Pergamon

Tetrahedron 57 (2001) 2365–2370

TETRAHEDRON

Functionalised organotitanium compounds: from lithium to titanium intermediates in chemoselective reactions with carbonyl compounds

Isidro M. Pastor and Miguel Yus*

Departamento de Química Orgánica, Facultad de Ciencias, Universidad de Alicante, Apdo. 99, E-03080 Alicante, Spain

Received 28 October 2000; revised 18 December 2000; accepted 19 January 2001

Abstract—The reaction of functionalised organolithium compounds 1 with an equimolecular mixture of two carbonyl compounds in the presence of 2 equiv. of triisopropoxytitanium chloride can discriminate between aldehyde and ketone, the process being selective for aldehydes at room temperature. Electronic and steric effects have been observed for different aldehydes. © 2001 Elsevier Science Ltd. All rights reserved.

1. Introduction

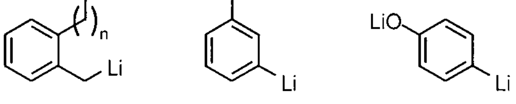
Carbon–carbon bond formation reactions use frequently organometallic intermediates and a carbonelectrophile. This process is especially interesting when the organometallic reagent bears a functionality because in this case at the same time, the functional group is transferred to the electrophilic component. The stability of functionalised organometallic compounds depends obviously on the compatibility between the functional group and the carbon–metal bond. Therefore the type of metal plays a fundamental role. In the last few years, we have been studying the use of functionalised organolithium compounds in synthetic organic chemistry.[1] These intermediates are very reactive species and, in general, they have to be handled at low temperatures in order to avoid their decomposition. In addition, due to their high reactivity, they are no too selective in order to discriminate different type of electrophilic groups. For these reasons, we thought that one way to modulate the reactivity and selectivity of functionalised organolithium compounds would be to replace the metal by another one less reactive but more selective such as titanium. In fact, organotitanium reagents[2] are interesting organometallic nucleophiles concerning their selectivity towards carbonyl compounds, being able to discriminate between aldehyde and ketone functionalities. In this paper, we describe the in situ preparation of functionalised organotitanium intermediates and their competitive reactivity with different carbonyl compounds, especially discriminating between aldehydes and ketones.

2. Results and discussion

For the lithium–titanium exchange, functionalised organolithium intermediates **1a**,[3a] **1b**,[3b] **1c**[3c] and **1d**[3c] were generated according to procedures developed in our laboratories, which involve an arene-catalysed lithiation at low temperature.[4–6] Once intermediates **1** were generated (2 mmol scale), a solution of triisopropoxytitanium chloride (4 mmol) in THF was added to the resulting clear solution at ca. −60°C and after 30 min stirring, allowing the temperature to rise to 20°C, an equimolecular solution of the corresponding mixture of carbonyl compounds (2.1 mmol each) was added at 0°C. Stirring was continued for 1.5 h allowing the temperature to rise to 20°C, being finally hydrolysed with hydrochloric acid, to give the expected alcohols **2** (Scheme 1, Charts 1 and 2 and Table 1).

$$\underset{\mathbf{1}}{R^{FG}Li} \xrightarrow{\text{i-iii}} \underset{\mathbf{2}}{R^{FG}C(OH)R^1R^2 + R^{FG}C(OH)R^3R^4}$$

Scheme 1. *Reagents and conditions*: (i) $(Pr^iO)_3TiCl$; (ii) R^1R^2CO/R^3R^4CO; (iii) H_2O.



1a: n = 2
1b: n = 1

1c

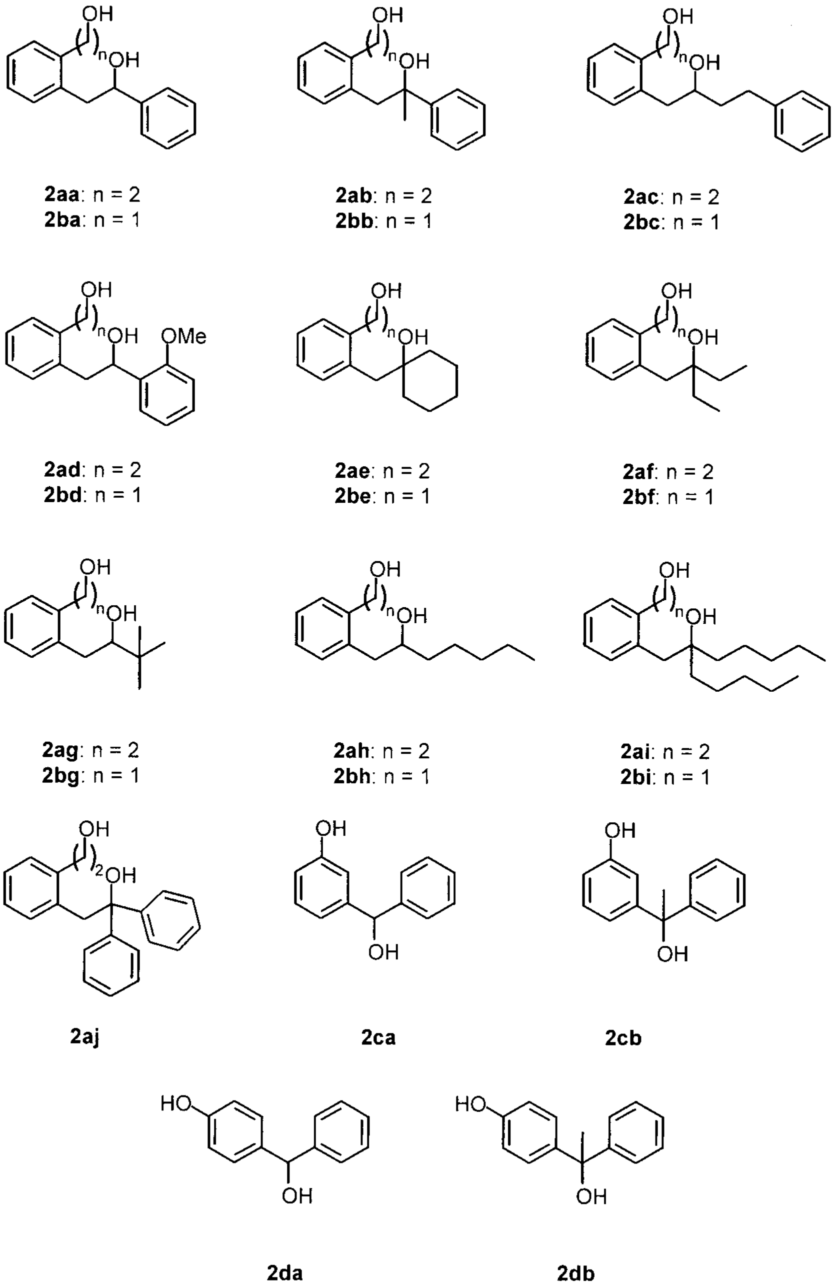
1d

Chart 1. Functionalised organolithium compounds $R^{FG}Li(\mathbf{1})$ used.

Keywords: organotitanium compounds; functionalised organolithiums; carbonyl compounds.

* Corresponding author. Tel.: +34-96-5903548; fax: +34-96-5903549; e-mail: yus@ua.es

PII: S0040-4020(01)00103-X



2aa: n = 2
2ba: n = 1

2ab: n = 2
2bb: n = 1

2ac: n = 2
2bc: n = 1

2ad: n = 2
2bd: n = 1

2ae: n = 2
2be: n = 1

2af: n = 2
2bf: n = 1

2ag: n = 2
2bg: n = 1

2ah: n = 2
2bh: n = 1

2ai: n = 2
2bi: n = 1

2aj

2ca

2cb

2da

2db

Chart 2. Compounds **2** prepared.

The following remarks can be extracted from the results included in Table 1, concerning competitive reactions with two carbonyl compounds:

(a) in almost all cases, the reaction in absence of the titanium component gave a ca. equimolecular mixture, so any selectivity was almost observed (Table 1, entries 1, 6, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31 and 33);
(b) concerning the amount of the titanium compound employed with the intermediate **1a**, using one equivalent at room temperature (Table 1, entry 2 and footnote 1), only the 'reduced' compound 2-(2-methylphenyl)ethanol (resulting from a lithium–hydrogen exchange from the functionalised organolithium intermediate **1a**) was isolated, whereas with 2 equiv. of the titanium salt, only reaction with benzaldehyde was observed and nothing of the corresponding compound resulting from the reaction with acetophenone (Table 1, entries 2 and 4). A larger excess of the titanium compound did not improve the former result (Table 1, entry 5). Two equivalents of the titanium compound are probably needed in order to substitute both lithium atoms by titanium in the intermediates **1**: due to the high titanium oxophilicity, the first titanium atom goes probably to the oxygen, so enhancing the reactivity of the remaining carbon–lithium bond towards proton abstraction from the reaction medium;
(c) the low temperature (−78°C) process, using **1a** and an equimolecular mixture of benzaldehyde/acetophenone, gave the same chemoselectivity but low yield in 1.5 h (Table 1, entry 3). However, after 12 h, almost the same result was obtained as at 20°C for 1.5 h (Table 1, entry 4 and footnote c). In general, the best discrimination result

Table 1. Preparation of compounds **2**

Entry	Functionalised organolithium	R^{1}R^{2}CO/R^{3}R^{4}CO	(Pr^{i}O)$_3$TiCl (equiv.)	T (°C)	Yield (%)[a] **2**
1	**1a**	PhCHO/PhCOMe	–	−78	**2aa/2ab**: 42/41
2			1	20	–[b]
3			2	−78	**2aa/2ab**: 10/–[c]
4			2	20	**2aa/2ab**: 60/–
5			4	20	**2aa/2ab**: 58/–
6	**1a**	PhCHO/PH$_2$CO	–	−78	**2aa/2aj**: 42/48
7			1	20	**2aa/2aj**: 26/10
8			2	20	**2aa/2aj**: 57/–
9	**1a**	PhCHO/Ph(CH$_2$)$_2$CHO	–	−78	**2aa/2ac**: 40/41
10			2	20	**2aa/2ac**: 6/49
11	**1a**	PhCHO/2-MeOC$_6$H$_4$CHO	–	−78	**2aa/2ad**: 45/38
12			2	20	**2aa/2ad**: 42/<1
13	**1a**	(CH$_2$)$_5$CO/Et$_2$CO	–	−78	**2ae/2af**: 22/44
14			2	20	**2ae/2af**: </1/<1
15	**1a**	Bu^{t}CHO/Me(CH$_2$)$_4$CHO	–	−78	**2ag/2ah**: 43/25
16			2	20	**2ag/2ah**: <1/43
17	**1a**	Me(CH$_2$)$_4$CHO/[Me(CH$_2$)$_4$]$_2$CO	–	−78	**2ah/2ai**: 35/51
18			2	20	**2ah/2ai**: 47/<1
19	**1b**	PhCHO/PhCOMe	–	−78	**2ba/2bb**: 40/53
20			2	20	**2ba/2bb**: 62/–
21	**1b**	PhCHO/Ph(CH$_2$)$_2$CHO	–	−78	**2ba/2bc**: 51/39
22			2	20	**2ba/2bc**: 8/62
23	**1b**	PhCHO/2-MeOC$_6$H$_4$CHO	–	−78	**2ba/2bd**: 45/42
24			2	20	**2ba/2bd**: 50/10
25	**1b**	(CH$_2$)$_5$CO/Et$_2$CO	–	−78	**2be/2bf**: 31/40
26			2	20	**2be/2bf**: <1/<1
27	**1b**	Bu^{t}CHO/Me(CH$_2$)$_4$CHO	–	−78	**2bg/2bh**: 45/27
28			2	20	**2bg/2bh**: <1/38
29	**1b**	Me(CH$_2$)$_4$CHO/[Me(CH$_2$)$_4$]$_2$CO	–	−78	**2bh/2bi**: 32/46
30			2	20	**2bh/2bi**: 52/<1
31	**1c**	PhCHO/PhCOMe	–	0	**2ca/2cb**: 23/30
32			2	20	**2ca/2cb**: 35/<1
33	**1d**	PhCHO/PhCOMe	–	0	**2da/2db**: 18/31
34			2	20	**2da/2db**: 27/2

[a] Yield deduced from the isolated crude mixture of compounds **2** by GLC.

[b] The only reaction product isolated (>99%) was 2-(2-methylphenyl)ethanol.

[c] Under the same reaction conditions, but during 12 h, **2aa/2ab**: 57/–.

was obtained at room temperature, in all cases the reaction time is of 1.5 h;

(d) for the couple benzaldehyde/benzophenone, the same results described in (c) were observed with **1a** (Table 1, entries 6–8);

(e) comparing an aromatic and an aliphatic aldehyde, the reaction with intermediate **1a** worked mainly with the second one (Table 1, entries 9 and 10);

(f) in the case of competing benzaldehyde and an electron-rich derivative (2-methoxybenzaldehyde), the reaction with **1a** showed to be very selective, reacting only with the non-substituted substrate (Table 1, entries 11 and 12);

(g) when a mixture of ketones such as cyclohexanone and 3-pentanone was used with **1a** under the standard conditions (2 equiv. of titanium salt, 20°C, 1.5 h), no reaction products could be detected: only the corresponding 'reduced' compound was isolated, resulting from a lithium–hydrogen exchange from the organolithium intermediate **1a** (Table 1, entry 14);

(h) steric effects play an important role. For instance, the reaction of intermediate **1a** with the equimolecular mixture of pivalaldehyde and hexanal under standard conditions (see above) yielded only the reaction product with the less hindered aldehyde (**2ah**) (Table 1, entry 16);

(i) as expected, when the aldehyde and ketone are aliphatic (Table 1, entry 18), only reaction of the aldehyde with intermediate **1a** occurred;

(j) a completely parallel behaviour was observed for intermediate **1b** (Table 1, entries 19–29) under the standard reaction conditions (2 equiv. of titanium compound, 20°C, 1.5 h): only aldehydes react in the presence of ketones, either aromatic or aliphatic (Table 1, entries 20 and 29); aliphatic aldehydes are more reactive than aromatic ones (Table 1, entry 21) and steric effects play an important role (Table 1, entry 27). Also here, electronic effects can be observed depending on the substitution at the aromatic ring in benzaldehyde (Table 1, entry 23);

(k) the use of intermediates **1c** and **d** under the mentioned standard conditions afforded the expected results when an equimolecular mixture of benzaldehyde and acetophenone was used (Table 1, entries 32 and 34);

(l) yields are in general modest due to the formation in some extension of the corresponding 'reduced' products coming from a metal–hydrogen exchange.

3. Conclusions

As a final conclusion, in this paper, we have demonstrated that functionalised organotitanium compounds (easily generated in situ from the corresponding organolithium intermediates) are chemoselective in the competitive reaction with carbonyl compounds: only aldehydes react in the presence of ketone. In addition, the reaction is rather sensitive to electronic and steric effects.

4. Experimental

4.1. General

For general information, see Ref. 7. Starting functionalised intermediates **1a**,[3a] **1b**[3b] and **1c**,**d**[3c] were generated according to the literature procedures.

4.2. Reaction of intermediates 1 with triisopropoxytitanium chloride and an equimolecular mixture of two carbonyl compounds: a competitive experiment

4.2.1. Isolation of compounds 2. *General procedure*—Once the corresponding functionalised organolithium reagent **1** was generated according to the literature,[3] the excess of lithium was filtered off and a solution of triisopropoxytitanium chloride (1.1 g, 4 mmol) in THF (3 ml) was added dropwise to the clear solution (2 mmol scale) at ca. −60°C. After 10 min, stirring was continued for 30 min allowing the temperature to rise to room temperature. Then, the corresponding equimolecular amount of two carbonyl compounds (2.1 mmol each) was added at 0°C and, after 1.5 h stirring allowing the temperature to rise to 20°C, the mixture was hydrolysed with 1 M HCl (10 ml). The resulting mixture was then extracted with ether (5×10 ml), the organic phase was dried over anhydrous $MgSO_4$ and evaporated. The resulting residue was analysed by quantitative GLC.

The competitive reactions without using the titanium salt were carried out under the same reaction conditions described above. The corresponding results are included in Table 1. For the characterization of the major products,[2] the corresponding isolation was performed by column chromatography (silica gel, hexane/ethyl acetate), so pure compounds **2** were obtained. Yields are given in Table 1. Compounds **2aa**,[3a] **2ab**,[3a] **2ae**,[3a] **2af**,[3a] **2ag**,[3a] **2ba**,[3b] **2bb**,[3b] **2be**,[3b] **2bf**[3b] and **2bg**[3b] were characterised by comparison of their spectroscopic and physical data with those described earlier by us. For new compounds or those partially described in literature,[8–10] physical, spectroscopic and analytical data follow:

4.2.2. 1-[2-(2-Hydroxyethyl)phenyl]-4-phenyl-2-butanol (2ac). R_f 0.21 (hexane/ethyl acetate: 2:1); ν (film) 3539–3140 (OH), 3060, 3024, 1494, 1453 (C=CH), 1044 cm^{-1} (C–O); δ_H 1.84–1.91 (2H, m, $CHCH_2CH_2$), 2.16 (2H, brs, 2×OH), 2.75, 2.82–2.97 (1H and 5H, respectively, 2m, 3×$ArCH_2$), 3.81 (3H, m, CH_2OH and $CHOH$), 7.15–7.30 (9H, m, ArH); δ_C 32.1, 35.5, 38.8, 40.5 (4×CH_2), 63.4 (CH_2OH), 72.0 (CHOH), 125.8, 126.6, 126.7, 128.4, 129.9, 130.4, 137.2, 137.4, 141.9 (12C. ArC); *m/z* 252 (M^+-18, 0.5%), 136 (74), 118 (49), 117 (53), 115 (11), 106 (51), 105 (54), 104 (10), 92 (19), 91 (100), 78 (11), 77 (18), 65 (17); HRMS: M^+- [H_2O], found 252.1495. $C_{18}H_{20}O$ requires 252.1514.

4.2.3. 2-[2-(2-Hydroxyethyl)phenyl]-1-(2-methoxyphenyl)-1-ethanol (2ad). R_f 0.25 (hexane/ethyl acetate: 2:1); ν (film) 3557–3107 (OH), 3064, 3031, 1491, 1452, 1439 (C=CH), 1056, 1022 cm^{-1} (C–O); δ_H 2.15, 2.75 (1H and 1H, respectively, 2brs, 2×OH), 2.85–3.07 (3H, m, $ArCH_2$ and $ArCHH$) 3.14 (1H, dd, *J*=14.1, 3.9 Hz, $ArCHH$), 3.80 (2H, m, CH_2OH), 3.84 (3H, s, CH_3O), 5.17 (1H, dd, *J*=9.0, 3.7 Hz, $CHOH$), 6.88 (1H, d, *J*=8.3 Hz, ArH), 6.96 (1H, t, *J*=7.3 Hz, ArH), 7.14–7.28 (5H, m, ArH), 7.40 (1H, dd, *J*=7.5, 1.7 Hz, ArH); δ_C 35.5, 40.7 (2×CH_2), 55.2 (CH_3), 63.6 (CH_2OH), 70.9 (CHOH), 110.3, 120.8, 126.4, 126.5, 126.7, 128.3, 129.9, 130.7, 132.2, 137.4, 137.6, 156.0 (ArC); *m/z* 254 (M^+-18, 5%), 137 (100), 121 (17), 118 (16), 117 (18), 107 (31), 91 (14), 77 (17); HRMS: M^+, found 272.1394. $C_{17}H_{20}O_3$ requires 272.1412.

4.2.4. 1-[2-(2-Hydroxyethyl)phenyl]-2-heptanol (2ah). R_f 0.34 (hexane/ethyl acetate: 2:1); ν (film) 3570–3131 (OH), 3060, 3018, 1466, 1452 (C=CH), 1043 cm^{-1} (C–O); δ_H 0.90 (3H, deformed t, *J*=6.7 Hz, CH_3), 1.34, 1.56 (4H and 4H, respectively, 2m, $CH(CH_2)_4CH_3$), 1.83 (2H, brs, 2×OH), 2.73–2.87, 2.89–3.04 (2H and 2H, respectively, 2m, 2×$ArCH_2$), 3.80–3.94 (3H, m, CH_2OH and $CHOH$), 7.21 (4H, m, ArH); δ_C 14.0 (CH_3), 22.6, 25.4, 31.8, 35.5, 37.2, 40.3 (6×CH_2), 63.3 (CH_2OH), 72.8 (CH), 126.4, 126.5, 129.9, 130.3, 137.4, 137.5 (ArC); *m/z* 218 (M^+-18, 0.3%), 136 (83), 119 (16), 118 (92), 117 (91), 115 (17), 106 (99), 105 (100), 104 (20), 103 (11), 92 (11), 91 (39), 83 (12), 79 (11), 78 (11), 77 (20), 57 (12), 55 (65), 44 (12), 43 (51), 41 (63); HRMS: M^+- [H_2O], found 218.1665. $C_{15}H_{22}O$ requires 218.1671.

4.2.5. 6-[2-(2-Hydroxyethyl)benzyl]-6-undecanol (2ai). R_f 0.52 (hexane/ethyl acetate: 2:1); ν (film) 3530–3137 (OH), 3060, 3019, 1465, 1458 (C=CH), 1046 cm^{-1} (C–O); δ_H 0.90 (6H, deformed t, *J*=6.8 Hz, 2×CH_3), 1.22–1.53 (16H, m, 2×$(CH_2)_4$), 2.20 (2H, brs, 2×OH), 2.82 (2H, s, CH_2COH), 2.98 (2H, t, *J*=6.5 Hz, CH_2CH_2OH), 3.82 (2H, t, *J*=6.5 Hz, CH_2OH), 7.15 (4H, m, ArH); δ_C 14.0 (2C, 2×CH_3), 22.6, 23.4, 32.35, 35.55, 38.9, 41.7 (10C, 10×CH_2), 63.2 (CH_2OH), 74.9 (COH), 125.8, 126.6, 129.7, 131.9, 136.1, 138.6 (ArC); *m/z* 288 (M^+-18, 2%), 171 (54), 136 (33), 129 (12), 118 (31), 117 (23), 115 (10), 106 (24), 105 (20), 97 (16), 91 (13), 83 (32), 71 (22), 69 (28), 57 (21), 55 (65), 43 (100), 41 (56); HRMS: M^+- [H_2O], found 288.2450. $C_{20}H_{32}O$ requires 288.2453.

4.2.6. 2-[2-(2-Hydroxyethyl)phenyl]-1,1-diphenyl-1-ethanol (2aj). R_f 0.38 (hexane/ethyl acetate: 2:1); ν (film) 3520–3343 (OH), 3059, 3021, 1493, 1446 (C=CH), 1042 cm^{-1} (C–O); δ_H 2.09, 3.13 (1H and 1H, respectively, 2brs, 2×OH), 2.75 (2H, t, *J*=6.4 Hz, CH_2CH_2OH), 3.71 (2H, s, CH_2C), 3.72 (2H, m, CH_2OH); 6.55 (1H, d, *J*=7.6 Hz, ArH), 6.88, 7.13, 7.27, 7.37 (1H, 2H, 6H and 4H, respectively, 4m, ArH); δ_C 35.2, 43.4 (2×CH_2), 63.3 (CH_2OH), 78.3 (COH), 125.6, 126.2, 126.6, 126.8, 127.9, 129.5, 131.6, 134.5, 138.8, 147.0 (18C, ArC); *m/z* 300 (M^+-18, 5%), 191 (12), 184 (13), 183 (96), 167 (64), 165 (12), 118 (10), 105 (100), 91 (23), 78 (10), 77 (69), 51 (19); HRMS: M^+- [H_2O], found 300.1521. $C_{22}H_{20}O$ requires 300.1514.

4.2.7. 1-(2-Hydroxymethylphenyl)-4-phenyl-2-butanol (2bc). R_f 0.31 (hexane/ethyl acetate:2:1); ν (film) 3583–3120 (OH), 3060, 3024, 1494, 1453 (C=CH), 1015 cm^{-1} (C–O); δ_H 1.90 (2H, m, CHC*H*$_2$CH$_2$), 2.64–2.86 (4H, m, C*H*$_2$CHCH$_2$C*H*$_2$), 3.52 (2H, brs, 2×OH), 3.77 (1H, m, CH), 4.43 (1H, d, *J*=11.8 Hz, HOC*H*H), 4.69 (1H, d, *J*=11.8 Hz, HOCH*H*), 7.15–7.31 (9H, m, ArH); δ_C 32.1, 39.3, 39.8 (3×CH$_2$), 63.2 (CH$_2$OH), 72.3 (CH), 125.9, 126.7, 128.4, 128.5, 130.0, 130.4, 137.9, 139.3, 141.8 (12C, ArC); *m/z* 238 (M$^+$−18, 1%), 116 (10), 105 (17), 104 (100), 91 (36), 91 (36), 77 (11); HRMS: M$^+$− [H$_2$O], found 238.1365. $C_{17}H_{18}O$ requires 238.1358.

4.2.8. 2-(2-Hydroxymethylphenyl)-1-(2-methoxyphenyl)-1-ethanol (2bd). R_f 0.30 (hexane/ethyl acetate: 2:1); ν (film) 3382–3079 (OH), 3033, 3011, 1493, 1464 (C=CH), 1059, 1007 cm^{-1} (C–O); δ_H 3.01–3.16 (2H, m, C*H*$_2$CH), 3.65 (2H, s, 2×OH), 3.89 (3H, s, OCH$_3$), 4.50 (1H, d, *J*=11.8 Hz, C*H*HOH), 4.80 (1H, d, *J*=11.8 Hz, CH*H*OH), 5.18 (1H, dd, *J*=8.9, 3.6 Hz, C*H*OH), 6.93 (1H, d, *J*=8.5 Hz, ArH), 6.99 (1H, t, *J*=7.5 Hz, ArH), 7.14–7.35 (5H, m, ArH), 7.43 (1H, dd, *J*=7.5, 1.6 Hz, ArH); δ_C 39.9 (CH$_2$), 55.3 (CH$_3$), 63.3 (CH$_2$OH), 70.9 (CH), 110.3, 120.8, 126.1, 126.8, 128.3, 128.5, 129.9, 130.6, 132.2, 138.0, 139.6, 156.0 (ArC); *m/z* 240 (M$^+$−18, 8%), 137 (25), 121 (12), 107 (145), 105 (11), 104 (100), 103 (10), 91 (13), 78 (14), 77 (19), 51 (11); HRMS: M$^+$, found 258.1256. $C_{16}H_{18}O_3$ requires 258.1256.

4.2.9. 1-(2-Hydroxymethylphenyl)-2-heptanol (2bh).[8] R_f 0.36 (hexane/ethyl acetate:2:1); ν (film) 3575–3103 (OH), 3064, 3020, 1455 (C=CH), 1019 cm^{-1} (C–O); δ_H 0.91 (3H, deformed t, *J*=6.7 Hz, CH$_3$), 1.29–1.59 (10H, m, (CH$_2$)$_4$ and 2×OH), 2.79 (2H, m, C*H*$_2$CH), 3.73 (1H, m, CH), 4.42 (1H, d, *J*=11.8 Hz, C*H*HOH), 4.70 (1H,d, *J*=11.8 Hz, CH*H*OH), 7.20, 7.27 (2H and 2H, respectively, 2m, ArH); δ_C 14.0 (CH$_3$), 22.6, 25.4, 31.8, 37.8, 39.7 (5×CH$_2$), 63.1 (CH$_2$OH), 73.1 (CH), 126.6, 128.3, 129.9, 130.3, 138.1, 139.4 (ArC); *m/z* 204 (M$^+$−18, 7%), 105 (17), 104 (100), 91 (10), 77 (10), 55 (11), 43 (11), 41 (14).

4.2.10. 6-(2-Hydroxymethylbenzyl)-6-undecanol (2bi). R_f 0.55 (hexane/ethyl acetate: 2:1); ν (film) 3545–3114 (OH), 3063, 3018, 1459 (C=CH), 1018 cm^{-1} (C–O); δ_H 0.91 (6H, deformed t, *J*=6.8 Hz, 2×CH$_3$), 1.26–1.54 (16H, m, 2×(CH$_2$)$_4$), 2.87 (2H, s, C*H*$_2$COH), 4.57 (2H, s, C*H*$_2$COH), 7.17, 7.11–7.29, 7.34 (1H, 2H and 1H, respectively, 3m, ArH); δ_C 14.1 (2C, 2×CH$_3$), 22.6, 23.4, 32.3, 39.0, 41.3 (9C, 2x(CH$_2$)$_4$ and ArC*H*$_2$C), 63.3 (CH$_2$OH), 74.5 (COH), 126.8, 127.6, 130.6, 131.9, 136.0, 140.5 (ArC); *m/z* 256 (M$^+$−36, 0.5%), 203 (16), 105 (21), 104 (100), 71 (11), 55 (23), 43 (53), 41 (28); HRMS: M$^+$− [H$_2$O]− [(CH$_2$)$_4$CH$_3$], found 203.1432. $C_{14}H_{19}O$ requires 203.1436.

4.2.11. 3-(Hydroxyphenyl)phenylmethanol (2ca).[9] R_f 0.31 (hexane/ethyl acetate: 2:1); ν (film) 3490–3238 (OH), 3087, 3025, 1451 (C=CH), 1255, 1037 cm^{-1} (C–O); δ_H 2.88 (2H, brs, 2×OH), 5.78 (1H, s, CH), 7.11–7.39 (9H, m, ArH); δ_C 79.1 (CH), 118.9, 126.5, 126.9, 127.1, 127.6, 127.9, 128.1, 128.2, 128.5, 129.7, 144.3, 152.1 (ArC); *m/z* 200 (M$^+$, 33%), 181 (16), 153 (12), 152 (10), 105 (99), 95 (72), 94 (64), 93 (18), 91 (13), 79 (36), 78 (21), 77 (100), 66 (11), 65 (41), 63 (21), 53 (15), 52 (13), 51 (45), 50 (16), 44 (18), 40 (23).

4.2.12. 1-(3-Hydroxyphenyl)-1-phenyl-1-ethanol (2cb).[10] R_f 0.38 (hexane/ethyl acetate: 2:1); ν (film) 3583–3150 (OH), 3062, 3042, 1492, 1447 (C=CH), 1267, 1235, 1067 cm^{-1} (C–O); δ_H 1.85 (3H, s, CH$_3$), 2.79 (2H, brs, 2×OH), 6.40, 6.67, 6.81, 6.91, 7.17–7.28, 7.33 (1H, 1H, 1H, 1H, 2H and 2H, respectively, 6m, ArH), 7.09 (1H, t, *J*=7.9 Hz, ArH); δ_C 30.5 (CH$_3$), 76.5 (C), 113.1, 114.1, 118.2, 125.8, 127.0, 128.1, 129.3, 147.4, 149.5, 155.6 (12C, ArC); *m/z* 214 (M$^+$, 7%), 199 (29), 196 (17), 121 (19), 105 (37), 77 (22), 65 (11), 51 (16), 43 (100).

4.2.13. 4-Hydroxyphenyl-phenylmethanol (2da). R_f 0.27 (hexane/ethyl acetate: 2:1); ν (film) 3483–3170 (OH), 3063, 3037, 1513, 1448 (C=CH), 1234, 1005 cm^{-1} (C–O); δ_H (CD$_3$OD) 2.37 (2H, brs, 2×OH), 5.76 (1H, s, CH), 6.77, 7.11–7.38 (2H and 7H, respectively, 2m, ArH); δ_C (CD$_3$OD) 75.2 (CH), 114.8, 126.1, 126.7, 127.8, 127.9, 135.1, 144.1, 155.8 (12C, ArC); *m/z* 200 (M$^+$, 25%), 199 (11), 183 (15), 182 (56), 181 (19), 154 (20), 153 (76), 152 (38), 151 (10), 128 (14), 123 (30), 122 (20), 121 (74), 96 (13), 94 (66), 93 (10), 79 (20), 78 (22), 77 (100), 76 (56), 75 (12), 74 (12), 66 (10), 65 (32), 64 (33), 63 (36), 62 (12), 55 (11), 53 (12), 52 (15), 51 (80), 50 (36); HRMS: M$^+$, found 200.0844. $C_{13}H_{12}O_2$ requires 200.0837.

4.2.14. 1-(4-Hydroxyphenyl)-1-phenyl-1-ethanol (2db).[10] R_f 0.35 (hexane/ethyl acetate: 2:1); ν (film) 3583–3130 (OH), 3060, 3044, 1490, 1445 (C=CH), 1265, 1230, 1052 cm^{-1} (C–O); δ_H 1.63 (3H, s, CH$_3$), 3.70 (2H, brs, 2×OH), 6.80, 7.13–7.49 (1H and 8H, respectively, 2m, ArH); δ_C 32.7 (CH$_3$), 77.2 (C), 114.9, 125.4, 125.7, 126.6, 128.3, 128.8, 129.6, 138.4, 155.4 (12C, ArC); *m/z* 202 (M$^+$−14, 25%), 154 (18), 153 (10), 142 (15), 141 (100), 115 (28).

Acknowledgements

The work was financially supported by the D.G.E.S. (no. PB97-0133) from the Spanish Ministerio de Educación y Cultura (M.E.C.) and Generalitat Valenciana (no. GVDOC99-2-4). I. M. P. thanks the Generalitat Valenciana for a fellowship.

References

1. For reviews, see: (a) Nájera, C.; Yus, M. *Trends Org. Chem.* **1991**, *2*, 155–181. (b) Nájera, C.; Yus, M. *Recent Dev. Org. Chem.* **1997**, *1*, 67–96. (c) Yus, M.; Foubelo, F. *Rev. Heteroatom Chem.* **1997**, *17*, 73–107.
2. For reviews, see: (a) Reetz, M. T. *Top. Curr. Chem.* **1982**, *106*, 1–54. (b) Weidmann, B.; Seebach, D. *Angew. Chem., Int. Ed. Engl.* **1983**, *22*, 31–45. (c) Seebach, D.; Beck, A. K.; Schiess, M.; Widler, L.; Wonnacott, A. *Pure Appl. Chem.* **1983**, *55*, 1807–1822. (d) Seebach, D.; Weidmann, B.; Wider, L. In *Modern Synthetic Methods*, Scheffold, R., Ed.; Salle-Sauerländer: Aarau, 1983; pp 217–353. (e) Reetz, M. T. *Organotitanium Reagents in Organic Synthesis*; Springer Verlag: Berlin, 1986. (f) See, also: Reetz, M. T. (Ed.)

Organotitanium Reagents in Organic Synthesis, *Tetrahedron* **1992**, *48*, 5557–5754.

3. (a) Almena, J.; Foubelo, F.; Yus, M. *Tetrahedron* **1995**, *51*, 3365–3374. (b) Almena, J.; Foubelo, F.; Yus, M. *Tetrahedron* **1995**, *51*, 3351–3364. (c) Guijarro, A.; Ramón, D. J.; Yus, M. *Tetrahedron* **1993**, *49*, 469–481.
4. For reviews, see: (a) Yus, M. *Chem. Soc. Rev.* **1996**, 155–161. (b) Ramón, D. J.; Yus, M. *Eur. J. Org. Chem.* **2000**, 225–237 (Microreview).
5. For a polymer supported version of the process, see: (a) Gómez, C.; Ruiz, S.; Yus, M. *Tetrahedron Lett.* **1998**, *39*, 1397–1400. (b) Gómez, C.; Ruiz, S.; Yus, M. *Tetrahedron* **1998**, *55*, 7017–7026.
6. Previous paper on this topic for our laboratory: Alonso, F.; Falvello, L. R.; Fanwick, P. E.; Lorenzo, E.; Yus, M. *Synthesis* **2000**, 949–952.
7. Ramón, D. J.; Yus, M. *Tetrahedron: Asymmetry* **1997**, *8*, 2479–2496.
8. Antionioletti, R.; Bovicelli, P.; Crescenzi, B.; Lupattelli, P. *Tetrahedron Lett.* **1998**, *39*, 6751–6752.
9. Fukui, M.; Ikeda, T.; Oishi, T. *Tetrahedron Lett.* **1982**, *23*, 1605–1608.
10. Fischer, M.; Wan, P. *J. Am. Chem. Soc.* **1999**, *121*, 4555–4562.