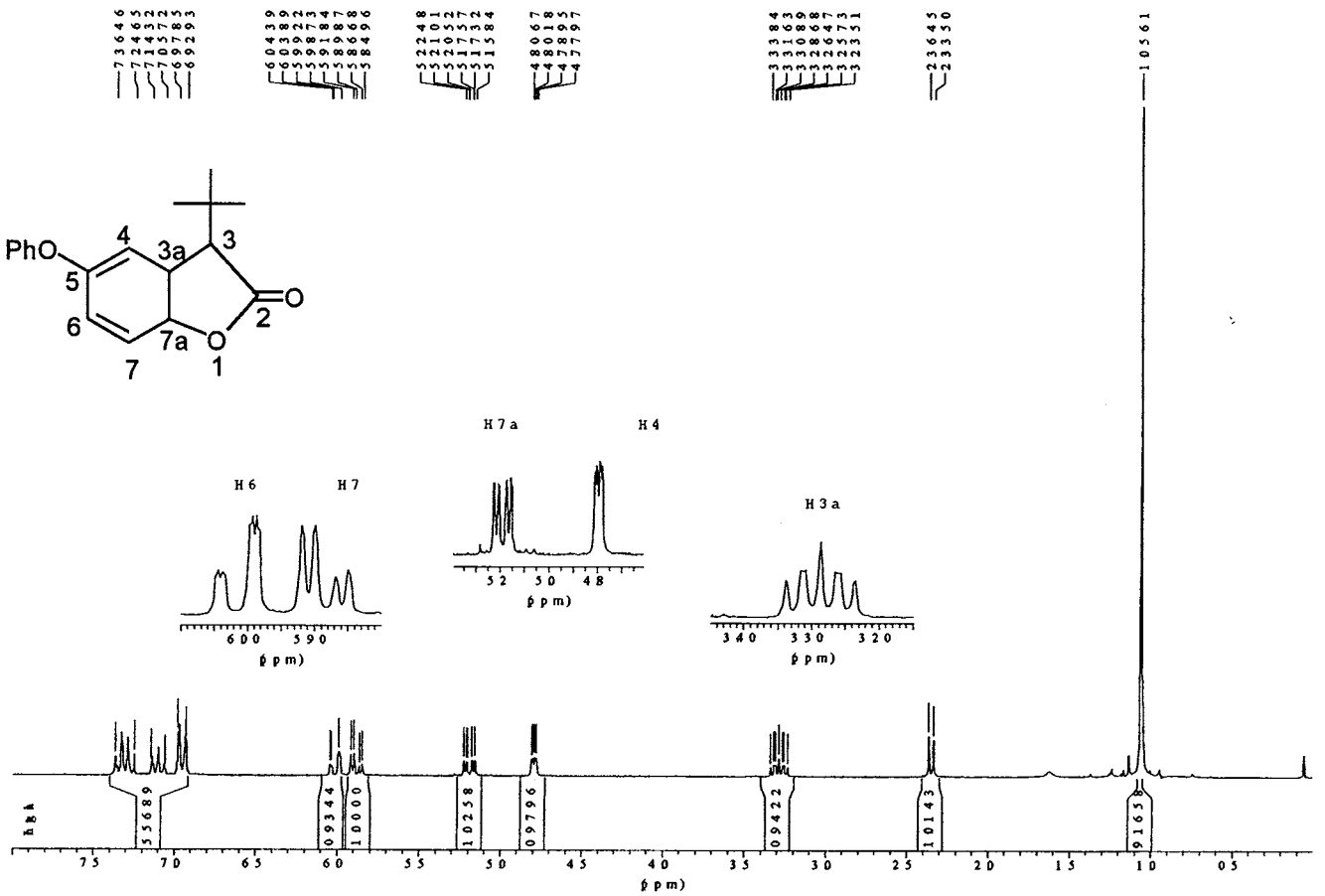


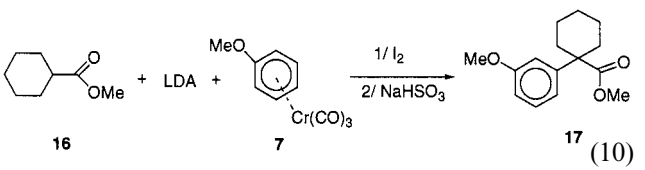
Fig. 3. ^{1}H-NMR spectrum of **15d** ($CDCl_3$, 400 MHz).

Surprisingly, in the reaction of acetal **2b** with complex **12**, the mono-addition product **13b** was the only product obtained in 58% yield.

2.4. Influence of the structure of the enolates on the course of the reaction: importance of the trimethylsilyl group for the formation of the lactones

The nucleophilic addition of enolates derived from carboxylic acid esters on arene tricarbonylchromium complexes leading to α-arylcarboxylic esters is a well established reaction [7–10]. No side products arising from a double nucleophilic addition have, to the best of our knowledge, been detected so far.

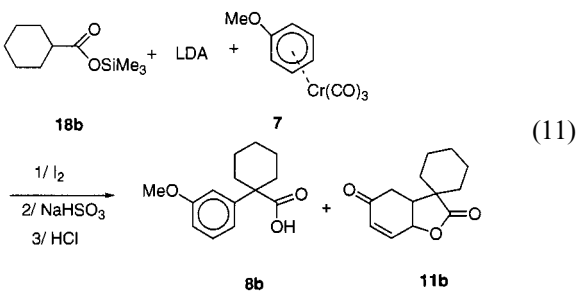
We confirmed this by carrying out a reaction involving the enolate of methylcyclohexanecarboxylate generated from the ester **16** and LDA, and complex **7**. Under the same conditions as above and as described in the literature, only the expected arylester **17** could be isolated after work up in 65% yield: no lactone even in trace amounts could be detected (Eq. (10)).



(10)

However, when the same reaction was carried out starting from the corresponding trimethylsilylester **18b** this led to two compounds, the expected carboxylic acid **8b** (5%) together with the lactone **11b** (30%).

Interestingly, the dianion of cyclohexanecarboxylic acid, which can be obtained from the corresponding acid and LDA did not react at all with the complex of anisole, even though the use of such dianions as enolate equivalents is well documented [12] (Eq. (11)).



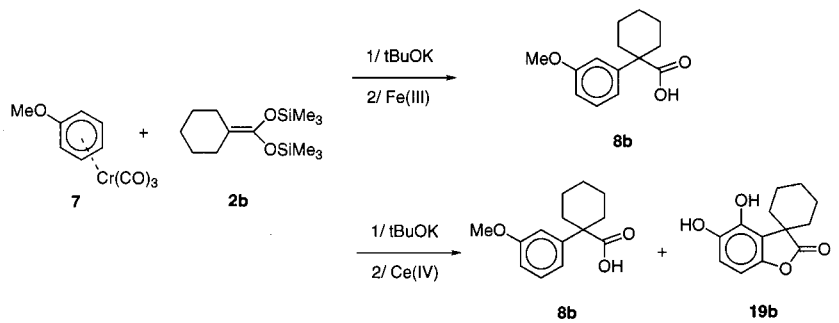
(11)

It appears, therefore, that the trimethylsilyl ester group was able to interact as a nucleophile with the aromatic ring during the oxidation step with formation of a carbon–oxygen bond while a common alkoxy ester was not, a result which confirms the beneficial influence of the TMS group.

2.5. Influence of the nature of the oxidant

According to the early work of Semmelhack [13], oxidants different from iodine could also be used to carry out the final demetallation step after the nucleophilic additions to arene tricarbonylchromium complexes. Among them, Fe(III) and Ce(IV) salts are reported to give the best results.

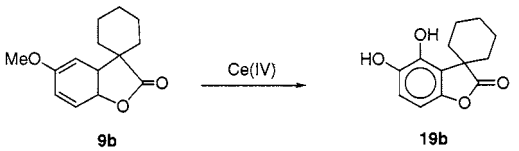
Since the second step of the reactions leading to lactones is the formation of a carbon–oxygen bond and is likely to be induced by the oxidation of the metal, we used, besides iodine, two other oxidants for the reaction between anisoletricarbonylchromium and the ketene acetal **2b**, $(Fe(DMF)_3Cl_2)(FeCl_3)$ and $Ce(NH_4)_2(NO_3)_6$ (CAN). Surprisingly, in the latter two cases, only trace amounts of the lactone **11b** were detected, the main product of the reaction is the arylcarboxylic acid **8b** (Eq. (12)).



(12)

In the case of CAN, small amounts (8%) of a second product having almost the same polarity as the lactone **11b** was isolated. This new product was fully characterized by its spectroscopic data.

From analysis of mass spectra and NMR data, this compound was determined to be **19b**, an α-*ortho*-diphenol containing a lactone. Both the ^{1}H- and ^{13}C-NMR spectra confirmed the presence of the γ-lactone but also the absence of an extra carbonyl group and of the methoxy group. Of significance were also the signals for two vicinal olefinic protons at δ 6.75 and 6.49 as two doublets and of a broad signal at δ 5.60 corresponding to two protons, which split into two broad signals in benzene. No other signals but those for the cyclohexyl group appeared in the spectrum. According to the mass spectrum, four oxygen atoms are present in the molecule: besides the two oxygen atoms of the lactone, two oxygen atoms belonging to two phenols are thus required. The presence of three quaternary carbons linked to oxygen is clearly indicated by three signals in the ^{13}C-NMR spectrum at δ 147.3, 142.2 and 139.6. Taken together, all these data agreed with the postulated structure **19b** (Eq. (13)).



(13)

That **19b** probably originated from the enol ether **9b**, and is thus an over-oxidized product confirmed by the following experiment: the oxidation of the dienol ether **9b** in the presence of CAN as above led to a 1:3 mixture of **19b** and the lactone **11b**.

The exact mechanism of this transformation, which combines an aromatization, a demethylation and a hydroxylation step, is still a matter of speculations although demethylation–oxidation reactions of methoxybenzenes by means of CAN are known [14].

2.6. Reaction of arene tricarbonyl chromium complexes with unsaturated ketene acetals: formation of unsaturated arylcarboxylic acids and also of a tetrahydrobenzofuran-1,5-dione containing an unsaturated side chain

Having established the limitations of the addition of enolates derived from various bis(trimethylsilyl) ketene acetals and having discovered an unprecedented double nucleophilic addition on a carbon–carbon double bond of aromatic ethers, we focused attention on the addition of enolates derived from unsaturated bis(trimethylsilyl) ketene acetals **20** which are easily synthesized from the corresponding unsaturated carboxylic acids[15], to a series of arenetricarbonylchromium complexes. It is indeed known that enolates originating from such ketene acetals behave like nucleophiles towards aldehydes and ketones to give unsaturated δ-

Table 2
Conjugated arylcarboxylic acids **21a–23d** from **20a–d**

Entry	Compound	R^1	R^2	R^3	R^4	X	Yield%
1	**21a**	H	H	H	H	H	41
2	**21b**	Me	H	H	H	H	59
3	**21c**	H	Me	H	H	H	14
4	**21d**	H	H	H	Me	H	43
5	**22b**	Me	H	H	H	OMe	41
6	**23a**	H	H	H	H	OPh	47
7	**23b**	Me	H	H	H	OPh	50
8	**23c**	H	Me	H	H	OPh	16
9	**23d**	H	H	H	Me	OPh	47

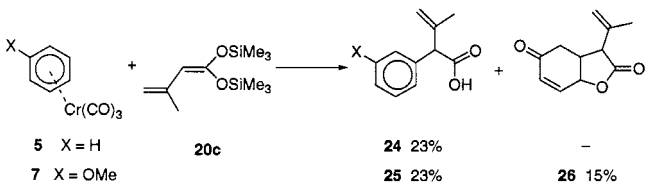
hydroxy acids (unpublished results from these laboratories). In turn, and in relation with the above results, their interaction with arenetricarbonylchromium complexes might thus lead to arylacrylic acids **21–23** which can be considered as precursors of important pesticides [16].

We first examined the feasibility of such a transformation by reacting a series of unsaturated ketene acetals **20** with benzenetricarbonylchromium **5**. Optimization of the reaction conditions was achieved on the substrate **20a** ($R^1 = R^2 = R^3 = H$). It appeared clearly that the best yields of acids were obtained by using a slight excess of acetal and by keeping the reaction mixture, before the oxidation step, at room temperature for 5 h. Interestingly, though the yields of addition products were low at −35°C, products due to a 1,2-addition reactions, giving branched unsaturated carboxylic acids, were detected (Eq. (14)).

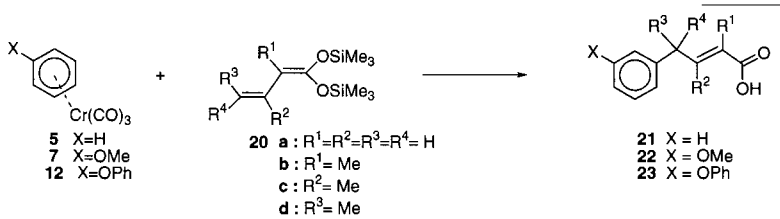
As shown in Table 2 (entries 1–4), the expected conjugated arylcarboxylic acids **21** were obtained in satisfactory yields in all the cases but for **21c** (entry 3).

Under similar conditions, the same trend was observed for the complex **12** derived from diphenylether. The molecular structure of **23c** was confirmed by an X-ray analysis. Fig. 4 shows the *meta* addition of the enolate originating from **22c**, via its γ-carbon (Table 3).

However, in neither case did we observe, under these conditions, products arising from a double nucleophilic addition which indeed could only be formed upon an α-enolate addition reaction. Finally we examined the behaviour of anisoletricarbonylchromium: again, a 41% of the expected acid **22b** was obtained from **20b**. Since small amounts of branched arylcarboxylic acids were only observed at low temperature, we repeated several reactions with the complexes derived from benzene and the arylethers under such conditions. Thus reaction of the acetal **20c** with complex **5** gave the vinyl arylcarboxylic acid **24**. Similarly, with complex **7**, besides the acid **25** (23%), a minor more polar product (15%) could be detected. Its NMR data were akin to those of the bicyclic compounds isolated so far and clearly indicating the presence of a lactone and a cyclohexenone (Eq. (15)).



(15)



(14)

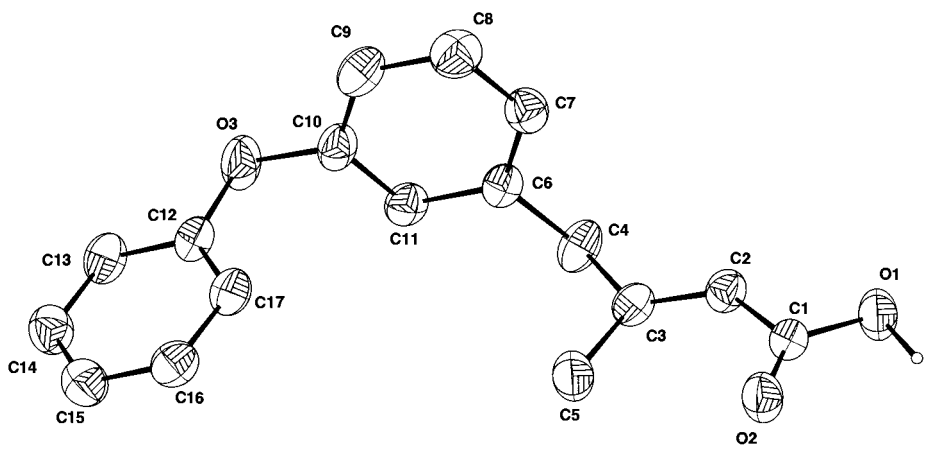


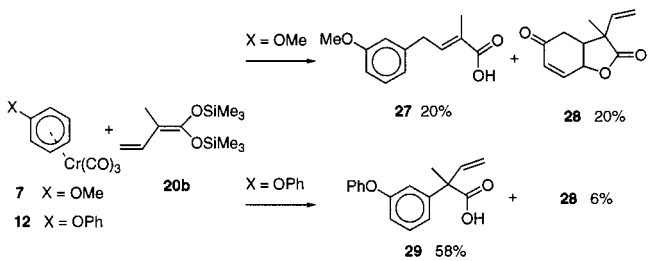
Fig. 4. X-ray structure of **23c**.

Table 3
X-ray data for **23c** ($C_{18}H_{20}O_3$)

Formula weight	284.35
Crystal system	Triclinic
Space group	$P\bar{1}$
Unit cell dimensions	
a (Å)	8.469(3)
b (Å)	10.491(2)
c (Å)	10.527(2)
α (°)	117.11(2)
β (°)	107.07(2)
γ (°)	96.42(2)
V (Å^3)	762.0(4)
Z	2
Linear absorption coefficient μ (cm^{-1})	0.78
Density ρ (g cm^{-3})	1.24
Diffractometer	CAD4 Enraf–Nonius
Radiation	Mo–K$_\alpha$ ($\lambda = 0.71069$ Å)
Scan type	$\omega/2\theta$
Scan range (°)	$0.8 + 0.345$ tgθ
θ Limits (°)	1–26
Temperature of measurement	295 K
Octants collected	0, 10; −12, 12; −12, 12
Number of data collected	3199
Number of unique data collected	2984
Number of unique data used for refinement	1628 $(F_o)^2 > 3\sigma(F_o)^2$
$R = ?\|\|F_o\| - \|F_c\|\|/?\|Fo\|$	0.0493
$R^*_w = [?w(\|F_o\| - \|F_c\|)^2/\Sigma wF_o^2]^{1/2}$ [a]	0.0597
S	1.13
Extinction parameter	none
Number of variables	192
$\Delta\rho$ min (e Å^{-3})	−0.17
$\Delta\rho$ max (e Å^{-3})	0.19

[a] $*w = w'[1 - ((\|\|F_o\| - \|F_c\|\|)/6\sigma(F_o))^2]^2$ with $w' = 1/\Sigma_r A_r T_r(X)$ with 3 coefficients 5.06, 0.622 and 3.43 for a Chebyshev Series, for which X is F_c/F_c(max).

Moreover, and as required for such a structure, two extra signals corresponding to two olefinic protons and to a methyl group (δ 5.22, 5.19 and 1.79, respectively) were present in the ^{1}H-NMR spectrum. Thus, all these data agreed with the structure of **26**, the product of the di-addition reaction. A similar behaviour was observed in the case of **7** and **12** with **20b**, the major products being in this case, respectively, the lactone **28** isolated in 21% yield and the acid **29** obtained in 58% yield.



(16)

3. Discussion

The initial goal of these investigations was to synthesize a wide variety of saturated and unsaturated arylcarboxylic acids in order to test their possible biological properties. This was achieved and additionally, we discovered unexpectedly a direct, new type of carbon–carbon double bond difunctionalization of aromatic systems, which appeared to be a double nucleophilic *exo* addition reaction. This broadened even more the scope of our approach since besides the α-arylcarboxylic acids, γ-lactones were formed, the biological properties of which are well-established [17].

To summarize, both reactions have a common feature which is not new: the interaction of a nucleophile with an arenetricarbonylchromium complex with the formation of a carbon–carbon bond.

The originality stems from two points:

- the use of bis(trimethylsilyl) ketene acetals to generate the enolates of TMS esters. This constitutes a very clean and efficient approach to these intermediates since it has been shown in these laboratories that they are formed in high yield upon the interaction of the acetals with *t*-BuOK in THF. Confirmation of this came from the results of the interaction of the enolates generated in this way with aldehydes and ketones which led almost quantitatively to α or γ-hydroxyacids [17].
- the arylcarboxylic acids are obtained directly in high to moderate yield, in a sequence which avoids the transformation of esters or nitriles into acids under severe conditions.

3.1. Mechanism of the formation of the tetrahydrobenzofuran-2,5-diones

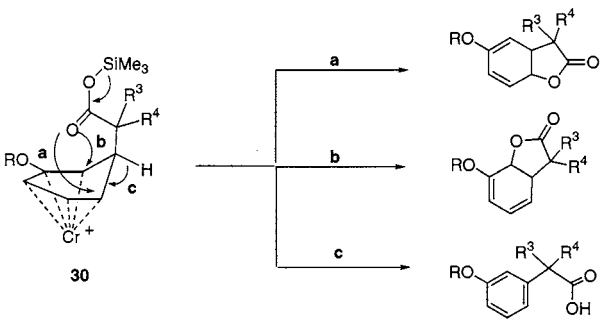
One of the benefits of these investigations is the unexpected formation of lactones by a two-step sequence that occurs in situ, thus intermediates need not to be isolated.

The first step of the reaction is common to both types of products: it leads to a new carbon–carbon bond. The second step, the formation of a carbon–oxygen bond, is specific to some ketene acetals and arenetricarbonylchromium complexes.

The first step involves the formation of cyclohexadienyl complexes of chromium upon addition of the enolate originating from the ketene acetal. Classically, such an intermediate can be oxidized by iodine to give, upon an aromatization reaction, the arylester. It can also be protonated by strong acids to give dienol ethers and, upon hydrolysis, cyclohexenones [11]. In the first sequence, the metal is oxidized and loss of a proton accounts for the rearomatization reaction [13], which probably occurs rapidly.

Of interest, in the second step is the structure and the reactivity of the intermediate oxidized chromium complex, which is likely to be a tricarbonylcyclohexadienylchromium(II) complex. Analogous complexes of iron are known, and according to the pioneering work of Pearson, they undergo nucleophilic addition reactions leading to diene complexes [18,19]. There exists, therefore, two ways for the oxidized intermediate to evolve:

- a rearomatization leading to an arylcarboxylic acid with loss of a proton according to *c*
- an intramolecular nucleophilic addition of the oxygen of the ester group according to *a* and *b* (Eq. (17)).



(17)

According to our results, path *a* and *b* do not exist for complexes derived from benzene. It is thus likely that the lifetime of the intermediate ionic species is too short in these cases to allow the second addition reaction to occur.

Consequently, since aromatic ethers evolve in both directions, the presence of the heteroatom slows down the rate of the aromatization reaction by stabilizing the ionic intermediate; competition between aromatization and a second intramolecular nucleophilic reaction can then take place.

The addition of the nucleophile, the oxygen atom of the ester group at either end of the cyclohexadienyl ligand might then lead to a five-membered ring lactone, a very favourable transformation.

Surprisingly, however, only trace amounts of lactone were observed for $R^3 = H$ and $R^4 = Me$. To increase the yield of lactone might be possible only by increasing the rate of the intramolecular cyclization with respect to the rate of the aromatization.

Evolutions of this type are well documented for related intramolecular cyclization reactions. Indeed, for the formation of five and six-membered ring systems, a beneficial effect is usually observed by the introduction of substituents giving rise to the gem dialkyl or Thorpe-Ingold effects [20], which has more recently been discussed by Bruice and Lightstone [21]. According to these authors, in such intramolecular reactions geminal substitution decreases the population of kinetically unprofitable conformers and increases the population of conformers which can undergo ring closure. Applied to the present cases, this means that the dialkylated ester and the carbon-termini of the cyclohexadienyl ligand must be in close proximity and hence increasing the probability of bond formation.

Obviously, this is the trend for the various enolates subjected to the nucleophilic addition to anisoletricarbonylchromium—increasing the number and the size of the substituents from methyl to spirocyclohexyl on the pendant carboxylate chain did indeed increase the yield of the lactones, a result which can be directly inferred to these kinetic effects.

A similar situation prevails in the case of the complex **12**. However, less clear-cut results are observed since small amounts of the expected lactone are observed from the acetal **2c** ($R^3 = i$-Pr, $R^4 = H$), and no lactone at all is formed when **2b** is used; the most significant observations occurred upon the interaction of **2d** with **12** which led mainly to cyclized products, the two dienol ethers **14d** and **15d** and the lactone **11d**. These results might be due to the interaction of the more crowded phenoxy group of **12** with the various substituents in the intermediate **30** (Eq. (16)), a situation which does not occur with the less sterically demanding methoxy group. Similar considerations might also explain the site-selective additions observed for the two arylethers—route *a* for anisole, while for diphenylether route *b* is predominant.

As far as the influence of the various oxidants is concerned, iodine as well as Fe(III) and Ce(IV) are suitable for the formation of arylcarboxylic acids. However, for the formation of the lactones not only their oxidizing power but also their Lewis acidity has to be taken into account. We observed indeed that iodine did not interact with the trimethylsilylesters. Such is not the case for Fe(III) and Ce(IV) which are powerful Lewis acids. Since they are used in excess during the demetallation reactions, they can interact directly with the nucleophilic centre of the ester group and thus prevent the formation of the lactones according to the second step of the reaction.

4. Conclusions

The results reported here confirm that lactones can be formed upon a double *exo* nucleophilic addition to arene complexes of potential dinucleophiles generated from bis(trimethylsilyl) ketene acetals and *t*-BuOK, together with α-arylcarboxylic acids, the mono-addition products. This reaction is not limited to anisole, but has been extended to diphenylether. Moreover, ketene acetals bearing a supplementary unsaturation can be subjected to the same type of transformations, leading, respectively to unsaturated arylcarboxylic acids and in

a few cases to lactones bearing various vinyl groups. Since we observe a highly specific formation of three contiguous chiral centres during the formation of the bicyclic lactones, we are focusing our efforts towards the asymmetric version of these reactions.

5. Experimental

5.1. General

All reactions were performed under a dry argon atmosphere. Solvents were distilled from sodium–benzophenone ketyl (diethyl ether, tetrahydrofurane), phosphorus pentoxide (CH_2Cl_2) and saturated with argon. Silica gel (Merck, type 60, 0.063–0.200 mm was used for column chromatography. ^{1}H-NMR: Bruker ARX-400 (400 MHz), DPX 250 (250 MHz), AC-200 (200 MHz). ^{13}C-NMR: Bruker ARX-400 (100 MHz), DPX-250 (60 MHz), AC-200 (50MHz). All NMR spectra were recorded in $CDCl_3$ unless stated otherwise with $CHCl_3$ as internal standard. MS and HRMS were recorded on a JEOL MS 700. Melting points were performed on a Reichert apparatus and are uncorrected. TLC: 0.25 mm Merck silica gel plates 60 F_{254}.

5.2. Preparation of **6**

A solution of benzene·$Cr(CO)_3$ **5** (1.07 g, 5 mmol) and ketene acetal **2** (10 mmol) in THF (10 ml) was treated at −70°C with a slight excess (1.1 equivalents) of a THF solution of *t*-BuOK (1 M) in the presence of DMF (6 ml). After 2 h at −35°C, the mixture is cooled to −70°C and a solution of I_2 (6.35 g, 5 equivalents) was slowly added. The solution was then progressively warmed to room temperature (r.t.) overnight. The mixture was treated with aqueous sodium dithionite solution, rapidly extracted by Et_2O and washed (brine, water). After drying over Na_2SO_4, the solvent was removed in vacuo to give **6** that was purified by chromatography with PE–Et_2O (90/10).

1-phenyl-cyclohexanecarboxylic acid **6b** (white solid, 45% yield, m.p. 113°C) [22]: ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.48–7.25 (m, 5H, Ph), 2.48 (m, 2H, cyclohexyl), 1.80–1.50 (m, 7H, cyclohexyl), 1.30 (m, 1H, cyclohexyl); ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 180.9 (C^2), 142.0 (*C* Ph), 128.6, 127.0 and 126.2 (*C*H Ph), 50.5 (C^1), 34.3, 25.6 and 23.6 (CH_2). HRMS Calc. for $C_{13}H_{17}O_2$ (MH^+) 205.1229. Found 205.1229.

3,3-dimethyl-2-phenyl-butyric acid **6d** (white solid, 75% yield) [23]: ^{1}H-NMR ($CDCl_3$, 250 MHz) δ 7.40–7.20 (m, 5H, Ph), 3.37 (s, 1H, H^2), 0.94 (s, 9H, CH_3); ^{13}C-NMR ($CDCl_3$, 60 MHz) δ 179.4 (C^1), 135.5 (*C* Ph), 129.8, 127.7 and 127.0 (*C*H Ph), 61.5 (C^2), 34.1 (C^3), 27.6 (3 CH_3).

5.3. Preparation of **8**, **9**, **10** and **11**

A solution of anisole·$Cr(CO)_3$ **7** (2 g, 7.8 mmol) and ketene acetal **2** (12.3 mmol) in THF (40 ml) was treated at −70°C with a slight excess (1.1 equivalents) of a THF solution of *t*-BuOK (1 M) in the presence of DMF (15 ml). After 3 h at −30°C, the mixture was cooled to −70°C and a solution of I_2 (8.3 g, 4 equivalents) was slowly added. The solution was then progressively warmed to r.t. overnight. The mixture was treated with an aqueous sodium dithionite solution, rapidly extracted with Et_2O and washed (water, brine). After drying over Na_2SO_4, the solvent was removed in vacuo to give **8a** or a mixture of four products, which were purified by silica gel chromatography. The arylcarboxylic acids **8** were eluted with PE–Et_2O (90/10), a mixture of **9** and **10** with PE–Et_2O (80/20) and tetrahydrobenzofuran-2,5-diones **11** with PE–Et_2O (40/60). Complexes **8** and **11**, except **8a**, were isolated as white crystals after recrystallization in a mixture of Et_2O–hexane for **8** and CH_2Cl_2–hexane for **11**.

The two compounds **9** and **10** were separated by preparative thin layer chromatography (hexane–AcOEt, 80/20) and recrystallized in a mixture of Et_2O–hexane.

2-(3-methoxy-phenyl)-propionic acid **8a** (yellow oil, 45% yield) [24]: ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.18 (t, $J_{HH} = 7.6$ Hz, 1H, H^8), 6.85 (d, $J_{HH} = 7.6$ Hz, 1H, H^7), 6.83 (s, 1H, H^5), 6.75 (dd, $J_{HH} = 7.6$ and 2.6 Hz, 1H, H^9), 3.72 (s, 3H, OCH_3), 3.66 (q, $J_{HH} = 7$ Hz, 1H, H^2), 1.44 (dd, $J_{HH} = 7$ Hz, 3H, CH_3); ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 181.5 (C^1, CO), 160.2 (C^6–OCH_3), 141.7 (C^4), 130.2 (C^8), 120.4 (C^7), 113.9 (C^5), 113.1 (C^9), 55.6 (OCH_3), 45.7 (C^2), 18.5 (CH_3). MS Calc. for $C_{10}H_{12}O_3$, 180 (M^+). Found 180.

1-(3-methoxy-phenyl)-cyclohexanecarboxylic acid **8b** (white crystals, 5% yield, m.p. 75°C): ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.27 (t, $J_{HH} = 7.9$ Hz, 1H, H^7), 7.03 (m, 2H, H^4 and H^6), 6.79 (dd, $J_{HH} = 7.9$ and 2.5 Hz, 1H, H^8), 3.80 (s, 3H, OCH_3), 1.80–1.22 (m, 10H, CH_2); ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 180.9 (C^1, CO), 159.7 (C^5–OCH_3), 144.7 (C^3), 129.5 (C^7), 118.6 (C^6), 112.7 (C^4), 111.9 (C^8), 55.2 (OCH_3), 50.5 (C^2), 34.4 (2C, CH_2), 25.5 (1C, CH_2), 23.6 (2C, CH_2). Anal. Calc. for $C_{14}H_{18}O_3$: C, 71.76; H, 7.75. Found: C, 71.62; H, 7.81%.

2-(3-methoxy-phenyl)-3,3-dimethyl-butyric acid **8d** (white crystals, 20% yield, m.p. 100°C): ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.24 (t, $J_{HH} = 8$ Hz, 1H, H^9), 7.0 (m, 2H, H^6 and H^8), 6.85 (dd, $J_{HH} = 8$ and 2 Hz, 1H, H^{10}), 3.82 (s, 3H, OCH_3), 1.05 (s, 9H, C(CH_3)$_3$); ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 179.0 (C^1, CO), 159.1 (C^7–OCH_3), 137.2 (C^5), 127.7 (C^9), 121.6 (C^{10}), 114.9 (C^6), 111.4 (C^8), 60.5 (C^2), 54.2 (OCH_3), 34.4 ($C(CH_3)_3$), 27.2 (3C, C(CH_3)$_3$). Anal. Calc. for $C_{13}H_{18}O_3$: C, 70.24; H, 8.16. Found: C, 70.17; H, 8.28%.

3,3′-cyclohexyl-5-methoxy-3a,7a-dihydro-3H-benzofuran-2-one **9b** (white crystals, 36% yield, m.p. 70°C): ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 5.97 (dd, $J_{HH}=10$ and 2.1 Hz, 1H, H^6), 5.91 (dd, $J_{HH}=10$ and 4.5 Hz, 1H, H^7), 5.06 (dd, $J_{HH}=8.6$ and 4.5 Hz, 1H, H^{7a}), 4.50 (m, 1H, H^4), 3.55 (s, 3H, OCH_3), 3.21 (dd, $J_{HH}=8.6$ and 3.5 Hz, 1H, H^{3a}), 1.84–1.65 (m, 6H, CH_2), 1.53–1.37 (m, 4H, CH_2); ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 180.5 (C^2, CO), 152.3 (C^5–OCH_3), 128.6 (C^6), 123.0 (C^7), 89.7 (C^4), 72.2 (C^{7a}), 54.4 (OCH_3), 46.7 (C^3), 42.4 (C^{3a}), 33.4, 30.1, 25.3, 22.5 and 22.2 (1C, CH_2). Anal. Calc. for $C_{14}H_{18}O_3$: C, 71.76; H, 7.75. Found: C, 71.59; H, 7.92%.

3,3′-cyclohexyl-7-methoxy-3a,7a-dihydro-3H-benzofuran-2-one **10b** (white crystals, traces): ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 5.91 (ddd, $J_{HH}=9.6$, 6.6 and 3 Hz, 1H, H^5), 5.30 (dd, $J_{HH}=9.6$ and 3 Hz,1H, H^4), 5.11 (d, $J_{HH}=6.6$ Hz, 1H, H^6), 4.85 (d, $J_{HH}=8$ Hz, 1H, H^{7a}), 3.59 (s, 3H, OCH_3), 3.25 (ddd, $J_{HH}=8$, 3 and 3 Hz, 1H, H^{3a}), 1.84–1.50 (m, 10H, CH_2); ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 179.3 (C^2, CO), 151.7 (C^7–OCH_3), 122.5 (C^5), 115.1 (C^4), 95.0 (C^6), 73.9 (C^{7a}), 54.2 (OCH_3), 46.0 (C^3), 43.5 (C^{3a}), 32.0, 29.3, 24.2, 21.6 and 21.0 (1C, CH_2). HRMS Calc. for $C_{14}H_{19}O_3$ (MH^+) 235.1334. Found 235.1334.

3-tert-butyl-7-methoxy-3a,7a-dihydro-3H-benzofuran-2-one **10d** (colorless oil, 5% yield): ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 5.89 (ddd, $J_{HH}=9$, 6.6 and 3 Hz, 1H, H^5), 5.20 (dd, $J_{HH}=9$ and 3 Hz, 1H, H^4), 5.14 (d, $J_{HH}=6.6$ Hz, 1H, H^6), 4.97 (d, $J_{HH}=9.6$ Hz, 1H, H^{7a}), 3.66 (s, 3H, OCH_3), 3.37 (dddd, $J_{HH}=9.6$, 3, 3 and 3 Hz, 1H, H^{3a}), 2.37 (d, $J_{HH}=3$ Hz, 1H, H^3), 1.13 (s, 9H, $C(CH_3)_3$); ^{13}C-NMR ($CDCl_3$ 100 MHz) δ 177.3 (C^2, CO), 152.5 (C^7–OCH_3), 122.0 (C^5), 121.9 (C^4), 95.7 (C^6), 76.5 (C^{7a}), 57.4 (C^3), 55.6 (OCH_3), 39.9 (C^{3a}), 34.3 ($C(CH_3)_3$), 27.9 (3C, $C(CH_3)_3$). HRMS Calc. for $C_{13}H_{19}O_3$ (MH^+) 223.1334. Found 223.1334.

3,3′-cyclohexyl-3,3a,4,7a-tetrahydro-benzofuran-2,5-dione **11b** (white crystals, 8% yield, m.p. 72°C): ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 6.88 (dd, $J_{HH}=10$ and 4.6 Hz, 1H, H^7), 6.19 (d, $J_{HH}=10$ Hz, 1H, H^6), 4.94 (ddd, $J_{HH}=5.6$, 4.6 and 1 Hz, 1H, H^{7a}), 2.83 (ddd, $J_{HH}=11.2$, 5.6 and 5.6 Hz, 1H, H^{3a}), 2.44 (dd, $J_{HH}=15.6$ and 5.6 Hz, 1H, $H^{4/4'}$), 2.30 (dd, $J_{HH}=15.6$ and 11.2 Hz, 1H, $H^{4/4'}$), 1.80–1.36 (m, 10H, CH_2); ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 197.4 (C^5, CO), 179.4 (C^2, CO), 140.8 (C^7), 133.2 (C^6), 70.4 (C^{7a}), 48.5 (C^3), 41.0 (C^{3a}), 35.4 (C^4), 31.9, 28.4, 25.4, 22.5 and 22.2 (1C, CH_2). Anal. Calc. for $C_{13}H_{16}O_3$: C, 70.89; H, 7.32. Found: C, 70.70; H, 7.33%.

3-tert-butyl-3,3a,4,7a-tetrahydro-benzofuran-2,5-dione **11d** (white crystals, 23% yield, m.p. 128°C): ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 6.71 (dd, $J_{HH}=10.2$ and 3 Hz, 1H, H^7), 6.13 (d, $J_{HH}=10.2$ Hz, 1H, H^6), 5.02 (ddd, $J_{HH}=7.2$, 3 and 1 Hz, 1H, H^{7a}), 3.03 (m, 1H, H^{3a}), 2.60 (m, 2H, $H^{4/4'}$), 2.10 (d, $J_{HH}=8$ Hz, 1H, H^3), 1.04 (s, 9H, $C(CH_3)_3$); ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 196.1 (C^5, CO), 175.6 (C^2, CO), 142.3 (C^7), 131.5 (C^6), 71.8 (C^{7a}), 54.5 (C^3), 39.5 (C^4), 36.3 (C^{3a}), 33.7 ($C(CH_3)_3$), 27.7 ($C(CH_3)_3$). Anal. Calc. for $C_{12}H_{16}O_3$: C, 69.21; H, 7.74. Found: C, 69.16; H, 7.80%.

5.4. Preparation of complexes **13**, **14**, **15** and **11**

Under the same conditions as for the anisole complex, the diphenylether complex (2 g, 6.54 mmol) reacted with ketene acetal **2d** (12.3 mmol) to give, after work up, a mixture of **13d**, **14d**, **15d** and **11d**. Chromatography on silica gel allowed separation of the compounds in the following order of elution: first, a mixture of **14d** and **15d** (PE–Et_2O 97/3), then **13d** as white crystals (PE–Et_2O 95/5) and finally **11d**. Complexes **14d** and **15d** were isolated pure as white crystals after separation with preparative thin layer (hexane–AcOEt, 90/10) and recrystallization in a mixture Et_2O–hexane.

1-(3-phenoxy-phenyl)-cyclohexanecarboxylic acid (**13b**) (white crystals, 55% yield, m.p. 148°C): ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.38–6.88 (m, 9H, Ph), 2.47 (m, 2H, cyclohexyl), 1.79–1.26 (m, 8H, cyclohexyl); ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 181.7 (C^2), 157.4 and 157.2 (*C*–O),145.3 (*C* Ph), 129.8, 129.7, 123.3, 121.3, 118.8, 117.3 and 117.2 (*C*H Ph), 50.6 (C^1), 34.3, 25.7 and 23.6 (CH_2). MS Calc. for $C_{19}H_{20}O_3$, 296 (M^+). Found 296.

2-(3-phenoxy-phenyl)-3,3′-dimethyl-butyric acid (**13d**) (white crystals, 17% yield, m.p. 106°C): ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.17–6.82 (m, 9H, Ph), 3.33 (s, 1H, H^2), 0.93 (s, 9H, $C(CH_3)_3$); ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 178.1 (C^1, CO), 156.2 (*C*–O), 155.6 (*C*–O), 136.6 (C^5), 128.7 (2C), 127.9, 123.9, 122.1, 119.8, 117.8, 117.6 and 116.7 (9C, *C*H, Ph), 60.4 (C^2), 33.4 (C^3), 26.8 (3C, $C(CH_3)_3$). MS Calc. for $C_{18}H_{20}O_3$, 284 (M^+). Found 284.

3,-tert-butyl-7-phenoxy-3a,7a-dihydro-3H-benzofuran-2-one (**14d**) (white crystals, 24% yield, m.p. 98°C): ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.28–7.00 (m, 5H, Ph), 5.69 (ddd, $J_{HH}=9.6$, 6.6 and 2.6 Hz, 1H, H^5), 5.18 (dd, $J_{HH}=9.6$ and 3 Hz, 1H, H^4), 5.10 (d, $J_{HH}=9.6$ Hz, 1H, H^{7a}), 5.01 (d, $J_{HH}=6.6$ Hz, 1H, H^6), 3.38 (dddd, $J_{HH}=9$, 3.6, 3 and 2.6 Hz, 1H, H^{3a}), 2.32 (d, $J_{HH}=3.6$ Hz, 1H, H^3), 1.07 (s, 9H, $C(CH_3)_3$); ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 175.9 (C^2, CO), 153.2 (*C*–O), 150.7 (*C*–O), 128.8 (2C, *C*H, Ph), 123.9 (C^4), 122.2 (C^5), 120.1, 119.9 and 116.9 (1C, *C*H, Ph), 100.8 (C^6), 74.6 (C^{7a}), 56.0 (C^3), 38.8 (C^{3a}), 33.0 ($C(CH_3)_3$), 26.5 ($C(CH_3)_3$, 3C). Anal. Calc. for $C_{14}H_{18}O_3$: C, 76.03; H, 7.09. Found: C, 75.86; H, 7.29%.

3-tert-butyl-5-phenoxy-3a,7a-dihydro-3H-benzofuran-2-one (**15d**) (colorless oil, 19% yield): ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.27–6.89 (m, 5H, Ph), 5.95 (dd, $J_{HH}=10$ and 2 Hz, 1H, H^6), 5.83 (dd, $J_{HH}=10$ and 4 Hz, 1H, H^7), 5.13 (ddd, $J_{HH}=10$, 4 and 2 Hz, 1H,

H^{7a}), 4.74 (m, 1H, H^4), 3.23 (ddd, $J_{HH} = 10$, 5.6 and 5.6 Hz, 1H, H^{3a}), 2.29 (d, $J_{HH} = 5.6$ Hz, 1H, H^3), 0.99 (s, 9H, $C(CH_3)_3$); ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 177.1 (C^2, CO), 155.3 (*C*–O), 149.5 (C^5), 128.8 (2C), 125.1, 123.8, 122.8, 1118.2 (2C) and 106.3 (*C*H, Ph), 73.8 (C^{7a}), 56.7 (C^3), 36.9 (C^{3a}), 33.9 ($C(CH_3)_3$), 27.9 ($C(CH_3)_3$, 3C). MS Calc. for $C_{18}H_{20}O_3$, 284 (M^+). Found 284.

5.5. Preparation of **17**

To a solution of lithium diisopropylamide (7.95 mmol) in THF (10 ml)was added dropwise a solution of carboxylic ester **16** (7.95 mmol) in THF (10 ml) at −70°C. The solution was stirred for 30 min at −70°C and was added slowly to a solution of anisole·$Cr(CO)_3$ (1.3 g, 5.3 mmol) at −70°C THF (10 ml) and DMF (10 ml). The mixture was stirred for 3 h at −30°C. After treatment with I_2 (4 equivalents), the solution was allowed to warm to r.t. overnight and was worked up as above. Complex **17** was isolated as a yellow oil after purification by chromatography.

1-(3-methoxy-phenyl)-cyclohexanecarboxylic acid methyl ester (**17**) (yellow oil, 65% yield): ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.16 (t, $J_{HH} = 8$ Hz, 1H, H^7), 6.89 (t, 1H, $J_{HH} = 8$ Hz, H^6), 6.86 (s, 1H, H^4), 6.69 (dd, $J_{HH} = 8$ and 2.5 Hz, 1H, H^8), 3.72 (s, 3H, $COOCH_3$), 2.41–2.37 (m, 2H, CH_2), 1.66–1.38 (m, 8H, CH_2); ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 176.0 (C^1, CO), 160.0 (C^5–OCH_3), 154.9 (C^3), 129.8 (C^7), 118.6 (C^6), 112.7 (C^4), 111.9 (C^8), 55.6 (OCH_3), 52.45 5 ($COOCH_3$), 51.32 (C^2), 35.1 (2C), 25.9 and 24.1 (2C) (CH_2). HRMS Calc. for $C_{15}H_{21}O_3$ (MH^+) 249.1491. Found 249.1495.

5.6. Preparation of **19b**

4,5-dihydroxy-3,3′-cyclohexyl-3H-benzofuran-2-one (**19b**) was obtained from complex **7** (4.4 mmol) and **2b** (6.6 mmol) upon oxidation with CAN (22 mmol) in acetonitrile (55 ml) at −70°C; (white solid, 8% yield, m.p. 101°C): ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 6.75 (d, $J_{HH} = 8$ Hz, 1H, H^6 or H^7), 6.50 (d, $J_{HH} = 8$ Hz, 1H, H^6 or H^7), 5.60 (broad, 2H, O*H*), 2.31–1.36 (m, 10H, CH_2); ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 179.7 (C^2, CO), 147.4, 142.2 and 139.6 (C^4, C^5 or C^{7a}, *C*–O), 119.7 (C^{3a}), 114.7 and 101.7 (C^6 or C^7), 47.2 (C^3), 31.4 (2C), 25.3 and 20.9 (2C) (CH_2). HRMS Calc. for $C_{13}H_{15}O_4$ (MH^+) 235.0970. Found 235.0970. This compound was also obtained upon oxidation of **9b** in acetonitrile with CAN at r.t. for 12 h together with the lactone **11b** and identified by its NMR spectra.

5.7. Preparation of **21**, **22** and **23**

The procedure is essentially the same as above with saturated acetal except the reaction temperature was held at r.t. after addition of *t*-BuOK. The products were isolated after the analogous work up.

4-phenyl-but-2-enoic acid (**21a**) (white solid, 41% yield, m.p. 54°C) [25]: ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.39–7.19 (m, 6H, H^3 and Ph), 5.85 (d, $J_{HH} = 15.5$ Hz, 1H, H^2), 3.58 (d, $J_{HH} = 6.7$ Hz, 2H, H^4); ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 172.1 (C^1, CO), 150.4 (C^3), 137.3 (C^5), 128.9 (2C), 128.8 (2C) and 126.9 (1C) (*C*H, Ph), 121.7 (C^2), 38.6 (C^4).

2-methyl-4-phenyl-but-2-enoic acid (**21b**) (white solid, 59% yield, m.p. 71°C) [26]: ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.39–7.10 (m, 5H, Ph), 7.08 (m, 1H, H^3), 3.60 (d, $J_{HH} = 7.6$ Hz, 2H, H^4), 1.94 (s, 3H, CH_3); ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 173.8 (C^1, CO), 143.0 (C^3), 138.7 (C^5), 128.6 (2C, *C*H, Ph), 128.6 (2C, *C*H, Ph), 128.3 (C^2), 126.6 (1C, *C*H, Ph), 35.1 (C^4), 11.7 (CH_3). Anal. Calc. for $C_{11}H_{12}O_2$: C, 74.98; H, 6.86. Found: C, 74.88; H, 6.87%.

3-methyl-4-phenyl-but-2-enoic acid (**21c**) (white solid, 14% yield, m.p. 72°C) [27]: ^{1}H-NMR ($CDCl_3$, 250 MHz) δ 7.38–7.18 (m, 5H, Ph), 5.75 (m, 1H, H^2), 3.49 (s, 2H, H^4), 2.16 (s, 3H, CH_3); ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 171.8 (C^1, CO), 161.5 (C^3), 137.5 (C^5), 129.2 (2C), 128.7 (2C) and 126.9 (1C) (*C*H, Ph), 116.7 (C^2), 47.4 (C^4), 19.0 (CH_3).

4-phenyl-pent-2-enoic acid (**21d**) (white solid, 43% yield, m.p. 45°C): ^{1}H-NMR ($CDCl_3$, 250 MHz) δ 7.27–7.12 (m, 6H, H^3 and Ph), 5.75 (dd, $J_{HH} = 15.6$ and 1.4 Hz, 1H, H^2), 3.59 (m, 1H, H^4), 1.38 (d, $J_{HH} = 7$Hz, 3H, CH_3); ^{13}C-NMR ($CDCl_3$, 60 MHz) δ 172.0 (C^1, CO), 155.7 (C^3), 143.3 (C^6), 129.1 (2C), 127.7 (2C) and 127.2 (1C) (*C*H, Ph), 119.7 (C^2), 42.15 (C^4), 20.4 (CH_3).

4-(3-methoxy-phenyl)-2-methyl-but-2-enoic acid (**22b**) (white solid, 41% yield, m.p. 48°C): ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.26 (m, 1H, H^9), 7.09 (m, 1H, H^3), 6.80 (m, 2H, H^8 and H^{10}), 6.75 (m, 1H, H^6), 3.82 (s, 3H, OCH_3), 3.55 (d, $J_{HH} = 7.6$ Hz, 2H, H^4), 1.97 (s, 3H, CH_3); ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 173.6 (C^1, CO), 159.9 (C^7–OCH_3), 142.8 (C^3), 140.2 (C^5), 129.8 (1C, *C*H, Ph), 127.8 (C^2), 120.96, 114.3 and 111.8 (1C, *C*H, Ph), 35.1 (C^4), 12.2 (CH_3). Anal. Calc. for $C_{12}H_{14}O_3$: C, 69.89; H, 6.84. Found: C, 69.88; H, 6.92%.

4-(3-phenoxy-phenyl)-but-2-enoic acid (**23a**) (colorless oil, 47% yield): ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.39–6.87 (m, 10H, H^3 and Ph), 5.84 (d, $J_{HH} = 15.6$ Hz, 2H, H^2), 3.54 (d, $J_{HH} = 6.8$ Hz, 2H, H^4); ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 172.1 (C^1, CO), 157.7 (*C*–O), 157.1 (*C*–O), 149.9 (C^3), 139.4 (C^5), 130.1 (2C), 129.9 (2C), 123.7 (1C) and 123.5 (1C) (*C*H, Ph), 122.0 (C^2), 119.3, 119.1 and 117.2 (1C, *C*H, Ph), 38.4 (C^4). MS Calc. for $C_{16}H_{14}O_3$, 254 (M^+). Found 254.

2-methyl-4-(3-phenoxy-phenyl)-but-2-enoic acid (**23b**) (white oil, 50% yield): ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.39–6.86 (m, 10H, H^3 and Ph), 3.54 (d, $J_{HH} = 7.6$ Hz, 2H, H^4), 1.96 (s, 3H, CH_3); ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 173.6 (C^1, CO), 157.5 (*C*–O), 157.1 (*C*–O),

142.5 (C^3), 140.7 (C^5), 130.0 (2C), 129.8 (2C), (*C*H, Ph)), 128.1 (C^2), 123.4 (2C), 119.0 (2C) and 116.9 (1C) (*C*H, Ph), 34.9 (C^4), 12.3 (CH_3). Anal. Calc. for $C_{17}H_{16}O_3$: C, 76.10; H, 6.01. Found: C, 76.09; H, 6.15%.

3-methyl-4-(3-phenoxy-phenyl)-but-2-enoic acid (**23c**) (white solid, 16% yield, m.p. 76°C): ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.39–6.88 (m, 9H, H^3 and Ph), 5.74 (s, 1H, H^2), 3.46 (s 2H, H^4), 2.16 (s, 3H, C*H*$_3$); ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 172.2 (C^1, CO), 161.0 (C^3), 157.5 (*C*–O), 157.1 (*C*–O), 139.5 (C^5), 130.0 (2C), 129.9 (2C), 124.1, 123.4, 119.8, 119.0 and 117.2 (*C*H, Ph), 117.1 (C^2), 47.1 (C^4), 19.1 (CH_3). MS Calc. for $C_{17}H_{16}O_3$, 268 (M^+). Found 268.

4-(3-phenoxy-phenyl)-pent-2-enoic acid (**23d**) (white solid, 47% yield): ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.38–6.86 (m, 10H, H^3 and Ph), 5.82 (d, $J_{HH} = 15.5$ Hz, 1H, H^2), 3.64 (m, 1H, H^4), 1.67 (d, $J_{HH} = 6.5$ Hz, 3H, C*H*$_3$); ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 172.3 (C^1, CO), 157.6 (*C*–O), 157.1 (*C*–O), 155.1 (C^3), 145.1 (C^6), 130.1, 129.9, 123.4 (2C) and 122.2 (*C*H,Ph), 119.7 (C^2), 119.0 (2C), 118.0 and 117.1 (*C*H, Ph), 42.1 (C^4), 20.1 (CH_3). HRMS Calc. for $C_{17}H_{16}O_3$, 269.1173 (MH^+). Found 269.1178.

3-methyl-2-phenyl-but-3-enoic acid (**24**) (white solid, 23% yield, m.p. 60°C) [28]: ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.38–7.28 (m, 5H, Ph), 5.06 (s, 1H, $H^{4/4'}$), 4.96 (s, 1H, $H^{4/4'}$), 4.36 (s,1H, H^2), 1.79 (s, 3H, C*H*$_3$); ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 178.5 (C^1), 142.4 (C^3), 136.6 (*C* Ph), 129.1, 128.9 and 128.0 (*C*H Ph), 114.8 (C^4), 58.9 (C^2), 22.1 (CH_3). MS Calc. for $C_{11}H_{12}O_2$, 176 (M^+). Found 176.

2-(3-methoxy-phenyl)-3-methyl-but-3-enoic acid (**25**) (colorless oil, 23% yield) [29]: ^{1}H-NMR ($CDCl_3$, 200 MHz) δ 7.23 (m, 1H, $H^{5'}$), 6.88 (m, 3H, $H^{2'}$, $H^{4'}$ and $H^{6'}$), 5.03 (s, 1H, $H^{4/4'}$), 4.95 (s, 1H, $H^{4/4'}$), 3.79 (s, 3H, OC*H*$_3$), 1.76 (s, 3H, C*H*$_3$); ^{13}C-NMR ($CDCl_3$, 50 MHz) δ 178.8 (C^1), 158.8 ($C^{3'}$), 142.0 (C^3), 137.8 ($C^{1'}$), 129.5 and 121.2 (*C*H Ph), 114.6 (C^4), 114.5 and 112.9 (*C*H Ph), 58.6 (C^2), 55.2 (O*C*H$_3$), 21.8 (CH_3).

3-isopropenyl-3,3a,4,7a-tetrahydro-benzofuran-2,5-dione (**26**) (white solid, 15% yield, m.p. 107°C): ^{1}H-NMR ($CDCl_3$, 200 MHz) δ 6.92 (dd, $J_{HH} = 10$ and 4.5 Hz, 1H,H^7), 6.25 (d, $J_{HH} = 10$ Hz, 1H, H^6), 5.22 (s, 1H, =C*H*$^{2/2'}$), 5.19 (s, 1H, =C*H*$^{2/2'}$), 4.88 (m, 1H, H^{7a}), 3.53 (d, $J_{HH} = 7.1$ Hz, 1H, H^3), 3.19 (m, 1H, H^{3a}), 2.26 (m, 2H, H^4), 1.79 (s, 3H, C*H*$_3$); ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 197.0 (C^5), 173.7 (C^2), 139.4 (C^7), 135.1 (*C*=CH$_2$), 133.8 (C^6), 117.8 (=*C*H$_2$), 70.9 (C^{7a}), 52.1 (C^3), 37.2 (C^4), 35.5 (C^{3a}), 23.7 (CH_3). HRMS Calc. for $C_{11}H_{13}O_3$, 193.0865 (MH^+). Found 193.0865.

3-methyl-3-vinyl-3,3a,4,7a-tetrahydro-benzofuran-2,5-dione (**28**) (white solid, 20% yield, m.p. 95°C): ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 6.83 (dd, $J_{HH} = 10.4$ and 2.9 Hz, 1H, H^7), 6.15 (dd, $J_{HH} = 10.4$ and 1.5 Hz, 1H, H^6), 5.68 (dd, $J_{HH} = 17.4$ and 10.8 Hz, *H*C=), 5.27 (d, $J_{HH} = 10.8$ Hz, 1H, =*CHH'*), 5.23 (d, $J_{HH} = 17.4$ Hz, 1H, =CH*H'*), 5.23 (ddd, $J_{HH} = 7.3$, 2.9 and 1.5 Hz, 2H, H^{7a}), 3.01 (ddd, $J_{HH} = 7.3$, 7.3 and 4.8 Hz,1H, H^{3a}), 2.66 (dd, $J_{HH} = 17.4$ and 7.3 Hz, 1H, $H^{4/4'}$), 2.56 (dd, $J_{HH} = 17.4$ and 4.8 Hz, 1H, $H^{4/4'}$), 1.42 (s, 3H, CH_3); ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 195.4 (C^5), 177.6 (C^2), 142.0 (C^7), 134.1 (H*C*=), 132.2 (C^6), 119.1 (=*C*H$_2$), 71.7 (C^{7a}), 49.3 (C^3), 44.4 (C^{3a}), 35.1 (C^4), 22.5 (CH_3). HRMS Calc. for $C_{11}H_{13}O_3$, 193.0865 (MH^+). Found 193.0870.

2-methyl-2-(3-phenoxy-phenyl)-but-3-enoic acid (**29**) (colorless oil, 58% yield): ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.38–6.89 (m, 9H, Ph), 6.42 (dd, $J_{HH} = 17.6$ and 10.6 Hz, 1H, H^3), 5.36 (d, $J_{HH} = 10.6$ Hz, 1H, $H^{4/4'}$), 5.24 (d, $J_{HH} = 17.6$ Hz, 1H, $H^{4/4'}$), 1.69 (s, 3H, C*H*$_3$); ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 180.9 (C^1, CO), 157.3 (*C*–O), 157.1 (*C*–O), 144,8 (*C*q, Ph),140.1 (C^3), 129.8, 123.4, 121.6, 118.8, 117.7, 117.3 (*C*H, Ph), 115.8 (C^4), 53.6 (C^2), 23.2 (CH_3). HRMS Calc. for $C_{18}H_{21}O_3$, 285.1484 ($M + CH_5^+$). Found 285.1491.

6. Structure solution and refinement

For products **14d** and **23c**, accurate cell dimensions and orientation matrices were obtained by least-squares refinements of 25 accurately centred reflections. No significant variations were observed in the intensities of two checked reflections during data collection. Complete data and collection parameters are listed in Table 2. Data was also collected for Lorentz and polarization effects. Computations were performed by using the PC version of CRYSTALS [30]. Scattering factors and corrections for anomalous absorption were taken from Ref. [31]. The structures were solved by Fo-Patterson technique or direct method (SHELXS [32]). Refinements were carried out by full-matrix least squares. All non-hydrogen atoms were anisotropically refined, hydrogen atoms were introduced in calculated positions. The drawing of the molecules was carried out with the CAMERON program [33].

7. Supplementary material

Fractional atomic coordinate anisotropic thermal parameters for hydrogen and non-hydrogen atoms, atomic coordinates for H atoms, complete lists of bond distances and bond angles have been deposited with the Cambridge Crystallographic data Centre, CCDC Nos 156560 for compound **14d** and 156561 for compound **23c**. Copies of the data may be obtained free of charge from The Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (Fax: +44-1223-336033; e-mail: deposit@ccdc.cam.ac.uk or www: http://www.ccdc.cam.ac.uk).

Acknowledgements

This research was supported by Centre National de la Recherche Scientifique, MENRT, ANVAR and AVENTIS-AGRO.

References

[1] See for example A.J. Pearson, S.L. Kole, T. Ray, J. Am. Chem. Soc. 106 (1984) 6060 and references therein.
[2] For recent applications, see for example (a) S. Kudis, G. Helmchen, Tetrahedron, 54 (1998) 10449. (b) N. Gathergood, K.A. Jorgensen, Chem. Commun. (1999) 1869. (c) C. Jonasson, M. Rönn, J.A. Bäckvall, J. Org. Chem. Soc. 65 (2000) 2122 and references cited therein.
[3] M. Bellassoued, E. Chelain, J. Collot, H. Rudler, J. Vaissermann, Chem. Commun. (1999) 187.
[4] H. Rudler, V. Comte, M. Bellassoued, E. Garrier, J. Vaissermann, J.C. Daran, C. R. Acad. Sci.Paris Serie IIc Chem. 3 (2000) 113.
[5] H. Rudler, A. Parlier, F. Cantagrel, P. Harris, M. Bellassoued, Chem. Commun. (2000) 771.
[6] For the synthesis of bis(trimethylsilyl) ketene acetals see (a) C. Ainsworth, Y.N. Kuo, J. Organomet. Chem. 46 (1973) 73. (b) M. Bellassoued, M. Gaudemar, Tetrahedron Lett. 31 (1990) 209.
[7] M.F. Semmelhack, Ann. N.Y. Acad. Sci. 295 (1977) 36.
[8] G. Jaouen, Ann. N. Y. Acad. Sci. 295 (1977) 59.
[9] F. Rose-Munch, E. Rose, Curr. Org. Chem. 3 (1999) 445.
[10] E.P. Kündig, Pure Appl. Chem. 57 (1985) 1855.
[11] For the formation of dienol ethers from anisoletricarbonylchromium and enolates, upon protonation, see for example (a) M.F. Semmelhack, A. Yamashita, J. Am. Chem. Soc. 102 (1980) 5924. (b) H.G. Schmalz, K. Schellhaas, Angew. Chem. Int. Ed. Engl. 35 (1997) 2146. (c) A.J. Pearson, A.V. Gontcharov, J. Org. Chem. 63 (1998) 152.
[12] P.L. Creger, J. Am. Chem. Soc. 89 (1967) 2500.
[13] M.F. Semmelhack, H.T. Hall, Jr., R. Farina, M. Yoshifuji, G. Clark, T. Bargar, K. Hirotsu, J. Clardy, J. Am. Chem. Soc. 101 (1979) 3535.
[14] P. Jacob, III, P.S. Callery, A.T. Shulgin, N. Castagnoli, Jr., J. Org. Chem. Soc. 41 (1976) 3627.
[15] For the synthesis of unsaturated bis(trimethylsilyl)ketene acetals see (a)W.T. Brady, M.O. Agho, J. Heterocycl. Chem. 20 (1963) 501. (b) M. Bellassoued, R. Enigrou, M. Gaudemar, J. Organomet. Chem. 338 (1988) 149. (c) M. Bellassoued, R. Ennigrou, M. Gaudemar, J. Organomet. Chem. 393 (1990) 19.
[16] J. Stetter, F. Lies, Angew. Chem. Int. Ed. Engl. 39 (2000) 1724 and references therein.
[17] R. Chamberlain, C. Koch, J. Org. Chem. 58 (1993) 2725.
[18] (a) A.J. Pearson, J. Chem. Soc. Chem. Commun. (1980) 488. (b) A.J.Pearson, Chi Wi Ong, J. Org. Chem. 47 (1982) 3780. (c) A.J. Pearson, A.R. Douglas, Organometallics, 17 (1998) 1448.
[19] M.-C.P. Yeh, L.W. Chuang, M.L. Lai, C.C. Chou, Organometallics 16 (1997) 4435.
[20] G.S. Hammond, in: M.S. Newman (Ed.), Steric Effects on Equilibrated Systems, Wiley, New York, 1956, p. 425.
[21] (a) F.C. Lightstone, T.C. Bruice, J. Am. Chem. Soc. 118 (1996) 2595. (b) T.C. Bruice, F.C. Lightstone, Acc. Chem. Res. 32 (1999) 127.
[22] S.N. Calderon, A.H. Newman, F.C. Tortella, J. Med. Chem. 34 (1991) 3159.
[23] C.F. Yao, K.H. Kao, J.T. Liu, C.M. Chu, Y. Wang, W.C. Chen, Y.M. Lin, M.C. Yan, J.Y. Liu, M.C. Chuang, J.L. Shiue, Tetrahedron 54 (1998) 791.
[24] W. Kübler, O. Petrov, E. Winterfeldt, Tetrahedron 44 (1988) 4371.
[25] T.H. Black, Y. Zhang, J. Huang, D.C. Smith, B.E. Yates, Synthetic Commun. 25 (1995) 15.
[26] R. Aumann, H.J. Weidenhaupt, Chem. Ber. 120 (1987) 23.
[27] M. Kuchar, B. Brunova, V. Rejholec, M. Jelinkova, J. Holubek, O. Nemecek, Collect. Czech. Chem. Commun. 49 (1984) 122.
[28] R. Knorr, E. Lattke, Chem. Ber. 114 (1981) 2116.
[29] Sumimoto Chemical Co. Ltd. Ger. Offen. 2 335 347, 1974, Japan, C.A. 80 (1974) 120746w.
[30] D.J. Watkins, C.K. Prout, J.R. Carruthers, P.W. Betteridge, Crystals Issue 10, Chemical Crystallography Laboratory, University of Oxford, UK, 1966.
[31] D.T. Cromer, International Tables for X-ray crystallography, vol. IV, Kynoch Press, UK, 1974.
[32] G.M. Sheldrick, SHELXS-86, Program for Crystal Structure Solution, University of Göttingen, 1986.
[33] D.J. Watkin, C.K. Prout, L.J. Pearce, Cameron Crystallography Laboratory, University of Oxford, UK, 1996.