Heck Reaction in Diols and Cascade Formation of Cyclic Ketals

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Abstract: The regioselective Heck arylation of butyl vinyl ether in alcohols is utilized for the formation of a variety of cyclic ketals. When carried out in ethylene glycol, propane-1,2-diol, or propane-1,3-diol, the palladium-catalyzed arylation afforded dioxolanes or dioxanes directly. With diols such as glycerol, 3-chloropropane-1,2-diol, and 2-methylpropane-1,3-diol, isolation of the Heck adducts and the use of an acid catalyst for the ketalization were necessary; an efficient phosphoric acid was identified. The procedure presented provides a new pathway for the synthesis of cyclic ketals, particularly those that are functionalized.

Key words: ketals, diols, olefins, Heck reaction, homogeneous catalysis

Cyclic ketals are widespread in organic chemistry as protecting groups of carbonyl compounds, and they also undergo some interesting transformations themselves.[1,2] Most interestingly, a number of biologically active molecules are known to contain the cyclic ketal moiety.[3] Figure 1 shows a few selected examples. Ketoconazole and propiconazole are both antifungal agents, the former being used in many medical applications, while the latter being a widely used agricultural fungicide.[4,5] Etoxadrol is a lead compound in the development of NMDA receptor antagonists, potential therapeutic agents for use in Alzheimer's disease, Parkinson's disease, epilepsy, and other central nervous system disorders.[6] B-12 has been identified as a promising candidate for use as an antagonist of the human pregnane X receptor, a receptor implicated in adverse drug reactions, increased cancer cell growth, and drug resistance.[7]

Because of their high importance, many methods exist for their preparation.[8]However, this is usually achieved by reacting the parent carbonyl compound with a suitable diol in the presence of a Brønsted or Lewis acid combined with the removal of water. Even so, there is still room for additional protocols, for instance, those that allow for protection of one carbonyl functionality in preference to another. Although protection of aldehydes in the presence of ketones can be achieved with excellent selectivity,[8a,d,e] methods for producing ketals containing unprotected ketones are less common.[9] Herein we describe a Heck reaction-based protocol, which allows for the easy synthesis of a diverse range of cyclic ketals, including those that contain carbonyl functionalities.

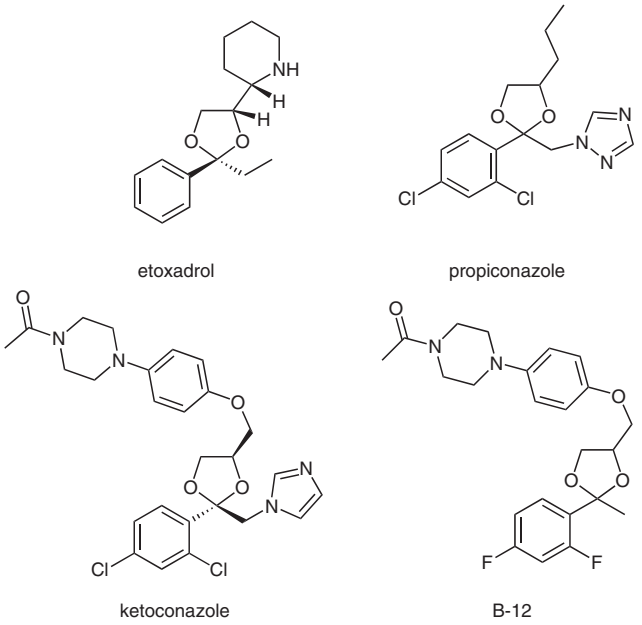
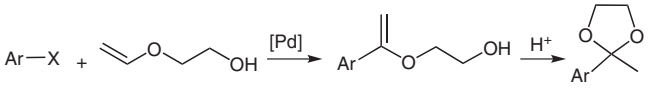


Figure 1 Examples of cyclic ketals that show biological activity

The Heck reaction is now regarded as one of the most useful C–C bond forming transformations in organic chemistry.[10] Scheme 1 shows an example of how the regioselective Heck reaction of an electron-rich hydroxy alkyl vinyl ether has been utilized to directly prepare cyclic ketals from aryl halides/triflates in a cascade-type reaction.[11] The arylated enol ether undergoes an intramolecular cyclization to form the cyclic ketal, either in situ under the reaction conditions[11a] or with addition of an anhydrous acid.[11b] This method has been utilized most successfully to produce five-membered cyclic ketals.



Scheme 1 Cyclic ketals from the Heck reaction of aryl bromides and hydroxy alkyl vinyl ethers

In order to obtain the ketal shown, the Heck reaction must proceed with internal or α-substitution (Scheme 2). Although the compounds resulting from β-substitution can be cyclized,[9a] the products of these reactions are cyclic benzylic acetals. It is, therefore, the regioselectivity of the

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initial Heck reaction that controls the nature of the final product. Unlike Heck reactions of electron-deficient olefins such as acrylates, which generally give exclusively β-substitution products,[10d,12] electron-rich olefins tend to give a mixture of products when allowed to react under the same conditions.[8f,10e,13] Two catalysts that exemplify this problem are the Hermann–Beller palladacycle[14] and Fu's Pd-P(*t*-Bu)$_3$ catalysts.[13h] Both are successful catalysts for reactions of electron-deficient olefins, providing β-products exclusively; yet when electron-rich olefins are employed a mixture of products are formed, with the β/α ratios becoming 13:10 and 1:4, for instance. It is now believed that the Heck reaction can proceed via two distinct pathways,[11a,13j–o,15] each leading to a different product in the case of electron-rich olefins, the feature being the nature of the ligand that dissociates from the palladium complex.[13k] Scheme 2 outlines these two different pathways, referred to as neutral or ionic, depending on the Pd species generated upon dissociation of a ligand. The former will be the result of an uncharged ligand, usually a phosphine, leaving the palladium, while the latter arises from the dissociation of the halide or triflate generated upon oxidative addition of the starting aryl compound. Evidence suggests that β-arylation of electron-rich olefins is the result of the neutral pathway whereas α-substitution arises from the ionic pathway.[15,16]

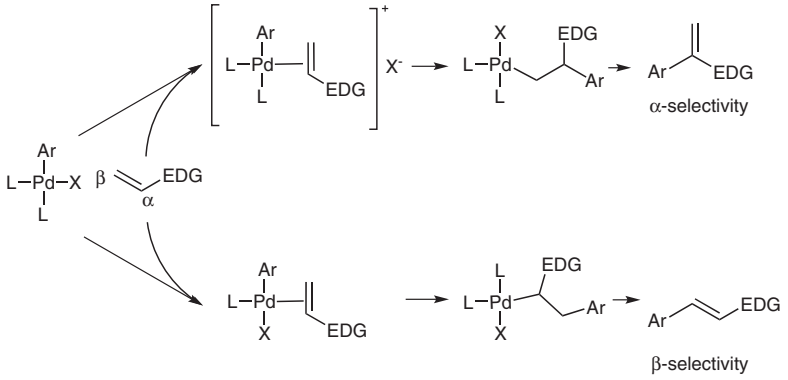
Based on this hypothesis several tactics have been employed to promote the ionic pathway and hence obtain arylation regioselectively at the α-position. The use of bidentate ligands such as bis-1,3-(diphenylphosphino)propane (dppp) was shown by Cabri to strongly influence the regioselectivity in favor of α substitution.[13j–m] Labile counterions such as triflate also help achieve this, as demonstrated by Hallberg.[17] However, these substrates are made less appealing by their high cost, limited availability or thermal lability.[15b,18] When arylating with aryl halides, silver and thallium salts can be used to act as halide scavengers and promote the ionic pathway. This method was used by Larhed and Hallberg for generating cyclic ketals of acetophenones via a Heck reaction of aryl bromides with hydroxy alkyl vinyl ethers (Scheme 1).[11b] Unfortunately the large quantities of required salt coupled with the cost of silver and toxicity of thallium present a potential problem for its application.[11b,15g] Ionic media such as

Biographical Sketches

Matthew McConville received his M.Chem. degree in Chemistry and Pharmacology from the University of Liverpool in 2005. His master's project in organocatalysis was supervised by Prof. Jiangliang Xiao. Since then he has been working towards his Ph.D. in the same group studying the regioselective Heck reaction. His research interests include organic synthesis, homogeneous catalysis, and tandem/domino reactions.

John Blacker received his B.Sc. from the University of Sheffield 1984 in Biochemistry and Chemistry, then moved to Université Louis Pasteur, Strasbourg to complete a DEA in Organic Chemistry and Ph.D. with Prof. Jean-Marie Lehn. Following post-doctoral studies with Prof. Sir Alan Fersht in Cambridge, in 1990 he joined ICI and ultimately became Technology Director at Piramal Healthcare responsible for chiral technology, process development, and commercial application. In 2006 he joined the University of Leeds part-time, to establish the Institute of Process Research and Development, and in 2009 was recruited full-time as iPRD Director and Chair of Process Chemistry.

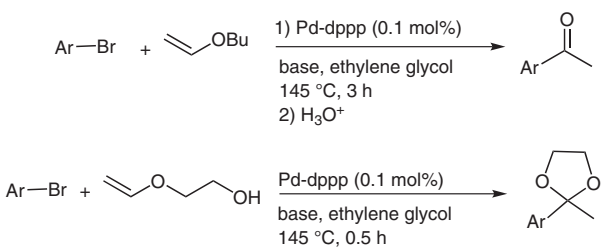
Jianliang Xiao received his B.Sc. in chemical engineering at Northwest University. This was followed by an M.Sc. in catalytic engineering with Profs. Chi Wu and JunYu Wang at the Research Institute of Petroleum Processing in China and a Ph.D. in chemistry with Prof. Marty Cowie at the University of Alberta. After a postdoctoral appointment with Prof. Richard Puddephatt, he joined the ERATO Molecular Catalyst Project directed by Prof. Noyori. In 1996 he took up a Principal Scientist position at the University of Liverpool and was appointed to a Lectureship in the Chemistry Department in 1999; this was followed by promotion to full Professor in early 2005. He is now Professor of Catalysis.



Scheme 2 Proposed ionic and neutral Heck pathways leading to different regioisomers

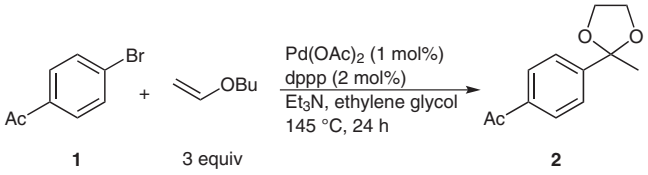
the imidazolium based ionic liquids provide an ideal environment for obtaining high α/β ratios when they are employed as solvents.[11a,19] Presumably, the ionic environment and the resulting high ionic strength promote the ionic pathway, thus affording the α selectivity; this is supported by the kinetic studies conducted by Amatore, Jutand, and co-workers.[16b] The reactions of aryl bromides with hydroxy alkyl vinyl ethers in these ionic media were found to yield cylclic ketals in good to excellent yields.[11a] The cyclizations occurred under the reaction conditions and no further heating or addition of acid was required.

Recent work has further shown that hydrogen bond donating additives such as $[H_2Ni\text{-}Pr_2][BF_4]$ have both a rate-accelerating and regioselectivity-promoting effect on the arylation of electron-rich olefins.[19b] These additives were expected to encourage dissociation of the halide ion from the Ar–Pd(II)–X intermediate, and were indeed found to be excellent replacements for the less desirable TlOAc for cyclic ketal synthesis via the Heck reaction. A further development of this work was the use of alcohols as solvents for the arylation of electron-rich olefins.[20] In particular, the highly hydrogen-bond-donating ethylene glycol has been identified as an excellent solvent for these reactions, circumventing the need for salt additives. Scheme 3 shows how the Pd-dppp/ethylene glycol system has been used for the production of ketones and cyclic ketals.[20a] The reactions proceed with >99% selectivity for α substitution and S/C ratios of up to 1000 have been achieved. The hydrogen-bonding capability of the solvent seemingly encourages the ionic pathway and hence highly selective and expedient reactions with a range of aryl bromides and olefins. There is also the added benefit of alcohol solvents being relatively environmentally benign compared to other solvents commonly employed for these reactions.



Scheme 3 Ketones and cyclic ketals via Heck reaction of aryl bromides in ethylene glycol

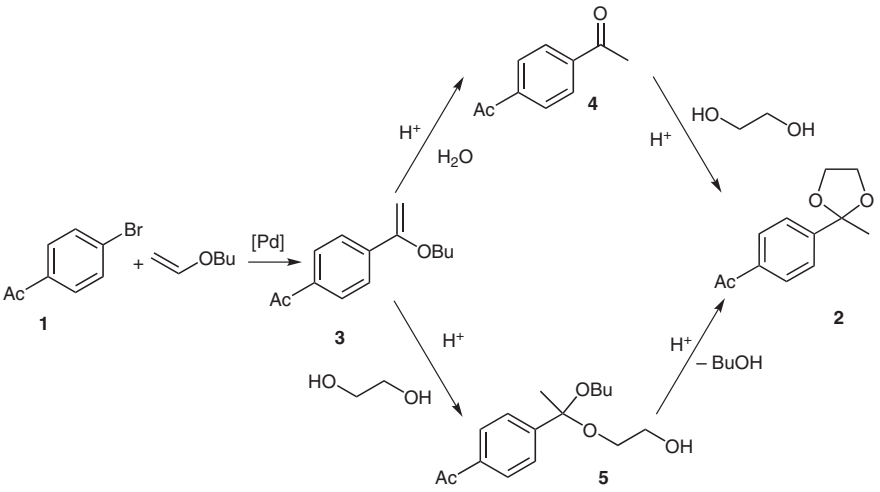
During our continued studies of the Heck reaction of electron-rich olefins, a curious observation was made. If left stirring under the reaction conditions, the Pd-catalyzed Heck coupling between 4-bromoacetophenone (**1**) and butyl vinyl ether (BVE) in ethylene glycol eventually led to the corresponding cyclic ketal **2** (Scheme 4). This was surprising because, as discussed earlier, the use of hydroxy vinyl ether is usually required to obtain such products (Scheme 1).[11] However, simple enol ethers are known to react with 1,2-diols such as those in carbohydrate chemistry as a means of protecting the latter.[21] Is **2** formed from a reaction of the arylated BVE with the solvent?



Scheme 4 Initial observation of the formation of **2** from **1**

Given the importance of ketal compounds, we thought the reaction in Scheme 4 might lead to a new method for easy ketal synthesis and therefore be worth pursuing. We envisaged two likely pathways for the reaction, proceeding via different intermediates with both acid-catalyzed (Scheme 5). The first is hydrolysis of the initially formed enol ether **3** to the diketone **4** followed by a classical ketalization with the ethylene glycol solvent. The second is acid-catalyzed formation of the mixed ketal **5** by addition of the solvent, followed by an intramolecular substitution reaction, eliminating butanol and generating **2**.

^{1}H NMR and TLC monitoring of the reaction was undertaken in order to identify the reaction intermediates. No trace of **4** was detected by either method, making the hydrolysis/cyclization pathway less likely. However, ^{1}H NMR showed that **5** was produced, increased and then decreased as formation of the ketal **2** was observed. A reaction profile is shown in Figure 2, showing that the Heck reaction to give the arylated BVE **3** is fast, **2** derives from



Scheme 5 Possible reaction pathways for cyclic ketals from enol ethers

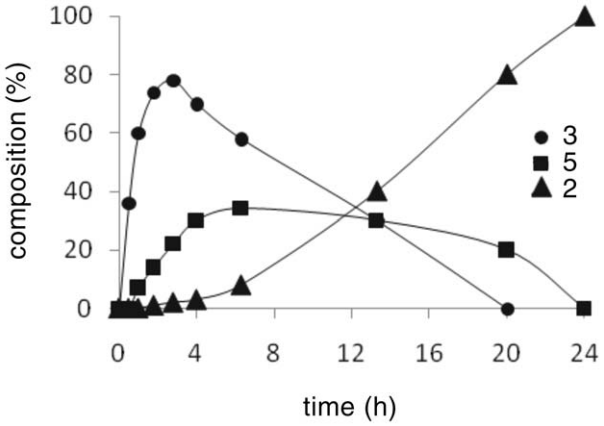
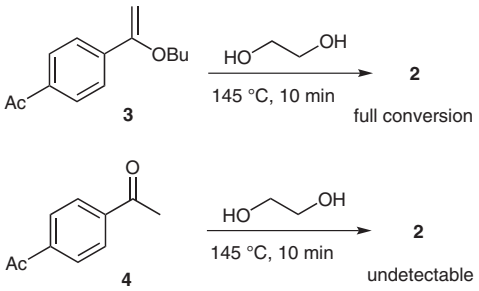


Figure 2 Composition (%) versus time for enol ether **3**, mixed ketal **5**, and cyclic ketal **2** in the reaction of **1** with BVE. Reaction conditions: $Pd(OAc)_2$ (0.25 mol%), dppp (0.5 mol%), **1** (3 mmol), BVE (9 mmol), Et_3N (9 mmol) in ethylene glycol (6 mL) at 145 °C.



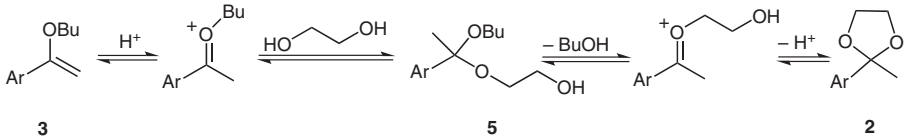
Scheme 6 Ketalization of enol ether **3** versus ketone **4** in ethylene glycol

3 most likely via the intermediacy of **5**, and the overall reaction to give **2** appears to be limited by the cyclization step. The intermediates **3** and **5** were characterized by stopping the reaction before completion.

Further evidence for this pathway comes from observing the reactions of **3** and **4** with ethylene glycol in the absence of base (Scheme 6). Whilst complete conversion of **3** to **2** took less than ten minutes, **4** produced only a trace (TLC) of the ketalized product under the same conditions. If the reaction were to go by the hydrolysis–ketalization sequence, then the reaction of **4** would be as fast as, if not faster than, that of **3**.

A possible mechanism is shown in Scheme 7. Protonation of **3** by $[Et_3NH]^+$ or by the ethylene glycol itself generates an oxocarbenium ion[11] that undergoes nucleophilic attack by ethylene glycol, and subsequent loss of a proton leads to the isolable mixed ketal **5**. Protonation of **5** followed by elimination of butanol gives a new oxocarbenium ion, an intermediate that the current reaction has in common with Heck/cyclization procedures that employ hydroxy alkyl vinyl ethers.[11b] Neighboring group participation assists the elimination and stabilizes the tertiary carbocation. Finally, an intramolecular nucleophilic attack by the pendant hydroxy function and loss of a proton release the final product **2**.

We have previously noted that the ketals undergo exchange with the ethylene glycol solvent under the Heck reaction conditions,[20a] a reaction likely to proceed via oxocarbenium ion and mixed ketal intermediates, adding weight to our suggested mechanism. A Spartan calculation reveals that the highest HOMO density of **3** locates at the terminal carbon of the C=C bond. Protonation at that

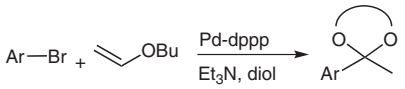


Scheme 7 Proposed mechanism for the conversion of **3** to **2** in ethylene glycol

carbon is therefore expected to take place easily, affording the oxocarbenium intermediate suggested.

Before exploring the scope of the catalysis for the synthesis of ketals, we undertook a limited screening using the coupling of **1** with BVE in ethylene glycol as a model reaction (Scheme 4). The results show that the catalyst loading could be reduced to as low as 0.1 mol%, without sacrificing yield. The temperature had to remain high in order to keep reasonable reaction times, however. Thus, at 80 °C the conversion to **2** was only 20% in 72 hours. With these observations, we then turned our attention to the scope of the reaction with respect to the aryl bromides used. Other diols were also considered, aiming to generate ketals other than dioxolanes. The results are presented in Table 1.

Table 1 Heck Arylation of BVE with Aryl Bromides in Diols Leading to Ketals[a]



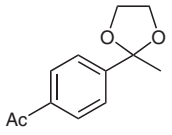
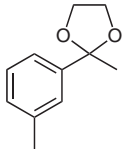
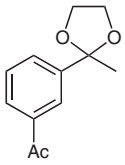
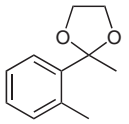
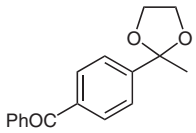
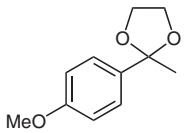
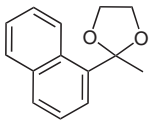
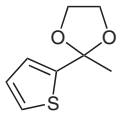
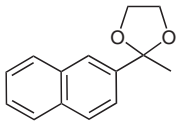
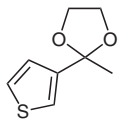
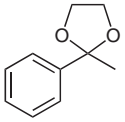
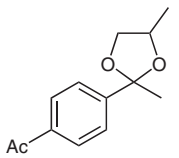
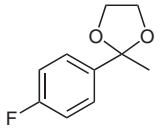
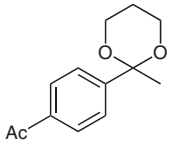
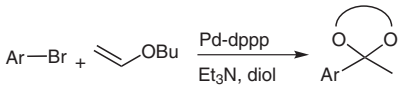
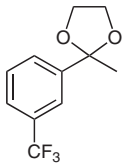
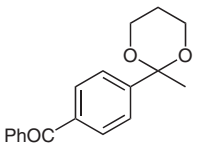
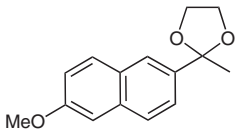
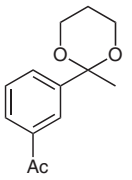
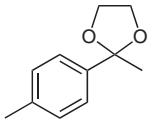
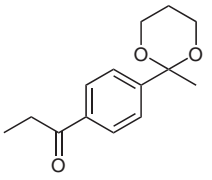
Entry	Product	Yield (%)[b]	Entry	Product	Yield (%)[b]
1	 **2**	82	11	 **15**	71
2	 **6**	75	12	 **16**	73
3	 **7**	80	13	 **17**	76
4	 **8**	73	14	 **18**	70
5	 **9**	66	15	 **19**	73
6	 **10**	77	16	 **20**	78[c]
7	 **11**	74	17	 **21**	72

Table 1 Heck Arylation of BVE with Aryl Bromides in Diols Leading to Ketals[a] (continued)



Entry	Product	Yield (%)[b]	Entry	Product	Yield (%)[b]
8	 **12**	72	18	 **22**	80
9	 **13**	74	19	 **23**	73
10	 **14**	75	20	 **24**	78

[a] Reaction conditions: $Pd(OAc)_2$ (0.1 mol%), dppp (0.2 mol%), ArBr (3 mmol), BVE (9 mmol), Et_3N (9 mmol) at 145 °C for 24–36 h.
[b] Yields given are for isolated products.
[c] dr = 60:40, determined by ^1H NMR spectroscopy.

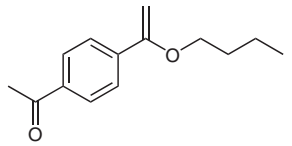
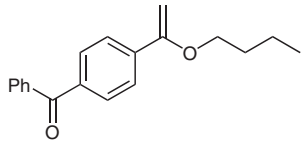
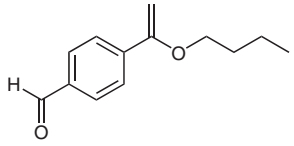
As can be seen, **1** reacted with BVE in ethylene glycol, affording the five-membered ketal **2** in a good yield of 82% (entry 1). In fact, a wide range of aryl groups can be tolerated, including electron-deficient (entries 1–3,8), electron rich (entries 9–13), and sterically demanding (entries 4,12). Heterocyclic aryl bromides also reacted to yield the cyclic ketals in good yields (entries 14,15). Of particular interest is that the compounds **2**, **6**, and **7** were obtained from aryl bromides that contain a carbonyl group, exhibiting excellent chemoselectivity with no diketalized product detected. When the solvent was changed from ethylene glycol to propane-1,2-diol, we were pleased to see that the substituted ketal **20** was produced, interestingly with some diastereoselectivity (60:40). An attempt to increase this selectivity by lowering the temperature to 80 °C once the Heck reaction had finished was not successful; the diastereomeric ratio remained at 60:40 and a yield of only 22% was obtained in 72 hours. Of further interest is that when the Heck reaction was carried out in propane-1,3-diol, six-membered dioxanes, including carbonyl-containing ones, were produced by reacting the appropriate aryl bromide, again in decent yields (entries 17–20).

Although the protocol developed thus far was tolerant of a range of bromides and alcohols, some compounds were not obtainable by this method. For example, 3-chloropropane-1,2-diol was unable to act as a solvent for the reaction; the Heck reaction did not proceed and the starting aryl bromide was recovered. Some other alcohols also proved problematic, 2-methylpropane-1,3-diol and glycerol being examples where either no desired product was obtained or sluggish reactions occurred.

Enol ethers such as 2-methoxypropene react with diols to form ketals as a means of diol protection and the reaction is promoted by Brønsted acids, typically *p*-toluenesulfonic acid.[21b] This, in conjunction with our suggested acid-catalyzed mechanism for cyclization, led us to investigate whether we could overcome these difficulties with an acid-catalyzed cyclization of isolated enol ethers. Hopefully this would also allow us to produce cyclic ketals from enol ethers under mild conditions. It was, therefore, necessary to isolate the enol ethers originally produced in the Heck reaction. As the Heck reaction was fast at 145 °C and ketal formation began shortly afterwards, an adjustment to the conditions was necessary in order to maximize the yield of the enol ether. Quickly we found that by dropping the reaction temperature to 100 °C, the formation of **5** and **2** from **1** and BVE were minimal whilst the Heck reaction remained fast. We also found that simple extraction with diethyl ether was sufficient to remove the arylated enol ether product **3** from the ethylene glycol without too much of the solvent being removed alongside it. Following this, a rapid column chromatography with a basified eluent allowed for isolation of **3** in 85% yield on a multigram scale. This further demonstrates the versatility of the Heck reaction of electron-rich olefins in this solvent, add-

ing a new product that is available in excellent yield from the same reaction components, depending on the reaction and/or work up conditions. The results for selected aryl bromides are shown in Table 2. In ketalization of enol ethers with diols to protect the diols, an excess of the enol ether is usually used. As a consequence, acidic hydrolysis of the enol ether to the corresponding ketone is not a particularly big problem. Given the reverse of this is true for the reaction under question, a protocol that minimizes the hydrolysis of the enol ether was required. A variety of acids were therefore tried using ethylene glycol as both the ketalization reagent and solvent. The results are shown in Table 3.

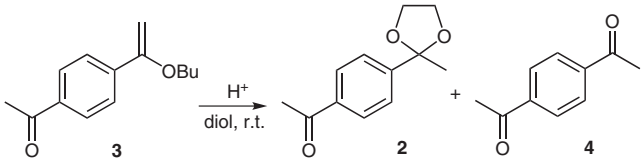
Table 2 Isolation of Arylated Enol Ethers from the Heck Reaction in Ethylene Glycol[a]

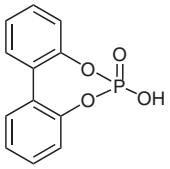
Entry	Product	Time (h)	Yield (%)[b]
1	 **3**	2	85
2	 **25**	3	90
4	 **26**	3	75

[a] Reaction conditions: $Pd(OAc)_2$ (1 mol%), dppp (2 mol%), ArBr (25 mmol), BVE (60 mmol), Et_3N (60 mmol) at 100 °C.
[b] Yields given are for isolated products.

As can be seen, different acids produced varying levels of success in terms of conversion and selectivity. Although full conversion could be achieved in almost instantaneous reactions with the strong acids in entries 1–5, the isolated yields of **2** were low due to high levels of hydrolysis to give **4**, even when care was taken to dry the diol and substrate. Acetic acid (pK_a 4.8) produced a very slow reaction, with only trace quantities of the ketal and hydrolysis product being obtained (entry 6). Other weak organic acids (entries 7, 8) (pK_a 4.2, 3.44, respectively) were not successful either for these reactions, giving only trace conversions to the ketal. The enol ether remained intact and only very small amounts of the hydrolysis product were detectable by TLC after 10 minutes. It is believed that a mixture of low solubility and insufficient acidity prevents these acids from successfully promoting the reaction.

Table 3 Effect of Various Acids on Ketalization of **3**[a]



Entry	Acid	Time (min)	Conv. (%)	Yield (%)[b] **2**	**4**
1	HBF_4	2	100	55	30
2	TfOH	2	100	50	25
3	HCl[c]	2	100	58	32
4	H_2SO_4	2	100	45	36
5	HNO_3	2	100	50	34
6	AcOH	10	10	trace	trace
7	$PhCO_2H$	10	<5	–	–
8	$4\text{-}O_2NC_6H_4CO_2H$	10	<5	–	–
9		2	100	74	<5

[a] Reaction conditions: **3** (0.25 mmol), 2% acid in ethylene glycol.
[b] Isolated yields.
[c] Used as a 4 M solution in dioxane.

The phosphoric acid in entry 9 (pK_a ~1.3)[22] gave a significantly better yield for **2** than the other acids tried, whilst retaining high activity. This relatively strong acid is easy to handle and dry, and is readily available. The acid allowed for a mild, catalytic, and high-yielding protocol for the production of **2** from **3**. In addition to the favorable conditions, the reaction was completely selective for the enol ether and no trace of the diketalized product was detected.

With an effective set of conditions established, we decided to expand the scope of the reaction to include functionalized diols and other carbonyl-containing enol ethers. The results are shown in Table 4. Both acetyl- and benzoyl-containing enol ethers are viable substrates, reacting with a range of diols to produce the respective ketals. Thus, ethylene glycol, propylene glycol, propane-1,2-diol, 3-chloropropane-1,2-diol and glycerol reacted with **3**, most being complete in short reaction times with very good yields. As aforementioned, some of these diols did not enter the ketalization under the in situ Heck conditions. The carbonyl group in the products can undergo further reactions, and of particular interest is that the ketals **27**, **28**, and **31** provide additional sites for functionalization. However, when the formyl-substituted enol ether **26** was reacted with ethylene glycol, the reaction was not selective, affording a mixture of products in which the

formyl group was always acetalized. Attempts to overcome this problem by performing the reaction in an organic solvent (3–10 equiv of diol) instead of neat diol failed; again a mixture of products were obtained. Further reduction to 1 equivalent of diol halted the reaction, with the enol ether remaining intact after two hours.

In conclusion, we have developed a simple, chemoselective, and efficient procedure for the production of cyclic ketals from aryl bromides via a regioselective Heck reaction of butyl vinyl ether in alcohol solvents. Following the Heck arylation, ketalization of the resulting arylated enol ether with the solvent takes place, leading to a variety of cyclic ketals. The method negates the use of more expensive hydroxy alkyl vinyl ethers and allows both five- and six-membered ketals containing sensitive functional groups to be prepared. Evidence shows that the reaction proceeds via a mixed ketal intermediate and not by hydrolysis to the corresponding ketone and subsequent ketalization. Further optimization identified a phosphoric acid, which is capable of catalyzing the ketalization of isolated enol ethers with problematic diols under mild conditions. Particularly noteworthy are some of the compounds found in Table 4, as they have a synthetic handle on the ketal ring in the form of C–Cl or C–OH bonds. Their similarity to intermediates in the synthesis of B-12 highlights that this method is a viable alternative for the synthesis of bioactive ketals, particularly when chemoselectivity is a concern.

All chemicals were purchased from commercial sources and either used as received or purified by standard procedures. NMR spectra were recorded on a 400 MHz Bruker Avance spectrometer with chemical shift (δ) values for ^{1}H (400 MHz) and ^{13}C (100 MHz) given in ppm with reference to $CDCl_3$ as an internal standard. Liquid glycols and glycerol were stored over 4Å molecular sieves and solid glycols stored in a vacuum desiccator. All reactions were conducted under N_2 using standard Schlenk technique. Column chromatography was performed using silica gel (300–400 mesh).

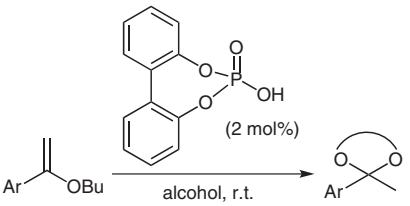
Catalyst Stock Solution

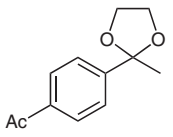
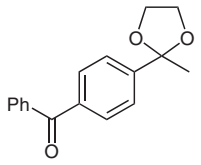
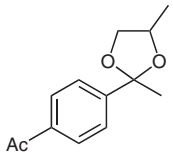
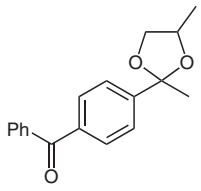
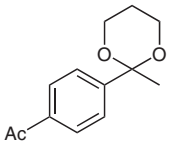
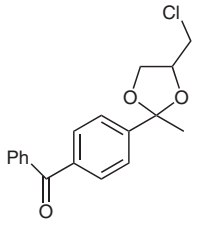
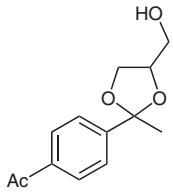
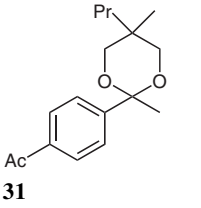
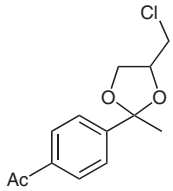
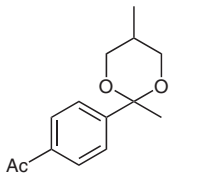
An oven-dried, two-necked round bottom flask was charged with $Pd(OAc)_2$ (7 mg, 0.03 mmol), dppp (25 mg, 0.06 mmol) and ethylene glycol (10 mL). The flask was evacuated and back-filled three times with N_2 and the solution stirred at r.t. for 3 h, at which time a homogeneous, bright yellow solution was obtained. The stock solution was kept under a slight pressure of N_2 and used immediately.

Heck Reaction of Aryl Bromides with Butyl Vinyl Ether in Alcohol Solvents to Form Aryl-Substituted Cyclic Ketals; 1-[4-(2-Methyl-1,3-dioxolan-2-yl)phenyl]ethanone (2); Typical Procedure

An oven-dried Schlenk tube was charged with 4-bromoacetophenone (**1**; 597 mg, 3 mmol) and ethylene glycol (5 mL). The flask was evacuated and back-filled three times with N_2. Et_3N (1.2 mL, 9 mmol) and the Pd-dppp stock solution (1 mL, 0.003 mmol, 0.1 mol% Pd) were added via a syringe and the tube placed in a parallel reactor (block temperature 145 °C). The mixture was vigorously stirred for 2–3 min after which time BVE (1.1 mL, 9 mmol) was injected and the reaction monitored by TLC until no trace of **1** or **5** remained. The flask was cooled to r.t. and H_2O (30 mL) was added. The aqueous layer was then extracted with Et_2O (3 × 20 mL) and the combined organic layers were washed with H_2O (20 mL). The solvent was removed in vacuo and the crude residue purified by flash chromatography on silica gel (hexanes–EtOAc, 95:5) to give **2**; yield: 506 mg (82%) (Table 1).

Table 4 Acid-Catalyzed Ketalization of Enol Ethers[a]



Entry	Product	Yield (%)[b]	Entry	Product	Yield (%)[b]
1	 **2**	74	6	 **7**	76
2	 **20**	75[c]	7	 **29**	75[c]
3	 **21**	70	8	 **30**	77[c]
4	 **27**	80[d]	9	 **31**	75[e]
5	 **28**	78	10	 **32**	79

[a] Reaction conditions: enol ether (1 mmol), phosphoric acid (0.02 mmol), alcohol (2 mL), and up to 1 h reaction time.
[b] Isolated yields.
[c] dr = 60:40.
[d] dr = 70:30.
[e] Reaction conducted in the molten diol at 60 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.94 (d, *J* = 8.4 Hz, 2 H), 7.58 (d, *J* = 8.4 Hz, 2 H), 4.10–4.01 (m, 2 H), 3.81–3.75 (m, 2 H), 2.61 (s, 3 H), 1.66 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 198.2, 148.9, 137.1, 128.8, 126.0, 108.9, 64.98, 27.8, 27.1.

HRMS (EI): *m*/*z* [M + H]$^+$ calcd for $C_{12}H_{15}O_3$: 207.1021; found: 207.1026.

Anal. Calcd for $C_{12}H_{14}O_3$: C, 69.88; H, 6.84. Found: C, 70.20; H, 6.87.

1-{4-[1-Butoxy-1-(2-hydroxyethoxy)ethyl]phenyl}ethanone (5)
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.95 (d, *J* = 8.4 Hz, 2 H), 7.61 (d, *J* = 8.4 Hz, 2 H), 3.82–3.74 (m, 2 H), 3.59–3.52 (m, 1 H), 3.52–3.44 (m, 1 H), 3.44–3.36 (m, 1 H), 3.35–3.29 (m, 1 H), 2.61 (s, 3 H), 1.69–1.55 (m, 2 H), 1.59 (s, 3 H), 1.47–1.36 (m, 2 H), 0.94 (t, *J* = 7.6 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 198.4, 148.9, 136.8, 128.6, 126.9, 101.4, 63.2, 62.5, 61.6, 32.3, 27.2, 27.0, 20.1, 14.3.

HRMS (ES): *m*/*z* [M + Na]$^+$ calcd for $C_{16}H_{24}O_4$ + Na: 303.1572; found: 303.1558.

2-Methyl-2-(naphthalen-1-yl)-1,3-dioxolane (8)
^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.51 (d, *J* = 9.0 Hz, 1 H), 7.72–7.64 (m, 3 H), 7.40–7.27 (m, 3 H), 3.97–3.93 (m, 2 H), 3.68–3.65 (m, 2 H), 1.78 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 137.4, 133.5, 129.3, 128.0, 127.6, 125.3, 124.7, 124.3, 123.8, 122.6, 108.6, 61.2, 26.5.

HRMS (EI): *m*/*z* [M + H]$^+$ calcd for $C_{14}H_{15}O_2$: 215.1072; found: 215.1075.

Anal. Calcd for $C_{14}H_{14}O_2$: C, 78.48; H, 6.61. Found: C, 78.55; H, 6.65.

2-(4-Fluorophenyl)-2-methyl-1,3-dioxolane (11)
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.40–7.34 (m, 2 H), 6.96–6.89 (m, 2 H), 3.99–3.90 (m, 2 H), 3.72–3.63 (m, 2 H), 1.55 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 162.8 (d, $J_{C,F}$ = 244 Hz), 139.6 (d, $J_{C,F}$ = 3 Hz), 127.5 (d, $J_{C,F}$ = 8 Hz), 115.4 (d, $J_{C,F}$ = 21 Hz), 108.9, 64.8, 28.1.

HRMS (EI): *m*/*z* [M + H]$^+$ calcd for $C_{10}H_{12}FO_2$: 183.0821; found: 183.0824.

Anal. Calcd for $C_{10}H_{11}FO_2$: C, 65.92; H, 6.09. Found: C, 66.11; H, 6.12.

2-(6-Methoxynaphthalen-2-yl)-2-methyl-1,3-dioxolane (12)
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.88 (s, 1 H), 7.85–7.68 (m, 2 H), 7.65–7.51 (m, 1 H), 7.25–7.11 (m, 2 H), 4.25–4.05 (m, 2 H), 3.92 (s, 3 H), 3.91–3.79 (m, 2 H), 1.73 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.2, 138.8, 134.6, 130.1, 128.8, 127.3, 124.6, 124.3, 119.3, 109.4, 106.0, 64.9, 55.7, 28.0.

HRMS (EI): *m*/*z* [M + H]$^+$ calcd for $C_{15}H_{16}O_3$: 245.1099; found: 245.1101.

Anal. Calcd for $C_{15}H_{15}O_3$: C, 73.75; H, 6.60. Found: C, 73.93; H, 6.66.

2-Methyl-2-*p*-tolyl-1,3-dioxolane (14)
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.37 (d, *J* = 7.6 Hz, 2 H), 7.16 (d, *J* = 7.6 Hz, 2 H), 4.08–3.95 (m, 2 H), 3.82–3.72 (m, 2 H), 2.34 (s, 3 H), 1.65 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 140.8, 137.9, 129.3, 125.6, 109.3, 64.8, 28.1, 21.5.

HRMS (EI): *m*/*z* [M + H]$^+$ calcd for $C_{11}H_{15}O_2$: 179.1067; found: 179.1070.

Anal. Calcd for $C_{11}H_{14}O_2$: C, 74.13; H, 7.92. Found: C, 74.29; H, 7.96.

2-Methyl-2-*m*-tolyl-1,3-dioxolane (15)
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.57–7.53 (m, 2 H), 7.25–7.12 (m, 2 H), 4.05–3.95 (m, 2 H), 3.77–3.65 (m, 2 H), 2.50 (s, 3 H), 1.68 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 141.0, 136.0, 132.3, 128.3, 126.5, 126.0, 109.9, 64.4, 26.7, 21.1.

HRMS (EI): *m*/*z* [M + H]$^+$ calcd for $C_{11}H_{15}O_2$: 179.1067; found: 179.1064.

Anal. Calcd for $C_{11}H_{14}O_2$: C, 74.13; H, 7.92. Found: C, 74.30; H, 7.97.

2-Methyl-2-*o*-tolyl-1,3-dioxolane (16)
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.48–7.19 (m, 3 H), 7.18–7.09 (m, 1 H), 4.18–4.03 (m, 2 H), 3.92–3.73 (m, 2 H), 2.36 (s, 3 H), 1.66 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 143.6, 138.2, 129.0, 128.5, 126.3, 122.7, 109.3, 64.8, 28.1, 21.9.

HRMS (EI): *m*/*z* [M + H]$^+$ Calcd for $C_{11}H_{15}O_2$: 179.1067; found: 179.1068.

Anal. Calcd for $C_{11}H_{14}O_2$: C, 74.13; H, 7.92. Found: C, 74.38; H, 7.98.

2-(4-Methoxyphenyl)-2-methyl-1,3-dioxolane (17)
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.40 (d, *J* = 8.8 Hz, 2 H), 6.87 (d, *J* = 8.8 Hz, 2 H), 4.10–3.95 (m, 2 H), 3.87–3.76 (m, 2 H), 3.81 (s, 3 H), 1.70 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.6, 135.9, 126.9, 113.9, 109.2, 64.8, 55.7, 28.1.

HRMS (EI): *m*/*z* [M + H]$^+$ calcd for $C_{11}H_{15}O_3$: 195.1016; found: 195.1016.

Anal. Calcd for $C_{11}H_{14}O_3$: C, 68.02; H, 7.27. Found: C, 68.17; H, 7.30.

2-Methyl-2-(thiophen-3-yl)-1,3-dioxolane (19)
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.30–7.24 (m, 2 H), 7.07 (dd, *J* = 4.8, 1.6 Hz, 1 H), 4.10–3.98 (m, 2 H), 3.92–3.87 (m, 2 H), 1.68 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 145.6, 126.4, 126.2, 121.8, 107.8, 65.1, 27.4.

HRMS (EI): *m*/*z* [M + H]$^+$ calcd for $C_{11}H_{15}O_3$: 171.0474; found: 171.0474.

Anal. Calcd for $C_8H_{11}O_2S$: C, 56.44; H, 5.94. Found: C, 56.56; H, 6.00.

1-[4-(2,4-Dimethyl-1,3-dioxolan-2-yl)phenyl]ethanone (20)
Mixture of diastereoisomers (dr = 60:40).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.94 (d, *J* = 8.4 Hz, 2 H), 7.61 (d, *J* = 8.0 Hz, 1.2 H), 7.58 (d, *J* = 8.0 Hz, 0.8 H), 4.5–4.34 (m, 0.6 H), 4.17 (dd, *J* = 8.0, 6.0 Hz, 0.6 H), 4.11–3.97 (m, 0.4 H), 3.88 (t, *J* = 6.8 Hz, 0.4 H), 3.65–3.54 (m, 0.4 H), 3.27 (t, *J* = 8.0 Hz, 0.6 H), 2.61 (s, 3 H), 1.66 (s, 1.2 H), 1.63 (s, 1.8 H), 1.34 (d, *J* = 6.0 Hz, 1.2 H), 1.19 (d, *J* = 6.0 Hz, 1.8 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 198.3, 150.3, 149.5, 137.0, 136.9, 128.9, 128.8, 128.7, 128.6, 128.9, 125.8, 109.0, 73.7, 72.5, 71.6, 71.3, 28.6, 28.5, 19.2, 18.7.

HRMS (EI): *m/z* [M + H]$^+$ calcd for $C_{11}H_{15}O_2$: 221.1178; found: 221.1172.

Anal. Calcd for $C_{11}H_{14}O_2$: C, 70.89; H, 7.32. Found: C, 71.03; H, 7.37.

1-[4-(2-Methyl-1,3-dioxan-2-yl)phenyl]ethanone (21)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.05 (d, *J* = 8.0 Hz, 2 H), 7.55 (d, *J* = 8.0 Hz, 2 H), 3.94–3.88 (m, 2 H), 3.75 (td, *J* = 12.0, 2.6 Hz, 2 H), 2.63 (s, 3 H), 2.14 (qt, *J* = 12.6, 5.0 Hz, 1 H), 1.52 (s, 3 H), 1.31–1.24 (m, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 198.2, 147.2, 137.0, 129.3, 127.5, 100.7, 61.8, 32.4, 27.1, 25.7.

HRMS (EI): *m/z* [M + H]$^+$ calcd for $C_{13}H_{17}O_3$: 221.1178; found: 221.1179.

Anal. Calcd for $C_{13}H_{16}O_3$: C, 70.89; H, 7.32. Found: C, 70.97; H, 7.34.

[4-(2-Methyl-1,3-dioxan-2-yl)phenyl](phenyl)methanone (22)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.91–7.82 (m, 4 H), 7.65–7.56 (m, 3 H), 7.54–7.47 (m, 2 H), 3.98–3.89 (m, 2 H), 3.80 (td, *J* = 11.1, 2.5 Hz, 2 H), 2.22–2.08 (m, 1 H), 1.56 (s, 3 H), 1.34–1.25 (m, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 194.5, 144.3, 135.7, 135.2, 130.6, 128.8, 128.2, 126.5, 125.0, 98.6, 59.6, 30.2, 23.5.

HRMS (EI): *m/z* [M + H]$^+$ calcd for $C_{18}H_{19}O_3$: 283.1329; found: 283.1330.

Anal. Calcd for $C_{18}H_{19}O_2$: C, 76.57; H, 6.43. Found: C, 76.67; H, 6.49.

1-[3-(2-Methyl-1,3-dioxan-2-yl)phenyl]ethanone (23)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.03 (t, *J* = 1.8 Hz, 1 H), 7.92 (dt, *J* = 7.6, 1.4 Hz, 1 H), 7.66 (dt, *J* = 7.6, 1.4 Hz, 1 H), 7.52 (t, *J* = 7.6 Hz, 1 H), 3.98–3.88, (m, 2 H), 3.75 (dt, *J* = 12.0, 2.4 Hz, 1 H), 2.64 (s, 3 H), 2.24–2.07 (m, 1 H), 1.53 (s, 3 H), 1.36–1.24 (m, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 198.8, 142.9, 138.6, 132.3, 129.9, 128.4, 127.4, 100.9, 62.0, 32.9, 27.5, 26.1.

HRMS (EI): *m/z* [M + H]$^+$ calcd for $C_{13}H_{17}O_3$: 221.1172; found: 221.1175.

Anal. Calcd for $C_{13}H_{16}O_3$: C, 70.89; H, 7.32. Found: C, 71.10; H, 7.40.

1-[4-(2-Methyl-1,3-dioxan-2-yl)phenyl]propan-1-one (24)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.00 (d, *J* = 8.4 Hz, 2 H), 7.54 (d, *J* = 8.4 Hz, 2 H), 3.98–3.86 (m, 2 H), 3.76 (td, *J* = 12.4, 2.8 Hz, 2 H), 3.02 (q, *J* = 7.2 Hz, 2 H), 2.13 (qt, *J* = 12.8, 5.2 Hz, 1 H), 1.51 (s, 3 H), 1.35–1.24 (m, 1 H), 1.24 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 200.9, 147.0, 136.8, 128.9, 127.5, 100.7, 61.9, 32.4, 32.3, 25.7, 8.7.

HRMS (EI): *m/z* [M + H]$^+$ calcd for $C_{14}H_{19}O_3$: 235.1329; found: 235.1327.

Anal. Calcd for $C_{14}H_{18}O_3$: C, 71.77; H, 7.74. Found: C, 71.95; H, 7.76.

Heck Reaction of Aryl Bromides with Butyl Vinyl Ether in Alcohol Solvents to Form Aryl-Substituted Enol Ethers; 1-[4-(1-Butoxyvinyl)phenyl]ethanone (3); Typical Procedure

An oven-dried, two-necked round-bottomed flask fitted with a reflux condenser was charged with $Pd(OAc)_2$ (56 mg, 0.25 mmol), dppp (205 mg, 0.50 mmol), 4-bromoacetophenone (**1**; 5.05 g, 25 mmol), and ethylene glycol (40 mL). The flask was evacuated and back-filled three times with N_2 and Et_3N (9.6 mL, 75 mmol) was added via a syringe. The flask was immersed in an oil bath at 100 °C and stirred vigorously for 3–4 min until a bright yellow color developed, at which point BVE (8 mL, 75 mmol) was added via a syringe. After an appropriate time (1–3 h), the reaction was cooled and the crude reaction mixture was extracted with Et_2O (3 × 100 mL). The combined extracts were concentrated in vacuo and the crude residue was purified by flash chromatography (hexanes–EtOAc–Et_3N, 98:1:1) to give **3**; yield: 4.63 g (85%) (Table 2).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.91 (d, *J* = 8.8 Hz, 2 H), 7.70 (d, *J* = 8.8 Hz, 2 H), 4.76 (d, *J* = 2.8 Hz, 1 H), 4.76 (d, *J* = 2.8 Hz, 1 H), 3.86 (t, *J* = 6.4 Hz, 2 H), 1.90–1.73 (m, 2 H), 2.59 (s, 3 H), 1.65–1.46 (m, 2 H), 0.99 (t, *J* = 7.6 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 198.1, 159.2, 141.4, 137.1, 128.6, 125.7, 84.6, 68.1, 31.5, 27.1, 19.8, 14.1.

[4-(1-Butoxyvinyl)phenyl](phenyl)methanone (25)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.11–7.71 (m, 6 H), 7.70–7.56 (m, 1 H), 7.54–7.42 (m, 2 H), 4.80 (d, *J* = 2.8 Hz, 1 H), 4.34 (d, *J* = 2.8 Hz, 1 H), 3.91 (t, *J* = 6.4 Hz, 2 H), 2.00–1.78 (m, 2 H), 1.68–1.48 (m, 2 H), 1.05 (t, *J* = 7.5 Hz, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 196.2, 166.3, 141.6, 138.0, 134.0, 133.6, 132.8, 130.5, 130.1, 129.9, 85.6, 68.8, 31.7, 20.1, 14.3.

4-(1-Butoxyvinyl)benzaldehyde (26)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.00 (s, 1 H), 7.85 (d, *J* = 8.0 Hz, 2 H), 7.79 (d, *J* = 8.0 Hz, 2 H), 4.80 (d, *J* = 2.8 Hz, 1 H), 4.35 (d, *J* = 2.8 Hz, 1 H), 3.87 (t, *J* = 6.4 Hz, 2 H), 1.90–1.73 (m, 2 H), 1.66–1.49 (m, 2 H), 1.00 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 192.4, 159.1, 142.8, 136.4, 130.0, 126.2, 85.2, 68.1, 31.5, 19.9, 14.0.

Acid-Catalyzed Conversion of Enol Ethers to Cyclic Ketals in Alcohol Solvents; 1-[4-(2-Methyl-1,3-dioxolan-2-yl)phenyl]ethanone (2); Typical Procedure

An oven-dried, two-necked round-bottomed flask was charged with **3** (218 mg, 1 mmol), phosphoric acid (Table 3, entry 9) (2 mg, 0.02 mmol), and ethylene glycol (2 mL). The flask was sealed and stirred for an appropriate time until consumption of the starting material was confirmed by TLC. Et_3N (0.1 mL, 1 mmol) was added and the mixture extracted with Et_2O (3 × 15 mL), and washed with H_2O (2 × 10 mL). The combined organic extracts were concentrated in vacuo and the resulting crude residue purified by flash chromatography (hexanes–EtOAc, 97:3) to give **2**; yield: 152 mg (74%) (Table 4). For spectral data, see above.

1-{4-[4-(Hydroxymethyl)-2-methyl-1,3-dioxolan-2-yl]phenyl}ethanone (27)

Mixture of diastereoisomers (dr = 70:30).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.95 (d, *J* = 8.4 Hz, 2 H), 7.67–7.56 (m, 2 H), 4.20 (dd, *J* = 8.4, 6.4 Hz, 0.3 H), 4.17–4.04 (m, 0.3 H), 4.12–4.09 (m, 0.7 H), 3.90 (dd, *J* = 8.0. 5.2 Hz, 0.7 H), 3.87–3.74 (m, 1.4 H), 3.74–3.58 (m, 1 H), 3.57–3.43 (m, 0.6 H), 2.61 (s, 3 H), 1.68 (s, 2.1 H), 1.65 (s, 0.9 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 198.2, 149.6, 148.6, 137.2, 129.0, 128.9, 126.0, 125.6, 109.7, 77.9, 76.6, 66.8, 66.2, 63.7, 63.1, 28.3, 28.2(8), 27.1.

HRMS (EI): *m/z* [M + H]$^+$ calcd for $C_{13}H_{17}O_4$: 237.1121; found: 237.1118.

Anal. Calcd for $C_{13}H_{16}O_4$: C, 66.09; H, 6.83. Found: C, 68.93; H, 6.84.

1-{4-[4-(Chloromethyl)-2-methyl-1,3-dioxolan-2-yl]phenyl}ethanone (28)

Mixture of diastereoisomers (dr = 55:45).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.92–7.85 (m, 2 H), 7.53–7.43 (m, 2 H), 4.46–4.35 (m, 0.45 H), 4.22 (dd, *J* = 8.8, 6.0 Hz, 0.45 H),

4.20–4.10 (m, 0.55 H), 3.90 (dd, *J* = 4.8, 4.0 Hz, 0.55 H), 3.71 (dd, *J* = 8.8, 6.8 Hz, 0.55 H), 3.69–3.55 (m, 1 H), 3.54–3.41 (m, 1 H), 3.10 (dd, *J* = 11.2, 8.0 Hz, 0.45 H), 2.54 (s, 3 H), 1.60 (s, 1.65 H), 1.56 (s, 1.35 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 196.7, 147.9, 147.0, 135.8, 127.5, 127.4, 124.5, 124.3, 108.8, 75.3, 74.4, 67.6, 66.4, 43.6, 43.1, 27.0, 25.7.

HRMS (EI): *m*/*z* [M + H]$^+$ calcd for $C_{13}H_{16}ClO_3$: 255.0787; found: 255.0789.

Anal. Calcd for $C_{13}H_{15}ClO_3$: C, 61.30; H, 5.94. Found: C, 61.40; H, 5.96.

[4-(2,4-Dimethyl-1,3-dioxolan-2-yl)phenyl](phenyl)methanone (29)

Mixture of diastereoisomers (dr = 60:40).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.80–7.66 (m, 4 H), 7.62–7.45 (m, 3 H), 7.45–7.35 (m, 2 H), 4.35–4.24 (m, 0.6 H), 4.17 (dd, *J* = 8.0, 5.6 Hz, 0.6 H), 4.02–3.92 (m, 0.4 H), 3.82 (dd, *J* = 7.6, 6.4 Hz, 0.4 H), 3.54–3.44 (m, 0.4 H), 3.30–3.18 (m, 0.6 H), 1.59 (s, 1.2 H), 1.56 (s, 1.8 H), 1.25 (d, *J* = 6.0 Hz, 1.2 H), 1.11 (d, *J* = 6.0 Hz, 1.8 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 196.8, 149.6, 148.9, 138.0, 137.9(9), 137.5, 137.4, 132.9, 132.8, 130.5, 130.4(3), 130.4(1), 128.7, 125.7, 125.6, 109.1, 73.7, 72.5, 71.6, 71.3, 28.7, 28.5, 19.3, 18.7.

HRMS (EI): *m*/*z* [M + H]$^+$ calcd for $C_{17}H_{24}O_3$: 283.1329; found: 283.1332.

Anal. Calcd for $C_{11}H_{14}O_2$: C, 76.57; H, 6.43. Found: C, 76.60; H, 6.45.

{4-[4-(Chloromethyl)-2-methyl-1,3-dioxolan-2-yl]phenyl}(phenyl)methanone (30)

Mixture of diastereoisomers (dr = 60:40).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.93–7.77 (m, 4 H), 7.73–7.57 (m, 3 H), 7.57–7.46 (m, 2 H), 4.53–4.44 (m, 0.4 H), 4.31 (dd, *J* = 8.8, 6.4 Hz, 0.4 H), 4.28–4.20 (m, 0.6 H), 3.99 (dd, *J* = 8.4, 4.4 Hz, 0.6 H), 3.83 (dd, *J* = 8.4, 7.2 Hz, 0.6 H), 3.77–3.63 (m, 1 H), 3.62–3.44 (m, 1 H), 3.20 (dd, *J* = 10.8, 8.8 Hz, 0.4 H), 1.71 (s, 1.8 H), 1.67 (s, 1.2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 196.9, 132.9, 130.6, 130.5, 128.7(3), 128.6(8), 125.6, 125.5, 75.9, 69.1, 67.9, 66.3, 45.0, 44.6, 28.5, 28.4, 15.7.

HRMS (EI): *m*/*z* [M + H]$^+$ calcd for $C_{18}H_{18}ClO_3$: 317.0939; found: 317.0939.

Anal. Calcd for $C_{18}H_{17}ClO_3$: C, 68.25; H, 5.41. Found: C, 68.43; H, 5.42.

1-[4-(2,5-Dimethyl-5-propyl-1,3-dioxan-2-yl)phenyl]ethanone (31)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.94–7.89 (m, 2 H), 7.48–7.45 (m, 2 H), 3.47 (d, *J* = 11.6 Hz, 1 H), 3.39 (d, *J* = 11.0 Hz, 1 H), 3.31 (d, *J* = 11.0 Hz, 1 H), 3.24 (d, *J* = 11.6 Hz, 1 H), 2.55 (s, 3 H), 1.68–1.59 (m, 1 H), 1.46 (s, 1.5 H), 1.45 (s, 1.5 H), 1.31–1.25 (m, 1 H), 1.19 (s, 1.5 H), 1.15–1.01 (m, 1 H), 0.92 (t, *J* = 7.2 Hz, 1.5 H), 0.82–0.75 (m, 1 H), 0.71 (t, *J* = 7.2 Hz, 1.5 H), 0.44 (s, 1.5 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 198.2, 147.1, 147.0, 137.0, 129.2, 127.5, 100.6, 100.4, 71.7, 70.7 39.0, 37.0, 32.9(0), 32.8(6), 32.1, 31.9, 27.1, 20.2, 19.2, 17.3, 16.0, 15.3, 15.2.

HRMS (EI): *m*/*z* [M + H]$^+$ calcd for $C_{17}H_{24}O_3$: 277.1804; found: 277.1801.

1-[4-(2,5-Dimethyl-1,3-dioxan-2-yl)phenyl]ethanone (32)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.06–7.97 (m, 2 H), 7.62–7.57 (m, 2 H), 3.95–3.86 (m, 1.2 H), 3.84–3.77 (m, 0.8 H), 3.66–3.54 (m, 1.2 H), 3.30–3.21 (m, 0.8 H), 2.63 (s, 1.2 H), 2.62 (s, 1.8 H), 2.23–2.12 (m, 0.4 H), 1.59–1.50 (m, 0.6 H), 1.54 (s, 1.8 H), 1.51 (s, 1.2 H), 1.28 (d, *J* = 6.8 Hz, 1.8 H), 0.57 (d, *J* = 6.8 Hz, 1.2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 198.2, 147.5, 147.0, 137.0, 129.3, 129.1, 127.6, 127.2, 100.4, 68.3, 66.9, 32.5, 30.8, 29.5, 29.1, 15.8, 12.7.

HRMS (EI): *m*/*z* [M + H]$^+$ calcd for $C_{14}H_{19}O_3$: 235.1329; found: 235.1331.

Anal. Calcd for $C_{14}H_{18}O_3$: C, 71.77; H, 7.74. Found: C, 71.82; H, 7.75.

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