Pergamon

Tetrahedron Letters 43 (2002) 5537–5540

TETRAHEDRON LETTERS

The [(*E*,*E*,*E*)-1,6,11-tris(*p*-toluenesulfonyl)-1,6,11-triazacyclopentadeca-3,8,13-triene]Pd(0) complex in the hydroarylation of alkynes in ionic liquids. An approach to quinolines

Sandro Cacchi,[a,*] Giancarlo Fabrizi,[a] Antonella Goggiamani,[a] Marcial Moreno-Mañas[b] and Adelina Vallribera[b]

[a]*Dipartimento di Studi di Chimica e Tecnologia delle Sostanze Biologicamente Attive, Università degli Studi "La Sapienza", P.le A. Moro 5, 00185 Rome, Italy*

[b]*Department of Chemistry, Universitat Autònoma de Barcelona, Cerdanyola, 08193 Barcelona, Spain*

Received 10 June 2002; accepted 13 June 2002

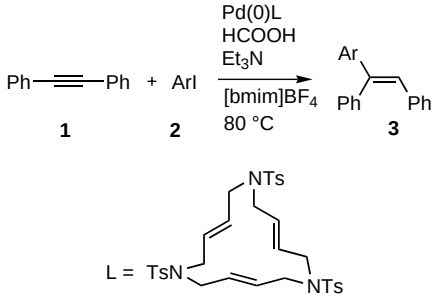
Abstract—The hydroarylation of alkynes can be successfully conducted in 1-butyl-3-methylimidazolium tetrafluoroborate ([bmim]BF_4) in the presence of the [(*E*,*E*,*E*)-1,6,11-tris(*p*-toluenesulfonyl)-1,6,11-triazacyclopentadeca-3,8,13-triene]Pd(0) complex. The catalytic ionic solution can be recycled for reuse in subsequent reaction runs. The procedure has been applied to the preparation of 3-arylquinolines through a domino hydroarylation/cyclization process.

The employment of room temperature ionic liquids in synthesis is emerging as an attractive alternative to that of classical molecular organic solvents. Some of their properties (no detectable vapor pressure, possible recycling, easy separation from the products, thermal robustness) make them promising candidates for the development of environmentally friendly synthetic methodologies. To date, a variety of reactions have been successfully carried out in these solvents,[1] and many of them describe the utilization of palladium catalysis,[2] thus establishing the feasibility of homogeneous palladium-catalyzed reactions in ionic liquids.

Our palladium-catalyzed hydroarylation and hydrovinylation reaction represents a useful tool for organic synthesis. The reaction has been examined with α,β-unsaturated carbonyl compounds,[3] norbornene derivatives,[4] and alkynes.[5] Sequential hydroarylation (hydrovinylation)/cyclization processes have been developed into new approaches to functionalized butenolides,[6] quinolines[7] and chromenes.[8] Intramolecular versions of the reactions have also been described.[9]

Here we wish to report that the palladium-catalyzed hydroarylation of alkynes can be conducted in 1-butyl-3-methylimidazolium tetrafluoroborate ([bmim]BF4),[10] a room temperature ionic liquid reported to be virtually insoluble in alkanes and diethyl ether but to dissolve many organic and organometallic compounds, in the presence of the [(*E*,*E*,*E*)-1,6,11-tris(*p*-toluenesulfonyl)-1,6,11-triazacyclopentadeca-3,8,13-triene]Pd(0) complex[11] (Scheme 1); the catalyst/ionic liquid system can be successfully reused in subsequent reaction runs.[12,13]

Initial attempts were made subjecting *p*-iodoanisole to diphenylacetylene in the presence of triethylamine, for-



Scheme 1.

Keywords: hydroarylation; palladium; macrocyclic ligands; ionic liquids; quinolines.

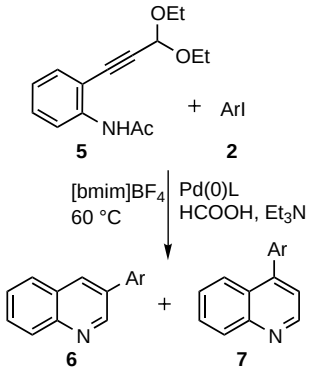
* Corresponding author. Fax: +39 (06) 4991-2780; e-mail: sandro.cacchi@uniroma1.it

0040-4039/02/$ - see front matter
PII: S0040-4039(02)01120-6

mic acid and classical Pd(0) donors such as $Pd(PPh_3)_4$ or $Pd_2(dba)_3$ at 80°C for 8 h. With $Pd(PPh_3)_4$ the desired hydroarylation derivative was isolated only in 41% yield. Employing $Pd_2(dba)_3$ increased the yield up to 82%, but a significant drop was observed on the first recharge (59% yield). Switching to [(*E*,*E*,*E*)-1,6,11-tris(*p*-toluenesulfonyl)-1,6,11-triazacyclopentadeca-3,8,13-triene]Pd(0) produced the corresponding hydroarylation product in 89% yield (comparable to the 92% yield obtained with the same catalyst system in DMF) and, what is more, allowed an extensive recycling of the ionic catalyst solution (vide infra). Keeping all the other parameters the same but substituting 1-butyl-3-methylimidazolium hexafluorophosphate ([bmim]PF_6) for [bmim]BF_4 produced the hydroarylation product in 41% yield, and the yield on the first recharge was only 25%. Therefore, [bmim]BF_4 was used as the solvent when the procedure was extended to include other aryl iodides. The unoptimized yields and stereoselectivity were usually satisfactory (Table 1).

The extension of the procedure to develop a domino hydroarylation/cyclization process was also investigated and the formation of substituted quinolines from 3,3-die-1-phenyl-1-propyne **5** and aryl iodides was chosen as the model reaction. The reaction (Scheme 2) proceeds in a straightforward fashion, producing quinoline derivatives in good overall yield and satisfactory regioselectivity. The new carbon–carbon bond is formed preferentially at the carbon bearing the acetal group and 3-arylquinolines **6** were isolated as the main products (Table 2).

One of the main tasks of this research effort was to develop an efficient procedure for recycling the catalyst/ionic liquid system. Therefore, we investigated the number of times that we could reuse the ionic catalytic solution by employing the reaction of diphenylacetylene with *p*-iodoanisole and ethyl *p*-iodobenzoate, models of electron-donating and electron-withdrawing aryl iodides. As shown in Table 3, the solution containing the catalytically active palladium species can be used at least six times with essentially no loss of activity with *p*-iodoanisole and only a modest decrease in activity with ethyl *p*-iodobenzoate.



Scheme 2.

Table 1. The hydroarylation of diphenylacetylene in [bmim]BF_4 in the presence of [(*E*,*E*,*E*)-1,6,11-tris(*p*-toluenesulfonyl)-1,6,11-triazacyclopentadeca-3,8,13-triene]Pd(0)[a]

Entry	Aryl iodide **2**	Reaction time (h)	**3** yield%[b]	*E*:*Z*[c]
1	*p*-MeO-C_6H_4-I	8	89[d]	94:6
2	*m*-MeOC_6H_4-I	60	59[d]	95:5
3	*p*-F-C_6H_4-I	480	45	>99:1
4	*p*-MeCO-C_6H_4-I	24	36	>99:1
5	*p*-EtOOC-C_6H_4-I	24	77	91:9
6	*p*-EtOOC-C_6H_4-I	24	69[d]	91:9
7	*m*-EtOOC-C_6H_4-I	48	70	94:6
8	2-NO_2-4-Me-C_6H_3-I	79	35	88:12

[a] Unless otherwise stated, reactions were carried out at 80°C using the following molar ratios: **1**:**2**:Et_3N:HCOOH:[Pd]=1:2:2:1.5:0.02.
[b] Yields refer to single runs and are given for isolated products. All products had satisfactory elemental analyses, and their spectra were consistent with the postulated structures.
[c] Calculated by NMR analysis.
[d] **1**:**2**:Et_3N:HCOOH:[Pd]=1:1.5:2:1.5:0.02.

Table 3. Recycling studies for the reaction of Scheme 1

Number of cycles	Yield% (with *p*-iodoanisole)	Yield% (with ethyl *p*-iodobenzoate)
1st	89	77
2nd	89	83
3rd	85	72
4th	74	72
5th	70	69
6th	86	58

Table 2. Synthesis of 3-arylquinolines in the presence of [(*E*,*E*,*E*)-1,6,11-tris(*p*-toluenesulfonyl)-1,6,11-triazacyclopentadeca-3,8,13-triene]Pd(0)[a]

Entry	Aryl iodide **2**	Reaction time (d)	Yield% of **6**[b]	Yield% of **7**[b]	**6**/**7**
1	*p*-MeO-C_6H_4-I	6	56	9	86:14
2	*p*-Me-C_6H_4-I	3	67	12	85:15
3	*p*-F-C_6H_4-I	3	67	13	84:16
4	*p*-EtOOC-C_6H_4-I	3	74	21	79:21

[a] Reactions were carried out at 60°C using the following molar ratios: **1**:**2**:Et_3N:HCOOH:[Pd]=1:2.4:3:2:0.025.
[b] Yields refer to single runs and are given for isolated products. All products had satisfactory elemental analyses, and their spectra were consistent with the postulated structures.

In summary, we have demonstrated that the [(*E*,*E*,*E*)-1,6,11-tris(*p*-toluenesulfonyl)-1,6,11-triazacyclopentadeca-3,8,13-triene]Pd(0) complex can be successfully employed for the hydroarylation of alkynes in 1-butyl-3-methylimidazolium tetrafluoroborate ([bmim]BF_4) and that the palladium-containing catalytically active species, ''immobilized'' in the ionic liquid, can be reused for subsequent runs with little loss in activity.

Acknowledgements

Work carried out in the framework of the National Project ''Stereoselezione in Sintesi Organica. Metodologie ed Applicazioni'' supported by the Ministero dell'Università e della Ricerca Scientifica e Tecnologica, Rome. Financial support of this research by the University ''La Sapienza'', Rome, is also gratefully acknowledged. Spanish partners acknowledge financial support from MEC (project PB98-0902) and Generalitat de Catalunya (project 2001-SGR0181). This work has been possible thanks to project COST D12/0011/98.

References

1. For reviews, see: (a) Chauvin, Y.; Olivier-Bourbigou, H. *Chemtech* **1995**, 26–30; (b) Welton, T. *Chem. Rev.* **1999**, *99*, 2071–2083; (c) Olivier, H. *J. Mol. Catal. A-Chem.* **1999**, *146*, 285–289; (d) Earle, M. J.; Seddon, K. R. *Pure Appl. Chem.* **2000**, *72*, 1391–1398; (e) Seddon, K. R.; Stark, A.; Torres, M.-J. *Pure Appl. Chem.* **2000**, *72*, 2275–2287; (f) Wasserscheid, P.; Keim, W. *Angew. Chem., Int. Ed. Engl.* **2000**, *39*, 3772–3789; (g) Bradley, D.; Dyson, P.; Welton, T. *Chem. Rev.* **2000**, *9*, 18–21; (h) Gordon, M. C. *Appl. Catal. A-Gen.* **2001**, *222*, 101–117.
2. (a) Kaufmann, D. E.; Nouzoorian, M.; Henze, H. *Synlett* **1996**, 1091–1092; (b) Dullius, J. E. L.; Suarez, P. A. Z.; Einloft, S.; de Souza, R. F.; Dupont, J.; Fischer, J.; De Cian, A. *Organometallics* **1998**, *17*, 815–819; (c) Zim, D. A.; de Souza, R. F.; Dupont, J.; Monteiro, A. L. *Tetrahedron Lett.* **1998**, *39*, 7071–7074; (d) Carmicaael, A. J.; Earle, M. J.; Holbrey, J. D.; McCormac, P. B.; Seddon, K. R. *Org. Lett.* **1999**, 997–1000; (e) Herrrmann, W. A.; Böhm, V. P. W. *J. Organomet. Chem.* **1999**, *572*, 141–145; (f) Chen, W.; Xu, L.; Chatterton, C.; Xiao, J. *Chem. Commun.* **1999**, 1247–1248; (g) Böhm, V. P. W.; Herrmann, W. A. *Chem. Eur. J.* **2000**, *6*, 1017–1025; (h) Reetz, M. T.; Westermann, E. *Angew. Chem., Int. Ed. Engl.* **2000**, *39*, 165–168; (i) Howarth, J.; Dallas, A. *Molecules* **2000**, *5*, 851–855; (j) Xu, L.; Chen, W.; Xiao, J. *Organometallics* **2000**, *19*, 1123–1127; (k) Calò, V.; Nacci, A.; Lopez, L.; Mannarini, N. *Tetrahedron Lett.* **2000**, *41*, 8973–8976; (l) Handy, S. T.; Zhang, X. *Org. Lett.* **2001**, 233–236; (m) Xu, L.; Chen, W.; Ross, J.; Xiao, J. *Org. Lett.* **2001**, 295–297; (n) Ross, J.; Chen, W.; Xu, L.; Xiao, J. *Organometallics* **2001**, *20*, 138–142; (o) Calò, V.; Nacci, A.; Monopoli, A.; Lopez, L.; di Cosmo, A. *Tetrahedron* **2001**, *57*, 6071–6077; (p) Calò, V.; Nacci, A.; Lopez, L.; Napola, A. *Tetrahedron Lett.* **2001**, *42*, 4701–4703; (q) Hagiwara, H.; Shimizu, Y.; Hoshi, T.; Suzuki, T.; Ando, M.; Ohkubo, K.; Yokoyama, C. *Tetrahedron Lett.* **2001**, *42*, 4349–4351; (r) Consorti, C. S.; Ebeling, G.; Dupont, J. *Tetrahedron Lett.* **2002**, *43*, 753–755.
3. (a) Cacchi, S.; Arcadi, A. *J. Org. Chem.* **1983**, *48*, 4236–4240; (b) Cacchi, S.; La Torre, F.; Calmieri, G. *J. Organomet. Chem.* **1984**, *268*, C48–C51; (c) Cacchi, S.; Calmieri, G. *Synthesis* **1984**, 575–577; (d) Arcadi, A.; Marinelli, F.; Cacchi, S. *J. Organomet. Chem.* **1986**, *312*, C27–C32; (e) Stokker, G. E. *Tetrahedron Lett.* **1987**, *28*, 3179–3182; (f) Wolff, S.; Hoffmann, H. M. R. *Synthesis* **1988**, 760–763; (g) Wada, A.; Yasuda, H.; Kanatomo, S. *Synthesis* **1988**, 771–775; (h) Amorese, A.; Arcadi, A.; Bernocchi, E.; Cacchi, S.; Cerrini, S.; Fedeli, W.; Ortar, G. *Tetrahedron* **1989**, *45*, 813–828; (i) Hoffmann, H. M. R.; Schmidt, B.; Wolff, S. *Tetrahedron* **1989**, *45*, 6113–6126; (j) Konopelski, J. P.; Chu, K. S.; Negrete, G. R. *J. Org. Chem.* **1991**, *56*, 1355–1357; (k) Wada, A.; Ohki, K.; Nagai, S.; Kanatomo, S. *J. Heterocyclic Chem.* **1991**, *28*, 509–512; (l) Benhaddou, R.; Czernecki, S.; Ville, G. *J. Org. Chem.* **1992**, *57*, 4612–4616; (m) Denmark, S. E.; Schnute, M. E. *J. Org. Chem.* **1995**, *60*, 1013–1019; (n) Hagiwara, H.; Eda, Y.; Morohashi, K.; Suzuki, T.; Ando, M.; Ito, N. *Tetrahedron Lett.* **1998**, *39*, 4055–4058; (o) Cacchi, S.; Fabrizi, G.; Gasparrini, F.; Pace, P.; Villani, C. *Synlett* **2000**, 650–652.
4. (a) Arcadi, A.; Marinelli, F.; Bernocchi, E.; Cacchi, S.; Ortar, G. *J. Organomet. Chem.* **1989**, *368*, 249–256; (b) Larock, R. C.; Johson, P. L. *J. Chem. Soc., Chem. Commun.* **1989**, 1368–1370; (c) Brunner, H.; Kramler, K. *Synthesis* **1991**, 1121–1124; (d) Sakuraba, S.; Awano, K.; Achiwa, K. *Synlett* **1994**, 291–292; (e) Sakuraba, S.; Okada, T.; Morimoto, T.; Achiwa, K. *Chem. Pharm. Bull.* **1995**, *43*, 927–934; (f) Montalbetti, C.; Savignac, M.; Genet, J.-P.; Roulet, J.-M.; Vogel, P. *Tetrahedron Lett.* **1996**, *37*, 2225–2228; (g) Otten, A.; Namyslo, J. C.; Stoermer, M.; Kaufmann, D. E. *Eur. J. Org. Chem.* **1998**, 1997–2001; (h) Kasyan, A.; Wagner, C.; Maier, E. *Tetrahedron* **1998**, *54*, 8047–8054; (i) Wållberg, A.; Magnusson, G. *Tetrahedron* **2000**, *56*, 8533–8537; (j) Wu, X.-Y.; Xu, H.-D.; Tang, F.-Y.; Zhou, Q. L. *Tetrahedron: Asymmetry* **2001**, *12*, 2565–2569.
5. (a) Arcadi, A.; Cacchi, S.; Marinelli, F. *Tetrahedron* **1985**, *41*, 5121–5131; (b) Arcadi, A.; Cacchi, S.; Marinelli, F. *Tetrahedron Lett.* **1986**, *27*, 6397–6400; (c) Cacchi, S.; Fabrizi, G.; Marinelli, F.; Moro, L.; Pace, P. *Tetrahedron* **1996**, *52*, 10225–10240; (d) Cacchi, S. *J. Organomet. Chem.* **1999**, *576*, 42–64.
6. (a) Arcadi, A.; Bernocchi, E.; Burini, A.; Cacchi, S.; Marinelli, F.; Pietroni, B. *Tetrahedron Lett.* **1989**, *30*, 3465–3468; (b) Arcadi, A.; Bernocchi, E.; Burini, A.; Cacchi, S.; Marinelli, F.; Pietroni, B. *Tetrahedron* **1988**, *44*, 481–490; (c) Arcadi, A.; Cacchi, S.; Fabrizi, G.; Marinelli, F.; Pace, P. *Eur. J. Org. Chem.* **1999**, 3305–3313.
7. Cacchi, S.; Fabrizi, G.; Marinellli, F.; Moro, L.; Pace, P. *Tetrahedron* **1996**, *52*, 10225–10240.
8. Arcadi, A.; Cacchi, S.; Fabrizi, G.; Marinelli, F.; Pace, P. *Eur. J. Org. Chem.* **2000**, 4099–4108.
9. (a) Burns, B.; Grigg, R.; Sridharan, V.; Worakun, T. *Tetrahedron Lett.* **1988**, *29*, 4325–4328; (b) Friestad, G.; Branchaud, B. P. *Tetrahedron Lett.* **1995**, *36*, 7047–7050; (c) Comins, D. L.; Joseph, S. P.; Zhang, Y.-M. *Tetrahedron Lett.* **1996**, *37*, 793–796.

10. 1-Butyl-3-methylimidazolium tetrafluoroborate ([bmim]-BF_4) was prepared according to Ref. 2l.
11. (a) Cortès, J.; Moreno-Mañas, M.; Pleixats, R. *Eur. J. Org. Chem.* **2000**, 239–243; (b) Cerezo, S.; Cortès, J.; Lago, E.; Molins, E.; Moreno-Mañas, M.; Parella, T.; Pleixats, R.; Torrejón, J.; Vallribera, A. *Eur. J. Inorg. Chem.* **2001**, 1999–2006.
12. **Typical procedure for the hydroarylation of alkynes:** To a 50 mL carousel reaction tube (Radley Discovery Technology) containing a magnetic stir bar were added [bmim]BF_4 (2 mL) and [(*E*,*E*,*E*)-1,6,11-tris(*p*-toluenesulfonyl)-1,6,11-triazacyclopentadeca-3,8,13-triene]Pd(0) (7.7 mg, 0.01 mmol). The mixture was stirred at 80°C for 1 h under argon. Then, diphenylacetylene (89.0 mg, 0.50 mmol), 4-iodoanisole (175.0 mg, 0.75 mmol), triethylamine (139 μL, 1.00 mmol) and formic acid (30 μL, 0.75 mmol) were added. The solution was stirred at 80°C for 8 h. After this time, the reaction mixture was cooled to room temperature and washed with diethyl ether (15 mL×5 times). The organic extracts were then combined, washed with water, dried over $NaSO_4$ and concentrated under reduced pressure. The residue was purified by chromatography on silica gel [*n*-hexane/ethylacetate 95/5 (v/v)] to give 0.126 mg (89% yield) of 1,2-diphenyl-1-(*p*-methoxyphenyl)ethylene as an approximately *E:Z* 96:4 stereoisomeric mixture. The two stereoisomers were separated by preparative HPLC and their configuration (NOE experiments did not provide clear-cut results) was assigned on the basis of our previous work that shows a general predominance of *cis* addition products following the carbopalladation step: (*E*)-isomer: oil; IR (neat): 2940, 1606, 1077 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.37–7.05 (m, 12H), 6.92–6.85 (m, 3H), 3.84 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 159.2, 142.1, 140.6, 137.6, 136.1, 130.4, 129.5, 129.4, 128.8, 127.9, 127.3, 126.5, 126.4, 113.6, 55.3; Anal calcd for $C_{21}H_{18}O$: C, 88.08; H, 6.34; Found: C, 88.17; H, 6.39; (*Z*)-isomer: oil; IR (neat): 2941, 1608, 1080 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.38–7.0 (m, 12H), 6.92–6.83 (m, 3H), 3.85 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 158.9, 143.8, 142. 2, 137.6, 132.5, 131.6, 1128.6, 128.1, 128.0, 127.8, 127.7, 127.5, 126.6, 114.0, 55.2; Anal calcd for $C_{21}H_{18}O$: C, 88.08; H, 6.34; Found: C, 88.19; H, 6.35. **Recycling of the catalyst/ionic liquid system**: After completion of the diethyl ether washes, diphenylacetylene (89.0 mg, 0.50 mmol), *p*-iodoanisole (175.0 mg, 0.75 mmol), triethylamine (139 μL, 1.00 mmol) and formic acid (30 μL, 0.75 mmol) were added to the ionic catalytic solution. The reaction mixture was stirred at 80°C for 8 h. After this time, the mixture was worked-up as before.
13. For use and recycle of a related [(*E*,*E*,*E*)-1,6,11-tris(arenesulfonyl)-1,6,11-triazacyclopentadeca-3,8,13-triene]Pd-(0) in butadiene telomerization see: Estrine, B.; Blanco, B.; Bouquillon, S.; Hénin, F.; Moreno-Mañas, M.; Muzart, J.; Pena, C.; Pleixats, R. *Tetrahedron Lett.* **2001**, *42*, 7055–7057.