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Borrowing Hydrogen: Indirect "Wittig" Olefination for the Formation of C–C Bonds from Alcohols

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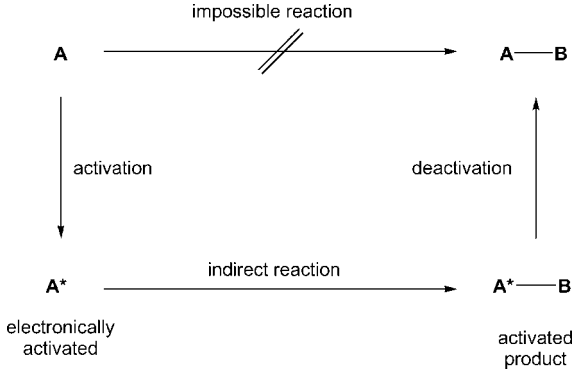
The successful development of an indirect three-step domino sequence for the formation of C–C bonds from alcohol substrates is described. An iridium-catalysed dehydrogenation of alcohol **1** affords the intermediate aldehyde **2**. The desired C–C bond can then be formed by a facile Wittig olefination, yielding the intermediate alkene **3**. In the final step the alkene is hydrogenated to afford the indirect Wittig product, the alkane **4**. The key to this process is the concept of borrowing hydrogen; hydrogen removed in the initial dehydrogenation step is simply borrowed by the iridium catalyst. Functioning as a hydrogen reservoir, the catalyst facilitates C–C bond formation before subsequently returning the borrowed hydrogen in the final step. Herein we present full details of our examination into both the substrate and reaction scope and the limitations of the catalytic cycle.

Introduction

Recent research in these laboratories has explored the use of domino reaction sequences[1] for the development of new reactions. Inspired by the powerful possibilities of domino chemistry, we envisioned that a sequence of domino transformations could accomplish an otherwise "impossible" reaction (Scheme 1). We reasoned that if an unreactive substrate **A** could be temporarily activated towards reaction (into electronically activated **A***) then the desired bond formation could proceed indirectly upon intermediate **A*** to afford the activated intermediate **A*–B**. The reaction cycle would then be completed by return of **A*–B** to the initial oxidation level, yielding the desired product **A**–**B**. We termed this concept Catalytic Electronic Activation.[2]

We were ultimately successful in employing this concept for the 1,4-addition of carbon nucleophiles to allylic alcohols[2] and the β-functionalisation of alcohols.[3,4] The key to these systems was an aluminium-catalysed (Meerwein–Ponndorf–Verley/Oppenauer[5]) oxidation–reduction couple to shuttle the alcohol–ketone equilibrium necessary for the indirect reaction (upon the ketone). In order to develop the scope of this concept, it was necessary to develop a more general oxidation/reduction couple. We believed that a transition-metal catalyst could function as a "hydrogen reservoir", borrowing hydrogen from the substrate to induce the reaction sequence and then subsequently return it in the final step (Scheme 2). In addition to the opportunity for reduction of a wider range of functional groups this would also eliminate the requirement for external hydride donors and/or acceptors.



Scheme 1.

We tested our "borrowing hydrogen" hypothesis by studying C–C bond formation upon alcohol substrates (Scheme 2). An alcohol **1** would undergo metal-catalysed dehydrogenation to afford an activated intermediate carbonyl compound **2**. The formation of a C=C bond should then proceed readily to provide the alkene intermediate **3**. The final hydrogenation step then returns the borrowed hydrogen to the intermediate alkene **3**, which generates the alkane product **4**. In contrast to most transfer hydrogenation reactions, this process requires the use of only one equivalent of the alcohol.[6] In addition, because the hydrogen is only borrowed temporarily, no overall net-oxidation transformation occurs.

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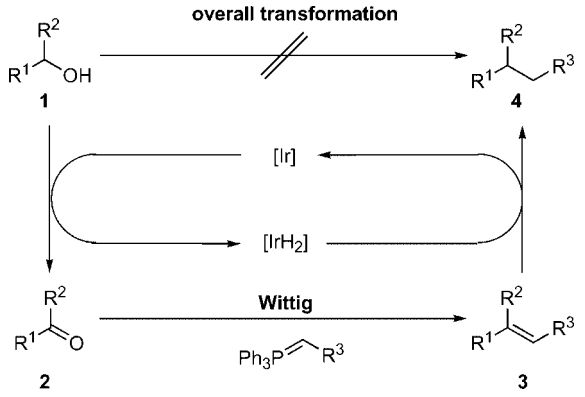


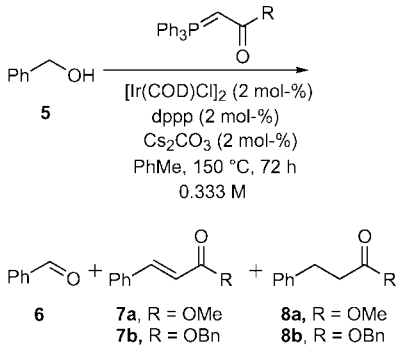
Scheme 2.

We communicated our preliminary findings[7] on this novel three-step domino sequence[8] in 2002 and subsequently reported an improved ruthenium-catalysed system that proceeds under milder conditions.[9] A related process for the α-alkylation of ketones or nitriles with alcohol substrates (albeit with an excess of alcohol) has been reported by various researchers.[10] In these reports the C–C bond is formed by a base-promoted aldol addition to the intermediate aldeyhde. Furthermore, the synthesis of amines from alcohols can also be achieved by an oxidation/imination/reduction sequence.[11] Subsequently we also applied the concept of borrowing hydrogen to the formation of C–N bonds with aza-Wittig and imine chemistry.[12] Herein we wish to report our full findings into the scope and pathway of iridium-catalysed C–C bond formation upon alcohols.

Results and Discussion

In our initial efforts, we used Wadsworth–Emmons olefination for the formation of the desired C–C bond.[7,13] Although we were able to obtain proof of principle from this chemistry, the low yields and complicated workup required made it less than ideal. The incompatibility of phosphonate nucleophiles made it apparent that an alternative olefination method was required. In theory, any C–C bond-forming method could be used. However, this method must be tolerant of the reaction conditions and functional groups involved. After careful consideration, we turned our attention towards Wittig olefination for formation of the crucial C–C bond. The added benefit of using stabilised phosphorane ylide nucleophiles is that no additional base is required. Thus, the domino sequence presented in Scheme 2 was examined.

In our previous studies,[7,13] we identified that modification of the iridium system reported by Ishii and coworkers[14] was optimal for the crossover transfer hydrogenation reaction. The starting point was to subject benzyl alcohol to the optimised conditions (5 mol-% Ir dimer, 150 °C, 72 hours, 0.333 M concentration) in the presence of the ester ylides **9** and **10** (Scheme 3). Although 5 mol-% of $[Ir(COD)Cl]_2$ was used in all the reactions described herein, we have insufficient evidence to propose the structure of the species that is catalytically active under the reaction conditions.



	conversion [%]	6 [%]	7a [%]	8a [%]	7b [%]	8b [%]
A: R = OBn, **9**	93	1	-	-	18	74
B: R = OMe, **10**	97	0	17	70	3	7

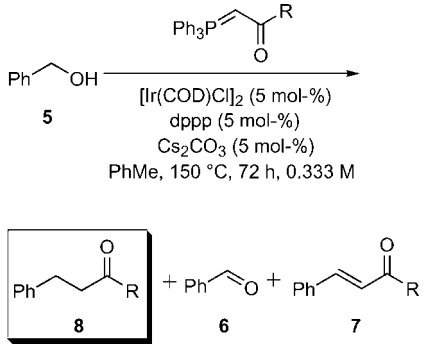
Scheme 3.

The results of these two initial experiments were gratifying; 74% of benzyl dihydrocinnamate **8b** and 70% of methyl dihydrocinnamate (**8a**) were obtained from the ylides **9** and **10**, respectively. Most importantly, these reactions generated considerably more product than our previous attempts with phosphonates. Furthermore, although some transesterification was still observed with the methyl ester ylide **10** (7% of benzyl ester **8b** was also obtained), this is minimal in comparison with the almost complete transesterification obtained with phosphonate nucleophiles.[15]

We undertook a brief optimisation of the reaction conditions and found that the conditions used previously provided the best yields of product. Of note was the observation that the use of excess phosphorane ylide inhibited the reaction, presumably by complexation to iridium; ylide complexes of metals do have literature precedent.[16] Recently, microwave irradiation of reactions has been shown to be beneficial to the promotion of many organic reactions,[17] the Wittig reaction included.[17,18] Although we were able to shorten the reaction times considerably under microwave irradiation (typically to less than one hour), considerable amounts of benzaldehyde and benzyl cinnamate were obtained. This was ultimately symptomatic of a problem we were to discover later in our synthetic runs; namely loss of hydrogen from the system by undetectable pathways (vide infra); thus we reverted to conventional heating.

We used the optimal reaction conditions to prepare a series of dihydrocinnamate derivatives (Scheme 4, Table 1). We were pleased to observe that the domino indirect Wittig process successfully afforded dihydrocinnamate derivatives **8a**–**8e** in 47–71% yield following chromatography and oxidative workup (to remove the otherwise inseparable alkene). The overall yields achieved were reasonable given that a three-step 51% yield equates to 80% yield for each discrete

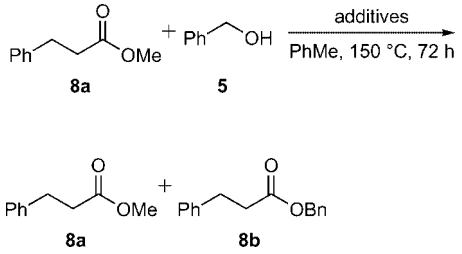
step. In all cases however, small amounts of both the aldehyde and alkene remained. The standard reaction with benzyl (triphenylphosphoranylidene)acetate (**9**) (Entry 2) proved to be best affording benzyl dihydrocinnamate (**8b**) in 71% isolated yield. When alternative ylides were used, a small amount of transesterification (4–13%) occurred under the reaction conditions, resulting in the formation of both (*E*)-benzyl cinnamate (**7b**) and benzyl dihydrocinnamate (**8b**). The steric bulk of the ester group was found to be unimportant in this process, even with the *tert*-butyl (Entry 3) and neopentyl esters (Entry 4) transesterification resulted. More surprisingly, even amide groups were affected (Entries 5–6). In view of the harsh reaction conditions and transesterification observed, the preparation of the synthetically useful Weinreb amide derivative **8f** in 47% yield (Entry 6) was notable.



Scheme 4.

Aside from the observed transesterification these reactions proved to be remarkably clean; this is indicative of the chemoselectivity of the reduction reaction. Only the alkene intermediate undergoes hydrogenation; benzyl esters, cyano groups and all the carboxylic acid derivatives proved to be inert to hydrogenation under these conditions.[20] The reaction with the *tert*-butyl ester ylide (Entry 3) proved to be an exception. Unsurprisingly, under the reaction conditions the *tert*-butyl ester underwent some thermal deprotection, resulting in (*E*)-cinnamic acid and dihydrocinnamic acid formation.[13,21] During these studies we also identified a novel fragmentation of (triphenylphosphoranylidene)succinic anhydride (not shown). When heated in the presence of alcohols, acrylate esters were obtained as the products together with triphenylphosphane. This observation subsequently led us to develop a phosphane-catalysed synthesis of acrylates from maleic anhydride.[22]

Before we could solve the problem of transesterification it was necessary to ascertain the cause. Thus an equimolar mixture of methyl dihydrocinnamate (**8a**) and benzyl alcohol (**5**) was subjected to three experiments in which the influence of the reaction components upon this process were examined (Scheme 5, Table 2). When the reagents were heated in the absence of additives (Entry 1), no transesterification occurred, even under the harsh reaction conditions. However, the addition of 5 mol-% of caesium carbonate caused considerable transesterification to occur (Entry 2). When all the reaction components were added (Entry 3) it was notable that a lower level of transesterification was observed. This is slightly misleading however, as some of the benzyl alcohol (**5**) underwent oxidation to benzaldehyde (**6**). Although, it is difficult to isolate the effect of the base from that of the catalyst, it is likely that both are involved in this process. It is also possible that transesterification occurs upon the phosphorane ylide. This is however impossible to verify since when the ylide and alcohol are heated together decomposition occurs.[23] Furthermore, a literature search revealed no reports of ylide esters undergoing transesterification. If transesterification does occur on the ylide, it is probably a relatively minor process. By way of comparison, the ester group of phosphonates which are known to undergo this process readily[15] exhibited almost complete transesterification.[7,13]



Scheme 5.

Table 1. Synthesis of dihydrocinnamate derivatives.[a]

Entry	Ylide R	Product	Conv.[b] [%]	**6** [%]	**7** [%]	**7b**[c] [%]	**8b**[c] [%]	**8** [%]	Yield [%][d]
1	OMe	**8a**	100	0	21	3	7	68	51
2	OBn	**8b**	100	2	18	–	–	80	71
3	O*t*Bu	**8c**	100[e]	0	15	3	10	63	45
4	OCH_2tBu	**8d**	96	4	20	2	4	71	54
5	NMe_2	**8e**	100	0	22	4	6	67	32[f]
6	NMe(OMe)	**8f**	99	11	11	2	2	75	47

[a] Reactions were carried out on 2.00-mmol scale in toluene (6 mL). [b] Total conversion of benzyl alcohol (**5**) into compounds **6**, **7** and **8** as determined by ^{1}H NMR spectroscopy. [c] Conversion into transesterification products (*E*)-benzyl cinnamate (**7b**) and benzyl dihydrocinnamate (**8b**). [d] Yield of isolated product after flash column chromatography and von Rudloff oxidative workup.[7,13,19] [e] The *tert*-butyl deprotection products (*E*)-cinnamic acid (1%) and dihydrocinnamic acid (8%) were also obtained. [f] Compound **8e** decomposed on silica; the product was therefore isolated by bulb-to-bulb distillation.

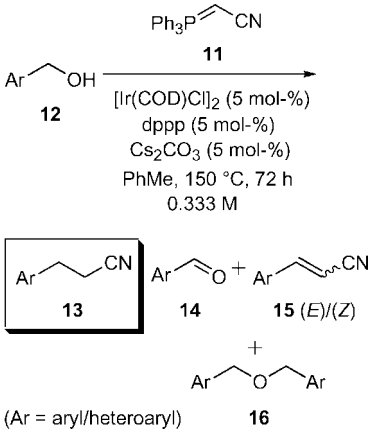
Table 2. Results of transesterification experiments.[a]

Entry	Cs_2CO_3 [mol-%]	$[Ir(COD)Cl]_2$ [mol-%]	dppp [mol-%]	Transesterification ratio[b] [**8a/8b**]
1	–	–	–	100:0
2	5	–	–	17:83
3	5	5	5	59:41

[a] Reactions were carried out on 1.00-mmol scale in toluene (3 mL). [b] Ratio of methyl dihydrocinnamate (**8a**) to benzyl dihydrocinnamate (**8b**) as determined by ^1H NMR analysis.

In view of the successful application of this domino process towards the synthesis of dihydrocinnamate derivatives, we wished to expand the methodology to a range of alcohols. We reasoned that this was unlikely with phosphorane ester ylides for two reasons: (i) transesterification issues and (ii) the tedious workup procedures required. In order to circumvent these issues we elected to remove the possibility of transesterification with the alternative stabilised ylide (triphenylphosphoranylidene)acetonitrile (**11**) as the olefinating reagent. We hoped the product(s) from these reactions would be amenable to purification by simple column chromatography; this we supposed would also improve the product yields.

The initial reaction with the cyano ylide **11** (Scheme 6, Ar = Ph) proved entirely successful, 80% conversion into the product dihydrocinnamonitrile (**13a**) being observed. The identification of 8% of dibenzyl ether was surprising, but can be attributed to the alcohol-promoted degradation of the ylide (vide infra). Most importantly, under the reaction conditions there was no evidence for any competing Pinner[24] or Ritter[25] reactions with the cyano functionality.



Scheme 6.

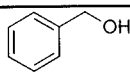
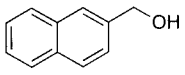
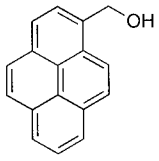
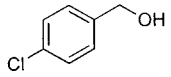
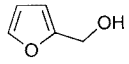
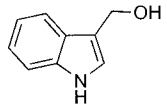
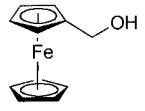
The application of cyano ylide **11** to a range of activated alcohols was then examined. Scheme 6 and Table 3 illustrate the substituted propionitriles obtained under these conditions.

These reactions afforded in all cases (in addition to the desired product) mixtures of the aldehyde, alkene, and ether derived from two molecules of alcohol substrate. Significantly, purification was facile; in all cases the product could be obtained by simple column chromatography without the need for oxidative workup. The yields obtained from these reactions were in the range 31–66%, similar to those obtained with the dihydrocinnamate series. The reaction of simple aryl alcohols (Entries 1–4) proceeded to afford the dihydrocinnamonitrile analogues **13a–d** in 46–66% yield. Most notably, pyren-1-ylmethanol afforded 3-(pyren-1-yl)-propionitrile (**13c**) in 52% yield (Entry 3). The reaction could also be extended to heteroaryl alcohols (Entries 5 and 6). Indol-3-ylmethanol proved to be a more suitable substrate than furfuryl alcohol. Presumably, in the case of furfuryl alcohol the reaction is retarded by chelation of the substrate to the metal centre, a structural impossiblity in the case of indol-3-ylmethanol. Attempts to use ferrocenylmethanol (Entry 7) proved entirely unsuccessful. This reaction converted all of the alcohol substrate into the ether product bis(ferrocen-1-ylmethyl) ether **17**; an 89% isolated yield of the ether being obtained.

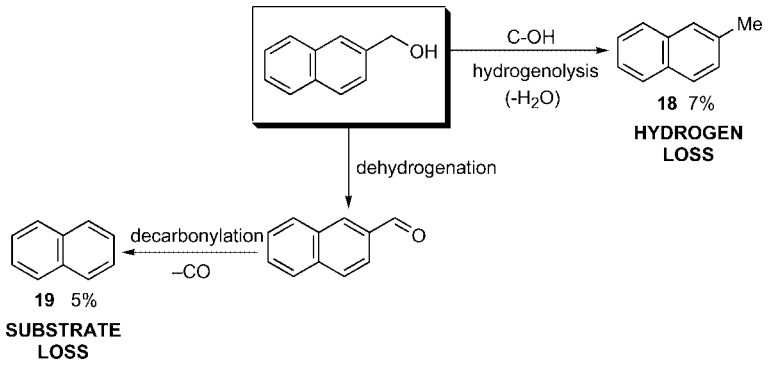
In all of the domino experiments it is evident that there is generally a 10–15% gap between the conversion into the product and the isolated yield obtained. This phenomenon was puzzling until work upon alternative alcohols with the cyano ylide **11** established that two distinct paths for hydrogen/substrate loss existed. From the reaction with naphthalene-2-ylmethanol, an inseparable 1.33:1 mixture of 2-methylnaphthalene (**18**) (7%) and naphthalene (**19**) (5%) was isolated. These components were identified upon the basis of ^1H NMR, ^{13}C NMR and GC-MS data. The isolation of these two components indicated that material can be lost by either a C–OH hydrogenolysis pathway or a decarbonylation pathway (Scheme 7). Hydrogenolysis of the C–OH bond removes hydrogen from the system, generating 2-methylnaphthalene (**18**) and water; this process is well known for heterogeneous systems.[26] The alternative pathway, decarbonylation removes alcohol from the system. The 2-naphthaldehyde intermediate formed by dehydrogenation is decarbonylated by the metal catalyst to yield naphthalene (**19**) and a carbonyl iridium complex.[27] Decarbonylation is well known for systems with ruthenium and particularly rhodium,[28] but it is less common for iridium. Hydrogen/substrate loss products were also isolated for additional examples (pyren-1-ylmethanol, indol-3-ylmethanol and undecan-1-ol all afforded such products – see supporting information; for supp. inf. see also the footnote on the first page of this article) thus it appears likely that this is a general cause of the loss of hydrogen and substrate.

The presence of ether in all of these reactions results from a process which has been known since the 1960s. In 1960 Grayson and Keough[23] reported that the alcohols **20** reacted with the phosphorane ylides **21** to afford the symmetric ether **22**, alkane **23** and phosphane oxide **24** as products (Scheme 8). Somewhat surprisingly ether formation is observed only in the reactions with the cyano ylide **11**; no ether product or acetate ester **23** was detected in any of the reactions with phosphorane ester ylides. During experiments to probe the extent of ylide degradation, we discovered an alternate un-catalysed pathway for formation of the

Table 3. Synthesis of substituted propionitriles.[a]

Entry	Alcohol [12]	Product	Conv.[b] (%)	**14** (%)	**15** (%)	**16** (%)	**13** (%)	Yield[c] (%)
1		**13a**	100	7	6	16	71	56
2		**13b**	>99	10	1	6	83	46
3[d]		**13c**	94	25	6	4	60	52
4		**13d**	96	9	8	4	83	66
5		**13e**	92	7	9	15	61	31
6		**13f**	99	1	17	0	82	50
7		–	100	0	0	100[e]	0	–

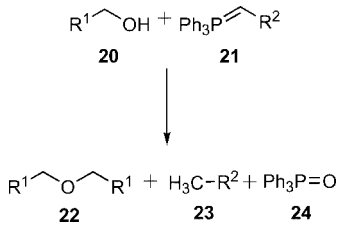
[a] Reactions were carried out on 2.00-mmol scale in toluene (6 mL). [b] Total conversion of alcohol **12** into compounds **13**, **14**, **15** and **16** as determined by ^{1}H NMR analysis. [c] Yield of isolated product after chromatographic purification. [d] Reaction was performed on a 1.5-mmol scale. [e] An 89% yield of bis(ferrocen-1-ylmethyl) ether (**17**) was obtained following chromatography.



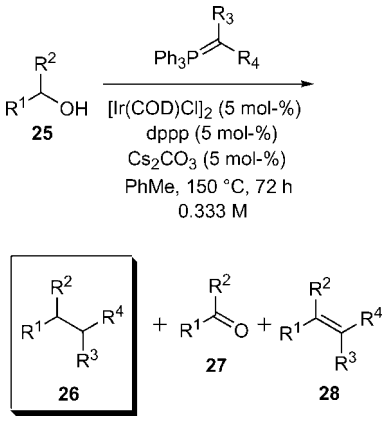
Scheme 7.

C–C bond resulting from direct reaction of the alcohol with the ylide. This pathway proceeds only to a small extent with the cyano ylide; for the ester ylides only trace amounts of product were observed. Subsequent work established that this was a process which proceeded only at high temperature and in the absence of possible alternate reactions; at 110 °C, and at lower temperatures, no reaction was observed. It is likely that this pathway contributes only minimally towards the product obtained from the domino reactions. We intend to publish our findings in this respect in a separate report in parallel with our development of an uncatalysed Wittig alkylation.

At the outset of this project, we envisaged that a successful domino process would enable the use of a wide range of alcohols and allow broad access to alkane products. Towards this goal, we decided to examine the full scope of this reaction in regard to the identity of the alcohol substrate and the phosphorane ylide. To glean the maximum possible information from these experiments we elected to use the cyano ylide **11** for the alternate alcohol runs and the



Scheme 8.



Scheme 9.

benzyl alcohol (**5**) for the alternate ylide runs. The results obtained under these conditions are illustrated in Scheme 9 and Table 4.

Unsurprisingly, aliphatic alcohol undecan-1-ol (Entry 1) proved to be somewhat unreactive, and significant amounts of unreacted alcohol remained; however tridecanenitrile (**26a**) was isolated in 32% yield. This is consistent with the lower oxidation potential of aliphatic alcohols.[29] Allylic alcohols proved to be poor substrates, the reactions generating extremely complex mixtures. Presumably this is explained by the facile isomerisation of allylic alcohols;[30] it is also possible that π-allyliridium complexes are culpable. Careful purification of the reaction mixture from cinnamyl alcohol[31] (Entry 2) afforded 15% of the expected alkane product (*E*)-5-phenyl-4-pentenenitrile (**26b**), and 26% of the alternative alkene reduction product 5-phenyl-2-pentenenitrile [as a mixture of (*E*)/(*Z*) isomers].[32] The observed non-discriminatory reduction suggests that allylic alcohols will probably not have any future synthetic application in this chemistry.

We examined two complementary approaches for the construction of tri-substituted alkanes. Firstly, the use of a secondary alcohol substrate, (±)-phenethyl alcohol (Entry 3), resulted only in a modest, albeit unsurprising, 14% yield of 3-phenylbutyronitrile (**26c**). The sluggish performance of ketones in Wittig olefination is well known, and many different approaches have been examined to overcome this problem.[33] In contrast, when the α-substituted ylide ethyl

Table 4. Examination of substrate scope.[a]

Entry	Alcohol R^1, R^2	Ylide R^3, R^4	Product		Conv.[b] (%)	**27**:**28**[c] (%)	**26**[d] (% yield)
1	*n*-$C_{11}H_{21}$, H	H, CN	*n*-$C_{10}H_{19}$(CN)	**26a**	57	<1:3	43(32)
2	PhCH=CH, H	H, CN	Ph(CN)	**26b**	[e]	–	(15)[f]
3	Ph, Me	H, CN	Ph(Me)(CN)	**26c**	81	28:9	19(14)
4	Ph, H	Me, CO_2Et	Ph(CO_2Et)(Me)	**26d**	100	0:32[g]	62(46)
5	Ph, H	H, C(O)Me	Ph(C(O)Me)	**26e**	99	0:12	87(16)
6	Ph, H	H, $C(O)CO_2Et$	Ph($C(O)CO_2Et$)	–	[h]	–	–
7	Ph, H	H, Ph[i]	Ph–Ph	**26f**	79	1:48	29(20)
8	Ph, H	H, *n*-C_3H_7[i]	Ph(Me)	**26g**	76	2:34	40(14)

[a] Reactions were carried out on 2.00-mmol scale in toluene (6 mL). [b] Total conversion of alcohol **25** into compounds **26**, **27**, and **28** as determined by ^{1}H NMR spectroscopy. [c] Conversion of alcohol **25** into components **27** and **28** respectively. [d] Conversion of alcohol **25** into product **26** and yield of isolated product after chromatography in parenthesis. [e] Conversions could not be determined due to the complex nature of the crude reaction mixture. [f] 26% Of a 1.15:1 (*E*)/(*Z*) mixture of 5-phenyl-2-pentenenitrile was also obtained. [g] 3% Of (*E*)-benzyl α-methylcinnamate and 4% of benzyl α-methylhydrocinnamate was also present. [h] No identifiable components were obtained from the reaction. [i] The phosphorane ylide was pre-formed from 1 equiv. of phosphonium halide and 1 equiv. of *n*-butyllithium (PhMe, 25 °C, 0.5 hour).

Table 5. Examination of alternative catalysts.

Entry[a]	Catalyst	Conv.[b] [%]	**14** [%]	**15** [%]	**13** [%]	Yield[c] [%]
1	[Ru(η^6-*p*-cymene)(*S*,*S*-TsDPEN)]	100	12	4	82	48
2[d,e]	[Ru(PCy_3)$_2$$Cl_2$(=CHPh)]	100	13	14	73	43
3[e]	[Ir(COD)(Py)(PCy_3)]PF_6	90	0	13	76	31
4	$RhCl(PPh_3)_3$	100	0	46	54	0

[a] Reactions were carried out on 2.00-mmol scale in toluene (6 mL) with 5 mol-% of the indicated catalyst. [b] Total conversion of benzyl alcohol (**5**) into compounds **13**, **14** and **15** as determined by ^{1}H NMR spectroscopy. [c] Yield of isolated product after chromatographic purification. [d] Reaction was performed on a 0.376-mmol scale. [e] 5 mol-% of Cs_2CO_3 was also added.

2-(triphenylphosphoranylidene)propionate was used (Entry 4) ethyl α-methylhydrocinnamate (**26d**) was isolated in 46% yield; small amounts of the transesterification products were also obtained. Thus, this is a much more feasible approach to tri-substituted alkanes. We expected that the use of a ketone ylide would lead to chemoselectivity problems due to competitive ketone reduction[14] (Entry 5). However, we were pleased to observe a clean reaction with no evidence for any reduction of the ketone. Despite the high conversion observed, only 16% of the product **26e** could be obtained after purification; this presumably indicates that alternative hydrogen loss pathways are operative here. In view of this result, we attempted the even more challenging reaction with a pyruvate-derived ylide (Entry 6); unfortunately, only decomposition resulted.

The final aspect of reactivity to be explored was the use of unstabilised and semi-stabilised phosphorane ylides. The use of these air- and moisture-sensitive ylides required in situ ylide formation. This was accomplished by pre-formation of the required ylide in toluene solution from phosphonium halide and *n*-butyllithium; the addition of the remainder of the reagents then enabled the domino reaction to proceed. Unstabilised ylides are reported to undergo facile decomposition in the presence of alcohols.[23,34] We were therefore delighted to observe that the corresponding domino product could be obtained from such reactions. Although the yield obtained is modest, despite the unoptimised nature of these experiments, the transformation of benzyl alcohol (**5**) into pentylbenzene (**26g**) in 14% yield[35] (Entry 8) is remarkable. The preparation of 1,2-diphenylethane (**26f**) from the semi-stabilised benzyl ylide was also achieved in 20% yield (Entry 8). When we attempted in situ ylide generation with KO*t*Bu, inferior results were obtained.

From the results presented above it is evident that a more active catalyst for the crossover hydrogenation was required.[36] The high temperatures and extended reaction times led also to the dual problems of transesterification and hydrogen loss. We were convinced that if a more active catalyst could be identified, then these problems could be eliminated and higher yields achieved. A preliminary step towards this goal was the examination of a number of alternative transfer-hydrogenation catalysts in the domino reaction between benzyl alcohol (**5**) and the cyano ylide **11** (Scheme 6, Table 5, Ar = Ph). Unfortunately, none of these catalysts proved to be superior to the original iridium system, although some product was obtained (Entries 1–3). In the case of Wilkinson's catalyst the intermediate aldehyde is presumably decarbonylated before any olefination can occur; the efficacy of rhodium catalysts for this process is well known.[28] These results were ultimately to lead to the development of a highly active ruthenium N-heterocyclic carbene catalyst for the domino indirect Wittig process; the results of which we have recently disclosed.[9]

Conclusions

In summary, we have described the successful development of a first-generation system for the indirect formation of C–C bonds with alcohols. Through the application of our borrowing hydrogen concept, we were able to couple (in a domino sequence) a Wittig olefination reaction with a crossover transfer hydrogenation. The concept of borrowing hydrogen, which we have further developed in the interim period, is under further investigation within these laboratories.

Experimental Section

All reactions were performed under dry argon in oven-dried (150 °C) ACE pressure tubes. Toluene was distilled from sodium wire, rigorously freeze/thaw degassed and stored in sealed Young's ampoules. All phosphorane ylides were freshly prepared prior to use and used immediately. Although several of these are commercially available, superior results were obtained with freshly prepared ylides. Flash chromatography was carried out with Davisil LC 60A silica gel (35–70 micron) purchased from Flurochem; thin-layer chromatographic detection (abbreviated det.) by the methods given. NMR spectra were performed in $CDCl_3$ with either a Bruker Avance 300 (300 MHz) or Varian WH-400 (400 MHz) instrument and recorded at the following frequencies: proton (^{1}H – 300/400 MHz) and carbon (^{13}C – 75.4/100.5 MHz). IR spectra were recorded with a Perkin–Elmer 1600 series FT-IR spectrophotometer (with internal background scan) in the range 600–4000 cm^{-1}. Mass spectra, including high-resolution spectra, were recorded with a Micromass Autospec spectrometer or a Finnigan MAT 8340 spectrometer using electron impact (EI+) ionisation, chemical ionisation (CI+ using isobutane or ammonia) and/or Fast Atom Bombardment (FAB+) ionisation. Melting points were measured with a Büchi 535 series instrument and are uncorrected. GC-MS was performed with a Fisons series 8000GC/Finnigan MAT 8340 spectrometer setup using an achiral 5% PH-ME siloxane, 20 m × 0.2 mm, column. *n*-Butyllithium was purchased from Acros organics, stored in a

Young's ampoule and titrated according to the procedure of Suffert[37] before use.

General Procedure 1: Preparation of Hydrocinnamate Derivatives: To an argon-purged ACE™ pressure tube containing $[Ir(COD)Cl]_2$ (67 mg, 0.1 mmol, 0.05 equiv.), dppp (41 mg, 0.1 mmol, 0.05 equiv.), caesium carbonate (33 mg, 0.1 mmol, 0.05 equiv.) and the phosphorane ylide (2.2 mmol, 1.1 equiv.) was added benzyl alcohol (**5**) (216 mg, 2.0 mmol, 197 μL, 1.0 equiv.) followed by degassed anhydrous toluene (6.0 mL). The tube was sealed, stirred vigorously and heated at 150 °C for 72 hours. The cooled reaction mixture was quenched by the addition of wet diethyl ether (50 mL) and concentrated in vacuo to afford the crude product. Conversion was determined by analysis of the ^{1}H NMR spectrum. Pre-adsorption of the crude mixture on silica and purification by flash column chromatography [SiO_2, petroleum ether (b.p. 40–60 °C)/diethyl ether eluent] afforded an inseparable mixture of the dihydrocinnamate product and cinnamate intermediate. This mixture was suspended in 50 mL of a 3:2 water/*tert*-butyl alcohol solution, and treated with potassium permanganate (20 mg), sodium metaperiodate (1.625 g) and potassium carbonate (125 mg) in a single portion. The resulting suspension was stirred for 2 hours at room temperature and then poured into water (50 mL). This mixture was extracted with diethyl ether (3 × 20 mL), the combined organic extracts washed with 1 M sodium hydroxide (2 × 25 mL), saturated brine (50 mL), dried ($MgSO_4$), filtered and concentrated in vacuo to yield the desired alkane product.

General Procedure 2: Preparation of Substituted Propionitriles: To an argon-purged ACE™ pressure tube containing $[Ir(COD)Cl]_2$ (67 mg, 0.1 mmol, 0.05 equiv.), dppp (41 mg, 0.1 mmol, 0.05 equiv.), caesium carbonate (33 mg, 0.1 mmol, 0.05 equiv.) and (triphenylphosphoranylidene)acetonitrile (**11**) (663 mg, 2.2 mmol, 1.1 equiv.) was added the required alcohol (2.0 mmol, 1.0 equiv.) followed by degassed anhydrous toluene (6.0 mL). The tube was sealed, stirred vigorously and heated at 150 °C for 72 hours. The cooled reaction mixture was quenched by the addition of wet diethyl ether (50 mL) and concentrated in vacuo to afford the crude product. Conversion was determined by analysis of the ^{1}H NMR spectrum. Pre-adsorption of the crude mixture on silica and purification by flash column chromatography [SiO_2, petroleum ether (b.p. 40–60 °C)/diethyl ether eluent] afforded the substituted propionitrile product.

General Procedure 3: Domino Indirect Wittig Reactions with Unstabilised Ylides: To an argon-purged ACE™ pressure tube containing a solution of the required phosphonium halide salt (2.20 mmol, 1.1 equiv.) in anhydrous toluene (6 mL) was added dropwise a solution of *n*-butyllithium [2.27 M in hexanes] (141 mg, 2.20 mmol, 1.1 equiv., 969 μL), and the mixture was stirred for 30 minutes at room temperature to form the phosphorane ylide.[38] $[Ir(COD)Cl]_2$ (67 mg, 0.1 mmol, 0.05 equiv.), dppp (41 mg, 0.1 mmol, 0.05 equiv.) and caesium carbonate (33 mg, 0.1 mmol, 0.05 equiv.) were added in a single portion followed by benzyl alcohol (**5**) (216 mg, 2.0 mmol, 197 μL, 1.0 equiv.) The reaction was then conducted in agreement with general procedure 1.

Methyl Dihydrocinnamate (8a): According to general procedure 2 using methyl (triphenylphosphoranylidene)acetate (**10**) (735 mg, 2.2 mmol, 1.1 equiv.) and petroleum ether (b.p. 40–60 °C)/diethyl ether (40:1) as the eluent afforded the title compound **8a** as a colourless oil (168 mg, 68% conversion, 51% yield). R_f = 0.67 (petroleum ether (b.p. 40–60 °C)/diethyl ether, 7:3, det. with *p*-anisaldehyde [orange]). ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, ppm): δ = 7.26–7.30 (m, 2 H, ArH), 7.18–7.22 (m, 3 H, ArH), 3.66 (s, 3 H, OCH_3), 2.95 (t, J = 8.2 Hz, 2 H, $PhCH_2$), 2.63 (t, J = 8.2 Hz, 2 H, CH_2CO_2Me). ^{13}C NMR (100.5 MHz, $CDCl_3$, 25 °C, ppm): δ = 173.5 (C=O), 140.7, 128.7, 128.4, 126.5, 52.0 (OCH_3), 36.1 (CH_2CO_2Me), 31.4 ($PhCH_2$). IR (liquid film): $\tilde{\nu}$ = 3086, 3025, 2951, 1734 (C=O), 1603, 1496, 1452, 1161, 1078 cm^{-1}. MS (EI+ = 70 eV): *m*/*z* (%) = 164 (39) [M$^{\cdot+}$], 133 (12), 105 (36), 104 (100), 91 (62), 77 (13). HRMS (EI+ = 70 eV): $C_{10}H_{12}O_2$ requires 164.0837, found 164.0838.

Benzyl Dihydrocinnamate (8b): According to general procedure 2 using benzyl (triphenylphosphoranylidene)acetate (**9**) (903 mg, 2.2 mmol, 1.1 equiv.) and petroleum ether (b.p. 40–60 °C)/diethyl ether (40:1) as the eluent afforded the title compound **8b** as a colourless oil (341 mg, 80% conversion, 71% yield). R_f = 0.73 (petroleum ether (b.p. 40–60 °C)/diethyl ether, 7:3, det. with *p*-anisaldehyde [red]). ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, ppm): δ = 7.24–7.37 (m, 7 H, ArH), 7.16–7.21 (m, 3 H, ArH), 5.10 (s, 2 H, OCH_2Ph), 2.96 (t, J = 7.4 Hz, 2 H, CH_2CO_2Bn), 2.67 (t, J = 7.4 Hz, 2 H, $PhCH_2$). ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C, ppm): δ = 172.8 (C=O), 140.6, 136.1, 128.8, 128.7, 128.5, 128.5, 126.5, 66.7 (OCH_2Ph), 36.3 (CH_2CO_2Bn), 31.4 ($PhCH_2$). IR (liquid film): $\tilde{\nu}$ = 3061, 3026, 2948, 1735 (C=O), 1603, 1495, 1453, 1159, 1077 cm^{-1}. MS (FAB+): *m*/*z* = 240 [M$^{\cdot+}$]. HRMS (FAB+): $C_{16}H_{16}O_2$ requires 240.1150, found 240.1139.

***tert*-Butyl Dihydrocinnamate (8c):** According to general procedure 2 using *tert*-butyl (triphenylphosphoranylidene)acetate (828 mg, 2.2 mmol, 1.1 equiv.) and petroleum ether (b.p. 40–60 °C)/diethyl ether (40:1) as the eluent afforded the title compound **8c** as a colourless oil (200 mg, 63% conversion, 49% yield). R_f = 0.54 (7:3 petroleum ether (b.p. 40–60 °C)/diethyl ether, det. with *p*-anisaldehyde [black]); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, ppm): δ = 7.19–7.23 (m, 2 H, ArH), 7.08–7.12 (m, 3 H, ArH), 2.83 (t, J = 7.1 Hz, 2 H, $PhCH_2$), 2.46 (t, J = 7.1 Hz, 2 H, CH_2CO_2tBu), 1.34 [s, 9 H, $OC(CH_3)_3$]. ^{13}C NMR (75.4 MHz, $CDCl_3$, 25 °C, ppm): δ = 171.2 (C=O), 139.8, 127.4, 127.3, 125.1, 79.3 [$OC(CH_3)_3$], 36.1 (CH_2CO_2tBu), 30.1 ($PhCH_2$), 27.0 [$OC(CH_3)_3$]. IR (liquid film): $\tilde{\nu}$ = 3086, 3063, 2976, 2930, 1729, 1604, 1496, 1453, 1146, 1078, 846, 743, 698 cm^{-1}. MS (EI+ = 70 eV): *m*/*z* (%) = 206 (1.5) [M$^{\cdot+}$], 150 (82), 133 (37), 105 (49), 104 (52), 91 (60), 57 (100). HRMS (EI+ = 70 eV): $C_{13}H_{18}O_2$ requires 206.1305, found 206.1306.

Neopentyl Dihydrocinnamate (8d): According to general procedure 2 using neopentyl (triphenylphosphoranylidene)acetate (859 mg, 2.2 mmol, 1.1 equiv.) and petroleum ether (b.p. 40–60 °C)/diethyl ether (100:1) as the eluent afforded the title compound **8d** as a colourless oil (237 mg, 71% conversion, 54% yield). R_f = 0.76 (7:3 petroleum ether (b.p. 40–60 °C)/diethyl ether, det. with *p*-anisaldehyde [black]). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, ppm): δ = 7.11–7.20 (m, 5 H, ArH). 3.69 (s, 2 H, OCH_2tBu), 2.89 (t, J = 7.5 Hz, 2 H, $PhCH_2$), 2.58 (t, J = 7.5 Hz, 2 H, $CH_2CO_2CH_2tBu$), 0.83 [s, 9 H, $C(CH_3)_3$]; ^{13}C NMR (75.4 MHz, $CDCl_3$, 25 °C, ppm): δ = 173.2 (C=O), 140.7, 128.6, 128.4, 126.4, 73.9 (OCH_2tBu), 36.0 ($CH_2CO_2CH_2tBu$), 31.4 [$CH_2C(CH_3)_3$], 31.2 ($PhCH_2$), 26.5 [$C(CH_3)_3$]. IR (liquid film): $\tilde{\nu}$ = 3063, 3028, 2959, 2869, 1732, 1604, 1497, 1478, 1456, 1377, 1366, 1291, 1244, 1160, 1078, 1014, 749, 694 cm^{-1}. MS (EI+ = 70 eV): *m*/*z* (%) = 220 (57) [M$^{\cdot+}$], 205 (7), 150 (61), 133 (47), 105 (77), 104 (69), 91 (84), 71 (100), 57 (25), 43 (47). HRMS (EI+ = 70 eV): $C_{14}H_{20}O_2$ requires 220.1463, found 220.1464.

***N*,*N*-Dimethyl-3-phenylpropionamide (8e):** The reaction was performed according to general procedure 2 using *N*,*N*-dimethyl-(triphenylphosphoranylidene)acetamide (764 mg, 2.2 mmol, 1.1 equiv.). Purification was achieved by bulb-to-bulb distillation (85 °C, 1 Torr) to yield a mixture of the desired product and transesterification product benzyl dihydrocinnamate. The product

proved to be unstable to silica, undergoing decomposition. Thus the mixture was dissolved in diethyl ether (15 mL), palladium on carbon [10 w/w%] (50 mg, 0.047 mmol) added and the mixture placed under 1 atm of hydrogen. The reaction mixture was stirred for 12 hours, diluted with diethyl ether (35 mL) and then filtered through a plug of celite. The filtrate was washed with 1 M sodium hydroxide (50 mL), saturated brine (50 mL), dried ($MgSO_4$), filtered and concentrated in vacuo to yield the title compound, **8e**, a colourless liquid (106 mg, 67% conversion, 32% yield). B.p. 85 °C/1 Torr (ABT). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, ppm): δ = 7.19–7.24 (m, 2 H, ArH), 7.11–7.16 (m, 3 H, ArH), 2.87 [s, 3 H, N(CH_3)$_2$], 2.85 [s, 3 H, N(CH_3)$_2$], 2.85 (partially obscured t, J = 7.5 Hz, 2 H, PhCH_2), 2.54 (t, J = 7.5 Hz, 2 H, CH_2CONMe$_2$). ^{13}C NMR (75.4 MHz, $CDCl_3$, 25 °C, ppm): δ = 172.3 (C=O), 141.6, 128.6, 128.5, 126.1, 37.3 [N(*C*H$_3$)$_2$], 35.5 [N(*C*H$_3$)$_2$], 35.4 (*C*H$_2$CONMe$_2$), 31.5 (Ph*C*H$_2$). IR (liquid film): $\tilde{\nu}$ = 3060, 3026, 2931, 1646 (C=O), 1495, 1453, 1398, 1345, 1266, 1141, 1076, 753, 700 cm^{-1}. MS (EI+ = 70 eV): *m*/*z* (%) = 177 (100) [M$^{\cdot+}$], 133 (8), 105 (46), 91 (64), 77 (24), 72 (42), 45 (39). HRMS (EI+, 70eV): $C_{11}H_{15}NO$ requires 177.1153, found 177.1157.

***N*-Methoxy-*N*-methyl-3-phenylpropionamide (8f):** According to General procedure 2 using *N*-methoxy-*N*-methyl(triphenylphosphoranylidene)acetamide (799 mg, 2.2 mmol, 1.1 equiv.) and petroleum ether (b.p. 40–60 °C)/diethyl ether (9:1 → 7:3) as the eluent afforded the title compound **8f** as a pale yellow oil (164 mg, 75% conversion, 47% yield). R_f = 0.13 (petroleum ether (b.p. 40–60 °C)/diethyl ether (7:3), det. with *p*-anisaldehyde [orange]). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, ppm): δ = 7.20–7.32 (s, 5 H, ArH), 3.61 [s, 3 H, NMe(OCH_3)], 3.18 [s, 3 H, NCH_3(OMe)], 2.97 (t, J = 7.5 Hz, 2 H, PhCH_2), 2.74 [t, J = 7.5 Hz, 2 H, CH_2CONMe(OMe)]. ^{13}C NMR (300 MHz, $CDCl_3$, 25 °C, ppm): δ = 173.8 (C=O), 141.4, 128.6, 128.5, 126.2, 61.3 (OCH_3), 33.9 [*C*H$_2$CONMe(OMe)], 32.3 (N*C*H$_3$OMe), 30.8 (Ph*C*H$_2$). IR (liquid film): $\tilde{\nu}$ = 3061, 3026, 2936, 1690, 1603, 1587, 1495, 1454, 1385, 1340, 1178, 1103, 1075, 1029, 989, 940, 751, 695 cm^{-1}. MS (EI+ = 70 eV): *m*/*z* (%) = 193 (44) [M$^{\cdot+}$], 133 (21), 105 (95), 91 (100), 77 (20), 61 (29). HRMS (EI+ = 70 eV): $C_{11}H_{15}NO_2$ requires 193.1103, found 193.1104.

Dihydrocinnamonitrile (13a): According to general procedure 3 using benzyl alcohol (**5**) (216 mg, 2.0 mmol, 197 μL, 1.0 equiv.) and petroleum ether (b.p. 40–60 °C)/diethyl ether (30:1) as the eluent afforded the title compound **13a** as a colourless oil (141 mg, 71% conversion, 56% yield). **13a**: R_f = 0.36 (petroleum ether (b.p. 40–60 °C)/diethyl ether (7:3), det. with *p*-anisaldehyde [orange]) ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, ppm): δ = 2.64 (t, J = 7.4 Hz, 2 H, CH_2CN), 2.98 (t, J = 7.4 Hz, 2 H, PhCH_2), 7.22–7.39 (m, 5 H, ArH). ^{13}C NMR (75.4 MHz, $CDCl_3$, 25 °C, ppm): δ = 138.5, 129.3, 128.7, 127.6, 119.6 (*C*≡N), 32.0 (Ph*C*H$_2$), 19.8 (*C*H$_2$CN). IR (liquid film): $\tilde{\nu}$ = 3063, 3029, 2931, 2246 (C≡N), 1603, 1496, 1454, 1079, 1030, 748, 699 cm^{-1}. MS (EI+ = 70 eV): *m*/*z* (%) = 131 (22) [M$^{\cdot+}$], 91 (100). HRMS (EI+ = 70 eV): C_9H_9N requires 131.0735, found 131.0733.

3-(Naphthalen-2-yl)propionitrile (13b): According to general procedure 3 using naphthalen-2-ylmethanol (316 mg, 2.0 mmol, 1.0 equiv.) and petroleum ether (b.p. 40–60 °C)/diethyl ether (19:1 → 9:1) as the eluent afforded the title compound **13b** as a colourless oil which solidified as a dense cream solid upon standing (168 mg, 83% conversion, 46% yield). M.p. 72–73 °C; R_f = 0.32 (petroleum ether (b.p. 40–60 °C)/diethyl ether (7:3), det. with *p*-anisaldehyde [red]). ^{1}H NMR ($CDCl_3$, 300 MHz, 25 °C, ppm): δ = 7.83–7.88 (m, 3 H, ArH), 7.72 (br. s, 1 H, ArH), 7.47–7.55 (m, 2 H, ArH), 7.37 (dd, J = 1.5, 8.4 Hz, 1 H, ArH), 3.16 (t, J = 7.4 Hz, 2 H, ArCH_2), 2.75 (t, J = 7.4 Hz, 2 H, CH_2CN). ^{13}C NMR (75.4 MHz, $CDCl_3$, 25 °C, ppm): δ = 135.6, 133.6, 132.6, 127.8, 127.8, 126.9, 126.5, 126.4, 126.0, 119.3 (*C*≡N), 31.8 (Ar*C*H$_2$), 19.4 (*C*H$_2$CN). IR (KBr): $\tilde{\nu}$ = 3054, 2954, 2926, 2885, 2243 (C≡N), 1597, 1507, 1448, 1422, 1368, 1273, 1202, 1126, 965, 951, 918, 900, 863, 828, 810, 749, 653 cm^{-1}. MS (EI+ = 70 eV): *m*/*z* (%) = 181 (33) [M$^{\cdot+}$], 141 (100), 115 (15). HRMS (EI+ = 70 eV): $C_{13}H_{11}N$ requires 181.0891, found 181.0892.

3-(Pyrene-1-yl)propionitrile (13c): According to General procedure 3 using pyren-1-ylmethanol (345 mg, 1.5 mmol, 1.0 equiv.), (triphenylphosphoranylidene)acetonitrile (**11**) (497 mg, 1.65 mmol, 1.1 equiv.), toluene (4.5 mL) and petroleum ether (b.p. 40–60 °C)/diethyl ether (30:1 → 7:3) as the eluent afforded the title compound **13c** as a yellow solid, which was subsequently recrystallised from dichloromethane/hexane to afford pale yellow microcrystals (199 mg, 60% conversion, 52% yield). M.p. 132–134 °C; R_f = 0.23 (petroleum ether (b.p. 40–60 °C)/diethyl ether (7:3), det. with *p*-anisaldehyde [mauve]). ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, ppm): δ = 8.16 (d, J = 7.4 Hz, 2 H, ArH), 8.10 (m, 3 H, ArH), 8.02 (s, 1 H, ArH), 8.01 (s, 1 H, ArH), 7.98 (d, J = 7.5 Hz, 1 H, ArH), 7.85 (d, J = 7.8 Hz, 1 H, ArH), 3.64 (t, J = 7.4 Hz, 2 H, ArCH_2), 2.80 (t, J = 7.4 Hz, 2 H, CH_2CN). ^{13}C NMR (75.4 MHz, $CDCl_3$, 25 °C, ppm): δ = 132.0, 131.7, 131.2, 131.1, 128.8, 128.6, 127.8, 127.7, 127.5, 126.5, 125.9, 125.6, 125.5, 125.4, 125.2, 122.4, 119.6 (*C*≡N), 29.6 (Ar*C*H$_2$), 19.7 (*C*H$_2$CN). IR (KBr): $\tilde{\nu}$ = 3041, 2927, 2241 (C≡N), 1604, 1586, 1466, 1457, 1431, 1418, 1318, 1248, 1187, 1098, 841, 755, 712 cm^{-1}. MS (EI+ = 70 eV): *m*/*z* (%) = 255 (27) [M$^{\cdot+}$], 220 (27), 215 (97), 213 (74), 205 (100), 105 (36), 71 (33), 57 (74), 43 (54). HRMS (EI+ = 70 eV): $C_{13}H_{13}N$ requires 255.1048, found 255.1051.

3-(*p*-Chlorophenyl)propionitrile (13d): According to general procedure 3 using *p*-chlorobenzyl alcohol (285 mg, 2.0 mmol, 1.0 equiv.) and petroleum ether (b.p. 40–60 °C)/diethyl ether (30:1 → 9:1) as the eluent afforded the title compound **13d** as a pale yellow oil (217 mg, 83% conversion, 66% yield). R_f = 0.28 (petroleum ether (b.p. 40–60 °C)/diethyl ether (7:3), det. with *p*-anisaldehyde [weak yellow]). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, ppm): δ = 7.31 (d, J = 8.3 Hz, 2 H, *ortho*-ArH), 7.17 (d, J = 8.3 Hz, 2 H, *meta*-ArH), 2.92 (t, J = 7.3 Hz, 2 H, ArCH_2), 2.60 (t, J = 7.3 Hz, 2 H, CH_2CN). ^{13}C NMR (75.4 MHz, $CDCl_3$, 25 °C, ppm): δ = 136.5 (C_{ipso}), 133.3 (C_{para}), 130.0 (C_{ortho}), 129.2 (C_{meta}), 119.0 (*C*≡N), 31.0 (Ar*C*H$_2$), 19.5 (*C*H$_2$CN). IR (liquid film): $\tilde{\nu}$ = 3029, 2932, 2869, 2246 (C≡N), 1598, 1493, 1427, 1424, 1408, 1092, 1015, 921, 832, 807, 776, 714 cm^{-1}. MS (EI+ = 70 eV): *m*/*z* (%) = 167/165 (7, 21) [M$^{\cdot+}$], 127/125 (33, 100). HRMS (EI+ = 70 eV): $C_9H_8N^{37}Cl$ requires 165.0345, found 165.0349.

3-(Furan-2-yl)propionitrile (13e): According to General procedure 3 using furfuryl alcohol (196 mg, 2.0 mmol, 174 μL, 1.0 equiv.) and petroleum ether (b.p. 40–60 °C)/diethyl ether (30:1) as the eluent afforded the title compound **13e** as a pale yellow liquid (76 mg, 61% conversion, 31% yield). R_f = 0.44 (petroleum ether (b.p. 40–60 °C)/diethyl ether (7:3), det. with *p*-anisaldehyde [turquoise]). ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, ppm): δ = 7.26 (d, J = 1.5 Hz, 1 H, ArH), 6.23 (app. t, J = 2.7 Hz, 1 H, ArH), 6.09 (d, J = 3.1 Hz, 1 H, ArH), 2.93 (t, J = 7.4 Hz, 2 H), 2.60 (t, J = 7.4 Hz, 2 H). ^{13}C NMR (75.4 MHz, $CDCl_3$, 25 °C, ppm): δ = 151.4, 142.2, 118.8 (*C*≡N), 110.6, 106.9, 24.4 (Ar*C*H$_2$), 16.7 (CH$_2$*C*N). IR ($CDCl_3$): $\tilde{\nu}$ = 2954, 2926, 2850, 2255 (C≡N), 1601, 1507, 1440, 1426, 1342, 1261, 1160, 1145, 1077, 1016, 927, 804 cm^{-1}. MS (EI+ = 70 eV): *m*/*z* (%) = 121 (22) [M$^{\cdot+}$]; 81 (100), 53 (26). HRMS (EI+ = 70 eV): C_7H_7NO requires 121.0527, found 121.0528.

3-(Indol-3-yl)propionitrile (13f): According to General procedure 3 using indol-3-ylmethanol (294 mg, 2.0 mmol, 1.0 equiv.) and petro-

leum ether (b.p. 40–60 °C)/diethyl ether (9:1 → 1:2) as the eluent afforded the title compound **13f** as a pale brown oil which solidified as a glassy pale brown solid on standing (170 mg, 82% yield, 50% yield). M.p. 66–68 °C; R_f = 0.22 (petroleum ether (b.p. 40–60 °C)/diethyl ether (1:1), det. with *p*-anisaldehyde [purple]). ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, ppm): δ = 8.13 (br. s, 1 H, N*H*), 7.59 (m, 1 H, ArH), 7.41 (dt, *J* = 1.1, 8.0 Hz, 1 H, ArH), 7.27 (dt, *J* = 1.1, 7.0 Hz, 1 H, ArH), 7.22 (dt, *J* = 1.1, 7.0 Hz, 1 H, ArH), 7.15 (br. d, *J* = 2.4 Hz, 1 H, ArH), 3.17 (t, *J* = 7.1 Hz, 2 H, ArCH_2), 2.73 (t, *J* = 7.1 Hz, 2 H, CH_2CN). ^{13}C NMR (75.4 MHz, $CDCl_3$, 25 °C, ppm): δ = 136.4, 126.7, 122.5, 122.3, 119.9 (*C*≡N), 119.8, 119.3, 112.7, 111.6, 21.8 (Ar*C*H$_2$), 18.8 (*C*H$_2$CN). IR ($CDCl_3$): $\tilde{\nu}$ = 3478, 3061, 2928, 2861, 2248 (C≡N), 1620, 1489, 1457, 1420, 1369, 1336, 1251, 1229, 1094, 1070, 1012 cm^{-1}. MS (EI+ = 70 eV): *m*/*z* (%) = 170 (24) [M$^{\cdot+}$]; 135 (27), 130 (100), 92 (91), 77 (15), 65 (15). HRMS (EI+ = 70 eV): $C_{11}H_{10}N_2O$ requires 170.0844, found 170.0846.

Tridecanenitrile (26a): According to General procedure 3 using undecan-1-ol (345 mg, 2.0 mmol, 416 μL, 1.0 equiv.) and petroleum (b.p. 40–60 °C)/diethyl ether (40:1) as the eluent afforded the title compound as a colourless liquid (126 mg, 43% conversion, 32% yield). R_f = 0.74 (petroleum (b.p. 40–60 °C)/diethyl ether (7:3), det. with *p*-anisaldehyde [weak green]). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, ppm): δ = 2.32 (t, *J* = 7.1 Hz, 2 H, CH_2CN), 1.64 (quint, *J* = 7.1 Hz, 2 H, CH_2CH_2CN), 1.38–1.45 (m, 2 H, $CH_2CH_2CH_2$CN), 1.26 (br. s, 16 H), 0.87 (t, *J* = 7.0 Hz, 3 H, CH_3). ^{13}C NMR (75.4 MHz, $CDCl_3$, 25 °C, ppm): δ = 14.3 (*C*H$_3$), 17.2, 22.8, 25.5, 28.8, 28.9, 29.4, 29.5, 29.6, 29.7, 32.0 (*C*H$_2$CN), 119.9 (*C*≡N). IR (liquid film): $\tilde{\nu}$ = 292, 2864, 2246 (C≡N), 1465, 1432, 1377, 722 cm^{-1}. MS (EI+ = 70 eV): *m*/*z* (%) 166 (17) [(M – Et$^{\cdot}$)$^+$], 152 (34), 138 (34), 124 (50), 110 (74), 97 (100), 96 (65), 83 (46), 82 (45), 69 (41), 57 (55), 55 (54), 43 (67), 41 (75). MS (FAB+): *m*/*z* = 196 [[M + H]$^+$]. HRMS (FAB+): $C_{13}H_{26}N$ [[M + H]$^+$] requires 196.2065, found 196.2067.

(*E*)-5-Phenyl-4-pentenenitrile (26b): According to General procedure 3 using cinnamyl alcohol (268 mg, 2.0 mmol, 1.0 equiv.) and petroleum ether (b.p. 40–60 °C)/diethyl ether (50:1 → 40:1 → 30:1 → 19:1 → 9:1 → 7:3) as the eluent a very complex mixture of fractions was isolated. From this mixture the title compound **26b** (47 mg, 15%) was isolated as a colourless liquid. R_f = 0.33 [petroleum ether (b.p. 40–60 °C)/diethyl ether (7:3), det. with UV]. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, ppm): δ = 7.15–7.30 (m, 5 H, ArH), 6.44 (d, *J* = 15.8 Hz, 1 H, PhC*H*=), 6.12 (dt, *J* = 6.5, 15.8 Hz, 1 H, PhCH=C*H*CH$_2$), 2.38–2.50 (m, 4 H). ^{13}C NMR (75.4 MHz, $CDCl_3$, 25 °C, ppm): δ = 137.0, 133.0, 128.7, 128.7, 126.4, 125.6, 119.6 (C≡N), 29.2 (*C*H$_2$CH$_2$CN), 18.0 (*C*H$_2$CN).

3-Phenylbutyronitrile (26c): According to General procedure 3 using (±)-*sec*-phenethyl alcohol (244 mg, 2.0 mmol, 242 μL, 1.0 equiv.) and petroleum ether (b.p. 40–60 °C)/diethyl ether (40:1) as the eluent afforded the title compound **26c** as a colourless oil (38 mg, 19% conversion, 14% yield). R_f = 0.25 [petroleum ether (b.p. 40–60 °C)/diethyl ether (7:3), det. with UV]. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, ppm): δ = 7.37–7.42 (m, 2 H, ArH), 7.27–7.34 (m, 3 H, ArH), 3.20 [app. sextet, *J* = 7.0 Hz, 1 H, PhC*H*(CH$_3$)CH$_2$CN], 2.67 (dd, *J* = 6.4, 16.6 Hz, 1 H, CH_aH$_b$CN), 2.58 (dd, *J* = 7.5, 16.6 Hz, 1 H, CH$_a$*H*$_b$CN), 1.49 (d, *J* = 7.0 Hz, 3 H, CH_3). ^{13}C NMR (75.4 MHz, $CDCl_3$, 25 C, ppm): δ = 143.2, 128.9, 126.6, 127.4, 118.7 (*C*≡N), 36.6 [Ph*C*H(CH$_3$)CH$_2$CN], 26.4 (*C*H$_2$CN), 20.7 (*C*H$_3$). IR ($CDCl_3$): $\tilde{\nu}$ = 3065, 3031, 2968, 2931, 2253 (C≡N), 1602, 1495, 1453, 1422, 1383, 1358, 1015 cm^{-1}. MS (EI+ = 70 eV): *m*/*z* (%) = 145 (17) [M$^{\cdot+}$], 105 (100), 77 (16). HRMS (EI+ = 70 eV): $C_{10}H_{11}N$ requires 145.0891, found 145.0891.

Ethyl 2-Methyl-3-phenylpropionate (26d): According to General procedure 2 using ethyl 2-(triphenylphosphoranylidene)propionate (718 mg, 2.2 mmol, 1.1 equiv.) and petroleum ether (b.p. 40–60 °C)/diethyl ether (40:1) as the eluent afforded the title compound, **26d**, as a colourless liquid (177 mg, 62% conversion, 46% yield). R_f = 0.57 (petroleum ether (b.p. 40–60 °C)/diethyl ether (7:3), det. with *p*-anisaldehyde [grey]). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, ppm): δ = 7.06–7.20 (m, 5 H, ArH), 3.99 (q, *J* = 7.1 Hz, 2 H, OCH_2CH$_3$), 2.85–2.97 [m, 1 H, PhCH$_2$C*H*(CH$_3$)CO$_2$Et], 2.53–2.68 (m, 2 H, PhCH_2), 1.04–1.11 (m, 6 H, CH_3). ^{13}C NMR (300 MHz, $CDCl_3$, 25 °C, ppm): δ = 176.7 (C=O), 140.0, 129.0, 128.6, 126.8, 60.8 (O*C*H$_2$CH$_3$), 42.1 [PhCH$_2$*C*H(CH$_3$)CO$_2$Et], 40.3 (Ph*C*H$_2$), 17.3 [PhCH$_2$CH(*C*H$_3$)CO$_2$Et], 14.7 (OCH$_2$*C*H$_3$). IR (liquid film): $\tilde{\nu}$ = 3063, 3028, 2977, 2935, 2876, 1732, 1604, 1495, 1454, 1376, 1350, 1282, 1173, 1117, 1094, 1028, 745, 700 cm^{-1}. MS (EI+ = 70 eV): *m*/*z* (%) = 191 (19) [M$^{\cdot+}$], 147 (7), 119 (22), 118 (61), 91 (100), 77 (7). HRMS (EI+ = 70 eV): $C_{12}H_{16}O_2$ requires 192.1150, found 119.1154.

4-Phenylbutan-2-one (26e): In analogy to general procedure 2 using alcohol **5** (216 mg, 2.0 mmol, 197 μL, 1.0 equiv.), (triphenylphosphoranylidene)acetone (700 mg, 2.2 mmol, 1.1 equiv.) and petroleum ether (b.p. 40–60 °C)/diethyl ether (40:1 → 19:1) as the eluent afforded the title compound **26e** as a colourless liquid (46 mg, 87% conversion, 16% yield). R_f = 0.33 (petroleum ether (b.p. 40–60 °C)/diethyl ether (7:3), det. with *p*-anisaldehyde [mauve]). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, ppm): δ = 7.16–7.22 (m, 2 H, ArH), 7.08–7.12 (m, 3 H, ArH), 2.81 (t, *J* = 7.5 Hz, 2 H, PhCH_2), 2.67 [t, *J* = 7.5 Hz, 2 H, CH_2C(O)Me], 2.05 (s, 3 H, CH_3). ^{13}C NMR (74.5 MHz, $CDCl_3$, 25 °C, ppm): δ = 206.9 (C=O), 140.0, 127.5, 127.3, 125.0, 44.1 [*C*H$_2$C(O)Me], 29.0 (Ph*C*H$_2$), 28.7 (*C*H$_3$). IR (liquid film): $\tilde{\nu}$ = 3061, 3027, 2924, 1717, 1602, 1579, 1496, 1453, 1409, 1356, 1282, 1216, 1161, 1080, 1030, 965, 750, 699 cm^{-1}. MS (EI+ = 70 eV): *m*/*z* (%) = 148 (77) [M$^{\cdot+}$], 133 (15), 105 (92), 91 (71), 77 (24), 43 (100). HRMS (EI+ = 70 eV): $C_{10}H_{12}O$ requires 148.0888, found 148.0892.

1,2-Diphenylethane (26f): According to general procedure 4 using benzyltriphenylphosphonium chloride (856 mg, 2.20 mmol, 1.1 equiv.) and petroleum ether (b.p. 40–60 °C)/diethyl ether (100:1) as the eluent afforded the title compound **26f** as a colourless oil that solidified as a cream solid upon standing (73 mg, 20% yield, 40% conversion). M.p. 47–49 °C, R_f = 0.67 [petroleum ether (b.p. 40–60 °C)/diethyl ether (7:3), det. with UV]: ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, ppm): δ = 7.33–7.38 (m, 4 H, ArH), 7.23–7.30 (m, 6 H, ArH), 3.00 (s, 4 H, PhCH_2). ^{13}C NMR (75.4 MHz, $CDCl_3$, 25 °C, ppm): δ = 141.9, 128.6, 128.4, 126.0, 38.1 (Ph*C*H$_2$). IR (KBr): $\tilde{\nu}$ = 3056, 3025, 2917, 2853, 1599, 1490, 1450, 1184, 1120, 1063, 1026, 750, 721, 697 cm^{-1}. MS (EI+ = 70 eV): *m*/*z* (%) = 182 (36) [M$^{\cdot+}$], 91 (100), 65 (13). HRMS (EI+ = 70 eV): $C_{10}H_{14}$ requires 182.1096, found 182.1096.

Pentylbenzene (26g): According to general procedure 4 using *n*-butyltriphenylphosphonium bromide (876 mg, 2.20 mmol, 1.1 equiv.) and petroleum ether (b.p. 40–60 °C)/diethyl ether (100:1) as the eluent afforded the a mixture of the title compound (40 mg, 14% yield, 40% conversion) and intermediate pent-1-enylbenzene following chromatography. Oxidative removal of the alkene by-product also leads to the destruction of the majority of the alkane product, although small amounts of alkane could be isolated. In order to confirm the identity of the product an alternative workup involving hydrogenation of the alkene (10% w/w Pd-C, 1 atm H_2, 2 hours) was employed. This furnished only the title compound **26g**, a colourless liquid. R_f = 0.76 [petroleum ether (b.p. 40–60 °C)/diethyl ether (7:3), det. with UV/weak $KMnO_4$]. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, ppm): δ = 7.17–7.22 (m, 2 H, ArH), 7.06–7.11 (m, 3 H, ArH), 2.51 (t, *J* = 7.6 Hz, 2 H, PhCH_2), 1.54 (app. quint, *J* =

7.0 Hz, 2 H, $PhCH_2CH_2$), 1.23 (m, 4 H, $CH_2CH_2CH_3$), 0.81 (t, J = 7.0 Hz, 3 H, CH_3). ^{13}C NMR (75.4 MHz, $CDCl_3$, 25 °C, ppm): δ = 141.1, 128.5, 128.3, 125.7 36.1 ($PhCH_2$), 31.7, 31.4, 22.7 (CH_3CH_2), 14.2 (CH_3). IR (liquid film): $\tilde{\nu}$ = 3062, 3026, 2956, 2927, 2856, 1604, 1496, 1453, 1377, 1111, 1030, 1026, 744, 697 cm^{-1}. MS (EI+ = 70 eV): *m/z* (%) = 148 (54) [$M^{\cdot+}$], 105 (16), 93 (65), 91 (100). HRMS (EI+ = 70 eV): $C_{11}H_{16}$ requires 148.1252, found 148.1249.

Supporting Information (see also the footnote on the first page of this article): Full characterisation data for all hydrogen/substrate loss compounds and isolated by-products.

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