Tetrahedron 67 (2011) 2670–2675

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Highly regioselective control of 1,2-addition of organolithiums to α,β-unsaturated compounds promoted by lithium bromide in 2-methyltetrahydrofuran: a facile and eco-friendly access to allylic alcohols and amines

Vittorio Pace [a,b], Laura Castoldi [a,c], Pilar Hoyos [a], José Vicente Sinisterra [a,d], Massimo Pregnolato [c], José Mª Sánchez-Montero [a,*]

[a] Biotransformations group, Organic and Pharmaceutical Chemistry Department, Pharmacy Faculty, Complutense University, Pza. Ramón y Cajal s/n, 28040 Madrid, Spain
[b] Department of Drug and Natural Products Synthesis, University of Wien, Althanstrasse 14, 1090 Wien, Austria
[c] Department of Pharmaceutical Chemistry, Pharmaceutical Biocatalysis Laboratories, University of Pavia, Via Taramelli 12, 27100 Pavia, Italy
[d] Industrial Biotransformations Service, Scientific Park of Madrid, C/Santiago Grisolia 2, Tres Cantos, 28760 Madrid, Spain

ARTICLE INFO

Article history:
Received 2 December 2010
Received in revised form 14 January 2011
Accepted 24 January 2011
Available online 28 January 2011

Keywords:
Regioselectivity
Green chemistry
Organometallic reagents
Addition
Enones

ABSTRACT

Very high regioselective 1,2-addition of organolithiums to α,β-unsaturated carbonyl-like compounds (ketones, aldehydes, and imines) in the presence of LiBr was achieved by carrying out reactions in the sustainable solvent 2-methyltetrahydrofuran. Excellent yields (in isolated product) of allylic alcohols and allylic amines were recovered under a simple experimental procedure at 0 °C.

1. Introduction

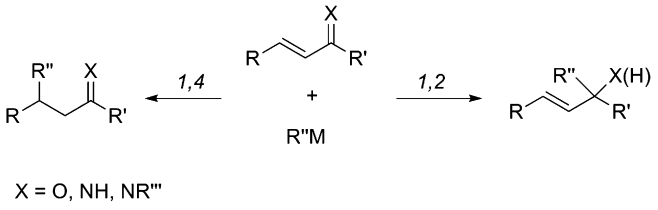
Allylic alcohols and allylic amines represent useful building blocks in organic synthesis because of their high versatility in a wide range of organic transformations including asymmetric total syntheses (e.g., cannabinoid-like compounds).[1–4] Furthermore, the importance of the hydroxyl motifs is well demonstrated by their inclusion in a plethora of biologically active structures such as the sesquiterpenes (*Z*)-α and (*Z*)-β santalol, recently isolated from *Santalum album*, active against *Helicobacter pylori* chlaritromicin resistant.[5] Analogously, the allylic aminic functionality is frequently found in a series of drugs, such as the antimicotic naftifine[6] or the calcium channel blocker flunarizine, active against peripheral vascular diseases.[7]

Considering the extreme importance of allylic alcohols, their preparation has been object of intense studies. Indeed, organic chemists have a series of protocols, among them the hydroboration of alkynes (i.e., the addition of alkenylzinc to aldehydes),[8–12] the Ni-catalyzed alkylative coupling between aldehydes and alkynes,[13,14] the carbonyl reverse prenylation from the alcohol or aldehyde oxidation level employing allenes,[15] or the Ti-catalyzed addition of vinylaluminum to carbonyls;[16] alternatively a distinct approach to allylic alcohols is based on the use of the Baylis–Hillman reaction.[17,18] Analogously, in the synthesis of allylic amines the use of transition metal (Pt,[19] Fe,[20] Pd,[21] Ru[22]) catalyzed amination of allylic compounds plays a central role.[1]

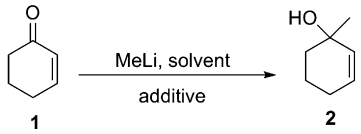
By far, the most simple approach to these structures is represented by the addition of organometallic species to opportune α,β-unsaturated carbonyl moieties, which formally is an operation of C–C bond formation. Since α,β-unsaturated carbonyl compounds may be viewed as ambient electrophiles, the reaction with an organometallic can provide two different products proceeding by the attack on the carbonyl carbon (1,2-addition) or, alternatively by the attack on the β carbon, that is, the so-called conjugate 1,4-addition.[23] (Scheme 1) For this reason, it is clear that the regioselective control that would allow the selective preparation of one of the two possible regioisomers, is the key step to achieve an effective synthetic strategy. Effectively, this control is the complex result of different kinetic and thermodynamic parameters, as well as it is strongly influenced by several factors, such as the nature of both organometallic species and substrate.[24] As a general rule, it was

* Corresponding author. Tel.: +34 91 3941820; fax: +34 91 3941822; e-mail address: jsanchez@farm.ucm.es (J.Mª Sánchez-Montero).

0040-4020/$ – see front matter © 2011 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2011.01.067



Scheme 1. Addition of organometallic species to an α,β-unsaturated carbonylic system.



Scheme 2. Addition of MeLi to cyclohexenone **1**.

demonstrated that organolithiums are by far the most popular reagents to promote 1,2-addition,[24] whereas organocuprates predominantly promotes conjugate addition.[25,26] In fact, according to Holm kinetic studies[27] on the addition of Grignard reagents to α,β-unsaturated compounds, the 1,2/1,4 ratio depends on both substrate and reagent: in particular, if the substrate assumes a *cisoid* conformation, only the 1,4-addition is observed. However, this same author notes that such theory does not explain the observed 1,4 reactivity for substrates that only adopt a *transoid* conformation (i.e., 2-cyclohexenone): thus, he rationalizes this behavior by invoking the concept of homolytic reaction mechanism, which is probably not generalizable. A different mechanistic approach proposed by Bryson[28] and Cohen[29] assumes that the regioselectivity of addition is function of the ion pair structure of the lithium reagent: thus, according to this model, contact ion pairs (CIP) with an intact C–Li association give 1,2-addition, while solvent-separated ion pairs (SIP) afford mainly the 1,4-addition products. Furthermore, an additional intriguing factor to be evaluated is the nature of the solvent and/or the presence of some additive. Hexamethylphosphoramide (HMPA) is frequently employed to accelerate organolithium reactions because its capability to coordinate the lithium cations is approximately 300 times more strongly than THF,[30] the presence (2 equiv) of such polar aprotic solvent maximizes the 1,4/1,2 ratio respect to the same reaction carried out in diethyl ether or THF.[31,32] Finally, the temperature plays a crucial role in that, cold providing mainly 1,4-additions[29] (conditions, which favors SIP formation[33]).

As a consequence of this high complexity of the regioselective control, carrying out reactions in the presence of Lewis acids seems to be a valuable strategy to maximize 1,2-adducts. In fact, the addition of Grignard reagents in the presence of catalytic amounts of $InCl_3$ affords predominantly 1,2-products.[34] However, as can be deduced by the opposite effect that the indium salt plays on different Grignard reagents, its applicability is not general. Some improvement has been detected by employing organocerium(III) reagents:[35] however, the use of this expensive lanthanide requires very low temperatures (−78 °C), thus complicating the possible scale-up process. For these reasons, it is necessary to develop synthetic procedures, with the goal of expanding the applicability on different substrates and to improve feasibility.

As a part of the development of synthetic methodologies with low ambient impact currently undergoing in our laboratory,[36–40] herein we show a simple and efficient protocol to allow an absolute1,2-regioselectivity in the addition of organolithiums to α,β-unsaturated carbonyl compounds based on the use of an additive (LiBr) in a green solvent, that is, 2-methyltetrahydrofuran at 0 °C.

2. Results and discussion

As a control reaction, we selected the addition of MeLi to 2-cyclohexenone **1**. Scheme 2 shows that the addition of LiBr is beneficial in terms of both regioselectivity and recovered yield. It must be stressed that the best results are observed when the ratio is higher than the stoichiometric, thus excluding the possibility of a catalytic pathway (Table 1, entries 1–4).

At first glance, the presence of LiBr seems to give an opposite result to the 1,4-fashion observed by Bertz and Dabbagh[41] that described an organocuprates protocol for the 1,4-addition. However, this apparent ambiguity can be explained by the different nature of organometallic species (organocuprates versus organolithiums), which can actually change the regioselectivity.

It is interesting to underline the better results obtained with LiBr compared to previously employed $CeCl_3$, which gave a 78% yield upon addition of MeLi at −78 °C.[42] Analogously, other Lewis acids afforded poor results with respect to LiBr (Table 1, entries 10–13). The solvent effect seems to be critical to the efficiency of the process, in fact, switching from normally used THF to its eco-friendly substitute 2-methyltetrahydrofuran[43,44] (MeTHF) enhances the reaction giving better results in shortest reaction time (entry 7). Diethyl ether (Table 1, entry 8) and THF (entry 9) gave lower yields respect to MeTHF (Table 1, entry 7). This effect is quite general and is also found at low temperatures (Table 1, entries 5–6). Schmalz noticed the same beneficial effect of MeTHF in promoting 1,4-addition with Grignard reagents.[45] Under optimized conditions [RLi (1.5 equiv), enone (1.0 equiv), LiBr (1.5 equiv), MeTHF, 0 °C], reactions proceeded cleanly without any side processes, such as 1,4-addition, enolization or reduction normally associated to organometallic reactions. The discovery of reactions in which the best results were obtained with the eco-friendly solvent MeTHF, it opens the interesting possibility of combining a high regioselective process with a sustainable organic synthesis. MeTHF, in fact, is a good substitute of THF for several reasons: (1) its precursor (furfural) is derived from renewable sources (corncobs or bagasse), in accordance with the seventh principle of Green Chemistry, the so-called 3*R* considerations (reduce, recycle, reuse). (2) Although this solvent does not show advantages on THF in terms of peroxides formation in the absence of stabilizers, it provides very clean organic-water phase separations with little tendency to form emulsions. Since THF is completely miscible with water, its substitution with MeTHF allows to avoid the use of other organic solvents (mainly diethyl ether) prior to quenching with water. (3) In general, organometallic reagents show improved solubility/stability profile in MeTHF compared to

Table 1
Reaction conditions screening

Entry	Additive	Solvent	Additive amount (equiv)	*T* (°C)	Reaction time (h)	Isolated yield of **2** (%)
1	–	THF	–	−78	12	70
2	LiBr	THF	0.15	−78	12	71
3	LiBr	THF	0.50	−78	9	73
4	LiBr	THF	1.00	−78	7	77
5	LiBr	THF	1.50	−20	6	79
6	LiBr	MeTHF	1.50	−20	4	93
7	LiBr	MeTHF	1.50	0	2	Quant.
8	LiBr	Et_2O	1.50	0	5	78
9	LiBr	THF	1.50	0	8	83
10	$LiClO_4$	MeTHF	1.50	0	4	85
11	LiCl	MeTHF	1.50	0	3.5	89
12	$ZnBr_2$	MeTHF	1.50	0	6	67

THF, increasing interest for the use of this solvent in organometallic reactions. (4) Although a comprehensive toxicological study is pending—and thus, MeTHF should not (yet) be regarded as 'green' solvent—it can be derived as mentioned above from biomasses and it is abiotically degraded in air.

On the basis of the shown data, it should be stressed that the best results in terms of selectivity and yields are obtained in the presence of the combined system LiBr–MeTHF. To the best of our knowledge, our protocol substantially improves previously described procedures. In fact, the addition of Grignard reagents to cyclohexenone seems to afford different results by using similar reaction conditions: Baba and co-workers reported only a modest yield (18%)[46] of **2**, while Whitwood obtained a 69% yield.[47]

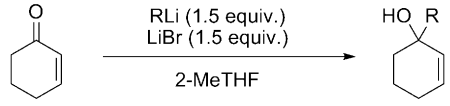
Subsequently, the protocol was tested with different organolithiums in order to expand its general applicability. As shown in Table 2, our protocol allowed to obtain excellent yields of the desired allylic alcohols **3**–**9** in short reaction times, without significant differences in the hybridization state of the carbanion, as well as the eventual presence of substituents (Table 2, entries 2–4). It is interesting to note that the highly basic *t*-BuLi requires low temperature (−20 °C) in order to add efficiently to cyclohexenone (Table 2, entries 3–4). On the contrary, less nucleophilic PhLi requires longer reaction time (Table 2, entry 5). Once again, our protocol proved to be superior to methodologies based on the use of Grignard reagents: the use of the aforementioned $InCl_3$,[34] gave a 1:1 mixture of alcohol **7** and its regioisomer derived by 1,4-addition, as well as it strikingly improve the amount of 1,4-addition products when PhMgBr or *t*-BuMgBr was used. Higher 1,2-addition selectivity was also observed with respect to previously reported *n*-BuLi addition in diethyl ether at −78 °C, which gave a poor 74% yield.[47]

By varying the nature of the α,β-unsaturated carbonyl compounds is possible to extend the applicability of the methodology to the regioselective synthesis of widely functionalized tertiary allylic alcohols. Acyclic ketone (entries 1–2) reacted efficiently without formation of byproducts as shown in Table 3. High regioselectivity (with an overall yield of 77%) has previously been achieved by employing a complex strategy based on the addition of Grignard reagents to expensive and not readily synthesized *N*-enoylsultams (Oppolzer sultams) at −78 °C[48]

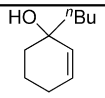
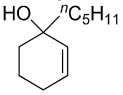
Analogously, aldehydes reacted smoothly regardless of their aromatic (Table 3, entries 3–4) or aliphatic nature (Table 3, entries 5–6): we observed better results by employing our combined LiBr–MeTHF strategy instead of simple organomagnesium reagents[49] or organolithiums added in the absence of LiBr.[50,51]

From a mechanistic point of view, the presence of LiBr favors the complexation between the Li cation and the carbonyl group of the α,β-unsaturated system. This proposed coordination would increase the positive charge in the carbon of C=O, reducing the positive charge of C-3. Even more, the R group would be very close the carbon of C=O. These effects would increase the reaction rate and the regioselectivity of the subsequent attack of the

Table 2
LiBr mediated 1,2-regioselective addition of different organolithiums in MeTHF to cyclohexenone[a]

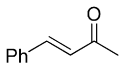
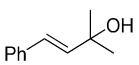
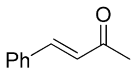
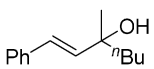
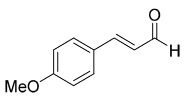
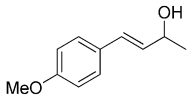
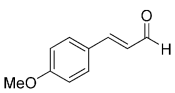
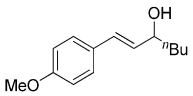
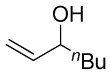
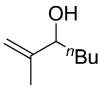


1 **3-9**

Entry	RLi	Reaction time (h) /temperature (°C)	Product	Isolated Yield (%)
1	*n*-Bu	2/0	 **3**	Quant.
2	*s*-Bu	4/0	 **4**	91
3	*t*-Bu	4/0	Complex mixture	–
4	*t*-Bu	5/−20	 **5**	86
5	Ph	7/0	 **6**	93
6	Et	2/0	 **7**	98
7	*n*-Pr	2/0	 **8**	95
8	*n*-Pentyl	2/0	 **9**	91

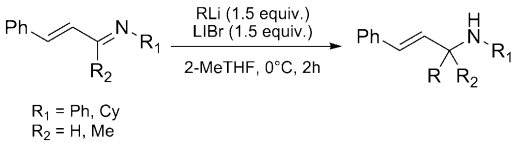
[a] Reaction conditions: substrate: RLi–LiBr (1:1.5:1.5), 2-MeTHF.

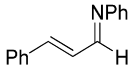
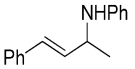
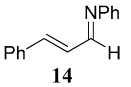
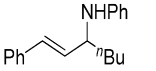
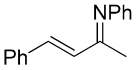
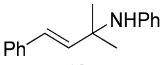
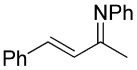
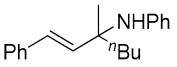
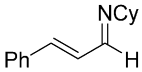
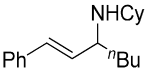
Table 3
LiBr promoted addition of organolithiums in 2-MeTHF to different α,β-unsaturated ketones and aldehydes[a]

Entry	Substrate	RLi	Product	Isolated yield (%)
1	 **10a**	Me	 **12a**	95
2	 **10b**	*n*-Bu	 **12b**	91
3	 **11a**	Me	 **13a**	97
4	 **11a**	*n*-Bu	 **13b**	92
5	 **11b**	*n*-Bu	 **13c**	88
6	 **11c**	*n*-Bu	 **13d**	94

[a] Reaction conditions: substrate: RLi–LiBr (1:1.5:1.5), 2-MeTHF, 0 °C, 2 h.

Table 4
LiBr promoted 1,2-regioselective addition of organolithiums in 2-MeTHF to different aryl and alkyl α,β-unsaturated imines[a]



Entry	Substrate	RLi	Product	Isolated yield (%)
1	 **14**	Me	 **17a**	98
2	 **14**	*n*-Bu	 **17b**	Quant.
3	 **15**	Me	 **18a**	95
4	 **15**	*n*-Bu	 **18b**	97
5	 **16**	*n*-Bu	 **19**	98

[a] Reaction conditions: substrate: RLi–LiBr (1:1.5:1.5), 2-MeTHF, 0 °C, 2 h.

organolithium. Effectively, this complexation enhances the rate of reaction with RLi since the complexed carbonyl group should be highly polarized as in other cases of acid catalysis of carbonyl compounds.

Encouraged by these results, we decided to probe the scope of our methodology for the preparation of allylic amines: in this regard, due to the poor electrophilicity of the azomethine carbon, addition of organometallics is often plagued by competitive enolization, reduction, or coupling reactions.[52] Furthermore, in the case of addition of organometallics to α,β-unsaturated imine compounds, the 1,2- and 1,4-selectivity has been shown to be dependent not only on the type of the organometallic,[53] but also on the nature of the imine.[54] Thus with such reagents, aromatic imines give predominantly 1,4-addition, while aliphatic ones give the 1,2-addition product.[55] By using our protocol (Table 4), we were able to add organolithiums in a 1,2-fashion regardless the electronic nature of the imine (aromatic or aliphatic), as well the fact that the imine is derived from a ketone or an aldehyde. Remarkably, the addition of highly basic and nucleophilic *n*-butyl lithium to *N*-cyclohexil imine (Table 4, entry 5) occurs with 1,2-regioselectivity, thus constituting a complementary technique to the use of the organolithiums in absence of LiBr that add in 1,4-fashion.[55] Furthermore, this methodology simplifies the previously $LaCl_3$-mediated 1,2-addition that requires the use of this expensive salt at low temperature,[56] thus representing a versatile procedure for the preparation of allylic amines.

3. Conclusions

In this work we show the efficiency of the binary system (LiBr–2-methyltetrahydrofuran) in promoting the additions of organolithiums to different α,β-unsaturated compounds, that allows a simple and high-yielding method for the preparation of allylic alcohols and allylic amines. This protocol allows to obtain very high 1,2-regioselectivity with no detection (^{1}H NMR) of undesired 1,4-adducts, as well contaminant products that normally affect organometallic mediated reactions. Notably, the use of the eco-friendly solvent 2-MeTHF allows to develop a green protocol, in which the addition of the organometallics takes place at not prohibitive low temperature (only 0 °C), thus constituting the bases for scale-up processes that are currently undergoing in our laboratory.

4. Experimental section

4.1. General method

All ^{1}H NMR, ^{13}C NMR, were recorded on a Bruker AC-250 spectrometer at 250 MHz and at 62.5 MHz, respectively, using a convenient deuterated solvent (reported in the characterization charts) and the residual peak as internal standard TMS in the case of CDCl3. Chemical shifts are reported in δ (ppm) referred to 1H (of residual protons) 13C of the deuterated solvents. IR absorption spectra were recorded on a Perkin–Elmer System 2000 FT-IR spectrophotometer. Compounds **1**, **10a**, **11a**, **11b**, **11c** as well all chemicals, solvents, and reagents were purchased from Sigma and were used without further purification. 2-Methyltetrahydrofuran was distilled under Na/benzophenone before use. LiBr was dried over P_2O_5. Imines **14**, **15**, and **16** were prepared according to the established procedures specified in the corresponding paragraphs.

4.2. Synthesis of imines 14, 15, and 16

*4.2.1. N-(3-Phenylallylidene)aniline (**14**).* A mixture of cinnamaldehyde (5.00 mmol, 660 mg), aniline (6.00 mmol, 559 mg), and $MgSO_4$ (5.00 mmol, 602 mg) was stirred in dried benzene (15 mL) for 1 h at room temperature. After filtration and removal of the solvent under reduced pressure, a yellow solid was obtained, which was recrystallized from methanol (767 mg, 74% yield). Mp: 107 °C (lit.[57] 106–108 °C). ^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm): 7.21 (m, 5H), 7.42 (m, 5H), 7.56 (m, 2H), 8.28 (dd, *J*=2.1, 6.5 Hz, 1H). ^{13}C NMR (62.5 MHz, $CDCl_3$) δ (ppm): 120.8, 126.3, 127.9, 129.0, 129.3, 129.4, 129.8, 134.9, 144.1, 152.0, 162.1. IR (NaCl) cm^{-1} 1630, 1598, 1572, 1486, 1445, 753, 689. Anal. Calcd for $C_{15}H_{13}N$: C, 86.92; H, 6.32; N, 6.76. Found: C, 86.74; H, 6.14; N, 6.44.

*4.2.2. N-(4-Phenylbut-3-en-2-ylidene)aniline (**15**).* A solution of 4-phenylbut-3-en-2-one (4.00 mmol, 584 mg), aniline (4.00 mmol, 372 mg), and anhydrous zinc(II) chloride (5 mol %, 27 mg) in benzene (10 mL) was refluxed for 6 h with azeotropic removal of water (Dean–Stark apparatus). Then, the catalyst was removed by filtration, the benzene was removed under reduced pressure, giving a yellow solid, which was purified by recrystallization from ethanol (65% yield, 575 mg). Mp: 107 °C (lit.[58] 106–108 °C). ^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm): 1.84 (s, 3H), 7.16–7.23 (m, 5H), 7.32–7.37 (m, 5H), 7.46–7.56 (m, 2H). ^{13}C NMR (62.5 MHz, $CDCl_3$) δ (ppm): 23.3, 120.6, 125.1, 126.6, 129.3, 129.7, 131.2, 132.0, 136.4, 143.6, 152.9, 165.0. IR (NaCl) cm^{-1} 1656, 1600, 1542, 739. Anal. Calcd for $C_{16}H_{15}N$: C, 86.84; H, 6.83; N, 6.33. Found: C, 86.49; H, 6.99; N, 6.18.

*4.2.3. N-(3-Phenylallylidene)cyclohexanamine (**16**).* A mixture of cinnamaldehyde (5.00 mmol, 660 mg), cyclohexylamine (6.00 mmol, 595 mg), and $MgSO_4$ (5.00 mmol, 602 mg) was stirred in dried benzene (15 mL) for 2 h at room temperature. After filtration and removal of the solvent under reduced pressure a colorless oil was obtained (906 mg, 85% yield). ^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm): 1.42–1.84 (m, 9H), 4.51–4.60 (m, 1H), 6.91 (m, 2H), 7.25–7.45 (m, 5H), 8.04 (m, 2H). ^{13}C NMR (62.5 MHz, $CDCl_3$) δ (ppm): 21.7, 24.2, 31.6, 65.2, 120.6, 128.1, 128.5, 130.3, 134.2,

137.8, 160.4. IR (NaCl) cm^{-1} 1622, 3081, 1598, 1562, 919. Anal. Calcd for $C_{15}H_{19}N$: C, 84.86; H, 8.98; N, 6.57. Found: C, 84.71; H, 8.69; N, 6.69.

4.3. General procedure for LiBr mediated 1,2-addition of different organolithiums in 2-MeTHF to α,β-unsaturated compounds

In a typical experiment a mixture of α,β-unsaturated compound (2.00 mmol, 1.0 equiv) and LiBr (3.00 mmol, 1.5 equiv) in freshly distilled 2-MeTHF (5 mL) was cooled at 0 °C. Organolithium reagents (3.00 mmol, 1.5 equiv) were then added drop-wise. After 2 h, reactions were quenched with saturated ammonium chloride aqueous solution (5 mL). After extraction with ethyl acetate (2×10 mL), desiccation over sodium sulfate, filtration, and solvent removal under reduced pressure, whenever necessary, the crude products were purified by liquid chromatography.

*4.3.1. 1-Methylcyclohex-2-enol (**2**).* ^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm): 1.29 (s, 3H), 1.59–1.91 (m, 7H), 5.63 (d, *J*=3.7, 4.1, 10.2 Hz, 1H), 5.70–5.74 (m, 1H, =CH). ^{13}C NMR (62.5 MHz, $CDCl_3$) δ (ppm): 19.7, 25.2, 29.4, 37.6, 67.7, 129.3, 133.9. IR (NaCl) cm^{-1} 3370, 1655. Anal. Calcd for $C_7H_{12}O$: C, 74.95; H, 10.78. Found: C, 74.76; H, 10.99.

*4.3.2. 1-n-Butylcyclohex-2-en-1-ol (**3**).* ^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm): 0.88 (t, *J*=7.2 Hz, 3H), 1.26–1.38 (m, 4H), 1.44–1.55 (m, 3H), 1.60–1.70 (m, 4H), 1.90–2.01 (m, 1H), 2.01–2.10 (m, 1H), 5.59–5.65 (m, 1H), 5.88 (ddd, *J*=3.1, 4.1, 10.2 Hz, 1H). ^{13}C NMR (62.5 MHz, $CDCl_3$) δ (ppm): 13.7, 23.7, 24.8, 35.1, 42.1, 70.4, 130.2, 132.5. IR (NaCl) cm^{-1}: 3365, 1660. Anal. Calcd for $C_{10}H_{18}O$: C, 78.87; H, 11.76. Found: C, 79.05; H, 11.93.

*4.3.3. 1-sec-Butylcyclohex-2-enol (**4**).* ^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm): 0.89 (t, *J*=7.0 Hz, 3H), 0.95 (d, *J*=6.8 Hz, 3H), 1.49 (m, 2H), 1.56–1.68 (m, 4H), 1.70 (m, 1H), 1.89–1.95 (m, 1H), 2.03–2.12 (m, 1H), 3.05 (br s, 1H), 5.56 (ddt, *J*=1.5, 2.6, 8.9 Hz, 1H), 5.81 (ddt, *J*=2.2, 4.6, 9.1 Hz, 1H). ^{13}C NMR (62.5 MHz, $CDCl_3$) δ (ppm): 16.2, 17.9, 18.4, 25.1, 25.6, 30.3, 36.8, 70.6, 131.0, 133.1. IR (NaCl) cm^{-1}: 3451, 1466, 1435. Anal. Calcd for $C_{10}H_{18}O$: C, 78.87; H, 11.76. Found: C, 79.58; H, 11.51.

*4.3.4. 1-tert-Butylcyclohexen-2-enol (**5**).* ^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm): 0.82 (s, 9H), 1.33–2.41 (m, 7H), 5.78 (d, *J*=10.3 Hz, 1H), 5.86 (ddd, *J*=1.9, *J*=10.3, 1H). ^{13}C NMR (62.5 MHz, $CDCl_3$) δ (ppm): 18.9, 25.1, 30.9, 36.8, 72.8, 129.5, 130.9. IR (NaCl) cm^{-1}: 3459, 2962. Anal. Calcd for $C_{10}H_{18}O$: C, 77.88; H, 11.74. Found: C, 77.56; H, 11.50.

*4.3.5. 1-Phenylcyclohex-2-enol (**6**).* ^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm): 1.59 (m, 1H), 1.75 (m, 1H), 1.83 (dd, *J*=12.6, 3.0 Hz, 1H), 1.98–2.20 (m, 4H), 5.72 (d, *J*=10.0 Hz, 1H), 6.02 (ddd, *J*=3.8, 4.0, 10.0 Hz, 1H), 7.18 (t, *J*=1.1, 7.2 Hz, 1H), 7.35 (t, *J*=7.9 Hz, 2H), 7.44 (d, *J*=7.9 Hz, 2H). ^{13}C NMR (62.5 MHz, $CDCl_3$) δ (ppm): 71.9, 124.9, 126.6, 128.2, 130.0, 131.8, 147.5. IR (NaCl) cm^{-1}: 3449, 2968, 1462. Anal. Calcd for $C_{12}H_{14}O$: C, 82.72; H, 8.10. Found: C, 82.49; H, 8.31.

*4.3.6. 1-Ethylcyclohex-2-enol (**7**).* ^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm): 0.85 (t, *J*=7.5 Hz, 3H), 1.48 (d, *J*=7.5 Hz, 2H), 1.61–2.23 (m, 7H), 5.59 (d, *J*=10.0 Hz, 1H), 5.66 (ddd, *J*=2.5, 4.1, 10.0 Hz, 1H). ^{13}C NMR (62.5 MHz, $CDCl_3$) δ (ppm): 18.1, 19.9, 24.6, 32.1, 33.8, 74.2, 128.4, 131.9. IR (NaCl) cm^{-1}: 3443, 3019, 2959, 2359, 2339, 2249, 1694, 1682, 1652, 1455, 1258, 1177, 1113. Anal. Calcd for $C_8H_{14}O$: C, 76.14; H, 11.18. Found: C, 76.36; H, 10.99.

*4.3.7. 1-n-Propylcyclohex-2-enol (**8**).* ^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm): 0.86 (d, *J*=7.5 Hz, 3H), 1.20–2.11 (m, 10H), 3.15 (br s, 1H), 5.56 (d, *J*=10.0 Hz, 1H), 5.73 (m, 1H). ^{13}C NMR (62.5 MHz, $CDCl_3$) δ (ppm): 13.7, 15.8, 18.1, 32.1, 34.4, 43.8, 74.2, 128.3, 132.1. IR (NaCl) cm^{-1}: 3444, 2957, 2357, 2339, 2247, 1694, 1682, 1652, 1557, 1454, 912, 731. Anal. Calcd for $C_9H_{16}O$: C, 77.09; H, 11.50. Found: C, 77.24; H, 11.35.

*4.3.8. 1-n-Pentylcyclohex-2-enol (**9**).* ^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm): 0.88 (t, *J*=7.0 Hz, 3H), 1.18–1.39 (m, 6H), 1.48–1.68 (m, 6H), 1.88–2.06 (m, 2H), 5.56 (d, *J*=9.8 Hz, 1H), 5.75 (m, 1H). ^{13}C NMR (62.5 MHz, $CDCl_3$) δ (ppm): 14.5, 19.5, 23.6, 25.6, 30.5, 32.8, 35.8, 42.7, 70.1, 130.1, 133.3. IR (NaCl) cm^{-1}: 3443, 3018, 2957, 1454. Anal. Calcd for $C_{11}H_{20}O$: C, 78.51; H, 11.98. Found: C, 78.70; H, 12.17.

*4.3.9. 2-Methyl-4-phenylbut-3-en-2-ol (**12a**).* ^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm): 1.47 (s, 6H), 2.02 (br s, 1H), 6.39 (d, *J*=16.1 Hz, 1H), 6.64 (d, *J*=16.1 Hz, 1H), 7.22–7.26 (m, 1H), 7.31–7.37 (m, 2H), 7.39 (m, 2H). ^{13}C NMR (62.5 MHz, $CDCl_3$) δ (ppm): 28.8 (×2), 70.0, 125.9, 127.4, 128.6, 128.9, 131.0, 135.8, 136.5. IR (NaCl) cm^{-1}: 3390, 3082, 1636. Anal. Calcd for $C_{11}H_{14}O$: C, 81.44; H, 8.70. Found: C, 81.20H, 8.99.

*4.3.10. 3-Methyl-1-phenylhept-1-en-3-ol (**12b**).* ^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm): 0.95 (t, *J*=7.2 Hz, 3H), 1.36–1.40 (m, 4H), 1.43 (s, 3H), 1.64 (m, 2H), 1.96 (br s, 1H), 6.33 (d, *J*=16.1 Hz, 1H), 6.63 (d, *J*=16.1 Hz, 1H), 7.24–7.46 (m, 5H). ^{13}C NMR (62.5 MHz, $CDCl_3$) δ (ppm): 13.1, 22.1, 25.2, 27.1, 41.6, 72.2, 125.3, 125.4, 125.8, 126.3, 126.4, 127.4, 135.8, 136.0. IR (NaCl) cm^{-1}: 3399, 3078, 1666, 1491, 1456, 936. Anal. Calcd for $C_{14}H_{20}O$: C, 82.30; H, 9.87. Found: C, 82.56; H, 10.05.

*4.3.11. 4-Phenylbut-3-en-2-ol (**13a**).* ^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm): 1.39 (d, *J*=6.5 Hz, 3H), 1.65 (s, 1H), 3.78 (s, 3H), 4.32 (br s, 1H), 6.11 (dd, *J*=6.5, 16.3 Hz, 1H), 6.54 (d, *J*=16.3 Hz, 1H), 6.86–7.36 (m, 4H). ^{13}C NMR (62.5 MHz, $CDCl_3$) δ (ppm): 23.9, 55.7, 69.5, 114.3, 127.9, 129.1, 129.6, 132.0, 159.5. IR (NaCl) cm^{-1}: 3389, 3074, 1660, 1484, 1442, 921. Anal. Calcd for $C_{14}H_{14}O_2$: C, 74.13; H, 7.92. Found: C, 73.90; H, 8.11.

*4.3.12. 1-Phenylhept-1-en-3-ol (**13b**).* ^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm): 0.81 (t, *J*=7.5 Hz, 3H), 1.26–1.38 (m, 4H), 1.46–1.53 (m, 1H), 2.07 (br s, 1H), 3.73 (s, 3H), 4.21–4.26 (m, 1H), 6.21 (dd, *J*=6.5, 16.2 Hz, 1H), 6.55 (d, *J*=16.2 Hz, 1H), 6.73–7.18 (m, 4H). ^{13}C NMR (62.5 MHz, $CDCl_3$) δ (ppm): 13.0, 21.6, 26.6, 36.1, 54.2, 72.2, 112.9 (×2), 126.6 (×2), 128.0, 130.1, 131.0, 153.3. IR (NaCl) cm^{-1}: 3391, 3062, 1612, 1434, 1422, 1324, 931, 716. Anal. Calcd for $C_{14}H_{20}O_2$: C, 76.33; H, 9.15. Found: C, 76.12; H, 9.36.

*4.3.13. Hept-1-en-3-ol (**13c**).* ^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm): 0.82 (t, *J*=6.9 Hz, 3H,), 1.11–1.32 (m, 6H), 1.91 (br s, 1H), 3.97 (dd, *J*=5.1, 7.2 Hz, 1H), 5.06 (dd, *J*=10.1, 17.2 Hz, 1H), 5.12 (dd, *J*=10.3, 17.2 Hz, 1H), 5.85 (ddd, *J*=6.5, 10.3, 17.0 Hz). ^{13}C NMR (62.5 MHz, $CDCl_3$) δ (ppm): 14.4, 23.0, 27.9, 37.1, 73.6, 114.9, 141.7. IR (NaCl) cm^{-1}: 3378, 3085, 1645. Anal. Calcd for $C_7H_{14}O$: C, 73.63; H, 12.36. Found: C, 73.89; H, 12.03.

*4.3.14. 2-Methylhept-1-en-3-ol (**13d**).* ^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm): 0.86 (t, *J*=7.0 Hz, 3H,), 1.13–1.31 (m, 4H), 1.46–1.52 (m, 2H), 1.74 (s, 3H), 3.99 (dd, *J*=5.0, 7.5 Hz, 1H), 4.75 (d, *J*=2.5 Hz), 4.86 (d, *J*=2.6 Hz). ^{13}C NMR (62.5 MHz, $CDCl_3$) δ (ppm): 13.0, 16.4, 21.6, 26.7, 33.6, 75.0, 109.9, 146.6. IR (NaCl) cm^{-1}: 3386, 3081, 1641, 899. Anal. Calcd for $C_8H_{16}O$: C, 74.94; H, 12.58. Found: C, 74.70; H, 12.42.

*4.3.15. N-(4-Phenylbut-3-en-2-yl)aniline (**17a**).* ^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm): 1.41 (t, *J*=7.1 Hz, 3H), 4.12–4.22 (m, 1H), 6.21 (dd, *J*=5.4, 16.0 Hz, 1H), 6.61 (d, *J*=16.0 Hz, 1H), 6.66–6.70 (m, 2H), 6.70–6.75 (m, 1H), 7.17–7.22 (m, 2H), 7.22–7.28 (m, 1H), 7.32 (dd,

J=7.0 Hz, 1H), 7.39 (m, 2H). ^{13}C NMR (62.5 MHz, $CDCl_3$) δ (ppm): 51.3, 114.0, 117.6, 125.9, 127.3, 129.0, 129.4, 129.5, 133.6, 137.8, 147.9. IR (NaCl) cm^{-1}: 3410, 2970, 1749, 1619, 1514, 1256, 975, 749, 698. Anal. Calcd for $C_{16}H_{17}$ N: C, 86.05; H, 7.67; N, 6.27. Found: C, 86.26; H, 7.48; N, 6.41.

*4.3.16. N-(1-Phenylhept-1-en-3-yl)aniline (**17b**).* ^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm): 0.84 (t, J=7.0 Hz, 3H), 1.25–1.38 (m, 4H), 1.56–1.63 (m, 2H), 3.78 (br s, 1H), 3.86–3.89 (m, 1H), 6.05 (dd, J=7.5, 17.5 Hz, 1H), 6.45–6.63 (m, 4H), 7.04–7.30 (m, 7H). ^{13}C NMR (62.5 MHz, $CDCl_3$) δ (ppm): 14.5, 23.1, 28.6, 36.5, 56.2, 113.8, 117.6, 126.8, 127.3, 128.9, 129.6, 130.5, 132.7, 137.5, 148.1. IR (NaCl) cm^{-1}: 3402, 3080, 2981, 1741, 1612, 1521, 1276, 981. Anal. Calcd for $C_{19}H_{23}$ N: C, 85.99; H, 8.74; N, 5.28. Found: C, 86.18; H, 8.48; N, 5.11.

*4.3.17. N-(2-Methyl-4-phenylbut-3-en-2-yl)aniline (**18a**).* ^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm): 1.36 (s, 6H), 3.51 (br s), 6.15 (d, J=16.8 Hz, 1H), 6.55 (d, J=16.9 Hz, 1H), 6.97–7.46 (m, 10H). ^{13}C NMR (62.5 MHz, $CDCl_3$) δ (ppm): 27.1 (×2), 59.9, 111.5, 118.0, 127.0, 128.1, 129.2, 129.4, 131.0, 133.5, 138.6, 147.9. IR (NaCl) cm^{-1}: 3409, 3086, 2990, 1731, 1616, 1534, 701. Anal. Calcd for $C_{17}H_{19}$ N: C, 86.03; H, 8.07; N, 5.90. Found: C, 86.30; H, 7.84; N, 5.66.

*4.3.18. N-(3-Methyl-1-phenylhept-1-en-3-yl)aniline (**18b**).* ^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm): 0.94 (t, J=7.1 Hz, 3H), 1.27–1.40 (m, 4H), 1.48–1.52 (m, 2H), 1.66 (s, 3H), 3.69 (br s, 1H), 6.11 (dd, J=6.4, 17.0 Hz, 1H), 6.57 (d, J=16.8 Hz, 1H), 6.62–7.36 (m, 10H). ^{13}C NMR (62.5 MHz, $CDCl_3$) δ (ppm): 14.9, 23.6, 29.4, 37.2, 63.2, 115.1, 119.0, 127.5, 127.9, 129.2, 130.9, 131.2, 131.8, 136.9, 146.8. IR (NaCl) cm^{-1}: 3414, 3079, 2984, 1736, 1623, 1542, 984, 712. Anal. Calcd for $C_{20}H_{25}$ N: C, 85.97; H, 9.02; N, 5.01. Found: C, 86.18; H, 8.84; N, 9.15.

*4.3.19. N-(1-Phenylhept-1-en-3-yl)cyclohexanamine (**19**).* ^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm): 0.86 (t, J=7.1 Hz, 3H), 1.26–1.65 (m, 16H), 2.20 (m, 1H), 3.68 (br s, 1H), 3.81–3.88 (m, 1H), 5.65 (dd, J=8.5, 15.7 Hz, 1H), 6.42 (d, J=15.7 Hz, 1H), 7.14–7.30 (m, 5H). ^{13}C NMR (62.5 MHz, $CDCl_3$) δ (ppm): 13.8, 21.4, 21.9 (×2), 25.2, 25.7, 28.0, 35.1, 36.6, 58.4, 63.2, 121.6, 129.1, 129.4, 131.7, 135.5, 138.9. IR (NaCl) cm^{-1} 3021, 2930, 2632, 1601, 1495, 1460, 1375, 1252, 1139, 1044, 975, 895, 760, 695. Anal. Calcd for $C_{19}H_{29}$ N: C, 84.07; H, 10.77; N, 5.16. Found: C, 84.41; H, 10.99; N, 5.59.

Acknowledgements

One of the authors (V.P.) thanks the Austrian Ministry of Education for an E. Mach postdoctoral grant. The present work was supported by a research Project CTQ2009-11801 of Spanish Ministry of Education and Science.

Supplementary data

Full experimental details for all compounds, as well spectral data can be founded in the Supplementary data. Supplementary data associated with this article can be found in online version at doi:10.1016/j.tet.2011.01.067.

References and notes

1. Johannsen, M.; Jorgensen, K. A. *Chem. Rev.* **1998**, *98*, 1689.
2. Jiang, H.; Holub, N.; Anker Jorgensen, K. *Proc. Natl. Acad. Sci. U.S.A.* **2010**, *107*, 20630.
3. Papahatjis, D. P.; Nikas, S. P.; Kourouli, T.; Chari, R.; Xu, W.; Pertwee, R. G.; Makriyannis, A. *J. Med. Chem.* **2003**, *46*, 3221.
4. Papahatjis, D. P.; Nahmias, V. R.; Nikas, S. P.; Andreou, T.; Alapafuja, S. O.; Tsotinis, A.; Guo, J.; Fan, P.; Makriyannis, A. *J. Med. Chem.* **2007**, *50*, 4048.
5. Ochi, T.; Shibata, H.; Higuti, T.; Kodama, K.-h.; Kusumi, T.; Takaishi, Y. *J. Nat. Prod.* **2005**, *68*, 819.
6. Kanno, H.; Taylor, R. J. K. *Tetrahedron Lett.* **2002**, *43*, 7337.
7. Marín, M. T.; Margarit, M. V.; Salcedo, G. E. *Il Farmaco* **2002**, *57*, 723.
8. Wu, H.-L.; Wu, P.-Y.; Uang, B.-J. *J. Org. Chem.* **2007**, *72*, 5935.
9. Salvi, L.; Jeon, S.-J.; Fisher, E. L.; Carroll, P. J.; Walsh, P. J. *J. Am. Chem. Soc.* **2007**, *129*, 16119.
10. Jeon, S.-J.; Fisher, E. L.; Carroll, P. J.; Walsh, P. J. *J. Am. Chem. Soc.* **2006**, *128*, 9618.
11. Chen, Y. K.; Walsh, P. J. *J. Am. Chem. Soc.* **2004**, *126*, 3702.
12. Chen, Y. K.; Lurain, A. E.; Walsh, P. J. *J. Am. Chem. Soc.* **2002**, *124*, 12225.
13. Yang, Y.; Zhu, S.-F.; Zhou, C.-Y.; Zhou, Q.-L. *J. Am. Chem. Soc.* **2008**, *130*, 14052.
14. Takai, K.; Sakamoto, S.; Isshiki, T. *Org. Lett.* **2003**, *5*, 653.
15. Han, S. B.; Kim, I. S.; Han, H.; Krische, M. J. *J. Am. Chem. Soc.* **2009**, *131*, 6916.
16. Biradar, D. B.; Gau, H.-M. *Org. Lett.* **2008**, *11*, 499.
17. Yadav, J. S.; Reddy, B. V. S.; Gupta, M. K.; Eeshwaraiah, B. *Synthesis* **2005**, 57.
18. Wei, H.-X.; Jasoni, R. L.; Hu, J.; Li, G.; Paré, P. W. *Tetrahedron* **2004**, *60*, 10233.
19. Ohshima, T.; Miyamoto, Y.; Ipposhi, J.; Nakahara, Y.; Utsunomiya, M.; Mashima, K. *J. Am. Chem. Soc.* **2009**, *131*, 14317.
20. Plietker, B. *Angew. Chem., Int. Ed.* **2006**, *45*, 6053.
21. Yan, H.; Beatty, A. M.; Fehlner, T. P. *Angew. Chem., Int. Ed.* **2001**, *40*, 4501.
22. Yi, C. S.; Yun, S. Y. *Org. Lett.* **2005**, *7*, 2181.
23. Pelmutter, P. *Tetrahedron Organic Chemistry Series*; Pergamon: Oxford, 1992; Vol. 9.
24. Sikorski, W. H.; Reich, H. J. *J. Am. Chem. Soc.* **2001**, *123*, 6527.
25. Feringa, B. L.; Badorrey, R.; Peña, D.; Harutyunyan, S. R.; Minnaard, A. J. *Proc. Natl. Acad. Sci. U.S.A.* **2004**, *101*, 5834.
26. López, F.; Minnaard, A. J.; Feringa, B. L. *Acc. Chem. Res.* **2007**, *40*, 179.
27. Holm, T. *Acta Chem. Scand.* **1991**, *45*, 925.
28. Dolak, T. M.; Bryson, T. A. *Tetrahedron Lett.* **1977**, *18*, 1961.
29. Cohen, T.; Abraham, W. D.; Myers, M. *J. Am. Chem. Soc.* **1987**, *109*, 7923.
30. Reich, H. J.; Kulicke, K. J. *J. Am. Chem. Soc.* **1996**, *118*, 273.
31. Reich, H. J.; Sikorski, W. H. *J. Org. Chem.* **1998**, *64*, 14.
32. Clark Still, W.; Mitra, A. *Tetrahedron Lett.* **1978**, *19*, 2659.
33. Esch, T. E. H.; Smid, J. *J. Am. Chem. Soc.* **1966**, *88*, 307.
34. Kelly, B. G.; Gilheany, D. G. *Tetrahedron Lett.* **2002**, *43*, 887.
35. Imamoto, T.; Kusumoto, T.; Tawarayama, Y.; Sugiura, Y.; Mita, T.; Hatanaka, Y.; Yokoyama, M. *J. Org. Chem.* **1984**, *49*, 3904.
36. Pace, V.; Martínez, F.; Fernández, M.; Sinisterra, J. V.; Alcántara, A. R. *Adv. Synth. Catal.* **2009**, *351*, 3199.
37. Pace, V.; Verniest, G.; Sinisterra, J.-V.; Alcántara, A. R.; De Kimpe, N. *J. Org. Chem.* **2010**, *75*, 5760.
38. Pace, V.; Martinez, F.; Fernandez, M.; Sinisterra, J. V.; Alcantara, A. R. *Org. Lett.* **2007**, *9*, 2661.
39. Pace, V.; Cortés-Cabrera, Á; Fernández, M.; Sinisterra, J. V.; Alcántara, A. R. *Synthesis* **2010**, 3545.
40. Pace, V.; Martínez, F.; Fernández, M.; Nova, C. I.; Sinisterra, J. V.; Alcántara, A. R. *Tetrahedron Lett.* **2009**, *50*, 3050.
41. Bertz, S. H.; Dabbagh, G. *J. Org. Chem.* **1984**, *49*, 1119.
42. Aggarwal, V. K.; Yu Fang, G. *Chem. Commun.* **2005**, 3448.
43. Aycock, D. F. *Org. Process Res. Dev.* **2007**, *11*, 156.
44. Pace, V.; Hoyos, P.; Fernandez, M.; Sinisterra, J. V.; Alcantara, A. R. *Green Chem.* **2010**, *12*, 1380.
45. Robert, T.; Velder, J.; Schmalz, H. G. *Angew. Chem., Int. Ed.* **2008**, *47*, 7718.
46. Saito, T.; Nishimoto, Y.; Yasuda, M.; Baba, A. *J. Org. Chem.* **2006**, *71*, 8516.
47. Coote, S. C.; O'Brien, P.; Whitwood, A. C. *Org. Biomol. Chem.* **2008**, *6*, 4299.
48. Cao, X.; Liu, F.; Lu, W.; Chen, G.; Yu, G.-A.; Liu, S. H. *Tetrahedron* **2008**, *64*, 5629.
49. Bassetti, M.; D'Annibale, A.; Fanfoni, A.; Minissi, F. *Org. Lett.* **2005**, *7*, 1805.
50. Chojnacka, A.; Obara, R.; Wawrzenczyk, C. *Tetrahedron: Asymmetry* **2007**, *18*, 101.
51. Katzenellenbogen, J. A.; Crumrine, A. L. *J. Am. Chem. Soc.* **1976**, *98*, 4925.
52. Bloch, R. *Chem. Rev.* **1998**, *98*, 1407.
53. Pridgen, L. N.; Mokhallalati, M. K.; Wu, M. J. *J. Org. Chem.* **1992**, *57*, 1237.
54. Inoue, I.; Shindo, M.; Koga, K.; Tomioka, K. *Tetrahedron* **1994**, *50*, 4429.
55. Tomioka, K.; Shioya, Y.; Nagaoka, Y.; Yamada, K.-i. *J. Org. Chem.* **2001**, *66*, 7051.
56. Qian, C.; Huang, T. *J. Organomet. Chem.* **1997**, *548*, 143.
57. Tomioka, K.; Shioya, Y.; Nagaoka, Y.; Yamada, K.-i. *J. Org. Chem.* **2001**, *66*, 7051.
58. Brady, W. T.; Shieh, C. H. *J. Org. Chem.* **1983**, *48*, 2499.