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[(NHC)Au^I]-Catalyzed Rearrangement of Allylic Acetates

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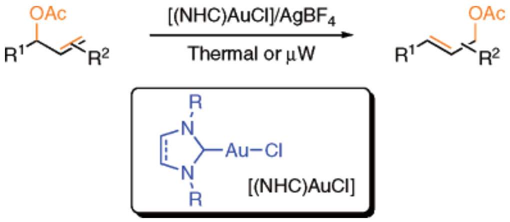
ABSTRACT



[(NHC)AuCl] complexes (NHC = N-heterocyclic carbene), in conjunction with a silver salt, were found to efficiently catalyze the rearrangement of allylic acetates under both conventional and microwave-assisted heating. The optimization of several reaction parameters (solvent, silver salt, and ligand) as well as a study of the reaction scope are reported. The steric hindrance of the ligand bound to gold was found crucial for the outcome of the reaction as only extremely bulky ligands permitted the isomerization.

Homogeneous gold catalysis has emerged lately as an efficient tool for the construction of complex organic molecules, notably through functionalization of alkynes and allenes.[1] Au^I and Au^{III} complexes generally act as soft π-acids and coordinate to the C≡C bond (or to the allene), triggering inter- and intramolecular nucleophilic attacks. This type of catalysis can be applied to alkenes as well but presents a more limited scope,[2] X−H addition (X = N, O) across the C=C bond being the most studied process.[3]

While propargylic acetates continue to be extensively studied for their valuable reactivity in the presence of gold catalysts,[4] almost no attention has been paid to their allylic counterparts.[5] Similarly to propargylic esters,[6] we envisaged that the acetate moiety might undergo a 1,3-shift upon complexation of Au$^+$ fragment onto the alkene, resulting ultimately in the formation of an isomerized allylic acetate. This reaction, namely the allylic rearrangement, provides an

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(1) For recent reviews, see: (a) Marco-Contelles, J.; Soriano, E. *Chem. Eur. J.* **2007**, *13*, 1350−1357. (b) Jiménez-Núñez, E.; Echavarren, A. M. *Chem. Commun.* **2007**, 333−346. (c) Zhang, L.; Sun, J.; Kozmin, S. A. *Adv. Synth. Catal.* **2006**, *348*, 2271−2296. (d) Hashmi, A. S. K.; Hutchings, G. J. *Angew. Chem., Int. Ed.* **2006**, *45*, 7896−7936. (e) Fürstner, A.; Davies, P. W. *Angew. Chem. Int. Ed.* **2007**, *46*, 3410−3449.

(2) For alkene activation in Au catalysis, see: (a) Hashmi, A. S. K.; Schwarz, L.; Choi, J.-H.; Frost, T. M. *Angew. Chem., Int. Ed.* **2000**, *39*, 2285−2288. (b) Dyker, G.; Muth, E.; Hashmi, A. S. K.; Ding, L. *Adv. Synth. Catal.* **2003**, *345*, 1247−1252. (c) Yao, X.; Li, C.-J. *J. Am. Chem. Soc.* **2004**, *126*, 6884−6885. (d) Alfonsi, M.; Arcadi, A.; Aschi, M.; Bianchi, G.; Marinelli, F. *J. Org. Chem.* **2005**, *70*, 2265−2273. (e) Xing, D.; Guan, B.; Cai, G.; Fang, Z.; Yang, L.; Shi, Z. *Org. Lett.* **2006**, *8*, 693−696. (f) Alfonsi, M.; Arcadi, A.; Bianchi, G.; Marinelli, F.; Nardini, A. *Eur. J. Org. Chem.* **2006**, 2393−2402.

(3) For N−H addition, see: (a) Zhang, J.; Yang, C.-G.; He, C. *J. Am. Chem. Soc.* **2006**, *128*, 1798−1799. (b) Brouwer, C.; He, C. *Angew. Chem., Int. Ed.* **2006**, *45*, 1744−1747. (c) Li, Z.; Ding, X.; He, C. *J. Org. Chem.* **2006**, *71*, 5876−5880. (d) Han, X.; Widenhoefer, R. A. *Angew. Chem., Int. Ed.* **2006**, *45*, 1747−1749. (e) Liu, X.-Y.; Li, C.-H.; Che, C.-M. *Org. Lett.* **2006**, *8*, 2707−2710. (f) Bender, C. F.; Widenhoefer, R. A. *Chem. Commun.* **2006**, 4143−4144. (g) Bender, C. F.; Widenhoefer, R. A. *Org. Lett.* **2006**, *8*, 5303−5305. For O−H addition, see: (h) Yang, C.-G.; He, C. *J. Am. Chem. Soc.* **2005**, *127*, 6966−6967. (i) Nguyen, R.-V.; Yao, X.; Li, C.-J. *Org. Lett.* **2006**, *8*, 2397−2399. (j) Skouta, R.; Li, C.-J. *Angew. Chem., Int. Ed.* **2007**, *46*, 1117−1119.

(4) For an overview, see: Marion, N.; Nolan, S. P. *Angew. Chem., Int. Ed.* **2007**, *46*, 2750−2752.

(5) During the redaction of this manuscript, a study on the isomerization of allenyl esters, a peculiar class of allylic acetates, catalyzed by Au^I complexes appeared, see: Buzas, A. K.; Istrate, F. M.; Gagosz, F. *Org. Lett.* **2007**, *9*, 985−988.

(6) For Au-mediated 1,3-shift of propargylic esters, see: (a) Fürstner, A.; Hannen, P. *Chem. Commun.* **2004**, 2546−2547. (b) Zhang, L. *J. Am. Chem. Soc.* **2005**, *127*, 16804−16805. (c) Zhang, L.; Wang, S. *J. Am. Chem. Soc.* **2006**, *128*, 1442−1443. (d) Buzas, A.; Istrate, F.; Gagosz, F. *Org. Lett.* **2006**, *8*, 1957−1959. (e) Wang, S.; Zhang, L. *J. Am. Chem. Soc.* **2006**, *128*, 8414−8415. (f) Wang, S.; Zhang, L. *Org. Lett.* **2006**, *8*, 4585−4587. (g) Oh, C. H.; Kim, A.; Park, W.; Park, D. I.; Kim, N. *Synlett* **2006**, 2781−2784. (h) Buzas, A.; Gagosz, F. *J. Am. Chem. Soc.* **2006**, *128*, 12614−12615. (i) Lemière, G.; Gandon, V.; Cariou, K.; Fukuyama, T.; Dhimane, A.-L.; Fensterbank, L.; Maiacria, M. *Org. Lett.* **2007**, *9*, 2207−2209.

10.1021/ol070843w CCC: $37.00

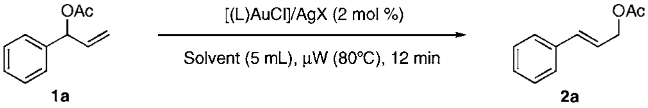
efficient and atom-economical access to primary oxo-derivatives. It has been described with various transition metals,[7] most studies focusing on Pd^{II},[8] but remains unprecedented,[5] to the best of our knowledge, in the presence of gold catalysts.

Herein, we report that [(NHC)AuCl] complexes (NHC = N-heterocyclic carbene), in conjunction with a silver salt, efficiently catalyze the isomerization of allylic acetates under thermal or microwave-assisted conditions.[9]

Capitalizing on catalytic systems we previously developed in the context of homogeneous gold catalysis,[10] we attempted the isomerization of allylic acetate **1a** with [(IPr)AuCl]/AgBF$_4$ in DCM (IPr = *N*,*N′*-bis(2,6-diisopropylphenyl)-imidazol-2-ylidene). We observed the formation of the rearranged product **2a** with complete selectivity for the *E*-isomer but results, under both thermal and microwave-assisted heating, were not reproducible. Nevertheless, encouraged by our preliminary findings, we engaged in a thorough optimization of the reaction conditions.[11]

As expected no conversion was obtained at room temperature.[12] Several solvents were tested under both conventional and microwave-assisted heating,[13] with equal results (Table 1, entries 1−5). The reaction performed best in polychlorinated solvents, DCE being the most efficient (Table 1, entry 2). We then decided to continue these studies using microwave conditions,[14] notably because of the great gain in time.

Table 1. Optimization of the Reaction Conditions



entry	L	AgX	solvent	**2a**[a]
1[b,c]	IPR	AgBF$_4$	DCM	60−90%
2[c]	IPR	AgBF$_4$	DCE	99%
3[c]	IPR	AgBF$_4$	toluene	16%
4[b,c]	IPR	AgBF$_4$	THF	<5−14%
5[c]	IPR	AgBF$_4$	H$_2$O	<5%
6	none	no catalyst	DCE	SM recovered
7	IPR	no catalyst	DCE	<5%
8[b]	none	AgBF$_4$	DCE	20−40%
9	IPR	AgPF$_6$	DCE	86%
10[d]	IPR	AgSbF$_6$	DCE	63%
11	IPR	AgOTf	DCE	98%

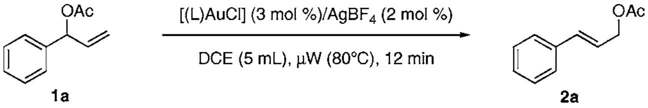
[a] ^{1}H NMR conversions, average of at least 2 runs. [b] Results were not repoductible. [c] Similar results were obtained under the following conditions: conventional heating, reflux for 12 h. [d] Substantial amount of oligomerization. DCM = dichloromethane; DCE = 1,2-dichloroethane; THF = tetrahydrofuran; Tf = triflate.

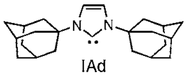
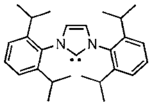
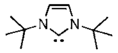
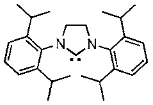
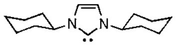
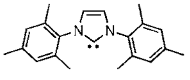
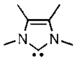
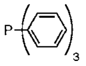
Next, three control experiments were carried out (entries 6−8). Acetate **1a** was fully recovered when neither Au nor Ag were added to the reaction (entry 6) and [(IPr)AuCl] alone showed very little catalytic activity (entry 7). On the other hand, AgBF$_4$ was found to catalyze the isomerization but in low yield and with no reproducibility (entry 8).

To avoid any "contaminating" silver(I) catalysis, we decided to employ an excess of gold(I) complex (3 mol % of Au and 2 mol % of Ag) to ensure a Au-catalyzed reaction. Finally, the influence of the counteranion was evaluated (entries 2 and 9−11). While BF$_4^-$, PF$_6^-$, and TfO$^-$ showed similar behavior, SbF$_6^-$ led to a significant amount of oligomerization.[11]

Next, we screened a number of NHCs with varying stereoelectronic properties (Table 2).[15] Interestingly, a strong steric effect was observed: only the most encumbering NHCs produced the isomerized acetate **2a** in quantitative yield (Table 2, entries 2, 3, 5, and 6).

Table 2. Influence of Ligand on the Rearrangement



entry	L	**2a**[a]	entry	L	**2a**[a]
1[b]	none	< 5%	5	 IAd	97%
2	 IPr	99%	6	 ItBu	98%
3	 SIPr	98%	7[b]	 ICy	< 5%
4[b]	 IMes	< 5%	8[b]	 ITM	< 5%
			9[b]		8%

[a] ^{1}H NMR conversions, average of 2 runs. [b] Substantial amount of oligomerization.

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(7) (a) Hg: Overman, L. E.; Campbell, C. B.; Knoll, F. M. *J. Am. Chem. Soc.* **1978**, *100*, 4822−4834. (b) Co: Mukhopadhyay, M.; Reddy, M. M.; Maikap, G. C.; Iqbal, J. *J. Org. Chem.* **1995**, *60*, 2670−2676. (c) Eu: Shull, B. K.; Sakai, T.; Koreeda, M. *J. Am. Chem. Soc.* **1996**, *118*, 11690−11691. (d) Yb: Krishna, P. R.; Kannan, V.; Sharma, G. V. M. *Synth. Commun.* **2004**, *34*, 55−64.

(8) (a) Henry, P. M. *J. Chem. Soc. D* **1971**, 328−329. (b) Henry, P. M. *J. Am. Chem. Soc.* **1972**, *94*, 5200−5206. (c) Overman, L. E.; Knoll, F. M. *Tetrahedron Lett.* **1979**, *4*, 321−324. (d) Shekhar, S.; Trantow, B.; Leitner, A.; Hartwig, J. F. *J. Am. Chem. Soc.* **2006**, *128*, 11770−11771.

(9) For reviews on microwave-assisted reactions, see: (a) Loupy, A., Ed. *Microwaves in Organic Synthesis*; Wiley-VCH: Weinheim, Germany, 2002. (b) Kappe, C. O. *Angew. Chem., Int. Ed.* **2004**, *43*, 6250−6284. (c) de la Hoz, A.; Díaz-Ortiz, A.; Moreno, A. *Chem. Soc. Rev.* **2005**, *34*, 164−178.

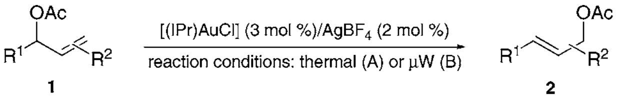
(10) (a) Marion, N.; de Frémont, P.; Lemière, G.; Stevens, E. D.; Fensterbank, L.; Malacria, M.; Nolan, S. P. *Chem. Commun.* **2006**, 2048−2050. (b) Marion, N.; Díez-González, S.; de Frémont, P.; Noble, A. R.; Nolan, S. P. *Angew. Chem., Int. Ed.* **2006**, *45*, 3647−3650. (c) Marion, N.; Carlqvist, P.; Gealageas, R.; de Frémont, P.; Maseras, F.; Nolan, S. P. *Chem.−Eur. J.* **2007**, *13*, DOI: 10.1002/chem.200700134.

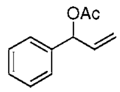
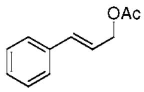
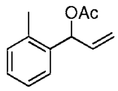
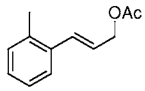
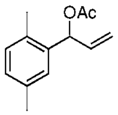
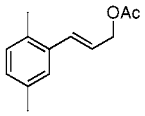
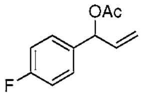
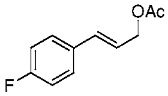
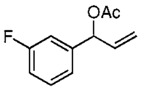
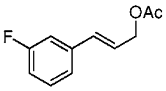
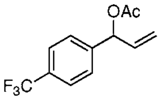
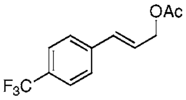
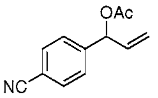
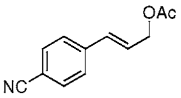
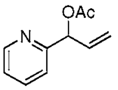
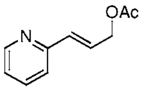
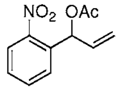
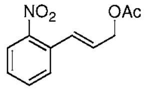
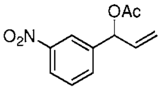
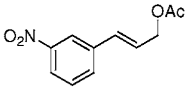
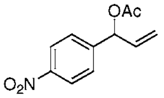
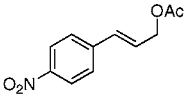
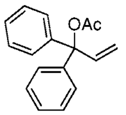
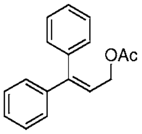
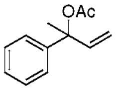
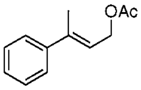
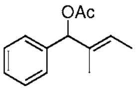
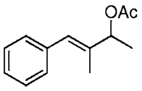
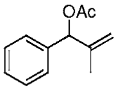
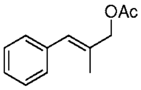
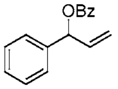
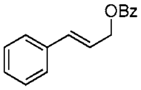
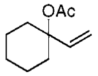
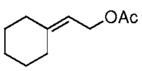
(11) We present here only the most significant results. For the complete set of optimization tables, and for a direct comparison with commonly used Pd catalysts, see the Supporting Information.

(12) Alkynes and allenes are typically activated at room temperature by Au while alkenes require prolonged heating, see refs 1−3.

(13) For a rare example of microwave-assisted gold-catalyzed reaction, see: Liu, X.-Y.; Li, C.-H.; Che, C.-M. *Org. Lett.* **2006**, *8*, 2707−2710.

Table 3. Au-Catalyzed Rearrangement of Various Allyl Esters[a]



entry	substrate	1	product	$\mathbf{2}^b$ (method)
1		1a		**2a**, 95% (A) 97% (B)
2		1b		**2b**, 92% (A) 90% (B)
3		1c		**2c**, 87% (B)
4		1d		**2d**, 95% (A) 95% (B)
5		1e		**2e**, 75% (A) 81% (B)
6		1f		**2f**, 94% (A) (E:Z, 93:7)[c]
7		1g		**2g**, n.r. (A) n.r. (B)
8		1h		**2h**, n.r. (A) n.r. (B)
9		1i		**2i**, n.r. (A) n.r. (B)
10[d]		1j		**2j**, 53% (B) (E:Z, 70/30)[c]
11		1k		**2k**, 96% (A) (E:Z, 92/8)[c] 98% (B) (E:Z, 95/5)[c]
12		1l		**2l**, 88% (B)
13		1m		**2m**, 78% (B) (E:Z, 75/25)[c]
14		1n		**2n**, 76% (B) (E:Z, 85/15)[c]
15		1o		**2o**, 93% (B) (E:Z, 85/15)[c]
16		1p		**2p**, 90% (B)
17		1q		**2q**, 97% (A) 98% (B)

[a] Reaction conditions. General: **1** (1 mmol), [(IPr)AuCl] (3 mol %), AgBF$_4$ (2 mol %), DCE (20 mL). Method A: oil bath, reflux, t = 12 h. Method B: μW, T = 80 °C, t = 12 min. [b] Isolated yields, average of two runs. [c] Ratio determined by ^{1}H NMR. [d] Substantial amount of oligomerization. n.r. = no reaction.

More strikingly, the less sterically demanding ligands did not lead to sluggish reactions or lower yields; they hardly produced the isomerized allyl and led mainly to oligomerization (entries 4 and 7−9). Since ItBu and IAd, which performed extremely well, are the most σ-donating ligands of the series,[16] an explanation relying on electronic properties was appealing. But it can be easily ruled out in view of the behavior of IPr and IMes that possess similar electronics and performed oppositely. A purely steric influence of the ligand on gold appears as the most plausible hypothesis—ItBu, IAd, IPr, and SIPr being the four most encumbered ligands of the series we tested. The greatest steric hindrance of the latter ligands could be seen as a protection of the gold center, preventing clusterization or precipitation of gold(0), which could inhibit the catalytic activity.

Even though a more thorough explanation remains elusive at the present time, it is noteworthy that the translation of the sterics of the ligand to the outcome of the reaction is unprecedented in this chemistry where we previously observed comparable performances for IPr and IMes.[10,17]

With a fully optimized catalytic system in hand, the scope of the reaction was examined and results are presented in

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(14) The amount of solvent, the reaction time, and the temperature have been optimized by using a scientific microwave reactor Biotage Initiator 2.0.

(15) For reviews, see: (a) Díez-González, S.; Nolan, S. P. *Coord. Chem. Rev.* **2007**, *251*, 874−883. (b) Hahn, F. E. *Angew. Chem., Int. Ed.* **2006**, *45*, 1348−1352. (c) Peris, E.; Crabtree, R. H. *Coord. Chem. Rev.* **2004**, *248*, 2239−2246. (d) Herrmann, W. A. *Angew. Chem., Int. Ed.* **2002**, *41*, 1290−1309. (e) Bourissou, D.; Guerret, O.; Gabbai, F. P.; Bertrand, G. *Chem. Rev.* **2000**, *100*, 39−92.

(16) For a study on the steric and electronic properties of NHCs, see: Dorta, R.; Stevens, E. D.; Scott, N. M.; Costabile, C.; Cavallo, L.; Hoff, C. D.; Nolan, S. P. *J. Am. Chem. Soc.* **2005**, *127*, 2485−2495.

(17) The sharp contrast between IPr and IMes in this reaction is currently being investigated.

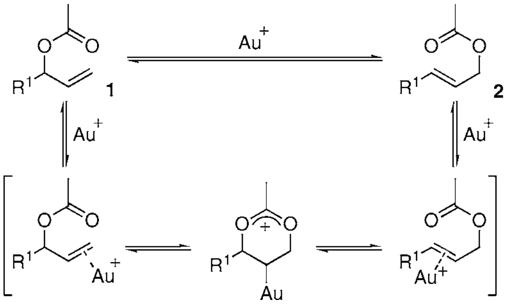
Table 3. It is important to note that the procedure is extremely simple to carry out and does not require anhydrous reagents or anaerobic conditions. Various substitution patterns on the phenyl ring did not alter the yield nor the stereochemistry of the isomerized products **2** (Table 3, entries 1−6). It was then surprising to observe the quantitative recovery of **1g** bearing a cyano group in the *para* position (entry 7). Despite repeated attempts using both methods A and B, we never detected the formation of **2g**. This could be due to coordination of the nitrile moiety of **1g** to the gold center, since linear two-coordinated cationic gold(I) complexes containing NHC ligands and acetonitrile have been reported as fairly stable compounds.[18] Hence, a hypothetical $[(\mathrm{IPr})\mathrm{Au}(\mathbf{1g})]^+\mathrm{BF}_4^-$ might be inert under the present reaction conditions. Decoordination of the nitrile upon workup would release **1g** unaffected. A similar feature was observed when a 2-pyridynyl group was attached to the allyl moiety (entry 8). Again, complexation of the substrate to the gold center is the most likely explanation, since in this case, in addition to a linear coordination of the nitrogen, formation of a 5-membered *N*,*O*-chelate is possible.

Examination of the results from entries 9−11 seems to corroborate this hypothesis.[19] When the nitro group is placed in the *ortho* position, no conversion is observed and the starting material is recovered (**1i**). Then, the conversion increases as a function of the distance between the nitro and the acetate (from *ortho* to *para*), resulting in quantitative formation of **2k** where the nitro group is located in the *para* position.

The formation of trisubstituted olefins, often challenging synthetically, was found efficient (entries 12−15 and 17). Tertiary acetates **1l** and **1m** were converted into **2l** and **2m** in good yields. Di- and trisubstituted alkenes participated as well in the isomerization reaction affording **2n** and **2o** in good yields and selectivity (entries 14 and 15).

Further expanding the scope of the reaction, a benzoate group at the allylic position isomerized similarly as an acetate (entry 16) and an alkyl-substituted allylic acetate produced in high yield the rearranged trisubstituted olefin (entry 17).

It is worth noting that several reactions were carried out with both conventional (i.e., oil bath) and microwave heating and produced very similar, if not identical, results even in terms of selectivity (entries 1, 2, 4, 5, 7−9, 11, and 17). In terms of mechanism, as depicted in eq 1, we propose that π-coordination of the alkene moiety onto the cationic gold center triggers an intramolecular nucleophilic attack of the carbonyl, leading to a 6-membered stabilized 1,3-acetoxonium. Completion of the 1,3-shift of the acetate would produce the isomerized olefin and regenerate the Au^+ fragment. By this proposal, which is in line with previous studies carried out with mercury[7a] and palladium,[8] we consider this reaction as a cyclization-induced rearrangement as defined by Overman.[20]



(1)

In summary, we have developed an efficient $[(\mathrm{NHC})\mathrm{Au}^{\mathrm{I}}]$-catalyzed rearrangement of allylic acetates under conventional or microwave-assisted heating that proved versatile. It was notably shown that an extremely bulky ligand bound to the gold center was crucial to obtain full conversions to the isomerized product. Studies aimed at understanding this feature and expanding further the scope of this reaction are ongoing in our laboratories.

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Supporting Information Available: Detailed optimization studies and experimental procedures as well as characterizations and references for all compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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[18] de Frémont, P.; Stevens, E. D.; Fructos, M. R.; Díaz-Requejo, M. M.; Pérez, P. J.; Nolan, S. P. *Chem. Commun.* **2006**, 2045−2047.

[19] Attempts to isolate one of the hypothetical complexes mentioned in the text were, to this point, unsuccessful.

[20] (a) Overman, L. E.; Campbell, C. B. *J. Org. Chem.* **1976**, *41*, 3338−3340. (b) Overman, L. E. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 579−587. (c) Overman, L. E.; Owen, C. O.; Pavan, M. M. *Org. Lett.* **2003**, *5*, 1809−1812. (d) Watson, M. P.; Overman, L. E.; Bergman, R. G. *J. Am. Chem. Soc.* **2007**, *129*, 5031−5044.