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Catalysis in water: Highly efficient synthesis of heptadienoic acids by rearrangement of allyl but-3-enoate promoted by Rh(I) complexes

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Abstract

A practical and efficient protocol has been developed to realize the catalytic rearrangement of allyl but-3-enoate to heptadienoic acids in $NaHCO_3$ saturated water, in the presence of catalytic amounts of a rhodium(I) complex, containing olefin, diene or phosphine ligands. The reaction mainly affords the sodium salt of *E*-2,6-heptadienoic acid, with high catalytic efficiency (3600 TON). A reaction scheme of the process is proposed. The reaction course differs from that observed in organic solvents, where *E*-3,6-heptadienoic acid is formed predominantly.

Keywords: Catalysis in water; C–C coupling; Green chemistry; Heptadienoic acids; Rhodium

1. Introduction

Heptadienoic acids and their derivatives are an important class of compounds, which have found application as useful intermediates for the synthesis of compounds of biological and pharmaceutical interest. Heptadienoic acid and its alkyl esters have in fact found extensive use as reported in the literature [1–11]. Unsaturated α-amino acids, key components in the synthesis of a class of biologically active peptides, were obtained in enantiomerically pure form starting from heptadienoic acid derivatives [12]. They are also useful chiral synthons and their synthetic interest has recently increased with the advent of ring closing metathesis (RCM) methodologies [13].

Several approaches to the synthesis of dienoic acids have been reported in the literature. A general organic procedure is based on the reaction of lithium dienenolates (obtained from unsaturated carboxylic acids, in particular but-3-enoic acids) with allylic halides [14]. However, it is characterized by poor γ-regioselectivity. An indirect way to achieve a γ-regioselective alkylation consists of a tandem process, in which the mixture of the α- and γ-alkylated products obtained from allylation of the lithium dienolate of an unsaturated carboxylic acid is subjected to Cope-rearrangement [15]. In the case of allylic halides as electrophiles, regioselective alkylation at the γ-carbon has also been attained by changing the counterion of the dienolate from lithium to Cu^+ [16,17]. An alternative approach to the stereospecific generation of 1,4- and 1,5-dienes developed by Corey et al. [18] is based on the addition of vinyl-copper and methallylcopper reagents to 2,4-pentadienoic esters to give (*E*)-3,6-heptadienoate and (*E*)-3,7-(7-methyl)octadienoate ester derivatives in good yields. Another protocol is based on the reaction of 1,5-hexadiene with a solution of cesium metal in THF, in the presence of 18-crown-6 at −75 °C, to afford a hexadienyl anion that can then undergo carbonatation to give a mixture of the cesium salts of 2-vinyl-4-pentenoic acid and (*E*) and (*Z*)-3,6-heptadienoic acid [19].

All the above-described procedures are suitable for small scale preparations. For larger scale syntheses, it is more convenient to follow an alternative way, based on the Wittig reaction, which makes use of unsaturated aldehydes and organic phosphorous compounds [7]. Nevertheless, techniques of this type require the preliminary preparation of the suitable aldehyde, as well as the stoichiometric use of a phosphorous reagent, which causes problems in connection with the present environmental

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requirements. This approach is therefore substantially not attractive for an industrial application. There are also known catalytic processes for the preparation of dienoic acids by reacting vinyl or allyl halides with acetylene and carbon monoxide in hydroxylated solvents in the presence of nickel carbonyl or precursor thereof [20]. Even these methods are not suitable for industrial applications, owing to the high toxicity of nickel carbonyl derivatives.

We now wish to propose an efficient, practical and environmentally friendly method for the preparation of heptadienoic acids and esters, based on the Rh(I)-catalyzed rearrangement of allyl but-3-enoate in aqueous media.

2. Experimental section

2.1. General

Elemental analyses were carried out with a Carlo Erba Elemental Analyzer Mod. 1106. ^{1}H and ^{13}C NMR spectra were taken on a Bruker AC300 (300 MHz) spectrometer. IR spectra were taken on a NICOLET 5700 FT-IR spectrometer. Mass spectra were obtained using a GC system HP6890 Series coupled with a HP 5973 Mass Selective Detector at 70 eV ionization voltage. All reactions were analyzed by TLC on silica gel 60 F_{254} or by GLC using a HRGC Mega 2 series Fisons Instruments equipped with a polymethylsilicone +5% phenylsilicone as a stationary phase (HP-5) capillary column. Column chromatography was performed on silica gel 60 (Merck, 70–230 mesh).

2.2. Materials

All reagents, ligands and rhodium complexes were obtained from commercial suppliers and used without further purification. The preparation of allyl ester **1** and substituted allyl esters of but-3-enoic acid **7**, **8** and **9**, the procedure for the preparation of rhodium complexes of 2,6- and 3,6-heptadienoic acids and the procedure for the catalytic isomerization of 2,2- and 3,3-heptadienoic acids are reported in the supplementary material. The substrates were purified by distillation or column chromatography using suitable eluents. ^{1}H, ^{13}C NMR, IR, mass spectra and elemental analyses confirmed the assigned structures (see Appendix B, Supplementary Material).

2.3. General procedure for the catalytic rearrangement of allyl but-3-enoate in organic solvents

The reactions described in Table 1 were carried out in a Schlenk flask under N_2 atmosphere. Allyl but-3-enoate (0.328 g, 2.6 mmol), $Rh(PPh_3)_3Cl$ (0.024 g, 2.6×10^{-2} mmol, or 1.3×10^{-2} mmol of rhodium dinuclear complexes) and, if required (di-isopropylethyl)amine (235.2 mg, 2.8 mmol) were dissolved in organic solvent (5 mL) and stirred at 100 °C for 18 h. Solvents and rhodium complexes are listed in Table 1. The reaction mixture was extracted with alkaline water (3× 10 mL) and the extract was acidified to pH 1 with 2 M HCl. The acidic aqueous phase was then extracted with diethyl ether (3× 20 mL). After removal of the solvent under vacuum, flash chromatography (silica gel) of the residue using a mixture of hexane/EtOAc (1/1) as eluent afforded acids **2-*E*** and **3-*E***.

2.4. General procedure for the catalytic rearrangement of allyl but-3-enoate in biphasic media

The biphasic reactions described in Tables 2 and 3 were carried out as follows: allyl but-3-enoate (2.071 g, 16.43 mmol) dissolved in the organic solvent (3 mL) was added to a $NaHCO_3$ saturated water solution (5 mL) in a Schlenk flask under N_2 atmosphere containing the Rh mononuclear complex (4×10^{-2} mmol) or the Rh dinuclear complex (2×10^{-2} mmol) and the mixture was stirred at 100 °C. Reaction times, solvents and rhodium complexes are listed in Tables 2 and 3. The crude organic layer was washed with aqueous $NaHCO_3$, and the organic phase was evaporated in vacuum to yield the crude neutral products (esters). After removal of the solvent under vacuum, flash chromatography (silica gel) of the residue using a mixture of hexane/EtOAc (8/1) as eluent afforded allyl esters **4-*E*** and

Table 1
Catalytic rearrangement reaction of allyl but-3-enoate 1 to heptadienoic acids 2–3 and esters 4–5 in organic solvents at 100 °C for 18 h[a]

Entry	Rhodium complex	Solvent (5 mL)	Conversion **1** (%)[b]	Yield (%)[b] (**2** + **3**)	Selectivity (%)		Yield (%)[b] (**4** + **5**)
					2/(**2** + **3**) 3,6-[(*E*) + (*Z*)][c]	**3**/(**2** + **3**) 2,6-(*E*)	
1	$Rh(PPh_3)_3Cl$	MeCN	≥99	84	97	3	7
2	$Rh(PPh_3)_3Cl$	C_3H_7CN	≥99[d]	82	93	7	7
3	$Rh(PPh_3)_3Cl$	CH_2Cl_2	79[d]	63	98	2	6
4	$Rh(PPh_3)_3Cl$	THF	96[d]	87	99	1	3
5	$Rh_2(C_2H_4)_4Cl_2$	MeCN	95[d]	75	92	8	8
6	$Rh_2(C_2H_4)_4Cl_2$	C_3H_7CN	≥99	86	94	6	6
7	$Rh_2(C_6H_{10})_2Cl_2$	MeCN	95	76	92	8	8
8	$Rh_2(C_6H_{10})_2Cl_2$	C_3H_7CN	≥99	86	95	5	6

[a] All reactions were carried out under the following conditions: **1** (2.6 mmol), $Rh(PPh_3)_3Cl$ (2.6×10^{-2} mmol), $[Rh(C_2H_4)_2Cl]_2$, $[Rh(C_6H_{10})_2Cl]_2$ (1.3×10^{-2} mmol), solvent (5 mL).
[b] Based on GLC analyses (after methylation of the products) referred to $C_6H_4Cl_2$ as an internal standard.
[c] (*E*/*Z*) molar ratios ranged from 3.7 to 5.6.
[d] 4-Allylhepta-2,6-dienoioc acid **6** (3–5%) was also formed.

Table 2
Catalytic rearrangement reaction of allyl but-3-enoate **1** to heptadienoic acids **2–3** and esters **4–5** in the biphasic system organic solvent/$NaHCO_3$ satd. water at 100 °C for 12 h[a]

Entry	Rhodium complex	Solvent (3 mL)	Conversion (%)[b]	Acids yield (%)[b] (**2** + **3**)	Selectivity (%)		Allylic esters yield (%)[b]	
					2/(**2** + **3**) 3,6-(*E*)	**3**/(**2** + **3**) 2,6-(*E*)	**4** (3,6)	**5** (2,6)
9	$Rh(PPh_3)_3Cl$	C_3H_7CN	91[c,d]	48		100	3	8
10	$[Rh(COD)Cl]_2$	C_3H_7CN	96[c,e]	67	28	72	2	3
11	$[Rh(COD)_2]BF_4$	C_3H_7CN	99[c,f]	78	14	86	0	4
12	$[Rh(C_6H_{10})Cl]_2$	C_3H_7CN	96[c,f]	77	18	82	1	5
13	$[Rh(C_2H_4)_2Cl]_2$	C_3H_7CN	≥99[f]	86	4	96	1	4
14	$[Rh(C_2H_4)_2Cl]_2$	CH_2Cl_2	89[c,f]	74	8	92	1	4
15	$[Rh(C_2H_4)_2Cl]_2$	DEE[g]	92[c,f]	78	7	93	1	3
16	$[Rh(C_2H_4)_2Cl]_2$	Toluene	90[c]	81	4	96		2
17	$[Rh(C_2H_4)_2Cl]_2$	C_6H_5Cl	93	83	4	96	1	3

[a] All reactions were carried out under the following conditions: **1** (16.43 mmol), $Rh(PPh_3)_3Cl$, $[Rh(COD)_2]BF_4$ (4.0×10^{-2} mmol), $[Rh(C_2H_4)_2Cl]_2$, $[Rh(C_6H_{10})_2Cl]_2$, $[Rh(COD)Cl]_2$ (2.0×10^{-2} mmol), $NaHCO_3$ saturated water solution (5 mL), organic solvent (3 mL).
[b] Based on GLC analysis (after acidification and methylation of the products) referred to $C_6H_4Cl_2$ as an internal standard.
[c] Butenoic acid recovered from reaction mixture completes the molar balance.
[d] Compound **6** (3%) was also formed.
[e] Compound **6** (2%) was also formed.
[f] Compound **6** (1%) was also formed.
[g] DEE: diethoxyethane.

5-*E*. The aqueous phases were combined with the crude aqueous layer obtained from the reaction, acidified to pH 1 with 2 M HCl, and then extracted with diethyl ether (3× 20 mL). After removal of the solvent under vacuum, flash chromatography (silica gel) of the residue using a mixture of hexane/EtOAc (1/1) as eluent afforded acids **2-*E***, **3-*E***, and **6**.

2.5. General procedure for the catalytic rearrangement of allyl but-3-enoate in aqueous media

The reactions described in Table 4 were carried out in a Schlenk flask under N_2 atmosphere. Allyl but-3-enoate (3.10 g, 24.65 mmol) was added to a $NaHCO_3$ saturated water solution (10 mL) containing the Rh mononuclear complex (1.2×10^{-2} mmol) or the Rh dinuclear complex (3.1×10^{-3} mmol) and, if required, 3,3′,3″-phosphinidynetris(benzene-sulfonic acid), trisodium salt (TPPTS, 1.2×10^{-2} to 3.6×10^{-2} mmol as specified in Table 4). The resulting mixture was stirred at 100 °C for the time indicated in Table 4. Rhodium complexes are listed in Table 4. The crude reaction mixture was diluted with satd. $NaHCO_3$ and extracted with diethyl ether (3× 20 mL) to recover the neutral products. The basic aqueous phase was acidified to pH 1 with 2 M HCl and then extracted with diethyl ether (3× 20 mL). The resulting organic phase was evaporated in vacuo to yield the crude acid products.

All yields were determined by GC according to the internal standard method. To obtain improved chromatographic peaks, organic acids were transformed in their respective methyl esters by treating with a CH_2N_2 solution in diethyl ether.

2.6. ICP analyses of rhodium

Quantitative determinations of rhodium by ICP technique were carried out at Chimica Generale ed Inorganica, Chimica Fisica, Chimica Analitica Department of Parma University. The samples were prepared according to a procedure reported in the literature [21].

2.7. Characterization of the products

All products were characterized by IR, ^1H NMR and ^{13}C spectroscopies, MS spectrometry, elemental analysis. ^1H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$ solutions at 300 MHz and 75 MHz, respectively, with Me_4Si as internal standard. Chemical shifts and coupling constants (*J*) are given in ppm (δ) and in Hz, respectively.

Table 3
Catalytic rearrangement of allyl but-3-enoate **1** to heptadienoic acids **2–3** in the biphasic system butyronitrile/$NaHCO_3$ satd. water at 100 °C for 1 h[a]

Entry	Solvent (mL)		Conversion (%)[b]	Acid yield (%)[b]	Selectivity (%)	
	H_2O	C_3H_7CN		(**2** + **3**)	**2**/(**2** + **3**) 3,6-(*E*)	**3**/(**2** + **3**) 2,6-(*E*)
18	5	3	20	18	4	≥96
19	5	1	34	32	–	≥99

[a] All reactions were carried out under the following conditions: **1** (5.0 mmol), $[Rh(C_6H_{10})_2Cl]_2$ or $[Rh(C_2H_4)_2Cl]_2$ (1.2×10^{-2} mmol), $NaHCO_3$ saturated water solution (5 mL) and butyronitrile.
[b] Based on GLC analysis (after acidification and methylation of the products) referred to $C_6H_4Cl_2$ as an internal standard.

Table 4
Catalytic rearrangement reaction of allyl but-3-enoate **1** to heptadienoic acids **2**–**3** and esters **4**–**5** in $NaHCO_3$ satd. water[a]

Entry	Rhodium complex	Substrate/Rh molar ratio	Satd. $NaHCO_3$ (mL)	Time (h)	Conversion (%)[b]	Yield (%)[b] **2** + **3**	Selectivity (%)		Yield (%) **4** + **5**[b]
							2/(**2** + **3**) 3,6-(*E*)	**3**/(**2** + **3**) 2,6-(*E*)	
20	$[Rh(C_6H_{10})\,Cl]_2$	200	5	1	65	63		≥99	-
21	$[Rh(COD)Cl]_2$	2000	10	16	99	82	21	79	7
22	$[Rh(COD)_2]BF_4$	2000	10	16	88	73	16	84	6
23	$[Rh(C_2H_4)_2Cl]_2$	2000	10	16	97	88	7	93	3
24	$[Rh(C_2H_4)_2Cl]_2$, 2 equiv. TPPTS	2000	10	16	89	62	13	87	-
25	$[Rh(C_2H_4)_2Cl]_2$, 4 equiv. TPPTS	2000	10	16	91	56	27	73	5
26	$[Rh(C_2H_4)_2Cl]_2$, 6 equiv. TPPTS	2000	10	16	94	28	40	60	-
27	$[Rh(C_6H_{10})Cl]_2$	2000	10	16	93	85	4	96	3
28	$[Rh(C_2H_4)_2Cl]_2$	4000	10	36	≥99[c]	90	11	89	3
29	$[Rh(C_6H_{10})Cl]_2$	4000	10	36	95[c]	83	4	96	4
30	$Rh(PPh_3)_3Cl$	2000	7.5	36	95[c]	53	34	66	4

[a] The reactions were carried out under the following conditions—entry 20: **1** (5.0 mmol), $[Rh(C_6H_{10})_2Cl]_2$ (1.2×10^{-2} mmol), in $NaHCO_3$ satd. water; entries 21 and 30: **1** (24.65 mmol), $Rh(PPh_3)_3Cl$, $[Rh(COD)_2]BF_4$ (1.2×10^{-2} mmol); entries 23–27–29: **1** (24.65 mmol), $[Rh(COD)Cl]_2$, $[Rh(C_2H_4)_2Cl]_2$, $[Rh(C_6H_{10})_2Cl]_2$ (3.1×10^{-3} mmol), in $NaHCO_3$ satd. water; entry 24: **1** (24.65 mmol), $[Rh(C_2H_4)_2Cl]_2$ (3.1×10^{-3} mmol), TPPTS (6.2×10^{-3} mmol), in $NaHCO_3$ satd. water; entry 25: **1** (24.65 mmol), $[Rh(C_2H_4)_2Cl]_2$ (3.1×10^{-3} mmol), TPPTS (1.24×10^{-2} mmol), in satd. $NaHCO_3$ entry 26: **1** (24.65 mmol), $[Rh(C_2H_4)_2Cl]_2$ (3.1×10^{-3} mmol), TPPTS (1.86×10^{-3} mmol), in $NaHCO_3$ satd. water.

[b] Based on GLC analysis (after acidification and methylation of the products) referred to $C_6H_4Cl_2$ as an internal standard.

[c] Butenoic acid recovered from reaction mixture completes the molar balance.

2.7.1. Hepta-3(E),6-dienoic acid **2**

Colourless oil. IR (film) ν_{max} (cm^{-1}) 2920 (m), 1709 (s), 1414 (m), 1289 (w), 990 (w), 970.1 (w), 914 (w). ^1H NMR (300 MHz) δ_H 2.79 (2H, dd, $J = 6.1$ Hz, $J = 6.4$ Hz, $CH_2{=}CHCH_2$), 3.09 (2H, d, $J = 5.4$ Hz, CH_2CO_2H), 4.98–5.08 (m, 2H, $H_2C{=}$), 5.55 (1H, dt, $J = 14.0$ Hz, $J = 6.1$ Hz, $HC{=}CHCH_2CO_2H$), 5.63 (1H, dt, $J = 14.0$ Hz, $J = 5.4$ Hz, $HC{=}CHCH_2CO_2H$), 5.80 (1H, ddt, $J = 17.1$ Hz, $J = 10.1$ Hz, $J = 6.4$ Hz $CH_2{=}CHCH_2$), 9.35 (s, 1H, OH). ^{13}C NMR (75 MHz) δ_C 36.4, 37.5, 115.2, 122.0, 131.0, 132.1, 177.3. MS *m/z* 126(M^+, 15), 81(100), 79(80), 41(50), 67(45), 53(35), 84(35), 97(10), 45(10). Anal. Calcd. for $C_7H_{10}O_2$: C, 66.63; H, 7.99. Found C, 66.55; H, 7.96.

2.7.2. Hepta-2(E),6-dienoic acid **3**

Colourless oil. IR (film) ν_{max} (cm^{-1}) 2926 (m), 1697 (s), 1651 (w), 1418 (m), 1288 (m), 1227 (w), 986 (w), 914 (w). ^1H NMR (300 MHz) δ_H 2.20–2.37 (m, 4H, CH_2CH_2), 5.00–5.09 (m, 2H, $H_2C{=}$), 5.73–5.87 (m, 2H, $H_2C{=}CHCH_2CH_2CH{=}CH$), 7.08 (dt, $J = 15.6$, $J = 6.8$ Hz, 1H, $CH{=}CHCO_2H$), 11.23 (s, 1H, OH). ^{13}C NMR (75 MHz) δ_C 31.5, 31.8, 115.6, 120.9, 136.8, 151.2, 171.6. MS *m/z* 126(M^+, 1), 81(100), 68(52), 54(38), 97(23), 51(13), 77(11), 57(9), 65(8), 85(7), 111(5), 108(5), 60(3), 125(3), 71(2), 74(2). Anal. Calcd. for $C_7H_{10}O_2$: C, 66.63; H, 7.99. Found C, 66.58; H, 7.95.

2.7.3. Methyl hepta-3(E),6-dienoate

Colourless oil. IR (film) ν_{max} (cm^{-1}) 2977 (m), 1738 (s), 1638 (w), 1437 (m), 1255 (w), 1165 (m), 995 (w), 971 (w), 914 (m). ^1H NMR (300 MHz) δ_H 2.76–2.80 (m, 2H, $H_2C{=}CHCH_2$), 2.78 (dd, $J = 6.4$ Hz, $J = 1.6$ Hz, 2H, CH_2CO_2Me), 3.66 (s, 3H, CO_2Me), 4.99–5.08 (m, 2H, $H_2C{=}$), 5.59 (dt, 1H, $J = 14.4$ Hz, $J = 5.0$ Hz, $CH{=}CHCH_2CO_2Me$) 5.73–5.87 (m, 2H, $H_2C{=}CHCH_2CH{=}CH$). ^{13}C NMR (75 MHz) δ_C 34.6, 37.7, 51.6, 115.3, 122.7, 131.4, 136.2, 172.2. MS *m/z* 140(M^+, 10), 125 (5), 111(10), 98 (45), 81(100), 67(20), 59(25), 53(25), 41(25). Anal. Calcd. for $C_8H_{12}O_2$: C, 68.53; H, 8.63. Found C, 68.48; H, 8.59.

2.7.4. Methyl hepta-2(E),6-dienoate

Colourless oil. IR (film) ν_{max} (cm^{-1}) 2950 (m), 1724 (s), 1656 (w), 1436 (m), 1271 (w), 1170 (w), 990 (w), 915 (w). ^1H NMR (300 MHz) δ_H 2.20–2.32 (m, 4H, CH_2CH_2), 3.63 (s, 3H, CO_2Me), 4.98–5.07 (m, 2H, $H_2C{=}$), 5.74–5.87 (m, 2H, $H_2C{=}CHCH_2CH_2CH{=}CH$), 6.95 (dt, $J = 15.6$ Hz, $J = 6.8$ Hz, 1H, $HC{=}CHCO_2Me$). ^{13}C NMR (75 MHz) δ_C 36.4, 37.7, 51.6, 115.4, 122.0, 130.1, 138.9, 172.2. MS *m/z* 140(M^+, 10), 125(3), 109(13), 98(35), 81(100), 67(25), 59(24), 53(30), 41(30). Anal. Calcd. for $C_8H_{12}O_2$: C, 68.53; H, 8.63. Found C, 68.48; H, 8.57.

2.7.5. Allyl hepta-3(E),6-dienoate **4**

Colourless oil. IR (film) ν_{max} (cm^{-1}) 2926 (m),1697 (s),1651 (w),1418 (m), 1288 (m), 1227 (w), 986 (w), 914 (w). ^1H NMR (300 MHz) δ_H 2.78–2.84 (m, 2H, $H_2C{=}CHCH_2CH{=}CH_2$), 3.07–3.14 (m, 2H, CH_2COO), 4.57–4.60 (m, 2H, CO_2CH_2), 5.00–5.08 (m, 2H, $H_2C{=}CHCH_2CH{=}$), 5.21–5.28 (m, 2H, $OCH_2CH{=}CH_2$), 5.60–5.65 (m, 2H, $HC{=}CHCH_2COO$), 5.77–5.93 (m, 2H, $H_2C{=}CHCH_2CH{=}CH + OCH_2CH{=}CH_2$). Noesy 1D experiments confirmed 3(*E*) geometry. ^{13}C NMR (75 MHz) δ_C 36.4, 37.9, 65.1, 115.4, 117.9, 122.6, 132.1, 132.0, 136.3, 171.5. MS *m/z* 166(M^+, 1), 151(1), 137(3), 125(25), 107(35), 83(40), 81(60), 79(100), 67(10), 53(30). Anal. Calcd for $C_{10}H_{14}O_2$: C, 72.25; H, 8.49. Found C, 72.20; H, 8.45.

2.7.6. Allyl hepta-2(E),6-dienoate ***5***

Colourless oil. IR (film) ν_{max} (cm^{-1}) 3080 (m), 2932 (m), 1724 (s), 1653 (m), 1446 (w), 1270 (w), 1170 (m), 990 (w), 971 (w). ^1H NMR (300 MHz) δ_H 2.16–2.33 (m, 4H, =CHCH_2CH_2CH=), 4.61 (ddd, J = 5.5 Hz, J = 1.3 Hz, J = 1.4 Hz, 2H, CO_2CH_2), 4.99–5.05 (m, 2H, CH_2=CHCH_2CH_2), 5.21 (ddt, J = 10.4 Hz, J = 1.1 Hz, J = 1.3 Hz, 1H, OCH_2CH=C*H*H), 5.30 (ddt, J = 17.1 Hz, J = 1.1 Hz, J = 1.4 Hz, 1H, OCH_2CH=CH*H*), 5.85 (dt, J = 15.6 Hz, J = 1.4 Hz, 1H, C*H*COO), 5.71–5.97 (m, 2H, H_2C=C*H*CH_2CH_2 + OCH_2C*H*=CH_2), 6.98 (dt, J = 15.6 Hz, J = 6.6 Hz, 1H, *H*C=CHCOO). MS *m/z* 166(M^+, 1), 151(3), 137(3), 125(20), 109(60), 81(100), 79(80), 68(25), 55(40). Anal. Calcd. for $C_{10}H_{14}O_2$: C, 72.25; H, 8.49. Found C, 72.20; H, 8.44.

2.7.7. Allyl 4-allyl-hepta-3,6-dienoate ***6***

Colourless oil. ^1H NMR (300 MHz) δ_H 2.76–2.79 [m, (4H, H_2C=CHCH_2)$_2$C=], 3.11 (d, J = 7.1 Hz, 2H, CH_2COO), 4.59 (dt, J = 5.7 Hz, J = 1.4 Hz, 2H, CO_2CH_2), 5.00–5.08 [m, 4H, (H_2C=CHCH_2)$_2$C=], 5.23 (ddd, J = 10.3, Hz, J = 1.3 Hz, J = 1.2 Hz, 1H, CO_2CH_2CH=C*H*H), 5.31 (ddd, J = 15.7, Hz, J = 1.6 Hz, J = 1.3 Hz, 1H, CO_2CH_2CH = CH*H*), 5.47 (t, J = 7.1 Hz, 1H, =*CH*CH_2), 5.70–5.96 [m, 3H, (H_2C=C*H*CH_2)$_2$C= + CO_2CH_2C*H*=CH_2]. MS *m/z* 206(M^+, 8), 187(5), 163(12), 145(30), 119(65), 105(45), 91(95), 79(100), 67(40), 55(30). Anal. Calcd. for $C_{13}H_{18}O_2$: C, 75.68; H, 8.80. Found C, 75.61; H, 8.72.

2.7.8. Octa-3(E),6(E)-dienoic acid ***10***

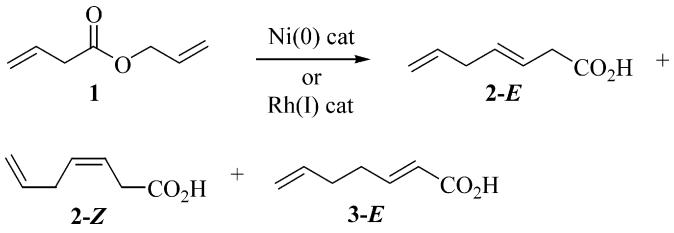
Colourless oil. ^1H NMR (300 MHz) δ_H 1.66 (d, J = 6.6 Hz, 3H, CH_3), 2.68–2.76 (m, 2H, CH_2CH=CHCH_2COO), 3.04 (d, J = 6.2 Hz, 2H, CH_2CH=CHCH_2COO) 5.33–5.46 (m, 2H, CH_3C*H*=C*H*), 5.48–5.84 (m, 2H, C*H*=C*H*CH_2COO), 9.80 (bs, 1H, OH). ^{13}C NMR (75 MHz) δ_C 17.8, 35.4, 37.7, 120.7, 126.2, 128.2, 133.7, 178.4. MS *m/z* 140(30), 122(5), 95(35), 81(80), 79(100), 67(50), 55(45), 41(50). Anal. Calcd. for $C_8H_{12}O_2$: C, 68.53; H, 8.63. Found C, 68.47; H, 8.62.

2.7.9. Octa-2(E),6(E)-dienoic acid ***11***

Colourless oil. ^1H NMR (300 MHz) δ_H 1.65 (dd, J = 6.7, J = 1.4 Hz, 3H, CH_3), 2.13–2.32 (m, 4H, CH_2CH_2), 5.28–5.64 (m, 2H, CH_3C*H*=C*H*), 5.83 (d, J = 15.9 Hz, 1H, C*H*COOH), 7.08 (dt, J = 15.9, J = 6.9 Hz, 1H, C*H*=CHCOOH), 9.80 (bs, 1H, OH). ^{13}C NMR (75 MHz) δ_C 17.8, 30.4, 32.2, 120.5, 129.3, 131.8, 151.8, 172.0. MS *m/z* 140(5), 122(1), 111(2), 95(5), 86(40), 79(5), 68(10), 55(100), 41(15). Anal. Calcd. for $C_8H_{12}O_2$: C, 68.53; H, 8.63. Found C, 68.46; H, 8.61.

3. Results and discussion

Several years ago it was reported that some phosphorous-containing Ni(0) and Rh(I) complexes were able to catalyze, in aprotic organic solvents and under mild conditions, the rearrangement of allyl but-3-enoate to a mixture of 2,6- and 3,6-heptadienoic acids (Eq. (1)) [22].

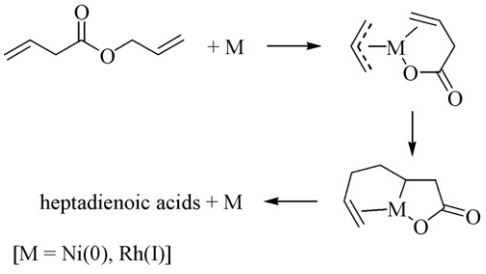


(1)

This approach took advantage of the chelating effect for achieving the formation of a new C–C bond [23,24]. In fact, the formation of a chelate complex can assist the oxidative addition to the metal center of the but-3-enoato group, which is thus held in the appropriate position for the double bond insertion (Scheme 1, ligands are not shown for clarity). A final β-H elimination step then leads to heptadienoic acids with regeneration of the metal catalyst [22].

Good yields were obtained with both nickel(0) and rhodium(I) catalytic systems. Reactions occurred between 20 and 80 °C under nitrogen. The $Rh(PPh_3)_3Cl$ complex in MeCN or THF at room temperature gave a 90% yield of 3,6-heptadienoic acids, predominantly the *E* one. The complex deriving from one molecule of $Ni(COD)_2 + P(OiPr)_3$ in anisole at room temperature gave a 66% yield of 2,6- and 3,6-heptadienoic acids in a ca. 9:1 molar ratio. The main by-products were the allyl esters of the heptadienoic acids. Catalytc efficiencies ranged from 180 TON for the Ni-catalyzed reactions to 255 TON for the Rh-catalyzed ones.

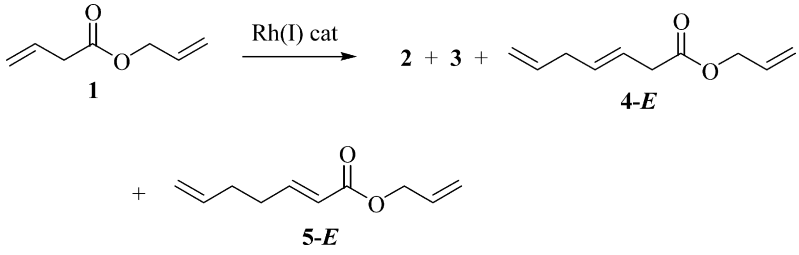
The two types of complexes exhibited a different catalytic activity depending on the environments provided by the nature of the phosphorus-containing ligands, which also affected the 2,6-/3,6-heptadienoic acid molar ratio. The $Rh(PPh_3)_3Cl$ complex reacted much more rapidly at room temperature than $Ni(COD)_2 + P(OiPr)_3$ and its activity was strongly influenced by solvents. Aprotic solvents, such as MeCN, $CHCl_3$, and THF, gave good results, while strongly coordinating solvents (like DMSO or DMF) were not effective. Interestingly, the reaction rates for both the rhodium and nickel-catalyzed processes were reduced in the presence of an excess of products, owing to the competition for the active sites on the metal.



Scheme 1.

3.1. Catalytic reactions in organic solvents

With the aim of developing a more efficient and practical version of this interesting approach to heptadienoic acids, we have investigated the possibility to improve the catalyst performance and to carry out the reaction in aqueous media. We have first investigated the catalytic activity of rhodium(I) complexes containing triphenylphosphine, ethylene, 1,5-hexadiene and cyclooctadiene (COD) ligands in the rearrangement reaction of allyl but-3-enoate in different organic solvents. Thus, $Rh(PPh_3)_3Cl$, $[Rh(C_2H_4)_2Cl]_2$, $[Rh(C_6H_{10})_2Cl]_2$, $[Rh(COD)Cl]_2$ and $[Rh(COD)_2]BF_4$ complexes were caused to react with allyl but-3-enoate in aprotic solvents at 100 °C for 18 h. The reaction led to a mixture of heptadienoic acids **2** and **3**, together with smaller amounts of their corresponding allyl esters **4** and **5** (formed by partial transesterification of **2** and **3** with **1**, Eq. (2)). The yields and selectivities obtained are reported in Table 1.



(2)

The reaction practically did not occur in hydrocarbon solvents such as methylcyclohexane or toluene in the presence of the complexes listed in Table 1. The $Rh(PPh_3)_3$ showed a satisfactory activity in aprotic solvents, such as MeCN, C_3H_7CN, THF, and CH_2Cl_2 at 100 °C (entries 1–4). Rhodium(I) complexes containing olefin or diolefin ligands (with the exception of the $[Rh(COD)Cl]_2$ and $[Rh(COD)_2]BF_4$ complexes, which were practically ineffective in all the above mentioned solvents) showed an activity similar to that of $Rh(PPh_3)_3$ only in nitrile solvents (entries 5–8), which likely act as electron donor ligands in the crucial oxidative addition step without interfering with the formation of the chelating ring. Rhodium complexes containing olefinic ligands showed a more marked decrease of activity at $T < 100$ °C with respect to that containing triphenylphosphine, which in its turn showed a stronger activity decrease in CH_2Cl_2 and THF in comparison with nitrile solvents.

Reaction selectivities did not vary significantly. The product distribution, using either ethylene or 1,5-hexadiene rhodium complexes under the same reaction conditions, were similar, as shown by the results reported in entries 5, 7 and 6, 8 of Table 1. This behavior may be ascribed to the fact that as soon as the formation of heptadienoic acids, particularly 2,6-heptadienoic acid, occurs, the rhodium coordinated olefinic ligands are replaced by the acid giving a new catalytic species. To confirm this hypothesis, $[Rh(C_2H_4)_2Cl]_2$ was caused to react with 2,6- and 3,6-heptadienoic acids in CH_2Cl_2 at room temperature to give yellow and red-brown powders, respectively. Elemental analyses agreed with a formula corresponding to $Rh(C_7H_{10}O_2)Cl$ for both solids, even though dinuclear species may be formed and different isomers may be present. These powders, scarcely soluble in organic solvents, were soluble in aqueous $NaHCO_3$. The ^1H NMR spectra in this medium did not allow a straightforward spectroscopic structure determination, however, since the signals were too broad. In any case, when these solids were used as catalysts in butyronitrile under the same experimental conditions similar results to the ones of entries 6 and 8 in Table 1 were obtained. On the other hand, a large excess of 3,6- and 2,6-heptadienoic acids in the reaction mixture (1:1 molar ratio with respect to allyl but-3-enoate) tended to prevent the coordination of allyl but-3-enoate to the metal center, thus causing a marked decrease of conversion. Clearly, the negative effect exerted by an excess of products on catalyst activity did not allow the achievement of high TON (Turn Over Number) in these reactions (TON were typically around 100 mol of product obtained per mol of catalyst used). However, the acidic nature of the products prompted out to investigate the possibility to carry out the reaction in a biphasic system, consisting of an organic solvent and an alkaline aqueous solution, in order to favor the transfer the products, as soon as they are formed, into the aqueous phase as carboxylates.

3.2. Catalytic reactions in biphasic media

The results obtained by using a biphasic system with a saturated $NaHCO_3$ solution as the aqueous phase are shown in Table 2. As it can be seen from the table, good yields of heptadienoates were indeed obtained under the biphasic conditions working with a substrate to rhodium molar ratio of ca. 400, thus confirming the validity of our hypothesis. Similar results were achieved when the substrate/catalytic complex molar ratio was raised to 800.

The use of $Rh(PPh_3)_3Cl$ or $[Rh(COD)Cl]_2$ led to a lower yield in heptadienoic acids **2** and **3** (entries 9 and 10) compared with the other olefin rhodium(I) complexes tested (entries 11–17). However, it is worth noting that the $[Rh(COD)Cl]_2$ complex was now able to promote the rearrangement process in biphasic media, in contrast with its inactivity in organic solvents (see above). Moreover, a reversed selectivity in favor of the 2,6-heptadienoic derivative instead of 3,6-isomer (the most abundant isomer formed in organic solvents) was observed in all cases.

3.3. Catalytic reaction in aqueous basic media

The effect of decreasing the amount of the organic solvent was examined by carrying out the reaction of **1** (in the presence of $[Rh(C_6H_{10})Cl]_2$ or $[Rh(C_2H_4)_2Cl]_2$ as catalyst for 1 h at 100 °C) in $NaHCO_3$ saturated water in mixture with diminishing amounts of butyronitrile (Table 3).

Very interestingly, a quantitative ICP determination of the rhodium dissolved in the organic phase and in the basic aqueous phase after reagent mixing as well as at the end of the reaction showed that more than 90% of the metal was actually in the aqueous phase. In a similar way, when the reagents were mixed in satd. $NaHCO_3$, without additional organic solvent, the ICP analysis of the mixture showed that more than 95% of the metal was in aqueous phase, with the remaining 5% lying into allyl but-3-enoate. We therefore expected that the reaction could also be carried out in the absence of added organic solvents. Indeed, the reaction carried out in satd. $NaHCO_3$, without any organic solvent, proceeded nicely and afforded the heptadienoates in high yield (Table 4, entry 20). Both the substrate conversion rate and product yields were actually higher compared to the reactions carried out in the biphasic system (compare entry 20 with entries 18 and 19).

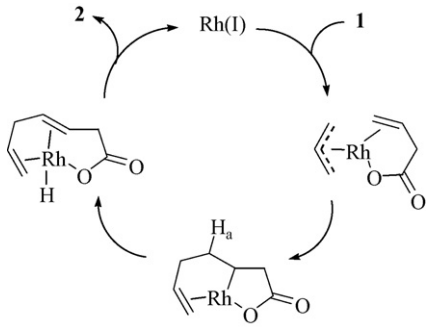
The basic aqueous phase then helps to speed up the reaction, since the heptadienoates, stabilized by ionic interaction with water, cannot interfere with the substrate for coordination to rhodium. The next experiments, aimed at optimizing catalytic efficiency and product yield, were therefore carried out in satd. $NaHCO_3$ at 100 °C in the presence of different rhodium(I) complexes, in some cases containing different molar ratios of TPPTS (3,3′,3″-phosphinidynetris(benzene-sulfonic acid), trisodium salt) and with a substrate/rhodium molar ratio up to 4000 (Table 4).

Very good yields (73–90%) were obtained with rhodium(I) complexes containing olefin or diolefin ligands (entries 21–23 and 27–29). Thus, the TON in the reaction carried out in the absence of organic solvents reached 3600. On the other hand, $Rh(PPh_3)_3Cl$ and $[Rh(C_2H_4)_2Cl]_2$ in presence of TPPTS led to less satisfactory results (entry 24–26, 30).

As in the case of the reactions carried out in biphasic media, the most abundant isomer formed in $NaHCO_3$ saturated water turned out to be the 2,6-heptadienoate (**3**) rather than the 3,6-unsaturated one (**2**).

The presence of a water soluble phosphine like TPPTS as an additional ligand (entries 24–26) decreased the reactivity of the system. This effect was more pronounced at higher TPPTS/Rh molar ratios. In additon, the selectivity of the reaction turned towards the 3,6-unsaturated isomer. The decreased reactivity can be attributed to a strong coordination of the phosphinic ligand to the metal, that prevents the coordination of the substrates. On the other hand, the increase of the amount of TPPTS enhances the electronic density on the metal, disfavouring the elimination of a proton from the β-carbon, thus shifting the selectivity towards the 3,6-unsaturated product.

In order to investigate the possible effect on selectivity, an organic base (di-isopropylethylamine) was also tested under the conditions described in Table 1. Actually, the selectivity of the reaction did not vary significantly, while the conversion was strongly decreased to 47% if $Rh(PPh_3)Cl$ was used as a catalyst and to 23% if $[Rh(C_2H_4)_2Cl]_2$ was used. This effect confirms that the active metal needs to be as free as possible from additional ligands to favor the coordination of the reagents and obtain the best performance.



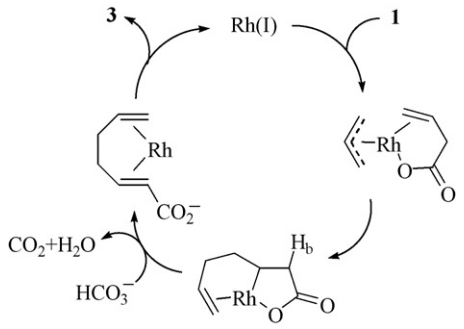
Scheme 2. Proposed reaction mechanism in organic solvents.

We have ascertained that no significant isomerization occurred when *E*-2,6- heptadienoic acid or the mixture of *E*-3,6- and *Z*-3,6-heptadienoic acids was heated at 100 °C for 16 h in butyronitrile in the presence of $Rh(PPh_3)_3Cl$ or in a mixture of basic water and butyronitrile in the presence of $[Rh(C_2H_4)_2Cl]_2$. These results demonstrate that isomeric heptadienoates **2** and **3** do not interconvert under the reaction conditions and therefore must derive from different catalytic steps.

Attempts to give a more general application of the rearrangement reaction were experienced extending the investigation to differently substituted allyl esters of but-3-enoic acid. Thus crotyl or cyclohex-2-enyl or 1-methylallyl but-3-enoate (2.6 mmol) was added to a solution of $[Rh(C_2H_4)_2Cl]_2$ (2.6×10^{-2} mmol) in CH_3CN (5 mL) and heated at 100 °C under stirring for 24 h. Alternatively, the same esters (4 mmol) were caused to react in biphasic solution of C_3H_7CN (3 mL) and $NaHCO_3$ saturated H_2O (3 mL) or in H_2O (5 mL) in the presence of $[Rh(C_2H_4)_2Cl]_2$ (2.0×10^{-2} mmol) under the same conditions. Only crotyl ester led to rearrangement products: 77% of 3,6- and 2,6-octadienoic acids (7:1 molar ratio) (**10** and **11**) at 90% conversion in homogeneous CH_3CN solution and 41% and 51% of 3,6- and 2,6-octadienoic acids (1:3 molar ratio) at 85% and 90% conversion in biphasic medium (41% of but-3-enoic acid from hydrolysis of the ester) and in water, respectively; whereas cyclohex-2-enyl and 1-methylallyl esters did not react yielding only hydrolysis products in biphasic medium or water.

Chelate effect brought about by bidentate phosphine ligands, such as ethylenebis(diphenylphosphine) completely inhibited the rearrangement process. Actually, bidentate ligands could prevent the right coordination of but-3-enoate double bond on rhodium(III) intermediate species.

Schemes 2 and 3 show the likely mechanistic pathways followed in organic solvent and in water, respectively (unreactive ligands are omitted for clarity). The first step is an oxidative addition of allyl but-3-enoate rhodium(I), assisted by double bond chelation, then double bond insertion occurs followed by β-hydrogen elimination with formation of a rhodium hydride intermediate, which eventually undergoes reductive elimination. In organic solvents, the β-hydrogen elimination takes place regioselectively from the less acidic hydrogen bonded to the γ-carbon (indicated in Scheme 2 as H_a) to afford 3,6-heptadienoic acids **2** as the main reaction products.



Scheme 3. Proposed reaction mechanism in aqueous media.

On the other hand, in basic water solution, the β-elimination preferentially occurs from the hydrogen bonded to the α-carbon atom of the chain (indicated in Scheme 3 as H_b), through proton abstraction by the base, eventually leading to 2,6-heptadienoic acids **3** as the main reaction products.

4. Conclusions

Summing up, we have showed that the use of an aqueous basic medium allows the rearrangement of allyl 3-butenoate to (*E*)-2,6-heptadienoate using Rh(I) complexes as catalysts with excellent yields and very high catalytic efficiencies (up to ca 3600 mol of product per mol of catalyst). This process resulted rather sensitive to the reagent structure pointing out that good results were obtained mainly with allyl but-3-enoate. This eco-friendly procedure may offer additional and practical usefulness and potentiality for the preparation of heptadienoic acids whose application in the synthesis of organic, bioorganic, pharmaceutical and natural products is more and more increasing.

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Financial support from The Ministero dell'Università e della Ricerca Scientifica e Tecnologica (Progetto d'Interesse Nazionale PRIN 2003039774) is acknowledged. The facilities of Centro Interfacoltà di Misure (Università di Parma) were used for recording NMR spectra.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.molcata.2007.04.030.

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