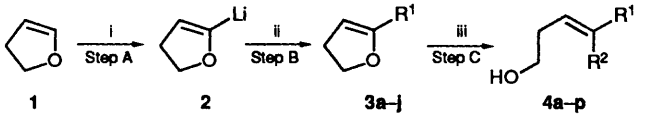
A Stereoselective Synthesis of Trisubstituted Alkenes. Part 1. Nickel-catalysed Coupling of Grignard Reagents with 5-Alkyl-2,3-dihydrofurans

Philip J. Kocieński,* Martin Pritchard, Sjoerd N. Wadman, Richard J. Whitby and Clive L. Yeates
Department of Chemistry, The University, Southampton, SO9 5NH, UK

5-Alkyl-2,3-dihydrofurans **3a–j** prepared by the alkylation of 5-lithio-2,3-dihydrofuran **2** with primary alkyl bromides and iodides, undergo Ni^0-catalysed coupling with Grignard reagents to give homoallylic alcohols. The yield and stereoselectivity depend on the structure of the Grignard reagent with the best results being obtained with long chain primary Grignard reagents and Grignard reagents lacking β-hydrogens (Me, Ph, Me_3SiCH_2). 5-(1-Hydroxyalkyl)-2,3-dihydrofurans **20** and **21** are poor substrates for the coupling reaction. Mechanisms are proposed for the coupling as well as competing reduction and isomerisation reactions.

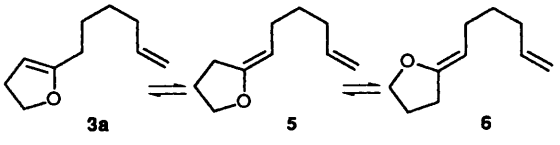
The transition metal-catalysed cross coupling of α-heteroalkenes with organometallic reagents is a highly stereoselective process in which the heterosubstituent is replaced, with retention of double bond geometry, by an alkyl, alkenyl or aryl group.[1,2] The reaction has been applied extensively to the synthesis of disubstituted alkenes; trisubstituted alkenes are less accessible because there are comparatively fewer methods for preparing the requisite heteroalkene precursors with stereocontrol.[3] Alkenyl halides are the most popular electrophilic partners in transition metal-catalysed coupling reactions but a wider range of heteroatom substituents have recently been explored. For example Julia and co-workers[4] have devised a highly stereoselective synthesis of trisubstituted alkenes that benefits greatly from the ease of preparation of the (*E*)-alkenyl sulfones which undergo efficient Ni- or Fe-catalysed cross coupling with Grignard reagents. The repertoire of α-heteroalkenes which participate readily in transition metal-catalysed cross coupling reactions has recently expanded to embrace phenylthioalkenes[5] as well as various enolate derivatives (enol phosphates, enol triflates, enol silanes).[6] We now report details[7] of a highly stereoselective synthesis of homoallylic alcohols in which cyclic α-metallated dihydrofurans are used as a^{1}d^1 reagents[8] as illustrated in Scheme 1.



Scheme 1 *Reagents and conditions:* i, Bu^{t}Li–pentane–THF, −40 to −5 °C, 1 h; ii, R^1X–pentane–THF, reflux, 2 h; iii, $[Ph_3P]_2NiCl_2$ (10 mol%), R^2MgX (2.2 equiv.), PhH–Et_2O, reflux

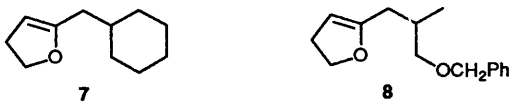
The three-step sequence involves the consecutive formation of two C–C bonds: the first by alkylation of the readily available 5-lithio-2,3-dihydrofuran **2**[9] and the second by a Ni^0-catalysed coupling of Grignard reagents with 5-alkyl-2,3-dihydrofurans **3** to give the desired homoallylic alcohols **4**. Under favourable circumstances these reactions can be run on a 100 mmol scale and afford a practical route to certain trisubstituted alkenes in which the high degree of regio- and stereo-control is a direct consequence of the rigorously defined double bond geometry of the cyclic enol ether precursor **3** and the high degree of retention of configuration in the Ni^0-catalysed coupling step. We now report the results of an extensive study of the scope and stereochemistry of the coupling reaction which was first reported by Wenkert and co-workers in 1979.[10] In the following discussion we examine in turn (a) some problems associated with the synthesis of the 5-alkyl-2,3-dihydrofuran precursors from lithiated dihydrofurans (step B); (b) the influence of Grignard structure and catalyst ligands on the rate and efficiency of the coupling (step C); and (c) the competition between coupling and substitution in the Ni^0-catalysed reaction of 5-(1-hydroxyalkyl)-2,3-dihydrofurans with Grignard reagents. In the accompanying paper we describe the results of a similar study using 6-alkyl-3,4-dihydro-2*H*-pyrans and acyclic enol ethers.

Preparation of 5-Substituted-2,3-dihydrofurans.—With the exception of the commercially available 5-methyl-2,3-dihydrofuran **3b**, all the dihydrofurans **3a** and **3c–j** used in this study were prepared in good yield (Table 1) by the alkylation of 5-lithio-2,3-dihydrofuran **2**. The resultant dihydrofurans were rather sensitive compounds which were prone to rearrangement of the double bond into the exocyclic position.[11]† The products could be stored in base-washed glassware for at least one week at −20 °C but traces of acid or prolonged heating caused rearrangement to take place. For example the dihydrofuran **3a** isomerised to an equilibrium mixture of **3a** and the exocyclic isomers **5** and **6** [eqn. (1)] in the ratio of 4:5:2, respectively, in deuteriochloroform at 20 °C in less than one hour.



(eqn. 1)

The alkylation reaction (step B, Scheme 1) was restricted to primary halides devoid of proximate branching. A substituent at C-2 of the halide thwarted displacement owing to competing elimination. Thus dihydrofurans **7** and **8** were not accessible by this route. Unfortunately attempts to suppress the basicity of the dihydrofuran **2** by converting it into the corresponding cuprate was prevented by the instability of the dihydrofuranylcuprates—a fact which can be turned to good account.[12]



Ni^0-catalysed Coupling of Grignard Reagents Lacking β-Hydrogens with 5-Substituted-2,3-dihydrofurans.—In their pion-

† Taskinen has investigated the equilibration of 2-alkylidenetetrahydrofurans and 5-alkyl-2,3-dihydrofurans and shown that an alkyl group stabilises the endocyclic isomer by about 3 kJ mol^{-1} in the gas phase but in the liquid phase the differences are less pronounced.

Table 1 Preparation of 5-substituted-2,3-dihydrofurans by the alkylation of 5-lithio-2,3-dihydrofuran **2** (Scheme 1, Step B)

Product	R^1	X	Yield (%)[a]
3a	$H_2C{=}CH{-}(CH_2)_4$	I	96
3b	Methyl	—	*b*
3c	Propyl	Br	65
3d	Pentyl	I	96
3e	$MeO(CH_2)_3$	I	82
3f	$PhCH_2O(CH_2)_3$	I	94[c]
3g	$Bu^tO(CH_2)_3$	Br	90
3h	$Bu^tMe_2SiO(CH_2)_3$	I	69
3i	Me_3Si	Cl	92
3j	Me_3Sn	Cl	83

[a] Yield of distilled product unless otherwise specified. [b] Commercially available (Aldrich). [c] Yield of product purified by column chromatography on grade 3 alumina eluting with Et_2O–hexane (1:5).

eering work on the Ni^0-catalysed coupling reaction of Grignard reagents with enol and phenol ethers, Wenkert and his associates examined a wide range of reaction parameters and noted that, in general, the reactions were sluggish and in many cases double bond isomers were obtained.[10] The formation of isomeric mixtures seemed surprising and unpredictable and we felt that a re-examination of the reaction might be worthwhile. In the event, we found that dihydrofurans were highly reactive substrates providing good yields and excellent stereoselectivity in most cases. The coupling reaction is easy to do and requires no special apparatus or cumbersome handling conditions. In a typical procedure MeMgBr in Et_2O (0.2 equiv.) is added at room temperature to a suspension of $(Ph_3P)_2NiCl_2$ (0.1 equiv.) in benzene to give the thermally unstable $(Ph_3P)_2NiMe_2$ which expels ethane to give an active, red Ni^0 catalyst. After 15 min, the appropriate Grignard reagent in Et_2O (2 equiv.) is added and the mixture concentrated under reduced pressure to about one fifth of its original volume whereupon benzene or toluene and the dihydrofuran (1 equiv.) are added and the mixture heated at reflux until the starting dihydrofuran is consumed (20 min to 24 h).

It became clear at an early stage that there were marked differences between the reactions of Grignard reagents not bearing β-hydrogens and the reactions of those that did: generally the former reacted faster and more cleanly than the latter. The figures compiled in Table 2 concern the coupling reactions of Grignard reagents lacking β-hydrogens, and from these results it may be seen that under optimal conditions, homoallylic alcohols **4a–4p** were obtained in good yields and excellent stereoselectivity.

The importance of a number of variables was examined and some of our observations are listed below:

(1) Various Ni^{II} salts could be used as precursors for catalytically active species, and these included $(Ph_3P)_2NiCl_2$, $(dppp)NiCl_2$,[13] $(dppe)NiCl_2$,[14] $(dmpe)NiCl_2$[15] and $(dppf)NiCl_2$.[15] Nickel acetylacetonate and $(Ph_3P)_4Pd^0$ were ineffective. The cheapest catalyst precursor, $(Ph_3P)_2NiCl_2$, was usually the most satisfactory both in terms of rate and yield. Stereoselectivity did not depend on the nature of the nickel catalyst. Reactions using $(dppf)NiCl_2$ or $(dmpe)NiCl_2$ as catalyst precursors gave the coupling products very cleanly, so that purification by chromatography was not required prior to distillation. However, the expense of the required ligands made the routine use of these salts unattractive. When Ph_3P, dppp and dppe ligands were used, the homoallylic alcohols had to be purified by column chromatography because they were contaminated with substantial amounts of biphenyl derived from competing cross-coupling with the phosphine ligands.[17]

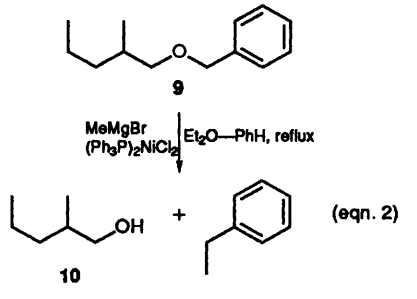
(2) The reactions were usually carried out in refluxing benzene because the ethereal solvents in which the Grignard reagents were prepared caused a marked decrease in rate and yield of the coupling reactions, and it was beneficial to concentrate the mixture containing the reduced nickel species to a fifth of the original volume and then reconstitute the solvent with neat benzene prior to introduction of the dihydrofuran. The final solvent composition (*ca.* 1:5 Et_2O–benzene) did not affect the catalyst adversely; moreover, with an especially reactive combination such as MeMgBr and dihydrofuran **3a**, the reaction could be carried out in neat Et_2O.

The presence of oxygen-substituents on the side chain of the dihydrofuran substrate also depressed the rate of coupling even with MeMgBr (Table 2, entries 11–14). However, the *tert*-butyl ether **3g** suffered only a slight diminution in rate (Table 2, entry 14) presumably because the bulky ether is a poor ligand and therefore does not deactivate the Ni catalyst to the same extent as methoxy or benzyloxy.

(3) In refluxing benzene the reactions of Me_3SiCH_2MgCl with dihydrofurans finished within 1.5 h, but the isomeric purity of the coupling products was variable. When these reactions were carried out at room temperature, much greater selectivity was observed (Table 2, entries 4 and 10). Similarly, allyl- and cinnamyl-magnesium bromides gave isomeric mixtures resulting from subsequent isomerisation of the initial coupling product but attempts to suppress isomerisation by carrying out the reactions at room temperature simply resulted in no reaction.

(4) The Ni^0-catalysed coupling of organometallic reagents to dihydrofurans was limited to Grignard reagents and dialkylmagnesiums. Attempts to accomplish similar couplings with reagents such as organolithiums, Me_3Al, Et_2Zn or EtZnCl failed.

(5) The use of reactive organometallic reagents both in the formation and ring opening of the dihydrofurans precluded the presence of most functional groups, but we found that suitably protected hydroxy groups could be carried through the sequence. While methyl- and *tert*-butyl ethers were unaffected in the ring opening reactions, silyl and benzyl ethers were cleaved at elevated temperatures. The instability of silyl ethers was not unexpected, but we were surprised by the cleavage of benzyl ethers. The occurrence of this process was confirmed by subjecting benzyl ether **9** to the usual reaction conditions, to give alcohol **10** and ethylbenzene [eqn. (2)], albeit in low conversion. No cleavage occurred in the absence of Ni^0 and the reaction would appear to be similar to the well-known Felkin reaction of allylic alcohols and ethers.[16]

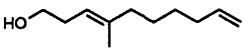
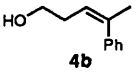
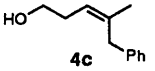
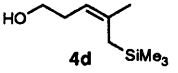
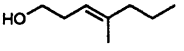
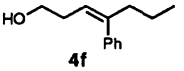
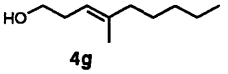
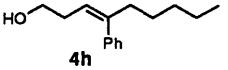
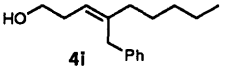
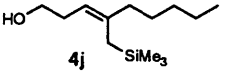
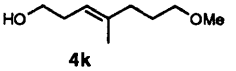
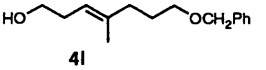
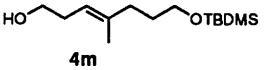
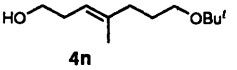
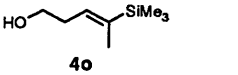
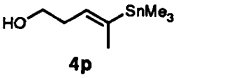


(eqn. 2)

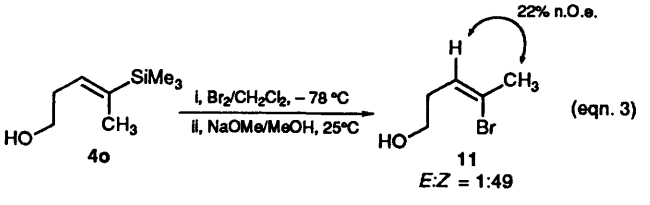
α-Silyl- or α-stannyl enol ethers are readily available from lithiated enol ethers,[17] and their participation in a Ni^0-catalysed coupling would provide easy access to the chemically versatile vinyl silanes and vinyl stannanes. We found that α-silyl- or α-stannyl-dihydrofurans **3i** and **3j** were less reactive than the related α-alkyl derivatives, and ring opening was observed only when using MeMgBr (Table 2, entries 15 and 16). Furthermore, the silyl derivative **3i** reacted faster and more efficiently than the tin congener and it provided the coupling product **4o** with higher stereoselectivity.

In order to prove the stereochemistry of **4o**, it was converted into the isomerically pure vinyl bromide **11** [eqn. (3)]. The

Table 2 Nickel-catalysed coupling of dihydrofurans with Grignard reagents lacking β-hydrogens

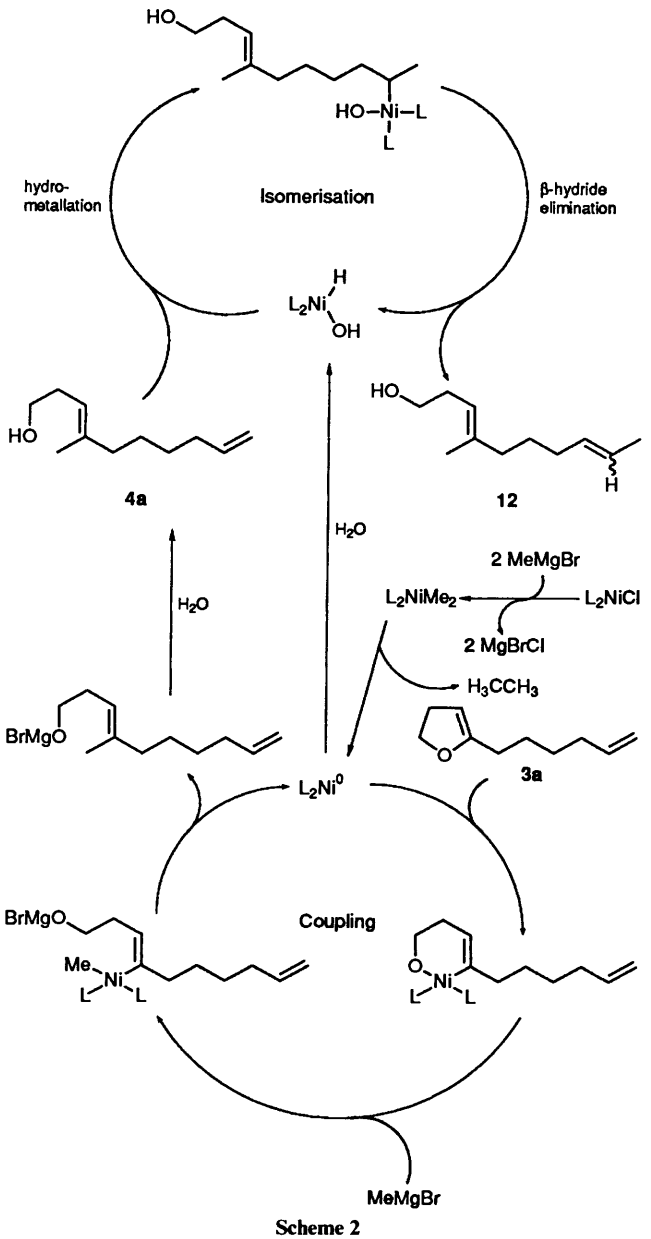
Entry	R^1	R^2	Catalyst[a,b]	Reaction time (h)	Product	Yield[d] (%)	Isomeric purity (%)[e]
1	$(CH_2)_4CH{=}CH_2$	Me	A	0.75	 **4a**	96	99
2	Me	Ph	A	0.33	 **4b**	85	96
3	Me	$PhCH_2$	A	1	 **4c**	91	>95[f]
4	Me	Me_3SiCH_2[c]	B	24	 **4d**	85	94
5	Propyl	Me	A	0.33	 **4e**	79	98
6	Propyl	Ph	A	0.33	 **4f**	85	>95[f]
7	Pentyl	Me	A	0.33	 **4g**	92	99
8	Pentyl	Ph	A	0.33	 **4h**	92	94
9	Pentyl	$PhCH_2$	A	1	 **4i**	79	>95[f]
10	Pentyl	Me_3SiCH_2[c]	B	36	 **4j**	77	>95[f]
11	$(CH_2)_3OMe$	Me	A	24	 **4k**	80	95
12	$(CH_2)_3OCH_2Ph$	Me	A	24	 **4l**	66	97
13	$(CH_2)_3OSiMe_2Bu^t$	Me	A	24	 **4m**	73	97
14	$(CH_2)_3OBu^t$	Me	A	0.66	 **4n**	82	98
15	$SiMe_3$	Me	A	1.5	 **4o**	97	98
16	$SnMe_3$	Me	A	4.5	 **4p**	62	90

[a] Catalyst A = $(Ph_3P)NiCl_2$; B = $(dppp)NiCl_2$. [b] Reaction run in refluxing Et_2O–PhH(1:5) unless otherwise specified. [c] Reaction run at room temperature. [d] Yields determined on samples purified by column chromatography and distillation. [e] Determined by capillary gas chromatography unless otherwise specified. [f] Determined by NMR spectroscopy at 270 MHz.



(eqn. 3)

proximity of 3-H and 5-H in the vinyl bromide **11** was confirmed by measurement of a strong nuclear Overhauser enhancement (22%) between these two nuclei, establishing the geometry of vinyl bromide **11** as drawn. Since the conversion of vinyl silanes into vinyl bromides occurs with complete inversion,[18] vinylsilane **4o** must have formed with retention of configuration in the coupling reaction.

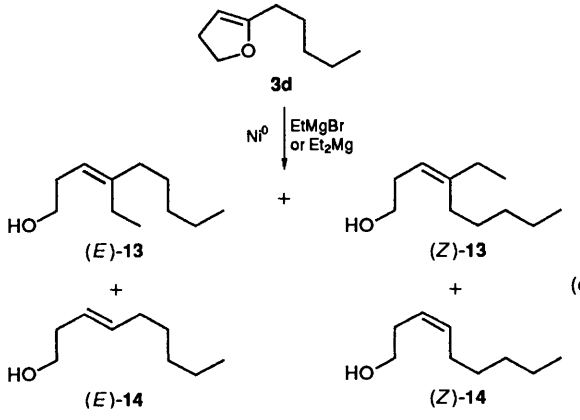


Scheme 2

The transformation **3a** ⟶ **4a** (Scheme 1) using the conditions described by Wenkert and co-workers[10] illustrates a problem which can occur when the side chain of the dihydrofuran bears a double bond. Early experiments indicated that the reaction gave a high yield of **4a** but attempts to scale the reaction up led to complex mixtures of products which included substantial amounts of isomeric dienes **12** (Scheme 2) in which the terminal alkene had rearranged one carbon into the chain (*E*- and *Z*-isomers). It was subsequently found that the formation of the isomeric products was strongly dependent on the method of work-up. If the aqueous quench was slow or stirring inefficient, the dienes **12** accounted for as much as 80% of the reaction mixture. However, if the reaction mixture was quenched by addition to a rapidly stirred solution of aqueous ammonium chloride the compound **4a** was obtained in 96% yield with greater than 99% (*E*)-stereoselectivity. These experiments suggest that a nickel hydride catalyst is generated on addition of water which can rapidly and efficiently isomerise double bonds by a reversible hydrometallation–elimination and that this same catalyst can be destroyed by excess water before it can do any damage by the simple expedient of rapid and efficient stirring in the work-up. One possible mechanism which accounts for the coupling and the isomerisation reactions is outlined in Scheme 2. It is noteworthy that the trisubstituted double bond was not affected by the putative nickel hydride catalyst under these conditions.

The critical importance of work-up procedure and some indication of the potential synthetic utility of the putative nickel hydride catalyst for the isomerisation of alkenes was confirmed in the following experiment. Reaction of 0.1 equiv. of $(Ph_3P)_2NiCl_2$ in benzene with 3 equiv. of MeMgBr in Et_2O followed by rotary evaporation of the solvent left a dark residue containing the Ni^0 catalyst. The residue was taken up in benzene and 1 equiv. of undec-10-en-1-ol was added and the mixture stirred at room temperature for 15 min. An aliquot was removed by syringe and quenched by addition to rapidly stirred aqueous ammonium chloride. Gas chromatography and NMR analysis of the crude reaction mixture showed clean recovery of starting material. The remainder was quenched by the slow addition of water to the stirred reaction mixture. Gas chromatography and ^{13}C NMR analysis now showed a mixture of three principal components: recovered undec-10-en-1-ol (5%) and approximately 90% of a 2:1 mixture of (*E*)- and (*Z*)-undec-9-en-1-ol. In addition the ^{13}C NMR spectrum showed minor amounts of other, presumably isomeric, components. These results indicate that the stereochemical variability reported previously[10] may have been caused in part by isomerisation during workup.

Ni^0-Catalysed Coupling of Grignard Reagents Bearing β-Hydrogens with 5-Substituted-2,3-dihydrofurans.—The Ni^0-catalysed coupling reactions of dihydrofurans with Grignard reagents bearing β-hydrogens were generally much slower, less stereoselective, and complicated by competing reduction. The results depended strongly on the length of the carbon chain in the Grignard reagent and the ligands on the Ni catalyst. Using 5-pentyl-2,3-dihydrofuran **3d** as the substrate we examined the coupling reactions of EtMgBr and Et_2Mg [eqn. (4)] since these were consistently the least selective of the Grignard reagents examined. The ratio of the isomeric coupling and reduction products (*E,Z*)-**13** and (*E,Z*)-**14** were ascertained by capillary gas chromatography or by NMR spectroscopy and their identity confirmed by comparison with authentic samples prepared as described in the Experimental section. As can be seen from the results summarised in Table 3, the ratio of coupling to reduction depended on the nature of the phosphine ligands, and the trends observed followed those established for transition metal-catalysed reactions of vinyl and aryl halides.[15] In the worst case involving Et_2Mg as the nucleophile, Ph_3P ligands gave nearly complete reduction in a reaction which proceeded over 20 h and gave poor yields (41%) whereas 1,2-bis(diphenylphosphino)ethane (dppe), 1,1-bis(diphenylphosphino)propane (dppp), and 1,1-bis(dimethylphosphino)ethane (dmpe) gave coupling and reduction products in roughly equal



(eqn. 4)

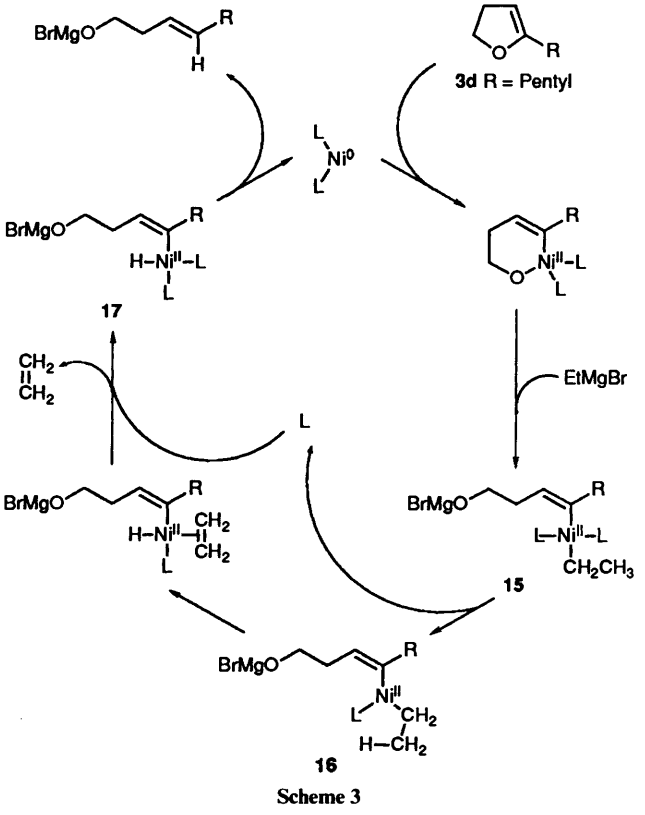
Table 3 Influence of ligands on the Ni^0-catalysed coupling of 5-pentyl-2,3-dihydrofuran **3d** with Et_2Mg and EgMgBr

Entry	Organomagnesium reagent	Catalyst precursor	Reaction time (h)	Yield (%)[a]	(*E*,*Z*)-**13**: (*E*,*Z*)-**14**	Coupling products (*E*)-**13**	Coupling products (*Z*)-**13**	Reduction products (*E*)-**14**	Reduction products (*Z*)-**14**
1	Et_2Mg	$(Ph_3P)_2NiCl_2$	20	41	1:49	1	1	87	11
2	Et_2Mg	(dppp)$NiCl_2$	20	64	1:0.8	52	4	30	14
3	Et_2Mg	(dppe)$NiCl_2$	20	61	1:0.8	34	26	21	19
4	Et_2Mg	(dppf)$NiCl_2$	2	81	1:2.5	25	4	63	8
5	Et_2Mg	(dmpe)$NiCl_2$	6	82	1:1	45	5	47	3
6	EgMgBr	(dppf)$NiCl_2$	4.5	80	3:2	—	—	—	—
7	EtMgBr	(dppp)$NiCl_2$	26	79	3:1	—	—	—	—
8	EtMgBr	(dppe)$NiCl_2$	28	80	5:1	—	—	—	—

[a] Yield refers to the combined yield of reduction and coupling products. The relative proportion of the products was determined by capillary gas chromatography.

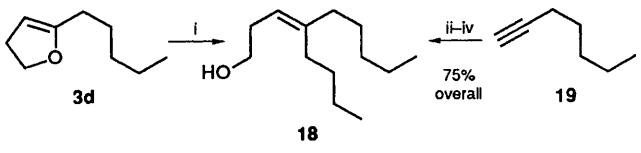
proportion. Much better ratios of coupling to reduction were observed when EtMgBr was used as the nucleophile.

A possible mechanism for the reduction is shown in Scheme 3. β-Hydride elimination is thought to be preceded by formation of a coordinatively unsaturated species **16**,[19] and the rate of elimination can be related to the thermal stability of the dialkylnickel species **15**. The relatively low thermal stability of **15** where the ligand is monodentate (*i.e.* Ph_3P) should result in facile β-hydride elimination, and consequently a large amount of reduction was observed (Table 3, entry 1). A further consequence of the β-hydride elimination pathway is the isomerisation of both the reduction and coupling products caused by the presence of nickel hydride complexes **17**, which can undergo reversible addition–elimination reactions with alkenes.[20] The gradual improvement in the ratio of coupling to reduction when EtMgBr was used as the nucleophile can also be explained in terms of catalyst stability (Table 3, entries 6–8): the relative stabilities of the corresponding platinum complexes have been measured[21] and follow the order (dppe) > (dppp) > (dppf).



Scheme 3

Two further aspects of the results presented in Table 3 merit comment. First, Grignard reagents bearing β-hydrogens appeared to react at roughly the same initial rates as observed for the corresponding reactions of Grignard reagents lacking β-hydrogens, but the complete consumption of the enol ether generally required much longer reaction times in the former case. This decreasing reaction rate (as indicated by gas chromatography) could result from gradual destruction of the catalyst during the reaction. Although addition of further amounts of Ni^0 catalyst did result in increased yields in some cases, a return to the initial reaction rate was never achieved. Secondly, β-hydride elimination and the consequent competing reduction process was not a problem as the length of the carbon chain in the Grignard reagent increased. For example, reaction of BuMgBr with 5-pentyl-2,3-dihydrofuran **3d** (Scheme 4) required only 2 h and gave exclusively the coupled product **18** whose stereochemistry was proven by independent synthesis *via* carbocupration of hept-1-yne. Indeed, Wenkert also observed a surprising selectivity in the reactions of longer chain primary alkyl Grignard reagents, and applied the reaction in the syntheses of several insect pheromones.[10b] It could be that in these cases β-hydride elimination, a process that requires precise coplanarity of four nuclei in the transition state,[22] is impaired by steric interactions, but the nature of these is not clear.

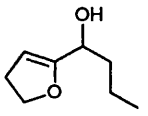
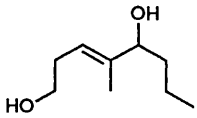
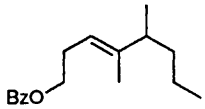
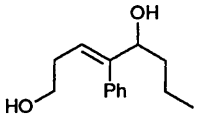
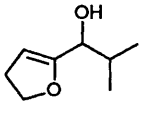
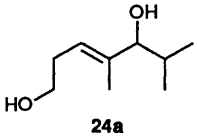
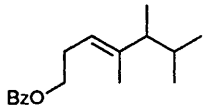
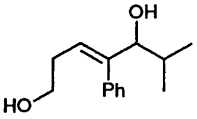


Scheme 4 *Reagents and conditions:* i, BuMgBr, Ni^0, Et_2O–PhH (5:1), reflux, 2 h, 82%; ii, BuCu·$MgBr_2$, Et_2O–Me_2S; iii, pentynyllithium; iv, oxirane

Ni^0-*Catalysed Coupling of Grignard Reagents with* 5-(1-*Hydroxyalkyl*)-2,3-*dihydrofurans*.—5-(1-Hydroxyalkyl)-2,3-dihydrofurans can undergo two different Ni^0-catalysed reactions with Grignard reagents: coupling with the enol ether moiety or displacement of the allylic hydroxy function.[16] In an attempt to establish whether either of these reactions was selective under appropriate conditions, we examined the reaction of **20** and **21** with MeMgBr and PhMgBr using $(Ph_3P)_2NiCl_2$ as the catalyst. It is clear from the low yields recorded in Table 4 that 5-(1-hydroxyalkyl)-2,3-dihydrofurans were poor substrates for the coupling reaction: the reactions were messier and much slower (24–30 h) than the corresponding reactions of dihydrofurans with simple hydrocarbon side chains.

With dihydrofurans **20** and **21** and MeMgBr the products **23** and **25** resulting from both coupling and displacement were obtained along with the desired coupling products **22a** and **24a** and such was the complexity of the product mixture that **23** and **25** could only be isolated as benzoate esters by HPLC. PhMgBr gave coupling products **22b** and **24b** but no displacement products. In all cases many minor unidentified products were

Table 4 Ni^0-Catalysed coupling of Grignard reagents with 5-(1-hydroxy-1-alkyl)-2,3-dihydrofurans

Dihydrofuran	Grignard reagent	Coupling product (yield, %)	Coupling/Substitution product (yield, %)
 **20**	MeMgBr	 **22a** (13)	 **23** (35)
	PhMgBr	 **22b** (35)	
 **21**	MeMgBr	 **24a** (29)	 **25** (16)
	PhMgBr	 **24b** (44)	

obtained including conjugated dienes resulting from formal dehydration of the resultant allylic alcohols and attempts to improve the efficiency and selectivity of the reactions by varying catalyst, reaction time, and temperature were to no avail. Similarly, protection of the hydroxy function in the dihydrofuran precursors **20** and **21** as the methyl or *tert*-butyldimethylsilyl ethers was fruitless.

In conclusion we have shown that dihydrofurans show exceptional reactivity in Ni^0-catalysed coupling with Grignard reagents and the synthetic value of the reaction largely depends on the structure of the Grignard reagent. In favourable cases (methyl, phenyl, benzyl, trimethylsilylmethyl and butyl) the coupling reactions were generally efficient and stereoselective; but there are numerous examples of Grignard reagents (ethyl, propyl, secondary alkyl, allyl and vinyl) whose coupling reactions were messy. Coupling of dihydrofurans with MeMgBr is an especially attractive method for the stereoselective synthesis of trisubstituted homoallylic alcohols in the terpene series[23,24] because it works well on at least a 100 mmol scale, does not require finicky control of temperature, and utilises cheap reagents. It would appear to have some advantages over popular current methods based on carbometallation of terminal alkynes which are often not generally suited to large scale work.[25] The principal disadvantage is the relative lability of the dihydrofurans as the heteroalkene precursor.

Experimental

Column chromatography was carried out on silica gel 60 (0.04–0.063 mm) with the eluent specified in parenthesis. All reactions requiring anhydrous conditions were conducted in a flame-dried apparatus under a static atmosphere of dry argon or nitrogen. Organic extracts were dried over $MgSO_4$ unless otherwise specified and evaporated at aspirator pressure on a rotary evaporator. Distillations in which the bath temperature is recorded were performed with a Kugelrohr apparatus. Grignard reagents were standardised by total base titration using Methyl Red as indicator and organolithium reagents were titrated in THF (tetrahydrofuran) under argon against 1,3-diphenylacetone toluene-*p*-sulfonylhydrazone.

^1H NMR spectra were recorded in $CDCl_3$ unless otherwise specified. Chemical shifts are reported in ppm relative to Me_4Si (δ 0.00) as an internal standard except in the case of silicon and tin compounds whose chemical shifts are quoted relative to $CHCl_3$ (δ 7.27). ^{13}C NMR spectra are quoted relative to $CDCl_3$ (δ 77.1) as an internal standard for silicon and tin compounds and Me_4Si (δ 0.00) otherwise. C–H coupling was analysed using the Distortionless Enhancement by Polarisation Transfer (DEPT) spectral editing technique with second pulses at 90° and 135°. Coupling is abbreviated s (no C–H coupling), d (CH), t (CH_2) and q (CH_3). *J* Values are given in Hz. Peak intensities in the IR spectra are defined as strong (s), medium (m) or weak (w). Accurate mass determinations and low resolution mass spectra were made on distilled compounds estimated to at least 95% pure by NMR spectroscopy and thin layer or gas chromatography. High resolution gas chromatography was performed on a Packard 436 capillary gas chromatography fitted with 220μ columns coated with CP Wax 52 or CP Sil 5.

5-*Hex*-5-*en*-1-*yl*-2,3-*dihydrofuran* **3a**.—A solution of *tert*-butyllithium in pentane (1.8 mol dm^{-3}; 117 cm^3, 0.21 mol) was added dropwise to a stirred solution of 2,3-dihydrofuran (17.3 g, 0.25 mol) in THF (50 cm^3) at a rate sufficient to maintain the internal temperature below −40 °C. A yellow precipitate formed which dissolved on slowly warming over 1 h to −5 °C to give a colourless solution. The mixture was cooled to −20 °C and 1-iodohex-5-ene (36.8 g, 0.175 mol) added over 10 min. The cooling bath was removed and the mixture allowed to warm to room temperature whereupon it was refluxed for 2 h, cooled to 0 °C and then poured slowly with vigorous stirring into saturated aqueous ammonium chloride (250 cm^3). The organic phase was diluted with Et_2O (250 cm^3) and washed with

aqueous $Na_2S_2O_3$ (20 cm^3) and brine (2 × 100 cm^3) before drying (Na_2SO_4) and rotary evaporation gave a residue which was rapidly distilled (Kugelrohr) using glassware which had been washed with aqueous NaOH (2 mol dm^{-3}) and water and dried overnight at 150 °C. The *title compound* (25.6 g, 0.168 mol, 96%) was obtained as a fragrant, colourless oil: b.p. 85 °C (bath)/20 mmHg; ν_{max}(film)/cm^{-1} 3080m, 2940s, 2865s, 1670m, 1640m and 930; δ_H(360 MHz) 5.81 (1 H, ddt, *J* 17.1, 10.3, 6.7), 5.01 (1 H, dq, *J* 17.1, 1.8), 4.95 (1 H, d, with fine splitting, *J* 10.3), 4.58 (1 H, br s), 4.30 (2 H, t, *J* 9.4), 2.60 (2 H, tq, *J* 9.2, 2.0), 2.0–2.1 (4 H, m) and 1.3–1.6 (4 H, m) (Found: M^+ 152.1197. $C_{10}H_{16}O$ requires *M*, 152.120 13). By similar procedures the dihydrofurans **3c–h** were prepared in the yields given in Table 1.

5-*Propyl*-2,3-*dihydrofuran* **3c**. B.p. 70 °C (bath)/20 mmHg; ν_{max}(CCl_4)/cm^{-1} 2980s, 2880s, 1670s, 1180s, 1050s and 940s; δ_H(60 MHz) 4.4 (1 H, t, *J* 2), 4.2 (2 H, t, *J* 6), 2.5 (2 H, m), 2.1–1.3 (4 H, m) and 1.0 (3 H, t) (Found: M^+ 112.0893. $C_7H_{12}O$ requires *M*, 112.088 82).

5-*Pentyl*-2,3-*dihydrofuran* **3d**. B.p. 70 °C (bath)/20 mmHg; ν_{max}(CCl_4)/cm^{-1} 2980s, 2880s, 1670s, 1180s, 1050s and 940s; δ_H(270 MHz) 4.57 (1 H, tt, *J* 2.3, *J'* 1.1), 4.31 (2 H, t, *J* 9.3), 2.60 (2 H, tq, *J* 9.3, *J'* 1.9), 2.09 (2 H, tq, *J* 7.4, *J'* 1.5), 1.50 (2 H, m), 1.3 (4 H, m) and 0.89 (3 H, t, *J* 6.8); δ_C(67.9 MHz), 159.14 (s), 93.34 (d), 69.69 (t), 31.64 (t), 30.08 (t), 27.94 (t), 26.50 (t), 22.54 (t) and 14.00 (q) (Found: M^+ 140.1201. $C_9H_{16}O$ requires *M*, 140.120 13).

5-(3-*Methoxypropyl*)-2,3-*dihydrofuran* **3e**. B.p. 90 °C (bath)/20 mmHg; ν_{max}(film)/cm^{-1} 2950s, 2880s, 1670s, 1190s, 1170s, 1130s and 930s; δ_H(360 MHz; CCl_4) 4.50 (1 H, s with fine splitting), 4.22 (2 H, t, *J* 9.2), 3.28 (2 H, t, *J* 6.2), 3.22 (3 H, s), 2.57 (2 H, t with fine splitting, *J* 9.2), 2.20 (2 H, apparent q with fine splitting, *J* 6.9) and 1.92 (2 H, m); δ_C(90 MHz) 158.5 (s), 95.0 (d), 75.7 (t), 72.5 (t), 60.9 (q), 33.2 (t), 30.0 (t) and 28.3 (t) (Found: M^+ 142.0990. $C_8H_{14}O_2$ requires *M*, 142.099 39).

5-(3-*Benzyloxypropyl*)-2,3-*dihydrofuran* **3f**. ν_{max}(film)/cm^{-1} 2940s, 2870s, 1670s, 1100s and 700s; δ_H(360 MHz; CCl_4) 7.42–7.20 (5 H, m), 4.62 (1 H, s with fine splitting), 4.56 (2 H, s), 4.34 (2 H, t, *J* 9.4), 3.54 (2 H, t, *J* 6.2), 2.66 (2 H, t with fine splitting, *J* 7.5), 2.30 (2 H, t with fine splitting, *J* 6.3) and 1.88 (2 H, tt, *J* 7.2, *J'* 6.2); δ_C(90 MHz; CCl_4) 159.09 (s), 139.15 (s), 128.28 (d), 127.52 (d), 127.36 (d), 93.49 (d), 72.89 (t), 69.64 (t), 69.57 (t), 30.34 (t), 27.30 (t) and 24.93 (t). A satisfactory HRMS was not obtained for this compound.

5-(3-tert-*Butoxypropyl*)-2,3-*dihydrofuran* **3g**. B.p. 110 °C (bath)/20 mmHg; ν_{max}(film)/cm^{-1} 2950s, 2880s, 1670s, 1190s, 1170s, 1130s and 930s; δ_H(270 MHz; [$^2H_6$]-acetone) 4.62 (1 H, s with fine splitting), 4.28 (2 H, t, *J* 6.5), 3.28 (2 H, t, *J* 6.8), 2.37 (2 H, tq, *J* 1.2, 7.4), 2.07 (2 H, m), 1.65–1.58 (2 H, m) and 1.14 (9 H, s); δ_C(67.5 MHz; [$^2H_6$]-acetone) 158.6 (s), 93.7 (d), 72.5 (t), 69.8 (t), 60.9 (t), 30.1 (t), 29.9 (t), 28.9 (t) and 27.6 (q) (Found: M^+ 184.1466. $C_{11}H_{20}O_2$ requires *M*, 184.14635).

5-(3-tert-*Butyldimethylsilyloxypropyl*)-2,3-*dihydrofuran* **3h**. B.p. 130 °C (bath)/1 mmHg; ν_{max}(film)/cm^{-1} 2990s, 1670s, 1260s, 1110s and 840s; δ_H(300 MHz) 4.57 (1 H, s with fine splitting), 4.28 (2 H, t, *J* 9.2), 3.62 (2 H, t, *J* 6.9), 2.58 (2 H, t with fine splitting, *J* 9.2), 1.97 (2 H, m), 1.87 (2 H, m), 0.85 (9 H, s) and 0.02 (6 H, s). A satisfactory HRMS was not obtained for this compound.

5-*Trimethylsilyl*-2,3-*dihydrofuran* **3i**. A solution of *tert*-butyllithium in pentanes (14.7 cm^3, 25 mmol) was added dropwise to a stirred solution of 2,3-dihydrofuran (1.40 g, 20.0 mmol) in dry THF (4.1 cm^3) cooled to −40 °C under argon. After stirring at 0 °C for 30 min, the mixture was cooled to −80 °C and a solution of chlorotrimethylsilane (2.12 cm^3, 16.7 mmol) in dry tetrahydrofuran (8.0 cm^3) was added dropwise. The mixture was allowed to warm to room temperature and was stirred for a further 1 h. The white suspension obtained was poured into saturated aqueous ammonium hydroxide (1 cm^3) in saturated aqueous ammonium chloride (9 cm^3). Extraction with light petroleum, drying ($MgSO_4$) and filtration through a column of basic alumina gave the *title compound* (2.10 g, 14.7 mmol, 88%) as a colourless oil after Kugelrohr distillation ν_{max}(film)/cm^{-1} 2960s, 1590m, 1250s, 1100s, 930s, 880s and 840s; δ_H(270 MHz) 5.19 (1 H, t, *J* 2.5), 4.27 (2 H, t, *J* 9.7), 2.58 (2 H, dt, *J* 2.5, 9.7) and 0.15 (9 H, s); δ_C(67.5 MHz) 162.4 (s), 111.2 (d), 70.5 (t), 30.7 (t) and −2.2 (q) (Found: M^+ 142.0820. $C_7H_{14}OSi$ requires *M*, 142.081 405).

5-*Trimethylstannyl*-2,3-*dihydrofuran* **3j**. Prepared by the same method as described for **3i**; b.p. 95 °C (bath)/15 mmHg; ν_{max}(film)/cm^{-1} 2960s, 2910s, 2870s, 1580s, 1050s, 920s and 770s; δ_H(270 MHz) 5.07 (1 H, m, *J* 2.4), 4.23 (2 H, t, *J* 9.6), 2.56 (2 H, m, *J* 2.5, 9.6) and 0.21 [9 H, s, *J*(^{117}Sn) 27.6, *J*(^{119}Sn) 28.8]; δ_C(67.5 MHz) 162.6 (s), 111.3 [d, *J*(^{117}Sn) 37.2, *J*(^{119}Sn) 39.1], 70.1 (t), 30.0 (t) and −9.7 (q). A satisfactory HRMS was not obtained for this compound.

(E)-4-*Methyldeca*-3,9-*dien*-1-*ol* **4a**.—*General Procedure for the Reaction of* 5-*Alkyl*-2,3-*dihydrofurans with Grignard Reagents*.—To $(Ph_3P)_2NiCl_2$ (6.85 g, 10.5 mmol) in dry benzene (150 cm^3) under argon at room temperature was added dropwise a solution of MeMgBr in Et_2O (3 mol dm^{-3}; 7 cm^3, 21 mmol). After stirring for 15 min at room temperature more methylmagnesium bromide in Et_2O (70 cm^3, 210 mmol) was added before the bulk of the solvent was removed under reduced pressure by rotary evaporation. The dark residue was suspended in benzene (200 cm^3) and dihydrofuran **3a** (15.9 g, 105 mmol) in benzene (20 cm^3) added. The mixture was refluxed for 45 min, cooled to 0 °C, and quenched by pouring as a slow stream into vigorously stirred saturated aqueous ammonium chloride (350 cm^3) at 0 °C. The stirring was continued for 20 min before the organic layer was separated and the aqueous phase extracted with Et_2O (4 × 200 cm^3). The combined extracts were dried, evaporated, and the residue chromatographed on silica gel (Et_2O–hexane 1:3–1:1 as eluent) to remove biphenyl impurity. Short path distillation gave the *title compound* **4a** (16.8 g, 99.9 mmol, 95%) as a colourless oil: b.p. 80–82 °C/0.5 mmHg; ν_{max}(film)/cm^{-1} 3330m, 2920s, 2870s, 1640m, 1080s and 920s; δ_H(360 MHz) 5.83 (1 H, m), 5.18 (1 H, t, *J* 7.1), 4.95–5.10 (2 H, m), 3.65 (2 H, t, *J* 6.8), 2.7 (1 H, br s, OH), 2.32 (2 H, dt, *J* 7.1, *J'* 6.8), 2.0–2.2 (4 H, m), 1.70 (3 H, s) and 1.60–1.35 (4 H, m); δ_C(90 MHz) 139.09 (d), 138.56 (s), 119.99 (d), 114.41 (t), 62.51 (t), 39.74 (t), 33.78 (t), 31.67 (t), 28.70 (t), 27.52 (t) and 16.18 (q). The 1-naphthylurethane derivative prepared in the usual way gave m.p. 41–43 °C (heptane) (Found: C, 78.1; H, 8.05; N, 4.15. $C_{22}H_{27}NO_2$ requires C, 78.3; H, 8.06; N, 4.15%).

(Z)-4-*Phenylpent*-3-*en*-1-*ol* **4b**. B.p. 135 °C (bath)/20 mmHg; ν_{max}(CCl_4)/cm^{-1} 3420s, 2980s, 1600m, 1450s, 1240s and 730s; δ_H(360 MHz) 7.30–7.13 (5 H, m), 5.45 (1 H, dq, *J* 7.4, *J'* 1.3), 3.50 (2 H, t, *J* 6.8), 2.41 (1 H, br s, OH), 2.18 (s H, dt, *J* 7.4, *J'* 6.8) and 2.02 (3 H, d, *J* 1.3); δ_C(90 MHz) 141.97 (s), 139.19 (s), 128.41 (d), 128.16 (d), 126.62 (d), 123.28 (d), 62.58 (t), 32.66 (t) and 25.66 (q). The ^{13}C NMR spectroscopic data compared favourably with literature data.[26]

(Z)-4-*Benzylpent*-3-*en*-1-*ol* **4c**. B.p. 140 °C (bath)/20 mmHg; ν_{max}($CDCl_3$)/cm^{-1} 3460m, 2970s, 1610m, 1490s, 1450s and 1050m; δ_H(360 MHz) 7.43–7.09 (5 H, m), 5.35 (1 H, tq, *J* 7.3, *J'* 1.2), 3.62 (2 H, t, *J* 6.7), 3.45 (2 H, s), 3.0 (1 H, br s, OH), 2.37 (2 H, dt with fine splitting, *J* 6.7, *J'* 7.3) and 1.63 (3 H, s with fine splitting); δ_C(90 MHz) 141.1 (s), 139.9 (s), 128.9 (d), 128.6 (d), 126.1 (d), 122.3 (d), 62.6 (t), 38.0 (t), 31.6 (t) and 23.5 (q); *m/z* (EI mode 176 ($M^{\cdot+}$, 21%), 91 (83), 67 (43) and 65 (100).

(Z)-4-(*Trimethylsilylmethyl*)*pent*-3-*en*-1-*ol* **4d**.—B.p. 90 °C (bath)/20 mmHg; ν_{max}(CCl_4)/cm^{-1} 3440m, 2960s, 1650w, 1250s, 1050s, 860s and 840s; δ_H(360 MHz) 4.95 (1 H, t, *J* 7.0), 3.54 (2 H, t, *J* 6.7), 2.30 (1 H, br s, OH), 2.16 (2 H, dt, *J* 7.0, *J'* 6.7), 1.67 (3 H,

s), 1.52 (2 H, s) and 0.02 (9 H, s); δ_C(90 MHz) 136.3 (s), 117.6 (d), 62.8 (t), 32.2 (t), 26.2 (q), 23.6 (t) and −0.7 (q); *m/z* (CI mode) 173 ($MH^{\bullet+}$, 29%), 73 (100) and 81 (17).

(E)-4-*Methylhept*-3-*en*-1-*ol* **4e**. B.p. 130 °C (bath)/20 mmHg; $\nu_{max}(CDCl_3)/cm^{-1}$ 3630m, 3460m, 2980s, 2880s, 1670w, 1460s, 1390s and 1050s; δ_H(360 MHz) 5.15 (1 H, tq, *J* 7.1, *J'* 1.4), 3.55 (2 H, t, *J* 6.8), 2.24 (2 H, dd, *J* 7.8, *J'* 6.8), 2.03 (2 H, t, *J* 6.9), 1.65 (3 H, s), 1.40 (2 H, m) and 0.93 (3 H, t, *J* 7.0); δ_C(90 MHz) 138.7 (s), 120.0 (d), 62.8 (t), 42.0 (t), 31.7 (t), 21.1 (t), 16.1 (q) and 13.7 (q). The ^{13}C NMR spectroscopic data was consistent with the data for **4e** prepared by an alternative route by the method of Helquist and co-workers.[27]

(Z)-4-*Phenylhept*-3-*en*-1-*ol* **4f**. B.p. 150 °C (bath)/20 mmHg; $\nu_{max}(CCl_4)/cm^{-1}$ 3620m, 3440m, 2990s, 2880s, 1600w, 1450s, 1220s and 730s; δ_H(360 MHz) 7.31–7.10 (5 H, m), 5.43 (1 H, t, *J* 7.3), 3.49 (2 H, t, *J* 6.8), 2.37 (1 H, br s, OH), 2.31 (2 H, t, *J* 7.5), 2.16 (2 H, dt, *J* 7.3, *J'* 6.8), 1.32 (2 H, dd, *J* 7.4, *J'* 7.5) and 0.86 (3 H, t, *J* 7.4); δ_C(90 MHz) 143.95 (s), 141.17 (s), 128.28 (d), 127.99 (d), 126.43 (d), 122.68 (d), 62.56 (t), 41.50 (t), 32.42 (t), 21.07 (t) and 13.47 (q); *m/z* (EI mode) 190 ($M^{\bullet+}$, 4%), 128 (27), 117 (100), 91 (61) and 41 (89).

(E)-4-*Methylnon*-3-*en*-1-*ol* **4g**. B.p. 155 °C (bath)/20 mmHg; $\nu_{max}(CCl_4)/cm^{-1}$ 3440m, 2980s, 2940s, 2880s, 1480s, 1380s and 1050s; δ_H(360 MHz) 5.12 (1 H, tq, *J* 8.6, *J'* 0.4), 3.59 (2 H, t, *J* 6.9), 2.26 (2 H, dt, *J* 7.8, *J'* 6.9), 1.98 (2 H, t with further fine splitting, *J* 7.6), 1.62 (3 H, s), 1.44–1.17 (6 H, m) and 0.88 (3 H, t, *J* 7.1); δ_C(90 MHz) 138.87 (s), 119.78 (d), 62.57 (t), 39.83 (t), 31.70 (t), 31.63 (t), 27.74 (t), 22.57 (t), 16.12 (q) and 13.97 (q).

The alcohol **4g** was identical by IR, ^1H NMR and ^{13}C NMR with an authentic sample prepared by the carboalumination of hept-1-yne according to the following procedure.[28] To a suspension of Cp_2ZrCl_2 (456 mg, 1.56 mmol) in 1,2-dichloroethane (5 cm^3) under nitrogen was added Me_3Al (4.7 cm^3 of a 2 mol dm^{-3} solution in toluene, 9.4 mmol) and the resulting green solution was stirred at room temperature for 10 min before the addition of hept-1-yne (300 mg, 3.12 mmol) in 1,2-dichloroethane (3 cm^3). The solution was stirred under nitrogen at room temperature for 72 h after which the solvent and excess Me_3Al was removed under reduced pressure. The residual alane was heated at 50 °C at 0.5 mmHg to remove the last traces of solvent and then extracted with dry pentane (4 × 3 cm^3). The yellow pentane solution was transferred to a flask cooled to −78 °C and BuLi added (1.5 cm^3 of a 2.5 mol dm^{-3} solution in hexane, 3.75 mmol). The resultant yellow suspension was allowed to warm to −30 °C over 1.5 h at which time ethylene oxide (1.26 cm^3 of a 10 mol dm^{-3} solution in Et_2O, 12.6 mmol) was added whereupon the suspension cleared to give two layers. The mixture was stirred at −30 °C for 1 h. The cooling bath was removed and water (10 cm^3) added to the cold mixture. The resultant white suspension was acidified to pH 2 (dilute HCl, suspension cleared) and Et_2O (75 cm^3) added. The organic layer was washed with brine, dried, and evaporated to give a pale green oil (430 mg) which was purified by column chromatography on silica gel eluting with Et_2O–hexane (1:3) followed by Kugelrohr distillation. The desired alcohol **4g** (327 mg, 67%) was obtained as colourless oil.

(Z)-4-*Phenylnon*-3-*en*-1-*ol* **4h**. B.p. 160 °C (bath)/20 mmHg; $\nu_{max}(CCl_4)/cm^{-1}$ 3350m, 3040m, 2970s, 2940s, 2390m, 1600m, 1485s, 1050s and 710s; δ_H(360 MHz) 7.32–7.09 (5 H, m), 5.43 (1 H, t, *J* 7.3), 3.53 (2 H, t, *J* 6.6), 2.33 (2 H, t, *J* 7.1), 2.18 (2 H, dd, *J* 7.3, *J'* 6.6), 1.25 (6 H, m) and 0.87 (3 H, t, *J* 7.0); δ_C(90 MHz) 144.61 (s), 141.36 (s), 128.45 (d), 128.04 (d), 126.60 (d), 122.52 (d), 62.81 (t), 39.54 (t), 32.61 (t), 31.54 (t), 27.86 (t), 22.53 (t) and 14.05 (q) (Found: C, 82.55; H, 10.4. $C_{15}H_{22}O$ requires C, 82.57; H, 10.17%).

(Z)-4-*Benzylnon*-3-*en*-1-*ol* **4i**. B.p. 170 °C (bath)/20 mmHg; $\nu_{max}(CHCl_3)/cm^{-1}$ 3620m, 3440m, 2970s, 2940s, 1600m, 1490m, 1450s and 1045s; δ_H(360 MHz) 7.4–7.1 (5 H, m), 5.30 (1 H, t, *J* 7.2), 4.60 (1 H, s, OH), 3.60 (2 H, t, *J* 6.7), 3.39 (2 H, s), 2.37 (2 H, dd, *J* 7.2, *J'* 6.7), 1.91 (2 H, d with further fine splitting, *J* 7.7), 1.41–1.14 (6 H, m) and 0.85 (3 H, t, *J* 7.1); δ_C(90 MHz) 141.26 (s), 140.19 (s), 128.55 (d), 128.53 (d), 128.36 (d), 125.92 (d), 121.68 (d), 65.17 (t), 62.65 (t), 36.82 (t), 36.27 (t), 31.81 (t), 31.63 (t), 27.76 (t), 22.52 (t) and 13.97 (q); *m/z* (EI mode) 232 ($M^{\bullet+}$, 10%), 110 (12), 101 (13), 91 (100) and 65 (41).

(Z)-4-(*Trimethylsilylmethyl*)*non*-3-*en*-1-*ol* **4j**. B.p. 150 °C (bath)/20 mmHg; $\nu_{max}(CCl_4)/cm^{-1}$ 3380m, 2960s, 2930s, 2880s, 1650w, 1250s and 860s; δ_H(360 MHz) 4.96 (1 H, t, *J* 7.2), 3.57 (2 H, t, *J* 7.0), 2.20 (2 H, dd, *J* 7.2, *J'* 7.0), 1.92 (2 H, t, *J* 7.7), 1.55 (2 H, s), 1.45–1.18 (6 H, m), 0.88 (3 H, t, *J* 7.1) and 0.02 (9 H, s); (Found: $M^{\bullet+}$ 228.1911. $C_{13}H_{28}OSi$ requires *M*, 228.19097).

(E)-7-*Methoxy*-4-*methylhept*-3-*en*-1-*ol* **4k**. B.p. 110 °C/20 mmHg; ν_{max}(film)/cm^{-1} 3700–3100s, 2980s, 2880s, 1680w, 1460s, 1390s, 1120s and 1050s; δ_H(360 MHz) 5.15 (1 H, dq, *J* 7.2, *J'* 1.2), 3.58 (2 H, t, *J* 6.9), 3.35 (2 H, t, *J* 6.7), 3.31 (3 H, s), 2.90 (1 H, br s, OH), 2.28 (2 H, dt, *J* 7.2, *J'* 6.9), 2.06 (2 H, distorted t, *J* 7.1), 1.68 (2 H, m) and 1.63 (3 H, s); δ_C(90 MHz) 137.44 (s), 120.28 (d), 72.40 (t), 62.23 (t), 58.24 (q), 36.12 (t), 31.54 (t), 27.76 (t) and 15.95 (q); *m/z* (EI) 158 ($M^{\bullet+}$, 7%), 140 (10), 113 (26), 109 (41), 93 (32), 81 (100), 71 (24), 55 (71) and 41 (40) (Found: C, 68.65; H, 11.7. $C_9H_{18}O_2$ requires C, 68.31; H, 11.47%).

(E)-7-*Benzyloxy*-4-*methylhept*-3-*en*-1-*ol* **4l**. ν_{max}(film)/cm^{-1} 3600–3100s, 2940s, 2860s, 1450s, 1360s, 1110s and 700s; δ_H(360 MHz) 7.40–7.18 (5 H, m), 5.11 (1 H, tq, *J* 7.2, *J'* 1.2), 4.45 (2 H, s), 3.49 (2 H, t, *J* 6.9), 3.40 (2 H, t, *J* 6.5), 3.00 (1 H, br s, OH), 2.21 (2 H, dt, *J* 7.2, *J'* 6.9), 2.05 (2 H, distorted t, *J* 7.5), 1.69 (2 H, tt, *J* 6.5, *J'* 7.5) and 1.60 (3 H, s); δ_C(90 MHz) 138.54 (s), 137.20 (s), 128.13 (d), 127.43 (d), 127.29 (d), 120.32 (d), 72.68 (t), 69.81 (t), 62.09 (t), 36.04 (t), 31.45 (t), 27.87 (t) and 15.91 (q); *m/z* (EI) 234 ($M^{\bullet+}$, 7%), 216 (5), 157 (31), 109 (42), 91 (100), 71 (27), 65 (30) and 51 (53) (Found: C, 76.75; H, 10.0. $C_{15}H_{22}O_2$ requires C, 76.88; H, 9.46%).

(E)-7-(tert-*Butyldimethylsilyloxy*)-4-*methylhept*-3-*en*-1-*ol* **4m**. B.p. 150 °C (bath)/0.1 mmHg; ν_{max}(film)/cm^{-1} 3600–3100m, 2930s, 2860s, 1255s, 1100s and 840s; δ_H(300 MHz) 5.12 (1 H, t, *J* 6.6), 3.55 (4 H, 2 superimposed t, *J* 6.8 and *J* 6.6), 2.62 (1 H, br s, OH), 2.23 (2 H, dt, *J* 7.1, *J'* 6.6), 2.00 (2 H, distorted t, *J* 7.6), 1.60 (3 H, s), 0.83 (9 H, s) and 0.02 (6 H, s); δ_C(75 MHz) 138.2 (s), 120.5 (d), 63.6 (t), 62.2 (t), 36.3 (t), 32.0 (t), 31.1 (t), 25.3 (q), 18.4 (s), 16.5 (q) and −5.0 (q) (Found: C, 65.05; H, 12.0. $C_{14}H_{30}O_2Si$ requires C, 65.06; H, 11.70%).

(E)-7-tert-*Butoxy*-4-*methylhept*-3-*en*-1-*ol* **4n**. B.p. 130 °C/15 mmHg; ν_{max}(film)/cm^{-1} 3600–3100s, 2980s, 2960s, 2880s, 1670w, 1390s, 1360s, 1300s and 1080s; δ_H(270 MHz) 5.11 (1 H, tq, *J* 1.2, 7.3), 3.55 (2 H, t, *J* 6.0), 3.28 (2 H, t, *J* 6.6), 2.24 (2 H, dt, *J* 6.6, 7.2), 2.07 (1 H, br s), 2.02 (2 H, t, *J* 7.6), 1.69–1.55 (2 H, m), 1.60 (3 H, s) and 1.14 (9 H, s); δ_C(67.5 MHz) 138.1 (s), 119.9 (d), 72.6 (s), 62.3 (t), 61.1 (t), 36.3 (t), 31.5 (t), 28.8 (t), 27.5 (q) and 16.1 (q); *m/z* 211 ($M^{\bullet+}$ − H_2O, 4%), 149 (11), 137 (17), 111 (19), 97 (40), 85 (56), 69 (100), 57 (60) and 93 (74).

(E)-4-*Trimethylsilylpent*-3-*en*-1-*ol* **4o**. A solution of MeMgBr in Et_2O (3.6 cm^3, 10.9 mmol) was added to a stirred suspension of $(Ph_3P)_2NiCl_2$ (0.22 g, 0.3 mmol) in dry benzene (10 cm^3) under dry nitrogen at room temperature. The resultant deep red mixture was stirred for 15 min, and the solvent was then replaced with dry benzene (15 cm^3). A solution of 5-trimethylsilyl-2,3-dihydrofuran **3i** (0.50 g, 3.4 mmol) in benzene (5 cm^3) was added and the mixture was heated to reflux. After 1.5 h, the mixture was cooled and poured into a solution of saturated ammonium hydroxide (2.0 cm^3) in saturated ammonium chloride (18 cm^3) with vigorous stirring. The mixture was stirred until decolourised and was then extracted with Et_2O. The combined extracts were dried ($MgSO_4$) and evaporated to leave a yellow oil which on Kugelrohr distillation yielded the *title compound* (0.53 g, 3.35 mmol, 97%) as a colourless oil: b.p. 90 °C (bath)/3 mmHg; ν_{max}(film)/cm^{-1} 3600–3100s, 2950s, 2900s, 1620m, 1250s,

1045s, 840s and 750s; δ_H(260 MHz) 5.70 (1 H, m, *J* 1.7, 6.9), 3.65 (2 H, t, *J* 6.7), 2.37 (2 H, dt, *J* 6.7, 6.9), 1.98 (1 H, br s), 1.69 (3 H, d, *J* 0.8) and 0.04 (9 H, s); δ_C(67.5 MHz) 139.9 (s), 134.2 (d), 62.1 (t), 31.9 (t), 14.7 (q) and −2.1 (q); *m/z* 158 ($M^{\cdot+}$, 2%), 143 (94), 125 (14), 115 (8), 89 (12), 75 (100) and 67 (32) (Found: 158.1126. $C_8H_{18}OSi$ requires *M*, 158.1127).

(E)-4-*Trimethylstannylpent*-3-*en*-1-*ol* **4p**. This compound was prepared as described for **4o** from 5-trimethylstannyl-2,3-dihydrofuran **3j** in 83% yield, and was obtained as an inseparable mixture of isomers (*E*:*Z* = 9:1). ν_{max}(film)/cm^{-1} 3700–3100s, 2980s, 2970s, 2910s, 1610w, 1430m, 1190m, 1045s and 770s; δ_H(270 MHz; peaks from both isomers) 5.98 (0.1 H, t), 5.56 (0.9 H, tq, with satellites 0.15 ppm off-centre, *J* 1.7, 6.0), 3.65 (2 H, m), 2.40 (1.8 H, dt, *J* 6.0, 7.4), 2.26 (0.2 H, dt), 1.88 (2.7 H, d, *J* 1.8), 1.82 (0.3 H, s) and 0.01 (9 H, s); δ_C(67.5 MHz) 142.2 (s), 136.2 (d), 135.5 (d, major), 62.2 (t, major), 62.1 (t), 31.7 (t), 26.5 (q), 18.5 (q, major) and −10.1 (q).

(Z)-4-*Bromopent*-3-*en*-1-*ol* **11**.—A solution of 4-trimethylsilylpent-3-en-1-ol **4o** (0.5 g, 3.1 mmol) in dry dichloromethane (6.2 cm^3) was cooled to −70 °C under nitrogen, and a solution of bromine in dichloromethane (1 cm^3, 3.1 mmol) was added dropwise. Decolouration occurred instantaneously, and addition was stopped when a faint yellow colouration persisted. Methanol (2.0 cm^3) was added and the mixture was decolourised with sodium thiosulfate. The organic material was extracted with Et_2O, dried ($MgSO_4$) and evaporated. The residue was taken up in a solution of sodium methoxide in methanol (4.6 cm^3, 4.6 mmol) and the mixture was stirred at room temperature for 5 min. After quenching with water, the mixture was concentrated under reduced pressure and was extracted with Et_2O, dried ($MgSO_4$) and evaporated. Column chromatography on silica gel (Et_2O–light petroleum, 1:1) gave the *title compound* (0.40 g, 2.44 mmol, 78%) as a colourless oil which rapidly turned brown on standing: ν_{max}(film)/cm^{-1} 3700–3100s, 2960s, 2940s, 2870s, 1730s, 1460s, 1370s, 1170s and 1110s; δ_H(360 MHz) 5.67 (1 H, tq, *J* 1.4, 6.8), 3.65 (2 H, t, *J* 6.4), 2.44 (1 H, s), 2.38 (2 H, dt, *J* 6.4, 6.7) and 2.28 (3 H, d, *J* 1.2); δ_C(67.5 MHz) 125.2 (d), 124.6 (s), 61.2 (t), 35.0 (t) and 28.9 (q) (Found: M^+, 163.9833. C_5H_9BrO requires *M*, 163.983 68). Differential NOE experiments were carried out to confirm the stereochemistry: (1-H/3-H) = 7.8%; (3-H/5-H) = 22%.

General Procedure for the Reactions of 5-*Pentyl*-2,3-*dihydrofuran* **3d** *with* Et_2Mg.—MeMgBr in Et_2O (0.1 cm^3, 0.2 mmol) was added to a suspension of the Ni^{II} salt (0.1 mmol) (see Table 3) in dry benzene (10 cm^3) under dry nitrogen and the mixture was stirred at room temperature for 15 min. A solution of Et_2Mg[29] in Et_2O (5.7 cm^3, 4.0 mmol) was added and the mixture was concentrated under reduced pressure to a fifth of its original volume. Dry benzene (10 cm^3) and a solution of 5-pentyl-2,3-dihydrofuran **3d** (0.28 g, 2.0 mmol) in dry benzene (5 cm^3) were added sequentially, and the mixture was then heated to reflux until TLC indicated complete consumption of the enol ether. The cooled mixture was then slowly poured into rapidly stirred saturated ammonium chloride (15 cm^3) and stirring was continued until the suspension decolourised. The organic products were extracted with Et_2O and the combined extracts were dried ($MgSO_4$) and evaporated. After removal of biphenyl derived from the phosphine ligands by column chromatography on silica gel (20% Et_2O in light petroleum) the relative composition of the alcohols (*E*)-**13**, (*Z*)-**13**, (*E*)-**14** and (*Z*)-**14** was ascertained by ^1H NMR spectroscopy and capillary gas chromatography at 130 °C on CP Wax 52 by comparison with authentic samples prepared as described below.

(E)-4-*Ethylnon*-3-*en*-1-*ol* (E)-**13**.—This compound was prepared by the method of Helquist and co-workers.[27] Me_2S (8.2 cm^3) was added to a suspension of CuBr·Me_2S complex (1.23 g, 6.0 mmol) in dry Et_2O (7.3 cm^3) to give a colourless solution which was cooled to −45 °C under dry nitrogen. Dropwise addition of an ethereal solution of EtMgBr (3.1 cm^3, 6.0 mmol) gave a yellow suspension which was stirred for 2 h. Hep-1-tyne (0.58 g, 6.0 mmol) was then added to give a green suspension which was stirred at −25 °C for 3 h, during which the mixture became homogeneous and turned black.

In a separate vessel, a solution of butyllithium in hexanes (2.3 cm^3, 6.0 mmol) was added dropwise to a solution of pent-1-yne (0.59 cm^3, 6.0 mmol) in HMPA (1.0 cm^3) and Et_2O (7.5 cm^3) at −78 °C under argon and the resulting solution was stirred for 40 min and then transferred to the mixture containing the organocopper reagent at −78 °C. The black mixture was stirred at −60 °C for 1 h and a solution of ethylene oxide in Et_2O (10 mol dm^{-3}, 0.6 cm^3, 6.0 mmol) was added. The mixture was stirred at −20 °C for 36 h whereupon saturated ammonium chloride solution (3 cm^3) was added and stirring was continued at room temperature for 2 h. Water (20 cm^3) was added and the organic products were extracted with Et_2O. The combined extracts were dried ($MgSO_4$) and concentrated to a yellow oil. Flash chromatography on silica gel (20% Et_2O in pentane) and Kugelrohr distillation gave the *title compound* (0.76 g, 4.47 mmol, 74%) as a colourless oil; b.p. 150 °C (bath)/20 mmHg; ν_{max}(film)/cm^{-1} 3340–3100m, 2985s, 2940s, 2880s, 1480s, 1385s and 1050s; δ_H(360 MHz) 5.08 (1 H, t, *J* 7.2), 3.59 (2 H, t, *J* 6.7), 2.42 (1 H, br s), 2.29 (2 H, m), 2.10–1.95 (4 H, m), 1.44–1.24 (6 H, m), 0.97 (3 H, t, *J* 7.5) and 0.89 (3 H, t, *J* 7.3), δ_C(90.6 MHz) 144.7 (s), 119.2 (d), 62.6 (t), 36.7 (t), 31.8 (t), 31.3 (t), 28.0 (t), 23.2 (t), 22.6 (t), 14.0 (q) and 13.2 (q).

(Z)-4-*Ethylnon*-3-*en*-1-*ol* (Z)-**13**. This compound was prepared in 63% yield by the carbocupration of but-1-yne (see above) using pentylmagnesium iodide followed by alkylation with ethylene oxide; b.p. 150 °C (bath)/20 mmHg; ν_{max}(film)/cm^{-1} 3400–3100s, 2980s, 2940s, 2880s, 1480s, 1380s and 1050s; δ_H(360 MHz) 5.12 (1 H, t, *J* 6.9), 3.59 (2 H, t, *J* 6.8), 2.35 (2 H, m), 2.12–1.95 (4 H, m), 1.49–1.20 (6 H, m), 1.03 (3 H, t, *J* 7.2) and 0.89 (3 H, t, *J* 7.2); δ_C(90.6 MHz) 142.4 (s), 117.9 (d), 62.3 (t), 36.9 (t), 31.7 (t), 31.2 (2), 27.9 (t), 23.3 (t), 22.6 (t), 14.1 (q) and 13.2 (q).

(E)-*Non*-3-*en*-1-*ol* (E)-**14**.—A solution of butyllithium in hexanes (7.7 cm^3, 20 mmol) was added dropwise at −50 °C to a stirred solution of hept-1-yne (2.6 cm^3, 20 mmol) in dry THF (25 cm^3) and HMPA (3.5 cm^3). The mixture was allowed to warm to −30 °C and a solution of ethylene oxide (10 mol dm^{-3}; 10 cm^3, 100 mmol) was added. The solution was stirred at −10 °C for 16 h whereupon saturated ammonium chloride solution was added. The organic material was extracted with ether, dried ($MgSO_4$) and subjected to flash chromatography on silica gel (10% Et_2O in light petroleum). Kugelrohr distillation of the major product gave non-3-yn-1-ol (2.4 g, 17.1 mmol, 86%) as a colourless oil; b.p. 115 °C (bath)/20 mmHg; ν_{max}(film)/cm^{-1} 3360m, 2940s, 1470s and 1050s; δ_H(60 MHz) 3.7 (2 H, t), 2.6–2.0 (4 H, m), 1.4 (6 H, m) and 0.9 (3 H, t). The non-3-yn-1-ol thus prepared (0.30 g, 2.14 mmol) was added dropwise to a stirred solution of sodium metal (0.18 g, 8.0 g atom) in liquid ammonia (25 cm^3) at −78 °C to give a dark mixture which was allowed to reflux for 1 h. Ammonium chloride (0.7 g) and Et_2O (20 cm^3) were added and the ammonia was allowed to boil off. The clear residual solution was washed with brine, dried ($MgSO_4$) and concentrated to a yellow oil from which the *title compound* (0.27 g, 1.90 mmol, 93%) distilled as a colourless oil; b.p. 125 °C (bath)/20 mmHg; ν_{max}(film)/cm^{-1} 3460–3100s, 2990s, 2935s, 1475w, 1460s, 1395s and 1050s; δ_H(360 MHz) 5.54 (1 H, dt with fine splitting, *J* 6.6, 15.2), 5.37 (1 H, dt with fine splitting, *J* 6.9, 15.3), 3.6 (2 H, t, *J* 6.6), 2.25 (2 H, m), 2.00 (2 H, m), 1.42–1.24 (6 H, m) and 0.89 (3 H, t, *J* 6.8);

δ_C(90.6 MHz) 134.1 (d), 125.9 (d), 62.2 (t), 36.1 (t), 32.7 (t), 31.5 (t), 29.4 (t), 22.6 (t) and 14.0 (q).

(*Z*)-*Non*-3-*en*-1-*ol* (Z)-**14**. To a solution of non-3-yn-1-ol (preparation described above) (0.35 g, 2.50 mmol) in dry methanol (16 cm^3) were added Pd (5%) on $BaSO_4$ (84 mg) and quinoline (40 mg) and the resulting mixture was stirred vigorously under an atmosphere of hydrogen for 2 h. The mixture was filtered through Celite, washing with methanol, and concentrated to a colourless oil. Kugelrohr distillation gave the *title compound* (0.34 g, 98%) as a colourless oil; b.p. 130 °C (bath)/20 mmHg; $\nu_{max}(CCl_4)/cm^{-1}$ 3630m, 3460m, 2985s, 2940s, 1670w, 1460s, 1395s and 1050s; δ_H(360 MHz) 5.55 (1 H, dt with fine splitting, *J* 6.5, 7.3), 5.40 (1 H, m), 3.62 (2 H, t, *J* 7.4), 2.35 (2 H, m), 2.05 (2 H, m), 1.42–1.25 (6 H, m) and 0.89 (3 H, t, *J* 6.8); δ_C (90.6 MHz) 134.2 (d), 125.1 (d), 62.4 (t), 36.1 (t), 32.7 (t), 31.0 (t), 29.2 (t), 22.5 (t) and 14.0 (q).

(E)-4-*Butylnon*-3-*en*-1-*ol* **18**.—This compound was obtained as a single isomer in 82% yield from the reaction of 5-pentyl-2,3-dihydrofuran **3d** with BuMgBr using 10 mol% (dppe)$NiCl_2$ as a catalyst precursor; b.p. 155 °C (bath)/20 mmHg; $\nu_{max}(CCl_4)/cm^{-1}$ 3640w, 3460s, 2960s, 2880s, 1660w, 1470m and 1050s; δ_H(360 MHz) 5.10 (1 H, t with fine splitting, *J* 7.4), 3.63 (2 H, t, *J* 6.6), 2.30 (2 H, m), 2.07–1.96 (4 H, m), 1.72–1.25 (10 H, m) and 0.92–0.87 (6 H, m); δ_C(90.6 MHz) 143.4 (s), 119.8 (d), 62.8 (t), 37.1(t), 31.8 (t), 31.5 (t), 30.9 (t), 30.1 (t), 28.1 (t), 22.9 (t), 22.6 (t), 14.0 (q) and 14.0 (q). In order to confirm the structure and stereochemistry an authentic sample of **18** was prepared by the carbocupration of hept-1-yne with BuMgBr followed by alkylation with oxirane according to the procedure of Helquist and co-workers[27] (see above).

5-(1-*Hydroxybutyl*)-2,3-*dihydrofuran* **20**.—To a solution of freshly distilled 2,3-dihydrofuran (1.09 g, 15.6 mmol) in dry THF (4 cm^3) under argon at −78 °C was added Bu^{t}Li (12.5 mmol, 7.35 cm^3 of a 1.7 mol dm^{-3} solution in pentane). The resulting solution was allowed to warm to 0 °C at which it was stirred for 1 h before lowering the temperature to −78 °C. Freshly distilled butanal (0.75 g, 10.4 mmol) in THF (4 cm^3) was added dropwise and the mixture allowed to warm slowly to room temperature. The reaction mixture was quenched by addition to a rapidly stirred mixture of saturated ammonium chloride–ammonia (9:1) and extracted with Et_2O. The organic extracts were dried and evaporated to give the *title compound* (1.22 g, 8.58 mmol, 81%) as an oil: ν_{max}(film)/cm^{-1} 3420s and 1670s; δ_H(60 MHz) 0.80–1.90 (7 H, m), 2.20 (1 H, OH), 2.65 (2 H, t, *J* 9) and 4.30 (3 H, m). The product rapidly deteriorated on standing and was used immediately in the next step without further purification.

5-(1-*Hydroxy*-2-*methylpropyl*)-2,3-*dihydrofuran* **21**. This compound was prepared (*ca.* 100% yield) by the same procedure as described for **20** and it too was used immediately in the next step: ν_{max}(film)/cm^{-1} 3400s and 1675s; δ_H(60 MHz) 0.85 (3 H, d, *J* 7), 1.0 (3 H, d, *J* 7), 1.7–2.2 (2 H, m including OH), 2.6 (2 H, m), 3.8 (1 H, m), 4.3 (2 H, t, *J* 9) and 4.8 (1 H, t, *J* 2).

Representative Procedure for the Reaction of Dihydrofurans **20** *and* **21** *with* MeMgBr *and* PhMgBr.—To a stirred suspension of $[Ph_3P]_2NiCl_2$ (0.1 equiv.) in benzene (5 cm^3) was added MeMgBr in Et_2O (0.3 equiv.). After stirring at room temperature for 15 min PhMgBr or MeMgBr in Et_2O (5 equiv.) was added and the solvent removed under reduced pressure. The residue was blanketed in Argon and benzene added (6 cm^3). The freshly prepared dihydrofuran in benzene (2 cm^3) was added dropwise and the mixture refluxed for 16–48 h until thin layer chromatography indicated the disappearance of starting material. The cooled reaction mixture was slowly poured into rapidly stirred aqueous ammonium chloride–ammonia (9:1) (50 cm^3) and the products extracted into Et_2O. The polar coupling products **22a**, **22b**, **24a** and **24b** were easily separated from the myriad non-polar products by column chromatography on silica gel eluting with 50% Et_2O in hexane. The substitution–coupling reaction products **23** and **25** were purified by conversion into the corresponding benzoates in the usual way followed by high performance liquid chromatographic separation on 9 mm × 30 cm Zorbax SIL columns eluting with 0.25% Bu^{t}OMe in hexane at a flow rate of 6 cm^3 min^{-1}.

Reaction of dihydrofuran **20** *with* MeMgBr. From dihydrofuran **20** (0.30 g, 2.1 mmol) was obtained (E)-4-*methyloct*-3-*ene*-1,5-*diol* **22a** (43 mg, 0.027 mmol, 13%): ν_{max}(film)/cm^{-1} 3350s; δ_H(360 MHz) 0.90 (3 H, t, *J* 7), 1.20–1.55 (4 H, m), 1.65 (3 H, s), 2.30 (2 H, m), 2.75 (2 H, br s, OH), 3.60 (2 H, m), 4.00 (1 H, t, *J* 6.7) and 5.40 (1 H, t, *J* 7.2) (Found: M^+, 158.1290. $C_9H_{18}O_2$ requires *M*, 158.1307) and (E)-1-*benzoyloxy*-4,5-*dimethyloct*-3-*ene* **23** (191 mg, 0.73 mmol, 35%): ν_{max}(film)/cm^{-1} 1720s; δ_H(360 MHz) 0.85 (3 H, t, *J* 7), 0.95 (3 H, d, *J* 7), 1.20 (4 H, m), 1.60 (3 H, s), 2.15 (1 H, m), 2.50 (2 H, m), 4.30 (2 H, t, *J* 7), 5.20 (1 H, t, *J* 7.2), 7.45 (2 H, dd with fine coupling, $J = J' = 8$), 7.55 (1 H, dd with fine splitting, $J = J' = 8$), 8.05 (2 H, d with fine splitting, *J* 8) (Found: $M^+ - PhCO_2H$, 138.1398. $C_{17}H_{24}O_2 - PhCO_2H$ requires *M*, 138.1404).

Reaction of dihydrofuran **20** *with* PhMgBr. From dihydrofuran **24** (200 mg, 1.4 mmol) was obtained (Z)-4-*phenyloct*-3-*ene*-1,5-*diol* **22b** (115 mg, 0.52 mmol, 35%): ν_{max}(film)/cm^{-1} 3350s; δ_H(360 MHz) 0.85 (3 H, m), 1.20–1.50 (4 H, m), 2.30 (2 H, q, *J* 6.3), 3.20 (1 H, br s, OH), 3.40 (1 H, br s, OH), 3.50 (2 H, t, *J* 6.1), 4.30 (1 H, br s), 5.70 (1 H, t, *J* 7.2), 7.15 (2 H, d, *J* 8) and 7.25 (3 H, m); δ_C(90 MHz) 13.94 (q), 18.96 (t), 32.02 (t), 37.83 (t), 62.30 (t), 76.41 (d), 124.49 (d), 126.99 (d), 127.90 (d), 128.16 (d), 129.29 (d), 138.55 (s) and 146.63 (s); (Found: M^+, 220.1448. $C_{14}H_{20}O_2$ requires *M*, 220.1458).

Reaction of dihydrofuran **21** *with* MeMgBr. From dihydrofuran **21** (350 mg, 2.46 mmol) was obtained (E)-4,6-*dimethylhept*-3-*ene*-1,5-*diol* **24a** (112 mg, 0.71 mmol, 29%); ν_{max}(film)/cm^{-1} 3400s; δ_H(360 MHz) 0.77 (3 H, d, *J* 7), 0.98 (3 H, d, *J* 7), 1.62 (3 H, s), 1.75 (1 H, m), 2.20–2.40 (2 H, m), 3.10 (2 H, br s, OH), 3.60 (3 H, m) and 5.35 (1 H, t, *J* 7.2); δ_C(90 MHz) 11.69 (q), 18.53 (q), 19.39 (q), 30.99 (d), 31.07 (t), 62.03(t), 83.64 (d), 123.34 (d) and 139.38 (s); *m*/*z* 158 ($M^{+\cdot}$, 1.3%) and (E)-1-*benzoyloxy*-4,5,6-*trimethylhept*-3-*ene* **25** (101 mg, 0.39 mmol, 16%); ν_{max}(film)/cm^{-1} 1725s; δ_H(360 MHz) 0.78 (3 H, d, *J* 7), 0.85 (3 H, d, *J* 7), 0.98 (3 H, d, *J* 7), 1.50 (1 H, m), 1.57 (3 H, s), 1.75 (1 H, m), 2.50 (2 H, m), 4.30 (2 H, t, *J* 7), 5.18 (1 H, br t, *J* 7), 7.45 (2 H, dd with fine splitting, $J = J' = 8$), 7.55 (1 H, dd with fine splitting, $J = J' = 8$) and 8.05 (2 H, d with fine splitting, $J = 8$) (Found: $M^+ - PhCO_2H$, 138.1398. $C_{17}H_{24}O_2 - PhCO_2H$ requires *M*, 138.1404).

Reaction of dihydrofuran **21** *with* PhMgBr. From dihydrofuran **21** (300 mg, 2.1 mmol) was obtained (Z)-6-*methyl*-4-*phenylhept*-3-*ene*-1,5-*diol* **24b** (206 mg, 0.94 mmol, 44%); m.p. 82–84 °C (Et_2O–hexane); ν_{max}(film)/cm^{-1} 3610s and 3420s; δ_H(360 MHz) 0.85 (3 H, d, *J* 7), 0.90 (3 H, d, *J* 7), 1.55 (1 H, m), 2.15 (2 H, dq, *J* 2.8, *J'* 6.4), 3.15 (2 H, br s, OH), 3.55 (2 H, t, *J* 6.1), 4.05 (1 H, d, *J* 6.1), 5.70 (1 H, t, *J* 6.4) and 7.15–7.40 (5 H, m); δ_C(90 MHz) 17.01 (q), 19.82 (q), 31.13 (d), 32.05 (t), 62.35 (t), 81.93 (d), 125.22 (d), 126.98 (d), 128.16 (d), 129.00 (d), 129.25 (d), 138.87 (s) and 145.47 (s) (Found: C, 76.3; H, 9.2. $C_{14}H_{20}O_2$ requires C, 76.36; H, 9.09%).

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