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Structural Effects in Radical Clocks and Mechanisms of Grignard Reagent Formation: Special Effect of a Phenyl Substituent in a Radical Clock when the Crossroads of Selectivity is at a Metal/Solution Interface

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A large class of radical clocks is based on the intramolecular trapping of a reactive radical by a suitably located unsaturated system. Depending on the substituents present on this unsaturated system, the rate of cyclisation may vary drastically. This property has been repeatedly used to diagnose the participation of very short-lived radicals in the mechanisms of a wide variety of reactions. For reactions occurring in homogeneous solution, a phenyl substituent capable of stabilizing the radical formed during the act of trapping has been one of the most widely used tools of this type. During study of the mechanisms of formation of Grignard reagents – reactions that occur at the interface of the metal and the solution – the phenyl substituent displayed a specific new behaviour pattern. Besides its stabilizing role, it was also able to play the role of mediator in redox catalysis of electron transfer. In this case, the first events on the pathway to the Grignard reagents involve a cascade of three (one intermolecular followed by two intramolecular) electron transfers. Introduction of a *p*-methoxy substituent on the phenyl ring, making the phenyl group a poorer electron acceptor, suppresses this specific second role. Applied to the mechanism of Grignard reagent formation, this *p*-methoxy effect is consistent with a triggering mechanistic act of electron transfer from the metal to the aryl halide rather than with a concerted oxidative addition. A similar change in selectivity is observed when a *p*-methoxy group is introduced onto a phenyl group that also bears a halogen, but its origin is different: this effect is associated with the shortening of the lifetime of the radical anion formed by the triggering electron transfer. These observations reemphasise our earlier proposals to use concepts originating from electrochemical kinetics to explain the selectivities of reactions occurring at metal/solution interfaces. This conjecture could possibly hold for any interface where the diffusion of reactive species plays a role in the settling of selectivity. These concepts emphasise the necessity to consider, for each reactive species, their average distance of diffusion away from the metal/solution interface.

Introduction

Radical clocks or radical probes have been some of the tools most widely used to demonstrate the participation of radical species in reaction mechanisms.[1–4] As proposed in a preceding work, radical clocks are radical probes for which reactive intramolecular rearrangements have been kinetically measured.[5] "Rearrangement" covers a variety of chemical acts occurring at the radical stage: racemisation, β-scission, hydrogen atom transfer, or addition to an unsaturated system. A review covering the use of these tools would demand the citation of more than two thousand references. Without going to this extreme, one may select references that show the use of these mechanistic tools in organic,[6–8] organometallic,[9–11] and inorganic chemistry,[12–17] in electrochemistry,[18–23] in photochemistry[24–26] and in enzymatic catalysis.[27–31] In this work we deal with radical probes based on intramolecular additions of aryl radicals to unsaturated systems suitably positioned in substituents situated in *ortho* positions to the aryl radicals. The reaction mechanism investigated is the formation of a Grignard reagent.

Curiously, although radical clocks based on intramolecular additions of fleeting radicals to unsaturated systems had been frequently used since 1975 for corroborating the participation of radicals during the formation of alkylMgX, the world had to wait to 1998 to see this concept applied to the study of arylMgX formation (Scheme 1, $R^1 = R^2 = R^3 = H$). Two teams independently used this type of tool

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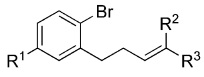
and observed the same surprising result: apparently, and in contrast with their alkyl counterparts, aryl halides were reacting with magnesium metal with almost no participation of radical species (here σ-type sp^2-C-centred radicals).[32,33] The unexpectedness of this observation was further accentuated by the fact that the rate constants of intramolecular addition to unsaturated systems were known to be higher for aryl radicals than for alkyl radicals (5×10^8 s^{-1} vs. 2×10^5 s^{-1}, room temperature). In his quantitative D model of reactivity, Garst was predicting that 64% of cyclised aryl Grignard should be formed, whereas less than 1% was experimentally observed in THF.[33,34]



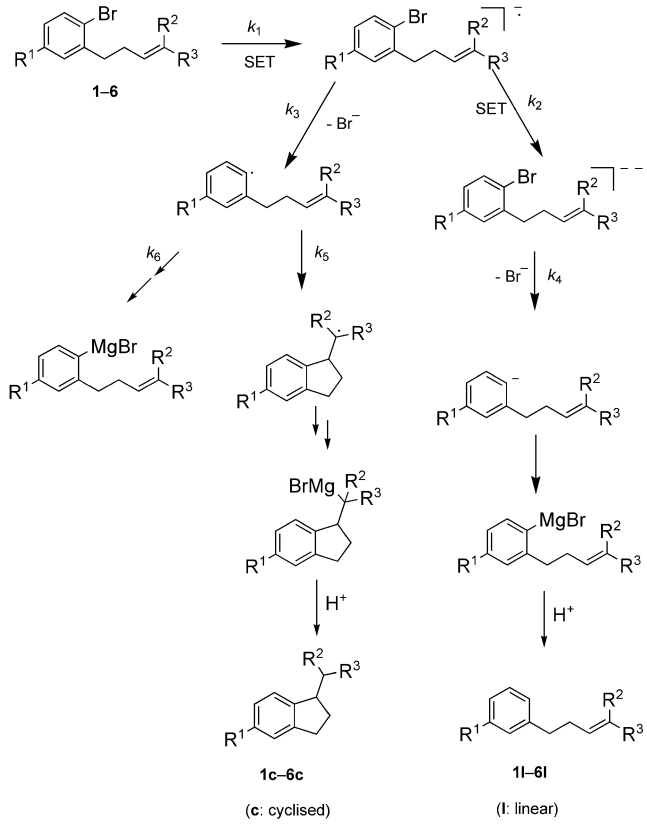
	R^1	R^2	R^3
1	H	H	H
(*E*)-**2**	H	H	Ph
2	H	Ph	H
3	H	Ph	Ph
4	H	*p*-OMe-C_6H_4	H
5	OMe	Ph	H
6	OMe	*p*-OMe-C_6H_4	H

Scheme 1.

The two teams provided diverging explanations for the same experimental observation. Garst's team proposed that the aryl halides, unlike their alkyl counterparts, were able to accept a second electron from the magnesium. This involves the intervention of dianion species or transition states (route k_1, k_2, k_4 dominant in Scheme 2, with weak participation of k_1, k_3...).[33] Our group proposed that the aryl radicals were indeed involved in the route to arylMgX much as alkyl radicals are on the route to alkylMgX (route k_1, k_3, k_5 or k_6 with no participation of k_1, k_2...). However, being much more reactive intermolecularly than alkyl radicals, the aryl radicals were far less readily trapped intramolecularly by the double bond than the alkyl radicals.[32,35]

The logical conclusion of such a hypothesis, then, was to synthesise aryl halides in which the side chain containing the unsaturated system is specifically designed to increase the rate constant of cyclisation. Radical clocks with higher cyclisation rates should display higher yields of rearranged products. Structural effects on the rate constants of radical cyclisations have been intensively explored.[3,4,36,37] Among the structural modifications that increase this rate, one of the most widely recognised is the substitution of the unsaturated system with a phenyl group (Scheme 1, R^2 or R^3 = Ph). The phenyl group indeed stabilises the incipient formed carbon-centred π radical formed by the addition of the radical species on the double bond.[38–42] This effect, could, however, become less important for the very rapid radical clocks.[43]

In this report we want to show that the introduction of phenyl groups on the *exo* double bonds of our radical clocks indeed leads to increases in production of cyclised products in reactions with metallic magnesium. Further studies, however, suggested that these increases were not the



Scheme 2.

consequences of simple classical substituent effects as we had postulated at the start.[35] A *p*-methoxy substituent placed on such a phenyl group would be expected to increase the quantity of cyclised product further.[44] Just the opposite was observed. This result, combined with electrochemical studies of these substrates, hints at a dual role for the phenyl group under the heterogeneous conditions of the Grignard reagent formation. The first role is the widely recognised radical stabilizing effect, but it is completed by a mediating effect. In this second role the phenyl substituent of the styryl group accepts one electron from the metal surface. As a consequence, the radical anion of the substrate aryl halide formed by addition of this electron displays a far longer lifetime than when the added electron directly adds in the π antibonding orbital of the aryl halide group. This leaves more time for the radical anion to diffuse away from the metal surface. We have previously shown that the participation of the radical route to the overall selectivity increases under such conditions.[45–47]

Results and Discussion

The range of structural modifications is shown in Scheme 1. In another report we have shown that with a radical clock bearing an oxygen atom instead of a benzylic CH_2 group (CH_2 replaced with O in (*E*)-**2**), high yields of cyclised product are obtained in the formation of Grignard reagent.[35] However, the effect of the phenyl group on the

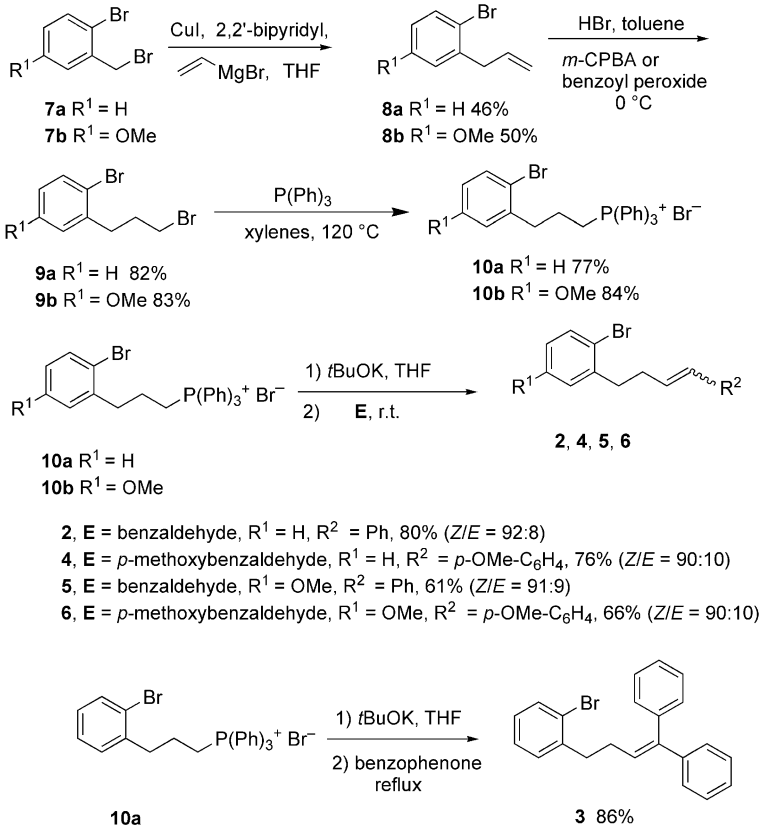
oxygen probe cyclisation rate constant is minor[43] and this more ambiguous[48] increase would deserve further investigation.

Scheme 1 shows stereochemically pure radical probes. Actually, we will see below that our method of preparation yielded mixtures of double bond isomers with the *Z* isomers in the majority, so radical probes **2**, **4**, **5** and **6** represent these mixtures (*Z*/*E* ≈ 90:10). Radical probe (*E*)-**2** represents the pure *E* isomer. In Scheme 2, **1c**–**6c** represent the corresponding cyclised products (e.g. **1c**: $R^1 = R^2 = R^3 =$ H) and **1l**–**6l** the corresponding linear products. The linear products of probes (*E*)-**2**, **2**, **4**, **5**, **6** are formed in *Z*/*E* ratios identical to those in the starting halogeno substrates [e.g. **2l**: R^1 = H, R^2 = Ph, R^3 = H with *Z*/*E* ≈ 90:10, whereas (*E*)-**2l** represents the pure *E* isomer].

Radical probes **2**–**6** were prepared as shown in Scheme 3. Treatment of **7a** or ether **7b** with vinylmagnesium bromide in the presence of CuI and 2,2′-bipyridyl yielded alkenes **8a** and **8b**, respectively. Treatment of **8a** and **8b** with HBr in toluene under radical conditions then gave the bromides **9a** and **9b**. The phosphonium salts **10a** and **10b** were prepared from the corresponding bromides and excess triphenylphosphane in xylenes at 120 °C. Radical traps **2**, **4**, **5** and **6** resulted from Wittig-type reactions between **10a**–**10b** and benzaldehyde or *p*-anisaldehyde as electrophiles. These reactions were carried out in THF at room temperature and yielded mixtures of isomers (*Z*/*E* ≈ 90:10). The Wittig reaction between the phosphonium salt **10a** and the less reactive benzophenone was performed in THF at reflux and afforded **3**. The *E* and *Z* isomers of **2**, **4**, **5** and **6** were identified by ^{1}H NMR spectroscopy, which showed the expected *cis*- and *trans*-vinyl coupling constants. Fortunately, the stereochemical composition does not depend on the methoxy group at the phenyl *para* position. Therefore, in Tables 1 and 2, the reported results for radical clocks in which *Z*/*E* isomerism exists refer to reactions between mixtures of stereoisomers (*Z*/*E* ≈ 90:10) and magnesium turnings.

Tables 1 and 2 summarise the experimental results obtained when structurally different radical clocks were treated with magnesium turnings in THF or diethyl ether at room temperature under nitrogen (Schlenk techniques). This experimental specification is particularly important. Indeed, a recent report shows that cyclisations of RZnX, formerly viewed as carbanionic ones, were actually chain radical cyclisations initiated by traces of dioxygen.[49] We ourselves have reported an example of a reduction with $LiAlH_4$ in which different products were obtained depending on the purity of argon used for the reaction.[50]

The solvent effect reported by Garst when the Grignard reaction was performed on halide **1** in THF or diethyl ether is found again with probes **2**–**6**: yields of cyclised products are higher in diethyl ether than in THF. We will return later to this point. With probes **2**, **4**, **5** and **6**, low yields of cyclised products were obtained in THF (< 1% to 1.5%), so the effect of the methoxy group is discussed mainly for diethyl ether.



Scheme 3.

Table 1. Reactions between radical probes and magnesium (turnings) in THF at room temperature.

Entry[a]	Radical probe[b]	Reaction time	RMgX (%)[c]	Relative yields (%)[d]	
				1c–6c	**1l–6l**[e]
1	**1**	2 h 05	96	< 1	> 99
2	(*E*)-**2**	3 h 15	94	5	95
3	**2**	3 h 30	96	< 1	> 99
4	**4**	3 h 25	94	< 1	> 99
5	**5**	3 h 15	97	1.5	98.5
6	**6**	3 h 15	93	< 1	> 99
7[f]	**3**	2 h 50	84[g]	8[h]	92[h]

[a] [RX] = 0.15 M, Mg/RX = 4.2–4.5, $BrCH_2CH_2Br$/RX = 0.38–0.39. The conversion was 100%. For halide **1**, see ref.[45]. [b] Radical probes **2**, **4**, **5**, **6** were mixtures of stereoisomers: *Z*/*E* ≈ 90:10. [c] Estimated by *o*-phenanthroline titration with 2-BuOH/xylene (0.5 M) as titration reagent. [d] GC determination: c = cyclised and l = linear. [e] *Z* and *E* linear products of probes **2**, **4**, **5**, **6** are formed in ratios identical to those in the starting halogeno substrates. [f] Benzophenone is also formed as byproduct: NMR measurement gives benzophenone/cy+lin ≈ 2:98. [g] Possibly approximate because the colour change during the titration was not sharp. [h] Average of three experiments.

Table 2. Reactions between radical probes and magnesium (turnings) in diethyl ether at room temperature.

Entry[a]	Radical probe[b]	Reaction time	RMgX (%)[c]	Relative yields (%)[d]	
				1c–6c	**1l–6l**[e]
1	**1**	2 h 05	84	9	91
2	(*E*)-**2**	3 h 25	73	20	80
3	**2**	3 h 30	82	17	83
4	**4**	3 h 20	78	2	98
5	**5**	3 h 10	85	11	89
6	**6**	3 h 10	68[f]	1.5	98.5
7[g]	**3**	3 h 30	81[h]	25[h]	75[h]

[a] [RX] = 0.15 M, Mg/RX = 4.2–4.5, $BrCH_2CH_2Br$/RX = 0.38–0.39. The conversion was 100%. For halide **1**, see ref.[45]. [b] Radical probes **2**, **4**, **5**, **6** are mixtures of stereoisomers: *Z*/*E* ≈ 90:10. [c] Estimated by *o*-phenanthroline titration with 2-BuOH/xylene (0.5 M) as titration reagent. [d] GC determination: c = cyclised and l = linear. [e] *Z* and *E* linear products of probes **2**, **4**, **5**, **6** are formed in ratios identical to those in the starting halogeno substrates. [f] The degree of conversion was 90%. [g] Benzophenone is also formed as a byproduct: NMR measurement gives benzophenone/cy+lin ≈ 0.5:99.5. [h] Average of two experiments.

Entries 2–3 in Tables 1 and 2 show that the stereoisomers display slight differences in terms of linear/cyclised selectivity, especially in THF. Kinetic studies on hex-5-en-1-yl radical cyclisations have indicated that *E* and *Z* isomers cyclise at similar rates.[44,51] In a previous report we showed that the linear/cyclised selectivity is best explained by use of the equations proposed by Saveant's group to interpret the selectivity observed in the yields of rearranged products in the vicinity of a cathode.[46,47,52] In these equations, the diffusion coefficients associated with the reactive species play a definite role. Several reports have suggested that the diffusion coefficients of isomers may slightly depend on the shapes of these isomers (here *Z* vs. *E* isomers).[53] This explanation is, however, not sufficient to explain the larger difference observed in THF. At this point we cannot explain the large differences in behaviour for the cyclisations performed in diethyl ether and in THF.

Comparison of Entries 1 and 2 in Tables 1 and 2 shows that the introduction of a phenyl group on the *exo* double bond indeed induces an increase in the formation of the cyclised product. In a previous report we used this observation to suggest that this experimental fact is better accounted for by considering the route that passes through an aryl radical stage (k_1, k_3 in Scheme 2).[35] This suggestion seems to be strengthened by consideration of Entries 7 in both tables: double substitution by phenyl increases the quantity of cyclised products still further. Such an effect has also been reported with cyclisable radical probes in homogeneous solutions.[4] The rate constants, in s^{-1} at 20 °C, for cyclisations of substituted hex-5-enyl radicals in which the double bonds are either terminally unsubstituted or substituted with two phenyl groups are 2×10^5 and 4×10^7, respectively.[4]

Garst, using radical probe **1**, showed that the product distributions in THF and in diethyl ether were not dependent on the reaction times. Moreover, (indanylmethyl)magnesium halides do not ring-open, so the yields of linear and cyclised Grignard products are kinetically controlled in both solvents.[33] With radical probe (*E*)-**2**, we found similar **2l/2c** ratios after reaction times of 3 h 15 or 1 h 40 in THF. Preparation of the Grignard reagent in the presence of *t*BuOH [2 equiv. relative to (*E*)-**2**], a proton donor, had not changed this ratio after 19 h of stirring. In diethyl ether, the same behaviour was found. The **2l/2c** ratios were similar after reaction times of 3 h 25 or 6 h. Addition of *t*BuOH [2 equiv. relative to (*E*)-**2**] had not changed this ratio after 21 h of stirring. Under our reaction conditions, therefore, addition of a phenyl group on the *exo* double bond does not allow the cyclisation of the aromatic Grignard reagent. Usually, five-membered ring cyclisations of alkenyl Grignard reagents are very slow processes. Phenyl substitution on the double bond appears modestly to accelerate the five-membered cyclisation.[54,55] When the reaction mixtures obtained from (*E*)-**2**, in THF or diethyl ether, were quenched with D_2O, more than 90% D incorporation was found in the cyclic product **2c** (–CHDPh, estimated from ^1H NMR 500 MHz), demonstrating the presence of the cyclised Grignard reagent in the mixture.

Garst more recently discussed possible complications with probes such as (*E*)-**2**, proposing that in such probes, "the reduction of the styryl group is a plausible first step of the Grignard reaction…One can envision subsequent pathways to cyclic products…These considerations cast doubt on the validity of these substrates as probes of mechanism of Grignard reagent formation and other reductions. Isomerisations in the corresponding Grignard reactions could be artefacts arising through other processes".[48] We discuss this proposition further later; starting from his first sentence explains why we tried other structural modifications on the probes shown in Scheme 1.

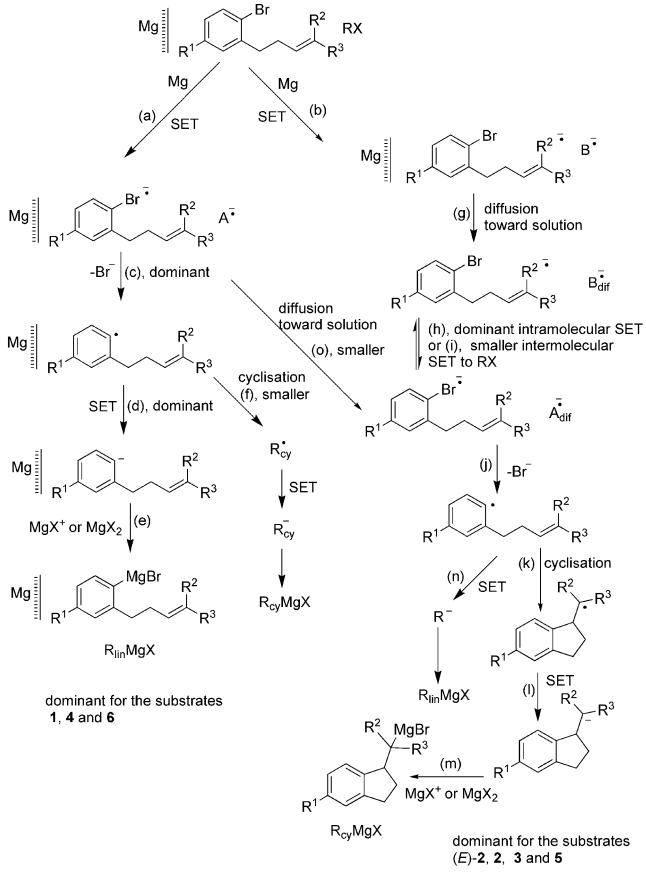
Suppose that the substitution of the phenyl group on the *exo* double bond does indeed have a double effect on the linear/cyclised product selectivity. Firstly, this group in-

creases the rate constant of radical cyclisation (k_5 in Scheme 2); secondly, it causes the first electron transfer from the metal to the substrate to occur on the styryl group rather than on the aryl halide group. The formation of the styryl-centred radical anion could, according to Garst's proposition, open a route to species forming cyclised products (deceptive ones with respect to actual radical probes). This author proposed that such cyclised products could form through attack on the halogen group by the thus-formed styryl radical anion. Such an attack could possibly lead to final products with exactly the same structures as those formed by step k_5 in Scheme 2. In electron transfer chemistry, deposition of an electron in an electrophoretic group followed by an intramolecular electron transfer to the actual reactive site has been repeatedly reported.[56–62]

If such is the case, the introduction of a *para*-methoxy group in the styryl component should change the situation. Such substituents are well known to decrease the electron acceptor character of the styryl group. On the other hand, available rate constants of cyclisation show that the radicals formed from substrate **4** should cyclise slightly more rapidly than those formed from substrate **2**.[44] This is also in line with the stabilisation conferred on a radical by a *para*-methoxy substituent.[63–70]

Therefore, application of Garst's line of thought to substrate **4** should let smaller amounts of cyclised products (mechanistically irrelevant ones) be expected, whereas the simple line of thought "unbiased radical probe **4**" would have suggested an increase in amounts of cyclised products with respect to (*E*)-**2** (Scheme 2, higher k_5). Entries 3 and 4 in Table 2 apparently converge to sustain Garst's proposition: in diethyl ether, smaller amounts of cyclised products are formed when a *p*-methoxy substituent diminishes the electron acceptor ability of the styryl block in the fast radical probes.

Electrochemical studies and application of electrochemical treatment of selectivity at electrode surfaces, however, offer an alternative explanation of this apparent convergence (Scheme 4). This interpretation is based on the participation of redox catalysis for the set of substrates (*E*)-**2**, **2**, **3**, and **5**. This redox catalysis demands the presence of electrophoretic groups on the *exo* double bonds; these electrophoretic groups must be better electron acceptors than the aryl halide part of the radical clock. The first electron transfer then occurs on the styryl part (path b in Scheme 4). In the anion radical thus formed, a reversible intramolecular electron transfer shuttle takes place (equilibrium h in Scheme 4). Overall, the equilibrium should favour the form in which the electron resides on the styryl group. Because of the irreversible carbon halogen bond cleavage (step j) occurring when the electron is in the aryl halide part, the equilibrium is nevertheless driven toward the production of the aryl radical. From the knowledge that the C–Br bond cleavage itself involves an intramolecular electron transfer (not represented in Scheme 4), the overall route corresponds to a cascade of three electron transfers (one intermolecular followed by two intramolecular).[62] Meanwhile, the radical anion and its counterion, possibly $MgBr^+$, have time to diffuse away from the metallic surface. The longer the overall set of three electron transfers takes to take place, the farther from the metallic surface the σ aryl radical will be formed. For the set of substrates **1**, **4** and **6**, in which the redox catalysis plays a negligible role, the cascade is simplified to two electron transfers (route a in Scheme 4). Such examples of intramolecular redox catalysis in the vicinity of a cathode have been explored.[71,72] This intramolecular redox catalysis is to be distinguished from the intermolecular redox catalysis involved in the arene catalysis of formation of organolithium compounds.[73] The electrochemical treatment of the cathodic reactivity of 9-chloroanthracene was a simplified case of intramolecular redox catalysis: here the cascade consisted of only two electron transfers.[52] Such cascades of intramolecular electron transfers driven by an irreversible last reaction provide simplified models for the electron transport chains involved in photosynthetic reaction centres.



Scheme 4.

For the fates of aryl radicals, we follow Bickelhaupt's group's proposition. This group proposed that the best way to explain their experimental results for aryl halides was to assume that aryl radicals were reduced to carbanions.[74–76] This was an original proposition, because up to their work it had been believed that the route from radicals to RMgX involved a direct coupling of radical R· with the paramagnetic MgX· species formed by reaction between Mg radical

cations and X anions.[77,78] In Bickelhaupt's and Garst's representations, RMgX results from reactions of R carbanions with MgX^+[75] and MgX_2,[48] respectively.

Solvent effects fit with this proposition. In diethyl ether, the cyclised/uncyclised ratio is higher than in THF. The viscosity of diethyl ether (0.194 cP) is about half that of THF (0.389 cP).[34,79] Everything proceeds as if the radical anion formed by heterogeneous electron transfer had more chances to get away from the metal surface in diethyl ether, therefore giving birth to the aryl radical farther away from the surface. This aryl radical would therefore, on average, have a lower probability of undergoing reduction than when the same succession of events occurs in THF. Bickelhaupt was the first author to propose the importance of viscosity in the selectivity of formation of Grignard reagents.[79] Later, Garst returned to this point and laid stress on polarity factors.[34,48] In this scheme of things, the polarity of the solvent plays a role in the value of k_3 (Scheme 2): more polar solvents increase its value.[80] The higher polarity of THF therefore fits with the lower yield of cyclised products obtained in this solvent: if the cleavage of the radical anion is faster, the aryl radical is created near the surface and has good chances of being reduced more rapidly.

Scheme 4 contains three oversimplifications. Firstly, although the route going through step a suggests the continuous presence of the magnesium surface in close proximity to the formed aryl radical, a better representation would be a short-distance shuttle of this radical between the metallic surface and the solution.[81,82] Scheme 4 emphasises the average proximity of the metallic surface, to contrast this situation with that in which intramolecular redox catalysis takes place.

Secondly, this scheme neglects the step of hydrogen atom transfer from the solvent to the aryl radical.[33,52] Ashby's contribution concerning the role of radicals in the formation of alkylMgX clearly showed such participation.[78] Saveant's report on the reactivity patterns of aryl halides suggests that the reduction of the σ aryl radicals formed by the cleavage of radical anions is fast enough to overcome their dimerisation and hydrogen abstraction reactivity.[52] The reduction (step d in Scheme 4) plays this predominant role because aryl radicals are better oxidizing agents than alkyl ones.[83–85] They are also better hydrogen atom abstractors than their alkyl counterparts (k abstraction from THF is $6 \times 10^7\ s^{-1}$ for aryl radicals at 25 °C vs. $7 \times 10^6\ s^{-1}$ for cyclopropyl radical).[34,37,86] The rates constants of cyclisation for the aryl-centred radical clocks are about $5 \times 10^8\ s^{-1}$,[37,87,88] or even higher when the double bond is stabilised by a phenyl group.[38–43] For the structures displayed in Tables 1 and 2, the H-abstraction reaction could become less negligible for the set of substrates relevant to intramolecular redox catalysis [(*E*)-**2**, **2**, **3** and **5**]. If predominant, this reaction would lead to increased yields of linear products, in contrast with the experimental trends for this set of substrates shown in Tables 1 and 2.

Thirdly, the complete electrochemical treatment of the selectivity observed when aryl halides react at a cathode includes, for some substrates, the possibility that the aryl radicals generated by the radical anion cleavage might be reduced in two different steps.[52] The first of these (step d or n in Scheme 4) involves a reduction of this radical by the metal surface. The second involves the reduction of this radical by radical anions migrating away from the metal surface. Its participation becomes non-negligible for radical anions of sufficient lifetime. In the original electrochemical treatment this corresponds to substrates such as 9-chloroanthracene or 9-bromoanthracene.[52] Substrates such as (*E*)-**2**, **2**, **3** and **5** would obviously be those for which this oversimplification would be the most damaging. The complete electrochemical treatment of intramolecular redox catalysis shows, however, that this neglect does not modify, overall, the interpretation of the experimental observations described in this report.

Cyclic voltammograms of radical clocks in DMF (NBu_4BF_4 as electrolyte) make it evident that, at a glassy carbon disk cathode, the first electron transfer occurs mainly on the halogenoaryl structural block only for the probes **1**, **4** and **6**. For (*E*)-**2**, **2**, **3** and **5** it occurs mainly on the styryl part.

The voltammograms of the radical probes (RBr) display either one or two peaks. One is connected with the reduction of the aryl halide structural block, the second is connected with the reduction of the substrate in which the bromine is replaced by hydrogen (reduction of the linear product RH). The cyclised products are not seen in the voltammograms because they are situated at too negative values. Within this general pattern of reactivity, the observed peaks are rather close. The voltammograms of substrate **1** show only the peak corresponding to the aryl halide group (–2.58 V vs. aq. SCE). For this substrate the reduced product (RH) peak lies at a value too negative to be seen. It is visible, however, for substrates **4** and **6** (**4**: peaks at –2.61 V for RBr and –2.79 V for RH, **6**: peaks at –2.65 V for RBr and –2.80 V for RH). The set of radical probes in which the electron transfer occurs predominantly on the styryl group displays a distinct pattern of voltammograms. For (*E*)-**2**, voltammograms show peaks at –2.46 V (RBr) and –2.63 V (RH). For **2** (*Z*/*E* 64:36), peaks displayed were similar (–2.47 V and –2.64 V). For substrate **3** these peaks are at –2.44 V (RBr) and –2.56 V (RH) and for substrate **5** they are seen at –2.50 V (RBr) and –2.64 V (RH). Under the same experimental conditions, styrene itself displays a unique peak at –2.52 V. Although the set of radical clocks in which the first electron transfer takes place on the stryryl part of the molecule shows a strong similarity with styrene itself, the peak values (RBr) for substrates **1**, **4** and **6** are not outstandingly distant from this styryl-type value (average difference of about 0.1 V). Competition between the two types of electrophores (aryl halide vs. styryl) is therefore possible.

The effect of a *p*-methoxy group on the styryl part, seen by comparison of the RH peaks of substrates **2** and **4** (difference of 0.15 V), gives a quantitative measure of the decrease in the electron acceptor ability of the styryl electrophoretic group *para*-substituted with a methoxy group.

These electrochemical observations therefore suggest an alternative to Garst's proposition: in the set of radical clocks (*E*)-**2**, **2**, **3** and **5**, intramolecular redox catalysis is made possible by the presence of the phenyl group. In previous reports, we proposed that the reductive strength of the magnesium surface was stronger than most of the homogeneous reductants (including the solvated electron).[46,47] As a consequence, an aryl radical created in close vicinity to this metallic surface should have less chance to cyclise because its rate of reduction into a carbanion would be very high. In contrast, when the radical is created at a greater distance from this metal surface, it would have better chances to cyclise. This situation will be met when the radical anions creating the aryl radical are long-lived enough to diffuse away from the metallic surface.[89,90] Radical clocks (*E*)-**2**, **2**, **3** and **5** illustrate this situation. For these radical clocks, the increase in the cyclised products has a double origin. *Firstly, because of intramolecular redox catalysis the σ aryl radicals are, on average, formed at a larger distance from the metallic surface. Secondly, because of the stabilizing effect of the phenyl group, the rate of radical cyclisation is increased.*

For substrate **3** one could have expected a relative yield of cyclised product higher than those given in Tables 1 and 2. The stabilisation of the radical formed during the cyclisation is certainly higher when it is substituted with two phenyl groups. These groups, however, could also hinder the attack on the double bond during the radical cyclisation.[4,91,92]

In the set of substrates in which intramolecular redox catalysis occurs, **5** is the member for which the relative quantity of cyclised compound is the lowest in diethyl ether (Entry 5, Table 2). A possible reason for this observation could be sought for in the effect of the *p*-MeO group on the rate of cyclisation (k_5, Scheme 2). If this group stabilises the σ aryl radical, this could induce a lower rate of cyclisation. Recent theoretical calculations suggest that this *p*-MeO group slightly destabilises this radical.[93] Another explanation for this experimental observation must therefore be provided. This pattern of reactivity may be qualitatively understood in terms of average distance from the metallic surface when the cleavage of the C–Br bond occurs in the formed radical anion. Besides the intrinsic diffusion coefficient of the species in the medium under consideration, this average distance depends on two parameters.[52,89,90] The first is the equilibrium constant of the first intramolecular electron transfer in the formed radical anion (step h in Scheme 4); for the radical anion formed from **5**, this equilibrium should be shifted toward the species in which the electron stays in the styryl part. The second is the rate of intramolecular electron transfer from the antibonding π cloud to the antibonding σ orbital of the C–Br bond in the aryl halide part. This second parameter has been repeatedly studied: in the radical anion of **5** an increase in this rate would be expected.[94–96] These two parameters play in opposite directions; comparison of Entries 3 and 5 in Table 2 suggests that the second parameter dominates. Everything takes place as if the average distance of cleavage for the C–Br bond of the radical anion formed from **5** were smaller than those related to radical anions from **2** and **3**.

The shared structural feature of **4** and **6** in the set of substrates **1**, **4** and **6** is the *para* substitution of the styryl group with a methoxy substituent. This substituent prevents, at least partly, the occurrence of the first electron transfer on the styryl part (induced difference in electrophoretic activity of 0.15 V). As a consequence, the patterns of reactivity of these two substrates directly parallel that of substrate **1** (in Tables 1 and 2, compare Entries 4 and 6 with Entry 1). In diethyl ether, the relative amount of cyclised compound for substrate **1** is even higher than that measured for the other two radical clocks of the set. This effect was not expected in terms of structural effects because the *para*-methoxyphenyl substituent should increase the rate of cyclisation for the aryl radical.[44] It disappears, however, in the electrochemical study. The data presented are not sufficient for discussion of its origin (counterion effects in the diffusion coefficients of the radical anions?). In comparison with the set of substrates (*E*)-**2**, **2**, **3** and **5**, this set is, overall, characterised by a shorter average distance of diffusion before the cleavage of the C–Br bond of the radical anion formed from the starting substrate.

Garst's proposal that the rapid radical clocks such as (*E*)-**2**, **2**, **3** and **5** could provide deceptive results because the initial electron transfer occurs on the styryl part of the molecule to yield a radical anion capable of reacting intramolecularly as a nucleophile to substitute the halogen of the aryl halide part of the molecule must be discussed further.[48] The best identified cases of ring-closure reactions triggered by an electron transfer and involving C–C bond formation are intramolecular $S_{RN}1$ reactions. These have recently been reviewed. The currently accepted mechanism involves a key step in which an aryl radical formed by cleavage of the radical anion reacts intramolecularly with a suitably situated carbanion in the same structure.[61] To the best of our knowledge, there are no precedents for S_NAr substitution in which the nucleophile is a radical anion. Usually, when an aromatic radical anion interacts with an aromatic halide, the interaction involves electron transfer between the interacting species driven by the cleavage of the C–X bond in the formed radical anion.[96] It might possibly be that future works will identify aromatic radical anions as nucleophiles at sp^2 carbon, as they have been on sp^3 ones.[97–99] At the present state of knowledge, however, such an intramolecular S_NAr substitution performed by a radical anion introduces a layer of complexity for which there is no evidence.

Theoretical and experimental approaches have given rise to the hypothesis that the formation of the Grignard reagent, rather than being triggered by an electron transfer from the metal, would be better understood in terms of a simple concerted oxidative addition of magnesium to the C–X bond.[100,101] In the terms of such an interpretation, it seems that substituent effects further than six atoms away from the C–X reactive centre should play a negligible role in the selectivity of the reaction. The results given in Table 1 and Table 2 display trends contrasting with this expectation.

A possible origin of this discrepancy could be sought for within the representation of Grignard reagent formation as a form of organic corrosion.[34,48] In such a representation, the kinetic measurements of metal consumption would have to be connected with an act of anodic dissolution. The donicity of the solvent, the importance of which in the rate of metal dissolution has been repeatedly shown by Maslennikov's team, could play its role at this anode.[102–104] The kinetic and selectivity results based on the fates of organic substrates and products, would, on their part, be connected to an act of cathodic reaction. The microanodes and microcathodes would be spatially distinct, although by not more than about five magnesium atoms.[34,48] Part of their reactivity could be coupled.[105,106] More work is needed to verify this kind of hypothesis.

Conclusions

This concomitant study of two complementary facets (electrochemical and synthesis) of selectivity in a series of structurally designed radical clocks sheds some fresh light on the mechanism of Grignard reagent formation and on the specificities of radical clocks used as mechanistic tools in heterogeneous media.

Firstly, the consistent reactivity patterns associated with structural variations when these substrates react to form ArMgX or to accept an electron from a cathode sustain the hypothesis of a single electron transfer from the magnesium surface as the triggering act of Grignard reagent formation. The proposition of a simple oxidative addition (magnesium atom insertion) of magnesium atoms to ArX is difficult to reconcile with the long-range substituent effects observed in this work.

Secondly, under the heterogeneous reaction conditions described here, the phenyl substituent effects classically encountered in radical reactions performed in homogeneous solutions become more complex. The widely acknowledged stabilisation of radicals by phenyl substituents has to be completed. This substituent may behave as a distant electrophoretic group where the first electron transfer may occur rather than going directly to the apparent centre. Under homogeneous reaction conditions this event would be of little importance in terms of selectivity because the electron would in any case be finishing its travel on the apparent centre. Spatially, at the end of the travel the molecule would be reacting in the same microscopic environment as was present when the electron was accepted. Under heterogeneous conditions, though, the molecule also has time to travel during the intramolecular electron transfer. This time, at the end of the travel, the molecule reacts in a microscopic environment that might be quite different from the one in which the electron was accepted. In Grignard reagent formation and in cathodic reduction, the heterogeneity is obvious. In some situations (particularly in biological media, colloidal solutions, forming polymers) the heterogeneity of the medium is less easy to recognise. The substituent effects described in this report could help in recognition of this.

Experimental Section

General: THF (S.D.S., 99.7%) and diethyl ether (S.D.S., 99.7%) were dried with sodium-benzophenone and distilled from purple solutions prior to use. Butan-2-ol was dried with K_2CO_3 and then distilled. Xylenes (mixture of isomers) was distilled from sodium/benzophenone ketyl. All glassware and transfer needles were oven-dried at 100 °C. 1,2-Dibromoethane (Acros, 99%), DMF (puriss absolute anhydrous, Fluka) and magnesium turnings (Aldrich, 99.98%) were used as received. NBu_4BF_4 was synthesised from ammonium tetrafluoroborate and tetrabutylammonium chloride (Fluka), recrystallised from petroleum ether, and then dried overnight before use.[107] Gas chromatography analysis was performed on a Fisons GC 8000 instrument with use of a BPX5 capillary column (SGE, 25 m, 0.22 mm internal diameter), helium as carrier gas and a flame ionisation detector (injector: 280 °C; detector: 250 °C). The following program temperature was used: 150 °C (3 min) to 250 °C (15 min) at 5 °C min^{-1}. Peak area integrations were performed by electronic integration on a SP4600 Integrator (Spectra Physics) and, if necessary, corrected by use of the ECN (effective carbon number) concept.[108] Petroleum ether (boiling range 40–65 °C) was distilled prior to use for liquid phase chromatography. Thin-layer chromatography (TLC) was performed with Merck silica gel (60 F_{254}) plates. Column chromatography was performed with Merck silica gel 60 (230–400 mesh particle size). Separations were monitored both by TLC and by gas chromatography (GC). $AgNO_3$-impregnated silica gel: $AgNO_3$ (2.5 g) and CH_3CN (150 mL) were introduced into a flask containing a magnetic stirrer. After the mixture had been stirred in the dark (10 min), silica gel (50 g) was added. The mixture was stirred for 2 h in the dark, and the solvent was then evaporated. Drying was achieved overnight in a oven. The column chromatography was performed in the dark. NMR spectra were run in $CDCl_3$ and were generally recorded at 300 MHz (^1H) and 75 MHz (^{13}C). NMR of compounds **2**, **4**, **5** and **6** were each run with two different mixtures of isomers ($Z/E \approx 90:10$ and $\approx 60:40$). ^{13}C NMR peak shifts are rounded off to the nearest 0.1 ppm except when greater precision is needed to distinguish closely spaced peaks. For compounds **4**, **5**, **6**, **3** and **4l**, signals may be blurred because of potential overlap. Gas chromatography/mass spectrometry (GC-MS) was performed by electronic impact at 70 eV. 1-Bromo-2-(but-3-enyl)benzene (**1**)[33,109] 1-bromo-2-[(3*E*)-4-phenylbut-3-enyl]benzene [(*E*)-**2**],[35] 4-bromo-3-(bromomethyl)-phenyl methyl ether (**7b**),[110] authentic samples of but-3-enylbenzene (**1l**)[33] and 1-methylindane (**1c**)[33,111] were prepared as described in literature. The reaction between bromide **1** and Mg has been described previously.[45]

Reactions between Bromides 2–6 and Magnesium: Magnesium (4.2–4.5 equiv.) was introduced into a Schlenk tube containing a magnetic bar. The Schlenk tube was successively degassed by three vacuum/nitrogen cycles, flame-dried in a flow of nitrogen and degassed again. Bromide (0.29–0.30 mmol, 1 equiv.) was introduced into a flask (10 mL) and this flask was flushed with nitrogen for about 10 min. Solvent (THF or diethyl ether, 2 mL) and 1,2-dibromoethane (0.38–0.39 equiv.) were added by syringe. The obtained solution was transferred by cannula to the Schlenk tube. After the allocated time of stirring (Teflon-coated stirring bars were used) at room temperature the Grignard reagent was titrated by Watson and Eastham's method.[112] A solution of *o*-phenanthroline (ca. 1 mg) in the reaction solvent (ca. 1 mL) was added by syringe. If Grignard reagent is present a purple or maroon colour develops. The mixture was then titrated to the endpoint with a solution of butan-2-ol in xylenes (0.5 M). After dilution with diethyl ether, the reaction mixture was successively washed with ammonium chloride (10%) and

water, dried ($MgSO_4$) and filtered. The crude product was analysed by GC and NMR spectroscopy. Components were identified by co-injection of authentic samples, GC-MS and NMR comparisons.

1-Bromo-2-(prop-2-enyl)benzene (8a) and 4-Bromo-3-(prop-2-enyl)-phenyl Methyl Ether (8b): These compounds were prepared by a modification of the method described by Knight and Parsons.[113]

1-Bromo-2-(prop-2-enyl)benzene (8a): A mixture of 2-bromobenzyl bromide (**7a**, 5.0 g, 20.0 mmol), THF (35 mL), CuI (0.42 g, 2.20 mmol) and 2,2′-bipyridyl (0.325 g, 2.08 mmol) was cooled to 0 °C and placed under nitrogen. A solution of vinylmagnesium bromide (20 mL of a 1 M solution in THF, 20 mmol) was transferred by cannula. The reaction mixture was stirred under nitrogen for 55 min at 0 °C and for 5 min without the ice bath. Solid NH_4Cl (8 g) was added, followed by Et_2O (90 mL) and water (80 mL). The solution was then transferred into a beaker and aqueous ammonia (33%, 5 mL) was added. After stirring (20 min), the organic phase was separated and the aqueous layer was extracted with Et_2O. The combined extracts were washed with aqueous HCl (10%) and saturated aqueous $NaHCO_3$, dried ($MgSO_4$) and concentrated. Chromatography on silica gel (petroleum ether) afforded **8a** as a colourless liquid (1.8 g, 46%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.51 (dt, J = 6.5, 1.5 Hz, 2 H), 5.04–5.14 (m, 2 H), 5.98 (ddt, J = 17.0, 10.2, 6.5 Hz, 1 H), 7.04–7.10 (m, 1 H), 7.21–7.30 (m, 2 H), 7.53–7.56 (m, 1 H) ppm. ^{1}H NMR spectroscopic data obtained agreed with published values.[113]

4-Bromo-3-(prop-2-enyl)phenyl Methyl Ether (8b): This compound was prepared by the same procedure with **7b** (5.667 g, 20.2 mmol), THF (38 mL), CuI (0.436 g, 2.29 mmol), 2,2′-bipyridyl (0.335 g, 2.15 mmol) and vinylmagnesium bromide (22 mL of a 1 M solution in THF, 22 mmol). Column chromatography on $AgNO_3$-impregnated silica gel (petroleum ether) afforded **8b** as a colourless liquid (2.28 g, 50%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.46 (dt, J = 6.6, 1.4 Hz, 2 H), 3.77 (s, 3 H), 5.05–5.15. (m, 2 H), 5.96 (ddt, J = 16.8, 10.2, 6.6 Hz, 1 H), 6.65 (dd, J = 8.7, 3.0 Hz, 1 H), 6.78 (d, J = 3.0 Hz, 1 H), 7.42 (d, J = 8.7 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 40.5, 55.5, 113.6, 115.1, 116.2, 116.8, 133.3, 135.6, 140.6, 159.2 ppm. $C_{10}H_{11}BrO$ (227.10): calcd. C 52.89, H 4.88, Br 35.18; found C 52.58, H 4.86, Br 33.96. The elemental analysis of this product is the average of three experimental measurements, except for Br, for which only one was performed.

1-Bromo-2-(3-bromopropyl)benzene (9a): A solution of **8a** (1.747 g, 8.86 mmol) and 3-chloroperbenzoic acid (ca. 70%, ca. 0.09 g, ca. 0.36 mmol) in toluene (33 mL) was prepared under nitrogen and cooled to 0 °C. An excess of HBr was bubbled through the mixture. HBr was prepared from the addition of Br_2 (3 mL, 58.4 mmol) to tetraline (7.3 mL, 53.4 mmol) over 1 h 15 min. At the halfway point of the addition, another portion of 3-chloroperbenzoic acid (ca. 70%, ca. 0.075 g, ca. 0.30 mmol) was added to the reaction mixture. With the addition of Br_2 finished, the reaction mixture was stirred at 0 °C for 30 min and left under air for 20 min at room temperature to allow HBr evaporation. The reaction mixture was then washed with aqueous Na_2SO_3 (20%) and water, dried ($MgSO_4$) and concentrated. Column chromatography of the residue (petroleum ether) afforded **9a** (2.013 g, 82%) as a colourless liquid. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.14–2.23 (m, 2 H), 2.91 (t, J = 7.5 Hz, 2 H), 3.43 (t, J = 6.6 Hz, 2 H), 7.05–7.11 (m, 1 H), 7.21–7.27 (m, 2 H), 7.54 (d, J = 7.7 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 32.6, 33.1, 34.6, 124.6, 127.6, 128.1, 130.8, 133.1, 140.0 ppm. ^{1}H and ^{13}C NMR spectroscopic data obtained agree with published values.[114]

4-Bromo-3-(3-bromopropyl)phenyl Methyl Ether (9b): For this experiment, benzoyl peroxide (ca. 75%, 0.2 g, ca. 0.62 mmol) was dissolved in toluene (3 mL), and water was removed by decantation. A solution of **8b** (1.1 g, 4.84 mmol) and benzoyl peroxide (1 mL of a 0.2 M solution in toluene, 0.2 mmol) in toluene (10 mL) was prepared under nitrogen and cooled to 0 °C. An excess of HBr was bubbled through the mixture. HBr was prepared by addition of Br_2 (3.2 mL, 62.3 mmol) to tetraline (13 mL, 95.1 mmol) over 1 h 40 min. During this addition, two further portions of benzoyl peroxide (1 mL, ≈0.4 mmol) were added to the reaction mixture. With the addition of Br_2 finished, the reaction mixture was stirred for 4 h and allowed slowly to reach room temperature. The reaction mixture was then washed with aqueous Na_2SO_3 (20%) and water, dried ($MgSO_4$) and concentrated. Column chromatography of the residue (petroleum ether, petroleum ether/Et_2O 99:1 and 98:2) afforded **9b** (1.24 g, 83%) as a pale yellow liquid. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.18 (quint, J = 7.0 Hz, 2 H), 2.86 (t, J = 7.4 Hz, 2 H), 3.43 (t, J = 6.6 Hz, 2 H), 3.78 (s, 3 H), 6.65 (dd, J = 8.8, 3.0 Hz, 1 H), 6.81 (d, J = 3.0 Hz, 1 H), 7.41 (d, J = 8.8 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 32.5, 33.2, 34.8, 55.6, 113.7, 114.9, 116.4, 133.6, 141.0, 159.1 ppm. $C_{10}H_{12}Br_2O$ (308.01): calcd. C 38.99, H 3.93; found C 39.29, H 3.79.

[3-(2-Bromophenyl)propyl](triphenyl)phosphonium Bromide (10a): A solution of **9a** (6.95 g, 25 mmol) and triphenylphosphane (13.1 g, 50 mmol) in xylenes (200 mL) was stirred under nitrogen at 120 °C (bath temperature). During the reaction, triphenylphosphane (60.3 g, 230 mmol) was added in five portions. The reaction time was 30 h. A solid was formed, and after cooling to room temperature the mixture was filtered through a Büchner funnel. This solid was then washed with xylenes and petroleum ether to afford pure **10a** (10.4 g, 77%) as a white solid; m.p. 222–223 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.93–2.06 (m, 2 H), 3.20 (t, J = 7.5 Hz, 2 H), 3.93–4.03 (m, 2 H), 7.05 (td, J = 7.7, 1.7 Hz, 1 H), 7.25 (td, J = 7.7, 1.2 Hz, 1 H), 7.44 (dd, J = 7.7, 1.2 Hz, 1 H), 7.60 (dd, J = 7.7, 1.7 Hz, 1 H), 7.63–7.70 (m, 6 H), 7.74–7.85 (m, 9 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 22.1 (d, $J_{C,P}$ = 50.5 Hz), 22.6 (d, $J_{C,P}$ = 3.3 Hz), 36.3 (d, $J_{C,P}$ = 17.6 Hz), 118.3 (d, $J_{C,P}$ = 86.2 Hz), 124.2, 128.0, 128.3, 130.5 (d, $J_{C,P}$ = 12.6 Hz), 132.3, 132.8, 133.7 (d, $J_{C,P}$ = 9.9 Hz), 135.1 (d, $J_{C,P}$ = 3.3 Hz), 139.5 (d, $J_{C,P}$ = 1.1 Hz) ppm; some chemical shifts and coupling constants were not definitely assigned. ^{31}P NMR (121 MHz, $CDCl_3$): δ = 24.8 ppm. $C_{27}H_{25}Br_2P$ (540.27): calcd. C 60.02, H 4.66; found C 59.92, H 4.50.

[3-(2-Bromo-5-methoxyphenyl)propyl](triphenyl)phosphonium Bromide (10b): This compound was prepared by the same procedure with **9b** (0.889 g, 2.89 mmol) and xylenes (24 mL). Triphenylphosphane (6.195 g, 23.6 mmol) was added in three portions: 2.529 g (initial time), 2.646 g (t = 7 h 30 min) and 1.020 g (t = 23 h).The reaction time was 29 h. Workup afforded pure **10b** (1.381 g, 84%) as a white solid; m.p. 174–175 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.93–2.07 (m, 2 H), 3.15 (t, J = 7.4 Hz, 2 H), 3.83 (s, 3 H), 3.93–4.03 (m, 2 H), 6.63 (dd, J = 8.7, 3.2 Hz, 1 H), 7.23 (d, J = 3.2 Hz, 1 H), 7.30 (d, J = 8.7 Hz, 1 H), 7.64–7.70 (m, 6 H), 7.75–7.86 (m, 9 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 22.1 (d, $J_{C,P}$ = 50.5 Hz), 22.5 (d, $J_{C,P}$ = 3.8 Hz), 36.6 (d, $J_{C,P}$ = 17.6 Hz), 56.1, 114.3, 115.1, 116.8, 118.3 (d, $J_{C,P}$ = 86.2 Hz), 130.5 (d, $J_{C,P}$ = 12.6 Hz), 133.2, 133.7 (d, $J_{C,P}$ = 10.4 Hz), 135.1 (d, $J_{C,P}$ = 2.7 Hz), 140.5 (d, $J_{C,P}$ = 1.1 Hz), 159.2 ppm; some chemical shifts and coupling constants were not definitely assigned. ^{31}P NMR (121 MHz, $CDCl_3$): δ = 24.8 ppm. $C_{28}H_{27}Br_2OP$ (570.30): calcd. C 58.97, H 4.77; found C 58.14, H 4.59.

1-Bromo-2-(4-phenylbut-3-enyl)benzene (2): tBuOK (0.215 g, 1.92 mmol) was added to a suspension of phosphonium salt **10a** (1.007 g, 1.86 mmol) in THF (8 mL) under a flow of nitrogen. The mixture was stirred under nitrogen for 15 min, and benzaldehyde

(0.19 mL, 1.87 mmol) was then slowly added by syringe. The mixture was stirred for 22.5 h at room temperature. The reaction was then quenched with HCl (1 M) and extracted with Et_2O. The organic layer was washed with water, dried ($MgSO_4$) and concentrated. Column chromatography of the residue (petroleum ether) afforded pure **2** (0.428 g, 80%, *Z*/*E* 92:8 from GC analysis) as a colourless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.53 (br. q, *J* = 7.4 Hz, 2 H *E*), 2.61–2.70 (m, 2 H *Z*), 2.86–2.94 (m, 2 H *Z* and 2 H *E*), 5.72 (dt, *J* = 11.6, 7.2 Hz, 1 H *Z*), 6.27 (dt, *J* = 15.7, 6.7 Hz, 1 H *E*), 6.42 (br. d, *J* = 15.7 Hz, 1 H *E*), 6.47 (br. d, *J* = 11.6 Hz, 1 H *Z*), 7.02–7.08 (m, 1 H *Z* and 1 H *E*), 7.19–7.34 (m, 7 H *Z* and 7 H *E*), 7.51–7.56 (m, 1 H *Z* and 1 H *E*) ppm. ^{13}C NMR (*Z* isomer, 75 MHz, $CDCl_3$): δ = 28.9, 36.4, 124.7, 126.7, 127.5, 127.8, 128.3, 128.8, 129.9, 130.6, 131.5, 132.9, 137.6, 141.0 ppm. $C_{16}H_{15}Br$ (287.19): calcd. C 66.91, H 5.26; found C 66.49, H 5.26.

4-[4-(2-Bromophenyl)but-1-enyl]phenyl Methyl Ether (4): The same procedure with phosphonium salt **10a** (1.008 g, 1.87 mmol), THF (8 mL), *t*BuOK (0.215 g, 1.92 mmol) and *p*-anisaldehyde (0.23 mL, 1.89 mmol) afforded, after column chromatography (petroleum ether and petroleum ether/Et_2O 95:5), compound **4** as a colourless oil (0.452 g, 76%), (*Z*/*E* 90:10 from GC analysis). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.50 (br. q, *J* = 7.4 Hz, 2 H *E*), 2.65 (br. q, *J* = 7.7 Hz, 2 H *Z*), 2.86–2.92 (m, 2 H *Z* and 2 H *E*), 3.798 (s, 3 H *E*), 3.802 (s, 3 H *Z*), 5.62 (dt, *J* = 11.6, 7.1 Hz, 1 H *Z*), 6.12 (dt, *J* = 15.8, 6.9 Hz, 1 H *E*), 6.36 (br. d, *J* = 15.8 Hz, 1 H *E*), 6.39 (br. d, *J* = 11.6 Hz, 1 H *Z*), 6.82–6.86 (m, 2 H *Z* and 2 H *E*), 7.02–7.08 (m, 1 H *Z* and 1 H *E*), 7.18–7.29 (m, 4 H *Z* and 4 H *E*), 7.53 (d, *J* = 7.7 Hz, 1 H *Z*), 7.54 (d, *J* = 7.9 Hz, 1 H *E*) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 28.89, 33.33, 36.36, 36.39, 55.32, 55.35, 113.70, 114.03, 124.59, 124.61, 127.22, 127.39, 127.49, 127.73, 127.76, 129.26, 129.85, 130.02, 130.07, 130.23, 130.52, 130.55, 130.59, 132.89, 132.91, 141.06, 141.15, 158.40, 158.89 ppm. $C_{17}H_{17}BrO$ (317.22): calcd. C 64.37, H 5.40, Br 25.19; found C 64.85, H 5.49, Br 24.84.

4-Bromo-3-(4-phenylbut-3-enyl)phenyl Methyl Ether (5): *t*BuOK (0.070 g, 0.62 mmol) was added to a suspension of phosphonium salt **10b** (0.328 g, 0.57 mmol) in THF (2.6 mL) under a flow of nitrogen. The mixture was stirred under nitrogen for 15 min. Benzaldehyde (0.049 g, 0.46 mmol) was then added under a flow of nitrogen, together with THF (0.4 mL) used for rinsing. The mixture was stirred for 25 h. at room temperature. The reaction mixture was then quenched with HCl (1 M) and extracted with Et_2O. The organic layer was washed with water, dried ($MgSO_4$) and concentrated. To induce oxidation of residual benzaldehyde and to make the purification easier, the crude product was exposed to air and daylight for about 24 h. Two chromatographic columns were necessary to obtain a pure product. A column of silica gel (petroleum ether/EtOAc 97:3) followed by a separation on silica gel impregnated with $AgNO_3$ (petroleum ether/EtOAc 98:2) afforded **5** as a colourless oil (0.09 g, 61%, *Z*/*E* 91:9). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.52 (br. q, *J* = 7.4 Hz, 2 H *E*), 2.61–2.69 (m, 2 H *Z*), 2.81–2.89 (m, 2 H *Z* and 2 H *E*), 3.74 (s, 3 H *Z*), 3.76 (s, 3 H *E*), 5.71 (dt, *J* = 11.5, 7.2 Hz, 1 H *Z*), 6.27 (dt, *J* = 15.8, 6.7 Hz, 1 H *E*), 6.43 (br. d, *J* = 15.8 Hz, 1 H *E*), 6.47 (br. d, *J* = 11.5 Hz, 1 H *Z*), 6.60–6.66 (m, 1 H *Z* and 1 H *E*), 6.75 (d, *J* = 3.2 Hz, 1 H *Z*), 6.80 (d, *J* = 3.0 Hz, 1 H *E*), 7.18–7.36 (m, 5 H *Z* and 5 H *E*), 7.40 (d, *J* = 8.7 Hz, 1 H *Z*), 7.42 (d, *J* = 8.7 Hz, 1 H *E*) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 28.82, 33.34, 36.43, 36.53, 55.50, 55.52, 113.36, 113.39, 115.04, 115.07, 116.21, 126.15, 126.75, 127.12, 128.28, 128.62, 128.85, 129.57, 129.89, 130.75, 131.41, 133.37, 133.40, 137.55, 137.76, 141.96, 142.06, 159.03, 159.05 ppm. $C_{17}H_{17}BrO$ (317.22): calcd. C 64.37, H 5.40, Br 25.19; found C 64.63, H 5.39, Br 25.14.

1-Bromo-4-methoxy-2-[4-(4-methoxyphenyl)but-3-enyl]benzene (6): *t*BuOK (0.132 g, 1.18 mmol) was added to a suspension of phosphonium salt **10b** (0.646 g, 1.13 mmol) in THF (5 mL) under a flow of nitrogen. The mixture was stirred under nitrogen for 10 min, and *p*-anisaldehyde (0.14 mL, 1.15 mmol) was slowly added by syringe. The mixture was stirred for 27.5 h at room temperature. The reaction was then quenched with HCl (1 M) and extracted with Et_2O. The organic layer was washed with water, dried ($MgSO_4$) and concentrated. Column chromatography of the residue (petroleum ether, petroleum ether/EtOAc 99:1 and 98:2) afforded **6** (0.26 g, 66%, *Z*/*E* 90:10) as a colourless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.49 (br. q, *J* = 7.5 Hz, 2 H *E*), 2.64 (br. q, *J* = 7.6 Hz, 2 H *Z*), 2.81–2.87 (m, 2 H *Z* and 2 H *E*), 3.75 (s, 3 H *Z*), 3.76 (s, 3 H *E*), 3.80 (s, 3 H *Z* and 3 H *E*), 5.62 (dt, *J* = 11.6, 7.0 Hz, 1 H *Z*), 6.12 (dt, *J* = 15.7, 6.9 Hz, 1 H *E*), 6.37 (br. d, *J* = 15.7 Hz, 1 H *E*), 6.40 (br. d, *J* = 11.6 Hz, 1 H *Z*), 6.62 (dd, *J* = 8.8, 3.0 Hz, 1 H *Z*), 6.63 (dd, *J* = 8.8, 2.8 Hz, 1 H *E*), 6.76 (d, *J* = 3.0 Hz, 1 H *Z*), 6.79 (d, *J* = 2.8 Hz, 1 H *E*), 6.81–6.87 (m, 2 H *Z* and 2 H *E*), 7.17–7.30 (m, 2 H *Z* and 2 H *E*), 7.41 (d, *J* = 8.8 Hz, 1 H *Z*), 7.42 (d, *J* = 8.8 Hz, 1 H *E*) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 28.82, 33.30, 36.53, 36.55, 55.30, 55.33, 55.43, 55.46, 113.30, 113.31, 113.68, 114.01, 115.00, 115.03, 116.18, 127.20, 127.33, 129.25, 129.79, 130.02, 130.07, 130.20, 130.56, 133.31, 133.33, 142.01, 142.13, 158.40, 158.88, 159.01 ppm. $C_{18}H_{19}BrO_2$ (347.25): calcd. C 62.26, H 5.52, Br 23.01; found C 62.17, H 5.54, Br 22.98.

1-Bromo-2-(4,4-diphenylbut-3-enyl)benzene (3): *t*BuOK (0.487 g, 4.34 mmol) was added to a suspension of phosphonium salt **10a** (2.167 g, 4.01 mmol) in THF (16 mL) under a flow of nitrogen. The mixture was stirred under nitrogen for 5 min, and benzophenone (0.652 g, 3.58 mmol) was added. The mixture was heated at reflux for 71.5 h. The reaction mixture was then quenched with HCl (1 M) and extracted with Et_2O. The organic layer was washed with water, dried ($MgSO_4$) and concentrated. Column chromatography of the residue on silica gel impregnated with $AgNO_3$ (petroleum ether) afforded **3** (1.125 g, 86%) as a yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.43 (q, *J* = 7.6 Hz, 2 H), 2.86 (t, *J* = 7.6 Hz, 2 H), 6.13 (t, *J* = 7.6 Hz, 1 H), 7.00–7.36 (m, 13 H), 7.49 (dd, *J* = 7.9, 1.1 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 30.14, 36.39, 124.68, 127.05, 127.33, 127.45, 127.74, 128.21, 128.30, 128.35, 129.95, 130.66, 132.89, 140.07, 141.01, 142.66, 142.70 ppm. $C_{22}H_{19}Br$ (363.29): calcd. C 72.73, H 5.27, Br 21.99; found C 72.81, H 5.26, Br 21.71.

Authentic Products: The aim of the following experiments was to isolate small amounts of pure samples of authentic products for the identification of Grignard reaction mixtures. Authentic samples of [(1*E*)-4-phenylbut-1-enyl]benzene [(*E*)-**2l**], (4-phenylbut-1-enyl)-benzene (**2l**), (1,4-diphenylbut-1-enyl)benzene (**3l**), 1-(diphenylmethyl)-2,3-dihydro-1*H*-indene (**3c**), methyl 4-(4-phenylbut-1-enyl)-phenyl ether (**4l**), methyl 3-(4-phenylbut-3-enyl)phenyl ether (**5l**) and 1-methoxy-3-[4-(4-methoxyphenyl)but-3-enyl]benzene (**6l**) were isolated (or identified) from Grignard reaction mixtures.

[(1*E*)-4-Phenylbut-1-enyl]benzene [(*E*)-2l]: Chromatography on silica gel (petroleum ether) afforded (*E*)-**2l**. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.54 (q, *J* = 7.9 Hz, 2 H), 2.80 (t, *J* = 7.9 Hz, 2 H), 6.26 (dt, *J* = 15.9, 6.7 Hz, 1 H), 6.42 (d, *J* = 15.9 Hz, 1 H), 7.19–7.23 (m, 4 H), 7.28–7.34 (m, 6 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 35.01, 36.02, 126.03, 126.13, 127.07, 128.50, 128.61, 128.63, 130.11, 130.51, 137.86, 141.90 ppm. GC-MS (70 eV): *m*/*z* (%) = 208 (14), 117 (100), 115 (39), 91 (51). NMR and MS data agree with published values.[115]

(4-Phenylbut-1-enyl)benzene (2l): This compound was directly identified from a crude reaction mixture (*Z*/*E* 92:8). ^{1}H NMR

(300 MHz, $CDCl_3$, *Z* isomer): δ = 2.61–2.70 (m, 2 H), 2.75–2.80 (m, 2 H), 5.70 (dt, *J* = 11.7, 7.0 Hz, 1 H), 6.44 (br. d, *J* = 11.7 Hz, 1 H), 7.16–7.34 (m, 10 H) ppm. GC-MS (70 eV): *m*/*z* (%) = 208 (19), 117 (100), 115 (38), 91 (46). ^{1}H NMR and MS data agree with published values.[115]

(1,4-Diphenylbut-1-enyl)benzene (3l) and 1-(Diphenylmethyl)-2,3-dihydro-1*H*-indene (3c): Chromatography on $AgNO_3$-impregnated silica gel (petroleum ether) afforded **3l** and **3c** as colourless oils.

Compound 3l: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.43 (q, *J* = 7.6 Hz, 2 H), 2.74 (t, *J* = 7.6 Hz, 2 H), 6.10 (t, *J* = 7.6 Hz, 1 H), 7.06–7.36 (m, 15 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 31.77, 36.30, 125.97, 127.00, 127.03, 127.34, 128.20, 128.27, 128.42, 128.65, 128.93, 129.94, 140.19, 141.79, 142.37, 142.78 ppm. ^{1}H NMR spectroscopic data obtained agree with published values.[116] GC-MS (70 eV): *m*/*z* (%) = 284 (8), 193 (100), 115 (85), 91 (65).

Compound 3c: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.73–1.84 (m, 1 H), 2.06–2.17 (m, 1 H), 2.70–2.87 (m, 2 H), 3.94 (d, *J* = 10.8 Hz, 1 H), 4.05–4.13 (m, 1 H), 6.37 (d, *J* = 7.6 Hz, 1 H), 6.88 (br t, *J* = 7.6 Hz, 1 H), 7.09 (br t, *J* = 7.3 Hz, 1 H), 7.13–7.33 (m, 11 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 31.0, 31.9, 48.8, 57.2, 124.5, 125.4, 125.7, 126.3, 126.5, 126.7, 128.3, 128.5, 128.6, 128.7, 144.6, 144.7, 144.8, 145.9 ppm. GC-MS (70 eV): *m*/*z* (%) = 167 (23), 117 (100), 115 (20).

Methyl 4-(4-Phenylbut-1-enyl)phenyl Ether (4l): This compound was directly identified from a crude reaction mixture (*Z*/*E* 90:10). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.50 (br. q, *J* = 7.2 Hz, 2 H *E*), 2.60–2.69 (m, 2 H *Z*), 2.73–2.80 (m, 2 H *Z* and 2 H *E*), 3.79 (s, 3 H *E*), 3.80 (s, 3 H *Z*), 5.61 (dt, *J* = 11.7, 6.9 Hz, 1 H *Z*), 6.11 (dt, *J* = 15.7, 6.8 Hz, 1 H *E*), 6.36 (br. d, *J* = 15.7 Hz, 1 H *E*), 6.37 (br. d, *J* = 11.7 Hz, 1 H *Z*), 6.82–6.87 (m, 2 H *Z* and 2 H *E*), 7.16–7.32 (m, 7 H *Z* and 7 H *E*) ppm. ^{13}C NMR (*Z* isomer, 75 MHz, $CDCl_3$): δ = 30.6, 36.3, 55.4, 113.7, 126.0, 128.5, 128.6, 128.9, 130.0, 130.4, 141.9, 158.4 ppm. GC-MS (70 eV): *Z* isomer *m*/*z* (%) = 238 (4), 147 (100), 115 (22), 103 (12), 91 (46); *E* isomer *m*/*z* (%) = 238 (2), 147 (100), 115 (32), 91 (24). ^{1}H NMR and MS data agree with published values.[117]

Methyl 3-(4-Phenylbut-3-enyl)phenyl Ether (5l): Chromatography on silica gel (petroleum ether/EtOAc 99:1) followed by chromatography on $AgNO_3$-impregnated silica gel (petroleum ether) afforded **5l** (*Z*/*E* 91:9). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.53 (br. q, *J* = 7.4 Hz, 2 H *E*), 2.61–2.69 (m, 2 H *Z*), 2.72–2.80 (m, 2 H *Z* and 2 H *E*), 3.78 (s, 3 H *Z*), 3.80 (s, 3 H *E*), 5.70 (dt, *J* = 11.7, 6.8 Hz, 1 H *Z*), 6.25 (dt, *J* = 15.9, 6.6 Hz, 1 H *E*), 6.42 (br. d, *J* = 15.9 Hz, 1 H *E*), 6.44 (br. d, *J* = 11.7 Hz, 1 H *Z*), 6.72–6.83 (m, 3 H *Z* and 3 H *E*), 7.17–7.34 (m, 6 H *Z* and 6 H *E*) ppm. ^{13}C NMR (*Z* isomer, 75 MHz, $CDCl_3$): δ = 30.4, 36.2, 55.2, 111.3, 114.4, 121.0, 126.7, 128.3, 128.9, 129.4, 129.6, 131.9, 137.7, 143.4, 159.8 ppm. GC-MS (70 eV): *Z* isomer: *m*/*z* (%) = 238 (7), 121 (25), 117 (100), 115 (32), 91 (32), 78 (12); *E* isomer: *m*/*z* (%) = 238 (4), 121 (23), 117 (100), 115 (32), 91 (33), 78 (14).

1-Methoxy-3-[4-(4-methoxyphenyl)but-3-enyl]benzene (6l): Column chromatography of the residue (petroleum ether/EtOAc 99:1) afforded **6l** (*Z*/*E* 90:10). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.50 (br. q, *J* = 7.4 Hz, 2 H *E*), 2.60–2.69 (m, 2 H *Z*), 2.71–2.78 (m, 2 H *Z* and 2 H *E*), 3.78 (s, 3 H *Z*), 3.79 (s, 6 H *E*), 3.80 (s, 3 H *Z*), 5.60 (dt, *J* = 11.6, 6.9 Hz, 1 H *Z*), 6.11 (dt, *J* = 15.8, 6.8 Hz, 1 H *E*), 6.34–6.39 (m, 1 H *E* and 1 H *Z*), 6.72–6.87 (m, 5 H *Z* and 5 H *E*), 7.16–7.28 (m, 3 H *Z* and 3 H *E*) ppm. ^{13}C NMR (*Z* isomer, 75 MHz, $CDCl_3$): δ = 30.5, 36.3, 55.3, 55.4, 111.3, 113.7, 114.4, 121.0, 129.0, 129.4, 130.1, 130.3, 130.4, 143.6, 158.4, 159.8 ppm. GC-MS (70 eV): *Z* isomer: *m*/*z* (%) = 268 (7), 121 (8), 147 (100), 115 (15), 91 (27), 78 (12); *E* isomer: *m*/*z* (%) = 268 (6), 121 (13), 147 (100), 115 (19), 91 (34), 78 (15).

1-Phenylmethyl-2,3-dihydro-1*H*-indene (2c): This compound was prepared by treatment of bromide (*E*)-**2** with Bu_3SnH in toluene at reflux. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.70–1.82 (m, 1 H), 2.08–2.19 (m, 1 H), 2.68 (dd, *J* = 13.6, 9.3 Hz, 1 H), 2.75–2.92 (m, 2 H), 3.14 (dd, *J* = 13.6, 5.7 Hz, 1 H), 3.44 (quint, *J* = 7.3 Hz, 1 H), 7.11–7.31 (m, 9 H) ppm. GC-MS (70 eV): *m*/*z* (%) = 208 (5), 117 (100), 116 (25), 115 (31), 91 (22). ^{1}H NMR spectroscopic data agree with published values.[118]

Cyclised products **4c**, **5c** and **6c** were also prepared by Bu_3SnH-induced radical cyclisation of the corresponding bromides: a solution of bromide **4**, **5** or **6** (0.22–0.26 mmol), AIBN (1.3–1.7 mg) and Bu_3SnH (0.14–0.15 mL) in THF (2.4–3.0 mL) was heated at reflux under nitrogen for 20–21 h. After concentration, the residue was purified by column chromatography.

4-(2,3-Dihydro-1*H*-inden-1-ylmethyl)phenyl Methyl Ether (4c): Chromatography on silica gel (petroleum ether, petroleum ether/EtOAc 99:1) afforded a colourless oil that crystallised on standing in a freezer. Recrystallisation from EtOH afforded a white solid; m.p. 44.5–46.5 °C (lit. 46–47 °C).[119] ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.69–1.81 (m, 1 H), 2.08–2.19 (m, 1 H), 2.64 (dd, *J* = 13.7, 9.1 Hz, 1 H), 2.73–2.93 (m, 2 H), 3.07 (dd, *J* = 13.7, 5.8 Hz, 1 H), 3.40 (quint, *J* = 7.4 Hz, 1 H), 3.80 (s, 3 H), 6.81–6.86 (m, 2 H), 7.10–7.23 (m, 6 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 31.3, 32.0, 40.6, 46.7, 55.4, 113.8, 124.0, 124.6, 126.1, 126.6, 130.1, 133.1, 144.3, 147.1, 158.0 ppm.

Methyl 1-Phenylmethyl-2,3-dihydro-1*H*-inden-5-yl Ether (5c): Chromatography on silica gel (petroleum ether, petroleum ether/EtOAc 99:1) afforded an oil that crystallised, in the presence of EtOH, on standing in a freezer. This white solid was washed with cold EtOH; m.p. 39–40 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.71–1.82 (m, 1 H), 2.09–2.20 (m, 1 H), 2.67 (dd, *J* = 13.6, 9.1 Hz, 1 H), 2.71–2.90 (m, 2 H), 3.08 (dd, *J* = 13.6, 5.9 Hz, 1 H), 3.38 (quint, *J* = 7.2 Hz, 1 H), 3.78 (s, 3 H), 6.68 (dd, *J* = 8.2, 2.5 Hz, 1 H), 6.77 (d, *J* = 2.5 Hz, 1 H), 6.98 (d, *J* = 8.2 Hz, 1 H), 7.18–7.32 (m, 5 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 31.5, 32.5, 41.9, 45.8, 55.5, 110.1, 112.0, 124.4, 126.0, 128.4, 129.2, 139.2, 141.1, 145.8, 159.0 ppm. GC-MS (70 eV): *m*/*z* (%) = 238 (2), 147 (100), 115 (13), 91 (29).

5-Methoxy-1-[(4-methoxyphenyl)methyl]-2,3-dihydro-1*H*-indene (6c): Chromatography on silica gel (petroleum ether, petroleum ether/EtOAc 95:5) afforded an oil that crystallised on standing at room temperature. Recrystallisation from EtOH afforded a white solid; m.p. 69–70 °C (lit.[120] 68–70 °C). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.69–1.81 (m, 1 H), 2.09–2.20 (m, 1 H), 2.62 (dd, *J* = 13.7, 8.8 Hz, 1 H), 2.70–2.89 (m, 2 H), 3.01 (dd, *J* = 13.7, 5.9 Hz, 1 H), 3.34 (quint, *J* = 7.3 Hz, 1 H) 3.78 (s, 3 H), 3.80 (s, 3 H), 6.68 (dd, *J* = 8.3, 2.3 Hz, 1 H), 6.77 (d, *J* = 2.3 Hz, 1 H), 6.81–6.86 (m, 2 H), 6.97 (d, *J* = 8.3 Hz, 1 H), 7.08–7.13 (m, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 31.5, 32.4, 41.0, 45.9, 55.4, 55.5, 110.0, 112.0, 113.8, 124.5, 130.1, 133.2, 139.3, 145.9, 158.0, 158.9 ppm. GC-MS (70 eV): *m*/*z* (%) = 268 (6), 121 (21), 147 (100).

Cyclic Voltammetry Experiments: The working electrode was a 3-mm diameter glassy carbon disk. It was carefully polished before each voltammogram. The counter electrode was a platinum wire and the reference electrode an aqueous SCE electrode. Cyclic voltammograms were recorded with a CHI600B potentiostat (CH Instruments, IJ Cambria Scientific, Burry Port, UK).

[1] D. Griller, K. U. Ingold, *Acc. Chem. Res.* **1980**, *13*, 317–323.

[2] J.-M. Surzur, in: *Reactive Intermediates* (Ed.: R. A. Abramovitch), Plenum Press, New York, **1982**, vol. 2, 121–295.
[3] M. Newcomb, *Tetrahedron* **1993**, *49*, 1151–1176.
[4] M. Newcomb, in: *Radicals in Organic Synthesis* (Eds.: P. Renaud, M. P. Sibi), Wiley-VCH, Weinheim, **2001**, vol. 1, pp. 317–336.
[5] K. E. Liu, C. C. Johnson, M. Newcomb, S. J. Lippard, *J. Am. Chem. Soc.* **1993**, *115*, 939–947.
[6] E. W. Della, C. H. Schiesser, D. K. Taylor, J. C. Walton, *J. Chem. Soc. Perkin Trans. 2* **1991**, 1329–1333.
[7] P. E. Eaton, Y. C. Yip, *J. Am. Chem. Soc.* **1991**, *113*, 7692–7697.
[8] M. Journet, M. Malacria, *J. Org. Chem.* **1992**, *57*, 3085–3093.
[9] R. R. Conry, J. M. Mayer, *Organometallics* **1991**, *10*, 3160–3166.
[10] W. E. Piers, D. J. Parks, L. R. Macgillivray, M. J. Zaworotko, *Organometallics* **1994**, *13*, 4547–4558.
[11] J. A. Franz, J. C. Linehan, J. C. Birnbaum, K. W. Hicks, M. S. Alnajjar, *J. Am. Chem. Soc.* **1999**, *121*, 9824–9830.
[12] D. Sattari, C. L. Hill, *J. Am. Chem. Soc.* **1993**, *115*, 4649–4657.
[13] E. I. Karasevich, V. S. Kulikova, A. E. Shilov, A. A. Shteinman, *Russ. Chem. Rev.* **1998**, *67*, 376–398.
[14] W. Adam, F. G. Gelalcha, C. R. Saha-Moller, V. R. Stegmann, *J. Org. Chem.* **2000**, *65*, 1915–1918.
[15] M. Costas, K. Chen, L. Que, *Coord. Chem. Rev.* **2000**, *200*, 517–544.
[16] R. H. Crabtree, *J. Chem. Soc., Dalton Trans.* **2001**, 2437–2450.
[17] F. Alonso, I. P. Beletskaya, M. Yus, *Chem. Rev.* **2002**, *102*, 4009–4091.
[18] M. L. Andersen, W. Long, D. D. M. Wayner, *J. Am. Chem. Soc.* **1997**, *119*, 6590–6595.
[19] J. M. Tanko, J. P. Phillips, *J. Am. Chem. Soc.* **1999**, *121*, 6078–6079.
[20] D. M. Fang, D. G. Peters, M. S. Mubarak, *J. Electrochem. Soc.* **2001**, *148*, E464–E467.
[21] H. Jensen, H. S. Sorensen, S. U. Pedersen, K. Daasbjerg, *J. Chem. Soc. Perkin Trans. 2* **2002**, 1423–1428.
[22] J. P. Stevenson, W. F. Jackson, J. M. Tanko, *J. Am. Chem. Soc.* **2002**, *124*, 4271–4281.
[23] T. Kjaersbo, K. Daasbjerg, S. U. Pedersen, *Electrochem. Acta* **2003**, *48*, 1807–1816.
[24] W. Adam, R. Finzel, *J. Am. Chem. Soc.* **1992**, *114*, 4563–4568.
[25] R. M. Wilson, K. A. Schnapp, *Chem. Rev.* **1993**, *93*, 223–249.
[26] C. Chatgilialoglu, A. Altieri, H. Fischer, *J. Am. Chem. Soc.* **2002**, *124*, 12816–12823.
[27] E. J. Corey, R. Nagata, *J. Am. Chem. Soc.* **1987**, *109*, 8107–8108.
[28] M. Sono, M. P. Roach, E. D. Coulter, J. H. Dawson, *Chem. Rev.* **1996**, *96*, 2841–2887.
[29] M. Newcomb, P. H. Toy, *Acc. Chem. Res.* **2000**, *33*, 449–455.
[30] M. Merkx, D. A. Kopp, M. H. Sazinsky, J. L. Blazyk, J. Muller, S. J. Lippard, *Angew. Chem. Int. Ed.* **2001**, *40*, 2782–2807.
[31] M. Newcomb, M. B. Manek, A. G. Glenn, *J. Am. Chem. Soc.* **1991**, *113*, 949–958.
[32] M. Chanon, J.-C. Négrel, N. Bodineau, J.-M. Mattalia, E. Péralez, A. Goursot, *Macromol. Symp.* **1998**, *134*, 13–28.
[33] J. F. Garst, J. R. Boone, L. Webb, K. E. Lawrence, J. T. Baxter, F. Ungváry, *Inorg. Chim. Acta* **1999**, *296*, 52–66.
[34] J. F. Garst, F. Ungváry, in: *Grignard Reagents: New Developments* (Ed.: H. G. Richey Jr.,), Wiley, Chichester, **2000**, pp. 185–275.
[35] N. Bodineau, J.-M. Mattalia, V. Timokhin, K. Handoo, J.-C. Négrel, M. Chanon, *Org. Lett.* **2000**, *2*, 2303–2306.
[36] A. L. J. Beckwith, K. U. Ingold, in: *Rearrangements in Ground and Excited States* (Ed.: P. de Mayo), Academic Press, New York, **1980**, vol. 1, pp. 161–310.
[37] L. J. Johnston, J. Lusztyk, D. D. M. Wayner, A. N. Abeywickreyma, A. L. J. Beckwith, J. C. Scaiano, K. U. Ingold, *J. Am. Chem. Soc.* **1985**, *107*, 4594–4596.
[38] E. A. Hill, C. L. Harder, R. Wagner, D. Meh, R. P. Bowman, *J. Organomet. Chem.* **1986**, *302*, 5–17.
[39] D. P. Curran, *Synthesis* **1988**, 417–439.
[40] D. G. Peters, in: *Organic Electrochemistry: An Introduction and a Guide* (Eds.: M. M. Baizer, H. Lund), 3rd edition, M. Dekker, New York, **1991**, pp. 361–400.
[41] T. A. Halgren, J. D. Roberts, J. H. Horner, F. N. Martinez, C. Tronche, M. Newcomb, *J. Am. Chem. Soc.* **2000**, *122*, 2988–2994.
[42] E. Martinez II, M. Newcomb, *J. Org. Chem.* **2006**, *71*, 557–561.
[43] A. Annunziata, C. Galli, M. Marinelli, T. Pau, *Eur. J. Org. Chem.* **2001**, 1323–1329.
[44] S. U. Park, S. K. Chung, M. Newcomb, *J. Am. Chem. Soc.* **1986**, *108*, 240–244.
[45] H. Hazimeh, J. M. Mattalia, C. Marchi-Delapierre, R. Barone, N. S. Nudelman, M. Chanon, *J. Phys. Org. Chem.* **2005**, *18*, 1145–1160.
[46] H. Hazimeh, J.-M. Mattalia, M. Attolini, N. Bodineau, K. Handoo, C. Marchi-Delapierre, E. Péralez, M. Chanon, *Indian J. Chem. Sect. B* **2006**, *45*, 2270–2280.
[47] H. Hazimeh, F. Kanoufi, C. Combellas, J.-M. Mattalia, C. Marchi-Delapierre, M. Chanon, *J. Phys. Chem. C* **2008**, *112*, 2545–2557.
[48] J. F. Garst, M. R. Soriaga, *Coord. Chem. Rev.* **2004**, *248*, 623–652.
[49] T. Cohen, H. Gibney, R. Ivanov, E. A. H. Yeh, I. Marek, D. P. Curran, *J. Am. Chem. Soc.* **2007**, *129*, 15405–15409.
[50] E. Péralez, J.-C. Négrel, M. Chanon, *Tetrahedron Lett.* **1995**, *36*, 6457–6460.
[51] A. L. J. Beckwith, I. A. Blair, G. Phillipou, *Tetrahedron Lett.* **1974**, *15*, 2251–2254.
[52] F. M'Halla, J. Pinson, J. M. Savéant, *J. Am. Chem. Soc.* **1980**, *102*, 4120–4127.
[53] A. Leahy-Dios, A. Firoozabadi, *J. Phys. Chem. B* **2007**, *111*, 191–198.
[54] H. G. Richey Jr., H. S. Veale, *Tetrahedron Lett.* **1975**, *16*, 615–618.
[55] E. A. Hill, in: *Advances in Organometallic Chemistry* (Eds.: F. G. A. Stone, R. West), Academic Press, New York, **1977**, vol. 16, pp. 131–165.
[56] M. Julliard, J. P. Scagliarini, M. Rajzmann, M. Chanon, *Chimia* **1986**, *40*, 16–19.
[57] H. Morrison, K. Muthuramu, G. Pandey, D. Severance, B. Bigot, *J. Org. Chem.* **1986**, *51*, 3358–3363.
[58] M. Chanon, M. Rajzmann, F. Chanon, *Tetrahedron* **1990**, *46*, 6193–6299.
[59] J. S. Duca, M. H. Gallego, A. B. Pierini, R. A. Rossi, *J. Org. Chem.* **1999**, *64*, 2626–2629.
[60] D. Laage, I. Burghardt, T. Sommerfeld, J. T. Hynes, *J. Phys. Chem. A* **2003**, *107*, 11271–11291.
[61] R. A. Rossi, A. B. Pierini, A. B. Penenory, *Chem. Rev.* **2003**, *103*, 71–167.
[62] N. Takeda, P. V. Poliakov, A. R. Cook, J. R. Miller, *J. Am. Chem. Soc.* **2004**, *126*, 4301–4309.
[63] J. M. Dust, D. R. Arnold, *J. Am. Chem. Soc.* **1983**, *105*, 1221–1227.
[64] A. M. de P. Nicholas, D. R. Arnold, *Can. J. Chem.* **1986**, *64*, 270–276.
[65] R. A. Jackson, M. Sharifi, *J. Chem. Soc. Perkin Trans. 2* **1996**, 775–778.
[66] J. P. Cheng, B. Liu, Y. Y. Zhao, Z. Wen, Y. K. Sun, *J. Am. Chem. Soc.* **2000**, *122*, 9987–9992.
[67] X. Zhang, W. M. Nau, *J. Phys. Org. Chem.* **2000**, *13*, 634–639.
[68] Z. Wen, Z. Li, Z. Shang, J.-P. Cheng, *J. Org. Chem.* **2001**, *66*, 1466–1472.
[69] L. W. Menapace, M. B. Loewenthal, J. Koscielecki, L. Tucker, L. C. Passaro, R. Montalbano, A. J. Frank, J. Marrantino, J. Brunner, *Organometallics* **2002**, *21*, 3066–3068.
[70] N. K. Singh, P. L. A. Popelier, P. J. O'Malley, *Chem. Phys. Lett.* **2006**, *426*, 219–221.

[71] S. Antonello, F. Maran, *J. Am. Chem. Soc.* **1998**, *120*, 5713–5722.
[72] S. Antonello, M. Crisma, F. Formaggio, A. Moretto, F. Taddei, C. Toniolo, F. Maran, *J. Am. Chem. Soc.* **2002**, *124*, 11503–11513.
[73] N. C. L. Wood, C. A. Paddon, F. L. Bhatti, T. J. Donohoe, R. G. Compton, *J. Phys. Org. Chem.* **2007**, *20*, 732–742.
[74] H. J. R. de Boer, O. S. Akkerman, F. Bickelhaupt, *Angew. Chem. Int. Ed. Engl.* **1988**, *27*, 687–689.
[75] G. P. M. van Klink, H. J. R. de Boer, G. Schat, O. S. Akkerman, F. Bickelhaupt, A. L. Spek, *Organometallics* **2002**, *21*, 2119–2135.
[76] F. Bickelhaupt, M. Newcomb, C. B. DeZutter, H. J. R. de Boer, *Eur. J. Org. Chem.* **2008**, 6225–6231.
[77] F. Kanoufi, C. Combellas, H. Hazimeh, J. M. Mattalia, C. Marchi-Delapierre, M. Chanon, *J. Phys. Org. Chem.* **2006**, *19*, 847–866.
[78] E. C. Ashby, J. Oswald, *J. Org. Chem.* **1988**, *53*, 6068–6076.
[79] H. W. H. J. Bodewitz, C. Blomberg, F. Bickelhaupt, *Tetrahedron* **1975**, *31*, 1053–1063.
[80] N. Kimura, S. Takamuku, *Radiat. Phys. Chem.* **1987**, *29*, 179–183.
[81] J. F. Garst, B. L. Swift, *J. Am. Chem. Soc.* **1989**, *111*, 241–250.
[82] J. F. Garst, *Acc. Chem. Res.* **1991**, *24*, 95–97.
[83] S. Antonello, M. Musumeci, D. D. M. Wayner, F. Maran, *J. Am. Chem. Soc.* **1997**, *119*, 9541–9549.
[84] C. P. Andrieux, J. Pinson, *J. Am. Chem. Soc.* **2003**, *125*, 14801–14806.
[85] Y. Fu, L. Liu, H.-Z. Yu, Y.-M. Wang, Q.-X. Guo, *J. Am. Chem. Soc.* **2005**, *127*, 7227–7234.
[86] B. Branchi, C. Galli, P. Gentili, *Eur. J. Org. Chem.* **2002**, 2844–2854.
[87] A. N. Abeywickrema, A. L. J. Beckwith, *J. Chem. Soc., Chem. Commun.* **1986**, 464–465.
[88] S. J. Garden, D. V. Avila, A. L. J. Beckwith, V. W. Bowry, K. U. Ingold, J. Lusztyk, *J. Org. Chem.* **1996**, *61*, 805–809.
[89] C. Amatore, in: *Organic Electrochemistry: An Introduction and a Guide* (Eds.: M. M. Baizer, H. Lund), 3rd edition, M. Dekker, New York, **1991**, pp. 207–232.
[90] C. Amatore, in: *Organic Electrochemistry* (Eds.: H. Lund, O. Hammerich), Fourth Edition, M. Dekker, New York, **2001**, pp. 183–205.
[91] C. Ha, J. H. Horner, M. Newcomb, T. R. Varick, B. R. Arnold, J. Lusztyk, *J. Org. Chem.* **1993**, *58*, 1194–1198.
[92] M. Newcomb, S.-Y. Choi, J. H. Horner, *J. Org. Chem.* **1999**, *64*, 1225–1231.
[93] F. De Vleeschouwer, V. Van Speybroeck, M. Waroquier, P. Geerlings, F. De Proft, *J. Org. Chem.* **2008**, *73*, 9109–9120.
[94] C. P. Andrieux, J. M. Savéant, D. Zann, *New J. Chem.* **1984**, *8*, 107–116.
[95] J. M. Savéant, in: *Advances in Physical Organic Chemistry* (Ed.: T. T. Tidwell), Academic Press, New York, **2000**, vol. 35, pp. 117–192.
[96] J. M. Savéant, *Elements of Molecular and Biomolecular Electrochemistry. An Electrochemical Approach to Electron Transfer Chemistry*, Wiley, Hoboken, **2006**.
[97] B. A. Selivanov, I. I. Bilkis, V. L. Varand, V. D. Shteingarts, *Zh. Org. Khim.* **1985**, *21*, 952–965.
[98] S. Fukuzumi, T. Suenobu, T. Hirasaka, R. Arakawa, K. M. Kadish, *J. Am. Chem. Soc.* **1998**, *120*, 9220–9227.
[99] S. Fukuzumi, D. M. Guldi, in: *Electron Transfer in Chemistry* (Ed.: V. Balzani), Wiley-VCH, Weinheim, **2001**, vol. 2, pp. 270–337.
[100] B. J. Beals, Z. I. Bello, K. P. Cuddihy, E. M. Healy, S. E. Koon-Church, J. M. Owens, C. E. Teerlinck, W. J. Bowyer, *J. Phys. Chem. A* **2002**, *106*, 498–503.
[101] P. G. Jasien, J. A. Abbondondola, *Theochem, J. Mol. Struct.* **2004**, *671*, 111–118.
[102] S. V. Maslennikov, E. N. Kirillov, N. V. Berezina, I. V. Spirina, A. V. Kondin, *Russ. J. Gen. Chem.* **1997**, *67*, 667–671.
[103] S. V. Maslennikov, A. V. Piskunov, L. N. Bochkarev, I. V. Spirina, *Russ. J. Gen. Chem.* **1998**, *68*, 907–909.
[104] S. V. Maslennikov, I. V. Spirina, A. V. Piskunov, S. N. Maslennikova, *Russ. J. Gen. Chem.* **2001**, *71*, 1741–1743.
[105] M. Spiro, in: *Modern Aspects of Electrochemistry* (Eds.: J. O. M. Bockris, B. E. Conway, R. E. White), Kluwer Academic, New York, **2001**, vol. 34, pp. 1–11.
[106] R. Akid, M. Garma, *Electrochem. Acta* **2004**, *49*, 2871–2879.
[107] C. Amatore, M. Azzabi, P. Calas, A. Jutand, C. Lefrou, Y. Rollin, *J. Electroanal. Chem.* **1990**, *288*, 45–63.
[108] J. T. Scanlon, D. E. Willis, *J. Chromatogr. Sci.* **1985**, *23*, 333–340.
[109] G. F. Meijs, J. F. Bunnett, A. L. J. Beckwith, *J. Am. Chem. Soc.* **1986**, *108*, 4899–4904.
[110] T. R. Hoye, L. Mi, *J. Org. Chem.* **1997**, *62*, 8586–8588.
[111] M. Adamczyk, D. S. Watt, D. A. Netzel, *J. Org. Chem.* **1984**, *49*, 4226–4237.
[112] S. C. Watson, J. F. Eastham, *J. Organomet. Chem.* **1967**, *9*, 165–168.
[113] J. Knight, P. J. Parsons, *J. Chem. Soc. Perkin Trans. 1* **1989**, 979–984.
[114] M. Oestreich, U. K. Schmid, G. Auer, M. Keller, *Synthesis* **2003**, 2725–2739.
[115] Y. S. Hon, L. Lu, R. C. Chang, S. W. Lin, P. P. Sun, C. F. Lee, *Tetrahedron* **2000**, *56*, 9269–9279.
[116] H. Uno, K. Sakamoto, F. Semba, H. Suzuki, *Bull. Chem. Soc. Jpn.* **1992**, *65*, 210–217.
[117] T. Satoh, N. Hanaki, N. Yamada, T. Asano, *Tetrahedron* **2000**, *56*, 6223–6234.
[118] M. Sindler-Kulyk, W. H. Laarhoven, *J. Am. Chem. Soc.* **1978**, *100*, 3819–3830.
[119] C. Courtot, *Ann. Chim.* **1916**, *9*, 52–108.
[120] D. M. Lynch, W. Cole, *J. Med. Chem.* **1968**, *11*, 291–295.

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