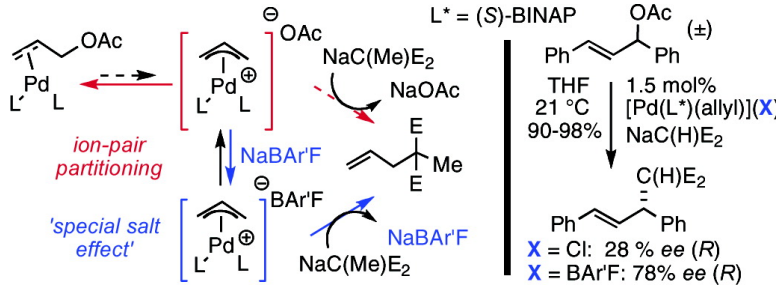
Communication

Counterintuitive Kinetics in Tsuji-Trost Allylation: Ion-Pair Partitioning and Implications for Asymmetric Catalysis

Louise A. Evans, Natalie Fey, Jeremy N. Harvey, David Hose, Guy C. Lloyd-Jones, Paul Murray, A. Guy Orpen, Robert Osborne, Gareth J. J. Owen-Smith, and Mark Purdie

J. Am. Chem. Soc., **2008**, 130 (44), 14471-14473 • DOI: 10.1021/ja806278e • Publication Date (Web): 08 October 2008



More About This Article

Additional resources and features associated with this article are available within the HTML version:

- Supporting Information
- Access to high resolution figures
- Links to articles and content related to this article
- Copyright permission to reproduce figures and/or text from this article

View the Full Text HTML

J|A|C|S
COMMUNICATIONS

Published on Web 10/08/2008

Counterintuitive Kinetics in Tsuji-Trost Allylation: Ion-Pair Partitioning and Implications for Asymmetric Catalysis

Louise A. Evans,[†] Natalie Fey,[†] Jeremy N. Harvey,[†] David Hose,[‡] Guy C. Lloyd-Jones,*[,†] Paul Murray,[‡] A. Guy Orpen,[†] Robert Osborne,[‡] Gareth J. J. Owen-Smith,[†] and Mark Purdie[§]

University of Bristol, Cantock's Close, Bristol, BS8 1TS, U.K., AstraZeneca, Avlon Works, Severn Road, Hallen, Bristol BS10 7ZE, and AstraZeneca, Bakewell Road, Loughborough, LE11 5RH, U.K.

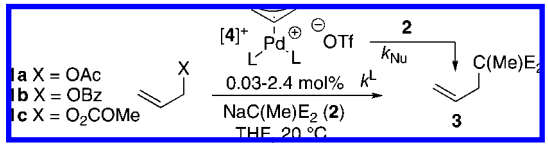
Received August 8, 2008; E-mail: Guy.Lloyd-Jones@bris.ac.uk

The Tsuji-Trost allylation of stabilized carbanions (**1** + **2** → **3**, Scheme 1) has evolved from a stoichiometric process[1] into one that is catalytic,[2] versatile, and extraordinarily selective.[3] The generic catalytic cycle outlined in Scheme 1, involving oxidative addition (k_{OA} → [**4**]$^+$), followed by nucleophilic attack (k_{Nu}) has become firmly established in the literature.[2b,3] The apparent simplicity of the mechanism and general robustness of the process accounts for its ubiquity as a "benchmarking reaction" in ligand design for asymmetric catalysis.[3] Herein we report on the kinetics of the catalytic reaction in the absence of interfering coligands such as halide or dba.[4h−l] We demonstrate that a variation of electron-demand in the phosphine ligand (L = i−xiii, Table 1)[5] leads to a counterintuitive spectrum of ligand-dependent turnover rates (k^L). This phenomenon has led us to use catalytic NaBAr′F (NaB[(3,5-$(CF_3)_2$)$C_6H_3)_4$])[6] to attenuate ion-pair return at the stage of the palladium allyl intermediate [**4**]$^+$||[X]$^-$; a process analogous to the "special salt effect" for carbocations.[7] Ion-pair partitioning by catalytic NaBAr′F provides new opportunities to accelerate allylation reactions, to reduce catalyst loadings, and to improve enantioselectivity, in this well-known reaction.

Despite extensive exploration of influence of ligands on the selectivity of allylation,[3] little has been documented regarding their influence on the overall reaction rate.[4] Nonetheless, there is a consensus that under catalytic conditions, rate = k_{obs}[Nu]^x.[4] This has given rise to the general assumption that the Pd-allyl intermediate ([**4**]$^+$), not L_2Pd, is the "resting-state" of the catalytic cycle.[3] The corollary of this assumption is that the turnover rate should depend primarily on the electrophilicity (k_{Nu}) of [**4**]$^+$, as modulated by ligands "L" (Scheme 1). The effect of a range of simple aryl and alkyl phosphine ligands (i−xiii) on the stoichiometric reactivity (k_{Nu}) of [**4**][OTf] toward **2** was readily assessed, Table 1. The data (normalized to k_{Nu}^{REL} = 1.00 for L = PPh_3, entry 4) shows the reactivity of [**4**]$^+$ spans about 1 order of magnitude and in the direction expected: electron withdrawing ligands (L) increase the electrophilicity (k_{Nu}).[4bc,f]

Under catalytic conditions the rate of reaction **1a** + **2**→**3** was found to be independent of the allyl acetate (**1a**) concentration: d[**3**]/dt = k^L[Pd_{tot}]^1[**2**]^1. While fully consistent with the generic catalytic cycle, Scheme 1, the trend in k^L is completely opposed to that of k_{Nu}, across the whole range of ligand systems tested. For example, the *p*-tolyl dppf complex [**4**(xiii)][OTf] generates a catalyst for the reaction of **1a** with **2** that is 166-fold more efficient (k^L) than its *p*-trifluoromethyl analogue [**4**(xii)][OTf] (Table 1, entries 12 and 13), yet the complex itself is 5-fold less reactive (k_{Nu}) toward **2**—a discrepancy of almost 3 orders of magnitude in the ratio of k^L/k_{Nu}.

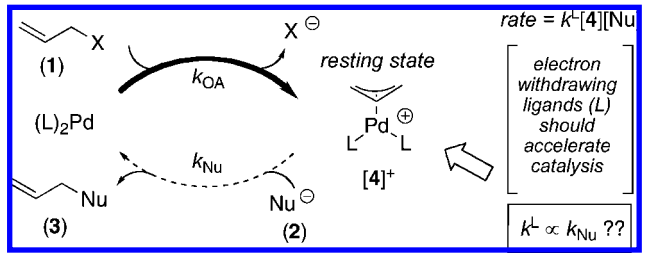
Table 1. Relative Rates (k_{Nu}^{REL}) for **2** + [**4**(L)$_2$][OTf]→**3**, Empirical Rate Constants (k^L) for **1** + **2**→**3** in THF Employing [**4**(L)$_2$][OTf] as Precatalyst, and Normalized Relative Rates in THF, DMF, and CH_2Cl_2



				k^L (M^{-1} s^{-1})[b]			$k^L{}_{REL}$[c]		
entry		L	k_{Nu}^{REL} [a]	**1a**	**1b**	**1c**	THF	DMF	CH_2Cl_2
1	(i)	P(*p*-$C_6H_4CF_3$)$_3$	2.64	0.73	1.9	53.1	0.03	0.02	5.58[d]
2	(ii)	P(*p*-C_6H_4Cl)$_3$	2.64	4.68					
3	(iii)	P(*p*-C_6H_4F)$_3$	2.15	8.32					
4	(iv)	PPh_3	1.00	26.9			1.00	1.00	1.00[d]
5	(v)	P(*p*-C_6H_4Me)$_3$	0.41	71.8	397	1980	2.67	1.34	0.37[b]
6	(vi)	P(*p*-C_6H_4OMe)$_3$	0.36	241					
7	(vii)	PPh_2Cy	0.49	71.8					
8	(viii)	$PPhCy_2$	0.13	99.7					
9	(ix)	PCy_3	0.20	36.9					
10	(x)	P(OPh)$_3$	3.01	0.91					
11	(xi)	dppf[e]	0.19	225					
12	(xii)	dppf-(*p*-CF_3)$_4$[e]	3.95	1.44					
13	(xiii)	dppf-(*p*-CH_3)$_4$[e]	0.75	239					

[a] Stoichiometric allylation: by first-order compensated fit of MS analysis of n in [$^{13}C_n$]-**3** obtained by competition of [**4**(ii−x)][OTf] and [**4**(x−xiii)][OTf] with [$^{13}C_1$-**4**(i)$_2$][OTf] for limiting **2**. [b] Linear regression of k_{obs} = k^L[Pd]$_{tot}$; k_{obs} from ln[**2**]$_0$/[**2**]$_t$ = $k_{obs}t$. [c] k^L for each solvent is normalized to k^L = 1.00 for L = PPh_3 (iv). [d] Using BSA/CH(Me)E_2 + cat. NaOAc. [e] Bidentate ligand.

Scheme 1. The Generic Catalytic Cycle for Tsuji-Trost Allylation.[1−3] [a]



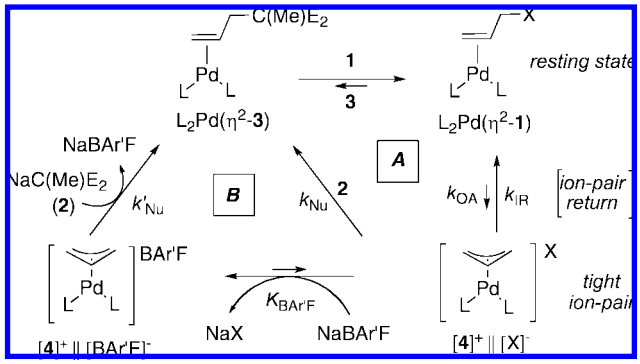
[a] k^L is the empirical rate constant for turnover as a function of ligand.

Replacing allyl acetate (**1a**) with allyl benzoate (**1b**) or allyl methyl carbonate (**1c**) led to substantially faster turnover, Table 1 entries 1 and 5, with **1c** increasing k^L values by just under 2 orders of magnitude over **1a**. However, as with **1a**, the more electron rich ligand P(*p*-tolyl)$_3$ (v) induced about 2 orders of magnitude faster turnover than the electron withdrawing ligand P(*p*-trifluorotolyl)$_3$ (i).[8]

[†] University of Bristol.
[‡] AstraZeneca, Avlon Works.
[§] AstraZeneca, Bakewell Road.

10.1021/ja806278e CCC: $40.75

Scheme 2. Modified Standard Cycle (**A**), with Ion-Pair Partitioning (k_{IR}/k_{Nu}) to Account for the Kinetics, Leaving Group (X) and Ligand Dependencies in the Pd-Catalyzed Reaction of **1a**−**c** with **2**, and Ion-Pair Metathesis Cycle (**B**)[a]



[a] $k^L \approx (k_{OA}/k_{IR})(k_{Nu} + K_{BAr'F}k'_{Nu}[NaBAr'F])$.

Since the trend in the electrophilicity (k_{Nu}) of $[\mathbf{4}]^+$ is opposite to the trend in turnover rate (k^L), the resting state of the catalytic system can not be $[\mathbf{4}]^+[X]^-$. Nonetheless, nucleophilic attack by **2** is turnover-limiting, suggesting that $[\mathbf{4}]^+[X]^-$ is generated reversibly in a low, steady-state, concentration. The catalytic cycle "**A**" outlined in Scheme 2, involving reversible generation of $[\mathbf{4}]^+[X]^-$ from $L_2Pd(\eta^2\text{-}\mathbf{1})$, is consistent with these observations.[9,10]

When **1a** and [$^{13}C_1$]-**1b** were coreacted there was no cross-over of leaving-group (X) detected in unreacted substrates. There is also no common-ion rate suppression by the NaX, which grows in parallel with **3**. Both of these results suggest that catalytic flux proceeds via a solvent-separated tight ion-pair $[\mathbf{4}]^+||[X]^-$.[4h−l,11] This ion-pairing accounts for the effects of the ligand, and the identity of X, on k^L. Thus, electron-withdrawing ligands, such as P(*p*-trifluorotolyl)$_3$ (i), increase the electrophilicity of $[\mathbf{4}]^+||[X]^-$ toward ion-pair return of X^- (k_{IR}) to a greater degree than they increase nucleophilic attack by **2** (k_{Nu}).[9] Better leaving groups (e.g., BzO, **1b**) reduce the rate of internal return, increasing the rate of catalytic turnover via nucleophilic attack by **2**.

As the partitioning of the ion-pair (k_{Nu}[**2**] versus k_{IR}, Scheme 2) appears to be a key parameter in controlling the turnover rate, we explored the use of NaBAr′F as a source of "naked" Na^+.[7] Generation of $[\mathbf{4}]^+||[BAr'F]^-$ from $[\mathbf{4}]^+||[X]^-$ will have the effect of attenuating[12] ion-pair return (k_{IR}) of X, analogous to Winstein's "special salt effect".[7] A key feature of this process is that the organic-soluble NaBAr′F is regenerated by **2** (k'_{Nu}) and can be employed in catalytic quantities, Scheme 2, cycle B.

The kinetics of Pd-catalyzed reactions of **1a** with **2** in the presence of catalytic NaBAr′F (0.6→2.2 mol%) were informative, Figure 1. A factor *a* has been employed to quantify the susceptibility of the catalyst system to acceleration through NaBAr′F mediated ion-pair partitioning, as compared to reactions with no added NaBAr′F (k^L_0, *y*-axis intercept).[13] The analysis clearly distinguishes that catalysts bearing moderately electron-rich ligands are the most substantially accelerated. For example, the catalyst bearing PPh_3 (iv, $a \approx 6 \times 10^3$ M^{-1}) undergoes 7-fold faster turnover with 1 mM NaBAr′F, while for the more electron rich ligand P(*p*-anisyl)$_3$ (vi) turnover is only increased 3-fold ($a \approx 2 \times 10^3$ M^{-1}). Catalysts bearing electron-poor ligands, which are already slow in the absence of NaBAr′F, for example, P(*p*-trifluorotolyl)$_3$ (i) are hardly accelerated at all ($a \approx -0.02 \times 10^3$ M^{-1}), Figure 1.

The ligand-dependency of the effect of NaBAr′F on attenuating ion-pair return was confirmed by ^{1}H NMR study of a stoichiometric mixture of L_nPd[14] and **1a** in d_8-THF, which does not generate any detectable π-allyl complex, [**4**(L)$_2$][OAc]). Addition of NaBAr′F

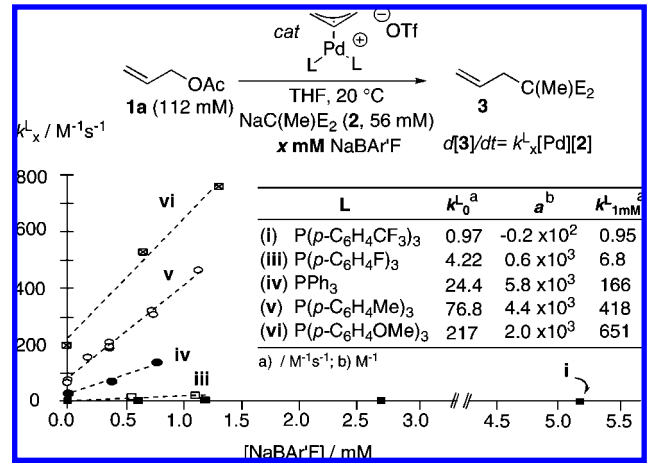


Figure 1. Ligand-selective acceleration of **1a** + **2**→**3** by catalytic [NaBAr′F]. Linear regression[7,13] is of $k^L = mx + k^L_0$; $a = (m/k^L_0)$; $k^L = k_{obs}/[Pd]_{tot}$. The acceleration factor *a* and predicted k^L values at 0 and 1 mM NaBAr′F (k^L_0 and $k^L_{1\ mM}$) are given for comparison.

(1.0 equiv) cleanly generated the π-allyl complex [**4**(**v**)$_2$][BAr′F] + NaOAc, when L = P(*p*-tolyl)$_3$ (v). However, the same reaction conducted with the electron-withdrawing ligand P(*p*-trifluorotolyl)$_3$ (i) did not generate any significant quantity of [**4**(i)$_2$][BAr′F], although both π-allyl complexes ([**4**(L)$_2$][BAr′F]) were smoothly generated by NaBAr′F addition to [**4**(L)$_2$][OTf] with cogeneration of NaOTf.[14b] This contrasting behavior clearly demonstrates the dependence of the energetics of formation of ($[\mathbf{4}]^+[BAr'F]^-$) on both the electron-donating ability of the ligand and the nature of X in $[\mathbf{4}]^+||[X]^-$.

The acceleration by NaBAr′F, Figure 1, is apparently a balance between having sufficient electron-donation available from the ligands (L) to make abstraction of X energetically accessible,[14b] but not having so much electron-donation available that it makes little impact on ion-pair return (k_{IR}) versus nucleophilic attack (k_{Nu}). For the range of simple aryl phosphines tested, PPh_3 appears to be about optimum in this regard.

Solvent obviously plays a key role on the ion-pairing in [**4**][X][4j] and was briefly explored. In the more ion-pair stabilizing solvent DMF the reactions proceeded about 3-fold faster than in THF, but there was no significant change in the effect of the ligand on the trend in turnover rates (k^L_{REL}, Table 1, entries 1, 4, 5). However, consistent with the generation of a more-dissociated ion-pair, the susceptibility to NaBAr′F acceleration was negligible. In stark contrast, the effect of the ligand on the trend in turnover rates was reversed in the less ion-pair stabilizing solvent CH_2Cl_2 (k^L_{REL}, Table 1, entries 1, 4, 5) using BSA/**2**-H for in situ nucleophile generation.[15] We are currently investigating the ligand influence on the energetics of ion-paired and neutral pathways, using computational methods, and will report on this in full in due course. Nonetheless, as with reactions in THF, NaBAr′F induces substantial acceleration in CH_2Cl_2 when the more electron rich ligands PPh_3 (iv) and P(*p*-tolyl)$_3$ (v) are employed ($a \approx 1 \rightarrow 3 \times 10^3$ M^{-1}), while reactions using P(*p*-trifluorotolyl)$_3$ (i) are unaffected.

Since the effect of NaBAr′F is to attenuate ion-pair return (k_{IR}) by X, the acceleration by NaBAr′F should be X-dependent, with poorer leaving groups such as OAc (**1a**) accelerated more than better ones, for example, OBz (**1b**). Competition between **1a** and **1b** for limiting **2** in THF yields their relative reactivity[16] (k_{1a}/k_{1b}, Figure 2). In all cases, acetate **1a** is substantially less reactive than benzoate **1b** ($k_{1a}/k_{1b} \ll 1$).[16] As predicted by Figure 1, with P(*p*-trifluorotolyl)$_3$ (i) as ligand ($a_a \approx 0$ M^{-1}) the selectivity is [NaBAr′F]-independent (Figure 2). However, with the more electron rich ligands PPh_3 (iv)

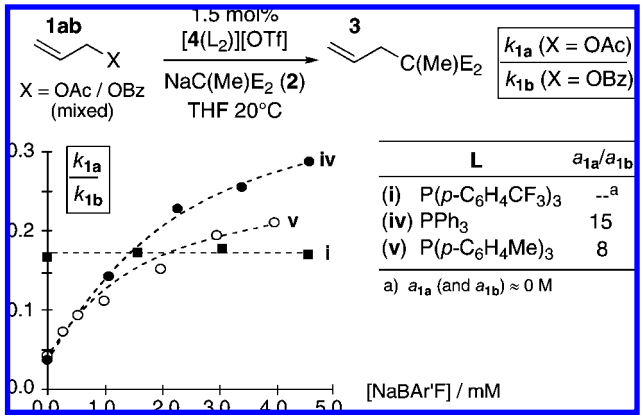
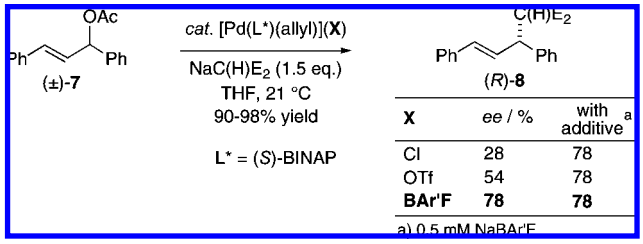


Figure 2. Selective acceleration of acetate (**1a**) over benzoate (**1b**) by [NaBAr′F]. k_{1a}/k_{1b} estimated by competition of **1a**/[^{13}C]-**1b** for limiting **2**. Nonlinear regression for (iv)/(v) is of $k_{1a}/k_{1b} = (\{k_{1a}/k_{1b}\}_0)((1 + a_{1a}x)/(1 + a_{1b}x))$. Note[16] that $k_{1a}/k_{1b} \neq k^{L(1a)}/k^{L(1b)}$.

Scheme 3. Impact of Cocatalytic NaBAr′F on Enantioselectivity[21]



and P(*p*-tolyl)$_3$ (v), acetate **1a** can be *differentially* accelerated ($a_{1a}/a_{1b} > 1$) over benzoate **1b**, by an order of magnitude.

Catalytic NaBAr′F is proposed to facilitate accelerated flux via generation of [**4**][BAr′F],[7,17] and thus a preliminary study[18] was conducted to investigate the impact of the degree of ion-pairing[19] at the point of nucleophilic attack (k_{Nu} versus k'_{Nu}, Scheme 2), on the selectivity of an archetypal asymmetric allylation, Scheme 3.[20]

In summary, counterintuitive ligand influences on the rate of Tsuji-Trost allylation[5] (**1** + **2** → **3**) can arise through reversible generation of a tight ion-pair ([**4**]$^+$||[X]$^-$) from a precomplexed resting state, $L_2Pd(\eta^2$-**1**),[22] Scheme 2. With appropriately electron-donating ligands, accelerated flux can be achieved by modulating the ion-pair partitioning with catalytic quantities of NaBAr′F (Scheme 2, cycle B).[14b,23] This process offers the potential to use lower catalyst loadings and to improve slow allylation reactions. It will also be an important consideration in chiral ligand design and the optimization of enantioselectivity.[19,20]

Acknowledgment. We thank AstraZeneca Global PR&D for generous financial support of this project and John M. Brown FRS, Oxford, for open exchange of information about ion-pairing.

Supporting Information Available: Preparation and characterization of catalysts; kinetic data and analysis. This material is available free of charge via the Internet at http://pubs.acs.org.

References

(1) (a) Tsuji, J.; Takahashi, H.; Moriwaka, M. *Tetrahedron Lett.* **1965**, *6*, 4387. (b) Trost, B. M.; Fullerton, T. J. *J. Am. Chem. Soc.* **1973**, *95*, 292.
(2) (a) Atkins, K. E.; Walker, W. E.; Manyik, R. M. *Tetrahedron Lett.* **1970**, *11*, 3821. (b) See reference 1 cited in ref 3a for an extensive list of reviews.
(3) Recent reviews: (a) Lu, Z.; Ma, S. *Angew Chem., Int. Ed.* **2007**, *47*, 258. (b) Trost, B. M.; Lee, C. *Catalytic Asymmetric Synthesis*, 2nd ed.; Ojima, I., Ed.; Wiley-VCH: New York, 2000; pp 593−649. (c) Pfaltz, A.; Lautens, M. *Comprehensive Asymmetric Catalysis*; Jacobsen, E. N., Pfaltz, A., Yamamoto, H., Eds.; Springer: Heidelberg, Germany, 1999; pp 833−886.
(4) Studies reporting on the kinetics of *catalytic* reaction: (a) Mackenzie, P. B.; Whelan, J.; Bosnich, B. *J. Am. Chem. Soc.* **1985**, *107*, 2046. (b) Åkermark, B.; Zetterberg, K.; Hansson, S.; Krakenberger, B.; Vitagliano, A. *J. Organomet. Chem.* **1987**, *335*, 133. (c) Ramdeehul, S.; Dierkes, P.; Aguado, R.; Kamer, P. C. J.; van Leeuwen, P. W. N. M.; Osborn, J. A. *Angew. Chem., Int. Ed.* **1998**, *37*, 3118. (d) Gais, H.-J.; Jagusch, T.; Spalthoff, N.; Gerhards, F.; Frank, M.; Raabe, G. *Chem.—Eur. J.* **2003**, *9*, 4202. Studies reporting on the kinetics of *stoichiometric amination* of π-allyl Pd complexes: (e) Vitagliano, A.; Åkermark, B. *J. Organomet. Chem.* **1988**, *349*, C22. (f) Kuhne, O.; Mayr, H. *Angew Chem. Int. Ed.* **1999**, *38*, 343. (g) Amatore, C.; Génin, E.; Jutand, A.; Mensah, L. *Organometallics* **2007**, *26*, 1875. Studies reporting on the kinetics of *stoichiometric* oxidative addition of allyl esters to generate π-allyl Pd complexes: (h) Amatore, C.; Jutand, A.; Meyer, G.; Mottier, L. *Chem.—Eur. J.* **1999**, *5*, 466. (i) Amatore, C.; Gamez, S.; Jutand, A. *Chem.—Eur. J.* **2001**, *7*, 1273. (j) Amatore, C.; Gamez, S.; Jutand, A.; Meyer, G.; Mottier, L. *Electrochim. Acta* **2001**, *46*, 3237. (k) Agenet, N.; Amatore, C.; Gamez, S.; Gérardin, H.; Jutand, A.; Meyer, G.; Orthwein, C. *Arkivoc* **2002**, *v*, 92. (l) Amatore, C.; Bahsoun, A. A.; Jutand, A.; Mensah, L.; Meyer, G.; Ricard, L. *Organometallics* **2005**, *24*, 1569.
(5) For a similar (but qualitative) trend, ascribed to an "ionic liquid effect", see: (a) Ross, J.; Chen, W.; Xu, L.; Xiao, J. *Organometallics* **2001**, *20*, 138. For a related acetate sequestering effect through H-bonding, that *suppresses* rate, see: (b) Ross, J.; Xiao, J. *Chem.—Eur. J.* **2003**, *9*, 4900.
(6) Brookhart, M.; Grant, B.; Volpe, A. F. *Organometallics* **1992**, *11*, 3920.
(7) (a) Winstein, S.; Klinedinst, P. E.; Robinson, G. C. *J. Am. Chem. Soc.* **1954**, *76*, 2597. (b) At present it is unclear whether the approximately linear plots in Figure 1 are the early phases of a special salt effect (which should progressively inflect to a normal salt effect) or the linear portion of a, rather powerful, normal salt effect. Scheme 3 supports the former.
(8) Crotyl acetate behaved analogously. See Supporting Information.
(9) An analogous conclusion was made by Jutand and co-workers, for Pd catalysed allylic amination, but based on the kinetics of *separate stoichiometric* reactions (K_{OA} and k_{Nu}), see reference 4g.
(10) Ligand association/dissociation equilibria are not implicated: the bidentate dppf ligands (entries 11−13) give identical trends. Addition of 1 equiv ligand v (entry 5) resulted in severe attenuation of turnover rate.
(11) Akermark, B.; Hansson, S.; Zetterberg, K.; Krakenberger, B.; Vitagliano, A. *Organometallics* **1984**, *3*, 679.
(12) Pregosin has demonstrated (from ^{19}F PGSE diffusion) that BAr′F engages in "very modest but not zero ion pairing", see: (a) Nama, D.; Butti, P.; Pregosin, P. S. *Organometallics* **2007**, *26*, 4942. (b) Pregosin, P. S. *Prog. Nucl. Magn. Reson. Spectrosc.* **2006**, *49*, 261.
(13) The approximation $d[\mathbf{3}]/dt \approx k^L(1 + a[NaBAr'F])[Pd_{tot}][\mathbf{2}]$ may only hold for low [NaBAr′F] concentrations. See also ref 7b.
(14) (a) A mixture of **1a** and (nominally) $(L)_2Pd$, was generated by reaction of $[Pd_2(allyl)_2(OAc)_2]$ with i and v (L/Pd = 2;−78→21 °C). For the analogous reaction with Cy_3P, see: Yamamoto, T.; Saito, O.; Yamamoto, A. *J. Am. Chem. Soc.,* **1981**, *103*, 5600. The precatalyst mixture gave an identical k^L value for **1a**→**3** to that obtained with [**4**$(L)_2$][OTf]. (b) ^{1}H-NMR isotherm-derived equilibrium constants for NaBAr′F + [**4**$(L)_2$][OTf] = NaOAc + [**4**$(L)_2$][BAr′F] are $K = 0.43 \pm 0.11$ (i), and $K = 193 \pm 147$ (v), see Supporting Information.
(15) Reactions were substantially slower than in THF, see Supporting Information, and proceeded with very approximately pseudo-zero-order kinetics, as might be expected from a steady-state concentration of [**2**].
(16) For other examples of pseudo-zero-order competitive networks see: (a) Ferretti, A. C.; Mathew, J. S.; Ashworth, I.; Purdy, M.; Brennan, C.; Blackmond, D. G. *Adv. Synth. Catal.* **2008**, *350*, 1007. (b) Blackmond, D. G.; Hodnett, N. S.; Lloyd-Jones, G. C. *J. Am. Chem. Soc.* **2006**, *128*, 7450. (c) Dominguez, B.; Hodnett, N. S.; Lloyd-Jones, G. C. *Angew. Chem., Int. Ed.* **2001**, *40*, 4289.
(17) Further evidence for a change in ion-pairing in **4**$^+$ at the point of nucleophilic attack comes from competition between **2** ($NaC(Me)E_2$) and the less sterically hindered $NaC(H)E_2$ for limiting **1a**. Using more electron rich ligands, the selectivity for **2** could be approximately doubled by addition of 3.0 mM [NaBAr′F], see Supporting Information.
(18) NaBAr′F (3.0 mM) increased k_{1a}/k_{1b} (0.15 → 0.50) with [**4**(BINAP)][OTf].
(19) The generation of a less-intimate ion-pair (see ref 12) may also modulate "memory effects". For leading references: (a) Trost, B. M.; Bunt, R. C. *J. Am. Chem. Soc.* **1996**, *118*, 235. (b) Lloyd-Jones, G. C.; Stephen, S. C.; Fairlamb, I. J. S.; Martorell, A.; Dominguez, B.; Tomlin, P. M.; Murray, M.; Fernandez, J. M.; Jeffery, J. C.; Riis-Johannessen, T.; Guerziz, T. *Pure Appl. Chem.* **2004**, *76*, 589. (c) Svensen, N.; Fristrup, P.; Tanner, D.; Norrby, P.-O. *Adv. Synth. Catal.* **2007**, *349*, 2631.
(20) Detrimental effects of halide on the selectivity of asymmetric allylation are known, see for example: Clark, T. P.; Landis, C. R. *J. Am. Chem. Soc.,* **2003**, *125*, 11792.
(21) Previously reported to proceed in 30% ee with X = Cl: Yamaguchi, M.; Shima, T.; Yamagishi, T. *Tetrahedron: Asymmetry* **1991**, *2*, 663.
(22) Cation-stabilizing allylic substituents (for example, 1,1,3-Ar_3) may decrease k_{IR} and/or k_{Nu} leading to a Pd-allyl species as resting state, see reference 4a.
(23) BAr′F, or analogous "non-interactive" (ref 12) anions are often employed in systems propagating via contiguous cationic catalytic intermediates. The results herein show that BAr′F can also be applied to catalytic cycles with neutral and cationic intermediates.

JA806278E