ORGANIC LETTERS

1999
Vol. 1, No. 13
2101−2104

Reactions of Alkenes, Alkynes, and Alkoxyallenes with New Polymer-Supported Electrophilic Reagents

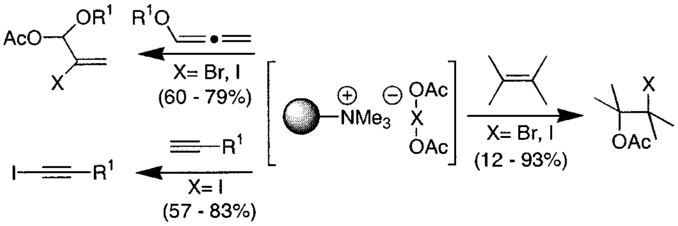
Holger Monenschein,[†] Georgia Sourkouni-Argirusi,[†] Katherine M. Schubothe,[‡] Thomas O'Hare,[‡] and Andreas Kirschning*,[†]

Institut für Organische Chemie der Technischen Universität Clausthal, Leibnizstrasse 6, D-38678 Clausthal-Zellerfeld, Germany, and Department of Chemistry, Willamette University, 900 State Street, Salem, Oregon 97301

andreas.kirschning@tu-clausthal.de

Received October 15, 1999

ABSTRACT



Preparation of new polymer-supported electrophilic reagents that efficiently promote 1,2-haloacetoxylations of alkenes and alkoxyallenes is described. Under very mild conditions and in high yields, alkenes are transformed into α-halo acetates while alkoxyallenes lead to vinyl iodides. In contrast to these results, terminal alkynes commonly afford synthetically valuable 1-iodo-alkynes.

Recently, development of polymer-supported reagents has been an area of intensive research.[1] Functionalized matrices can be used in excess to drive reactions in solution to completion and are finding application in high-throughput, automated parallel syntheses.[2] However, few polymer-supported reagents that perform the 1,2-cohalogention[3] or epoxidation of alkenic double bonds have been described so far.[4] Our interest in new electrophilic halogen−ate(I) complexes[5] has led to the development of the first polymer-bound iodine azide source which conveniently promotes azidoiodination of alkenes.[6] As a continuation of this work we describe the preparation of three resin-bound synthetic equivalents of acylated hypohalites and demonstrate that they are powerful electrophilic reagents for the selective oxidation of alkenes, alkynes, and alkoxyallenes.

[†] Technischen Universität Clausthal.

[‡] Willamette University.

(1) Reviews: (a) Shuttleworth, S. J.; Allin, S. M.; Sharma, P. K. *Synthesis* **1998**, 1217−1239. (b) Kaldor, S. W.; Siegel, M. G. *Curr. Opin. Chem. Biol.* **1997**, *1*, 101−106. (c) Hodge, P.; Sherringtom, D. C. In *Polymer-Supported Reaction in Synthesis*; Wiley: New York, 1990. (d) Laszlo, P., Ed. In *Preparative Chemistry using Supported Reagents*; Academic: San Diego, 1987.

(2) (a) Flynn, D. L.; Devraj, J. J. Parlow, *Curr. Opin. Drug Discovery Dev.* **1998**, *1*, 41−50. (b) Suto, M. J.; Gayo-Fung, L. M.; Palanki, M. S. S.; Sullivan, R. *Tetrahedron* **1998**, *54*, 4141−4150. (c) Parlow, S. S. *Tetrahedron Lett.* **1996**, *37*, 5257−5260. (d) Habermann, J.; Ley, S. V.; Scott, J. S. *J. Chem. Soc., Perkin Trans. 1* **1998**, 3127−3130. (e) Caldarelli, M.; Habermann, J.; Ley, S. V. *J. Chem. Soc., Perkin Trans. 1* **1999**, 107−110.

(3) Reviews: (a) Block, E.; Schwan, A. L. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Semmelhack, M. F., Eds.; Pergamon Press: Oxford, 1991; Vol. 4, pp 329−362. (b) Rodriguez, J.; Dulcère, J.-P. *Synthesis* **1993**, 1177−1205.

(4) (a) Olah, G. A.; Li, X.; Wang, Q.; Prakash, G. K. S. *Synthesis* **1993**, 693−699. (b) Zajc, B.; Zupan, M. *Tetrahedron* **1989**, *45*, 7869−7878. (c) Liu, C.-J.; Yu, W.-Y.; Li, S.-G.; Che, C.-M. *J. Org. Chem.* **1998**, *63*, 7364−7369.

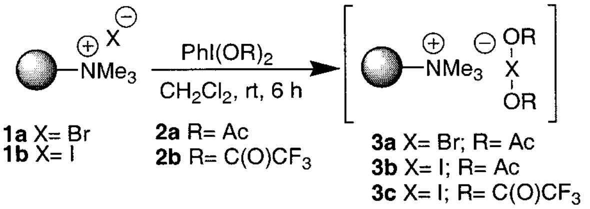
(5) (a) Kirschning, A.; Plumeier, C.; Rose, L. *Chem. Commun.* **1998**, 33−34. (b) Hashem, Md. A.; Jung, A.; Ries, M.; Kirschning, A. *Synlett* **1998**, 195−197. (c) Kirschning, A.; Hashem, Md. A.; Monenschein, H.; Rose, L.; Schöning, K.-U. *J. Org. Chem.* **1999**, *64*, 2720−2722.

(6) Kirschning, A.; Monenschein, H.; Schmeck, C. *Angew. Chem.* **1999**, *111*, 2720−2722; *Angew. Chem., Int. Ed. Engl.* **1999**, *38*, 2594−2596.

10.1021/ol991149m CCC: $18.00

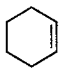
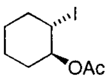
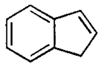
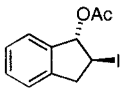
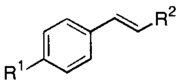
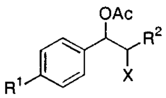
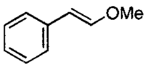
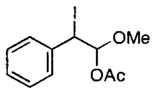
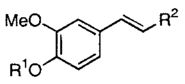
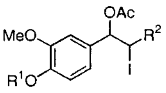
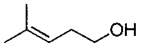
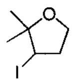
Preparation of these reagents was achieved by iodine(III)-promoted ligand transfer and hence oxidation of polystyrene-bound halides **1a**,**b**.[7] As a result of this transformation we presumably prepared polymer-bound di(acyloxy)halogenate(I) anions **3a**−**c** (Scheme 1).[5,8] Thus, reaction of bromide **1a** with (diacetoxyiodo)benzene **2a** afforded polymer **3a** while electrophilic reagents **3b** and **3c** were generated from polymer-bound iodide **1b** after treatment with **2a** and **2b**, respectively. We found that extensive washing of the resulting polymers does not result in their deactivation, which clearly supports the ionic character of the active species on the polymer. For resin **3b**, the weight increase served as an indicator for efficient ligand transfer onto polymer-bound halide and gave most reproducible results (about 90% conversion with respect to theoretical iodide).[7] Furthermore, both reagents can be stored below 0 °C for weeks without loss of activity.

Scheme 1

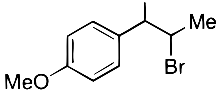


These electrophilic reagents promote 1,2-haloacetoxylation of various alkenes under very mild conditions with high efficiency (Table 1). Unlike classical reagents that have been employed for the haloacetoxylation of olefinic double bonds, immobilized reagents **3a** and **3b** do not require glacial acetic acid[9] or heavy metals.[10] 1,2-Functionalization of alkenes **4**−**12** using reagent **3b** typically afforded a single cohalogention product. The addititon proceeded with *trans* selectivity as demonstrated for cyclohexene **4**, indene **5**, and styrenes **7**−**10**.[11,12] Halogenated substrates **6** and **9** reacted very sluggishly at room temperature; at 80 °C, complete consumption of alkenes was achieved. Under these conditions,

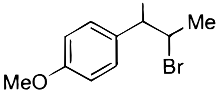
Table 1. Haloacetoxylation of Alkenes

	Alkene, R^1, R^2	Reagent (equiv.)	Product[a]		Yield %[b]
		→			
4		**3b** (3)		**13**	73 (90/80)
		→			
5		**3b** (3)		**14**	67 (90/75)
		→			
6	Br, H	**3b** (4)[c]	X= I	**15**	57 (80/70)
7	MeO, Me	**3a** (5)	X= Br	**16**[d]	43 (>95/50)
		3b (3)	X= I	**17**[e]	88 (>95/95)
8	H, CH_2Cl	**3b** (5)[c]	X= I	**18**[f]	12 (>95/95)
		→			
9		**3b** (4)		**19**[e]	79 (>95/95)
		→			
10	Me, Me	**3b** (3)		**20**[e]	74 (>95/90)
11	Bn, H	**3b** (4)		**21**	76 (90/85)
		→			
12		**3b** (4)		**22**	93 (>95/85)

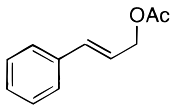
[a] For experimental details, refer to ref 11. [b] All yields refer to isolated pure products. Values in parentheses refer to yields/purities of the crude products. The differences relative to the isolated yields are due in part to decomposition during the course of chromatographic purification. [c] Reaction temperature, 80 °C. [d] Additionally, **23** (26%) and **24** (8%) were isolated. [e] Very labile 1,2-addition products. [f] Additionally, **25** (77%) was isolated.



23
two diastereoisomers
(1 : 1.5)



24
two diastereoisomers
(1 : 2.5)



25

---

(7) **General Procedure for the Preparation of Polymer-Bound Reagents 3a−c:** A suspension of polymer bound halide (available from Fluka; 3.2 g/mmol for bromide; 2.9 mmol/g for iodide) and $PhI(OAc)_2$ or $PhI(O_2CCF_3)_2$ (1.8 equiv) in dry CH_2Cl_2 (3 mL/mmol halide anion) under nitrogen was shaken at 300 rpm for 6 h at room temperature. The brownish suspension was protected from light. Filtration and washing of the resin with CH_2Cl_2 (3×) and drying in vacuo afforded the light yellow reagents **3a** and **3b** or pink resin **3c**.

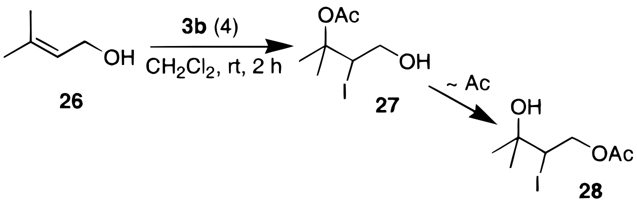
(8) (a) Doleschall, G.; Tóth, G. *Tetrahedron* **1980**, *36*, 1649−1665. (b) Szántay, C.; Blaskó, G.; Bárcrczai-Beke, M.; Péchy, P.; Dörnei, G. *Tetrahedron Lett.* **1980**, *21*, 3509−3512. (c) Matsuo, K.; Ishida, S.; Takuno, Y. *Chem. Pharm. Bull.* **1994**, *42*, 1149−1150.

(9) (a) Mangoni, L.; Adinolfi, M.; Barone, G.; Parrilli, M. *Tetrahedron Lett.* **1973**, 4485−4486. (b) Mangoni, L.; Adinolfi, M.; Barone, G.; Parrilli, M. *Gazz. Chim. Ital.* **1975**, *105*, 377−383. (c) Adinolfi, M.; Parrilli, M.; Barone, G.; Laonigro, G.; Mangoni, L. *Tetrahedron Lett.* **1976**, 3661−3663.

(10) (a) Birckenbach, L.; Goubeau, J.; Berninger, E. *Ber.* **1932**, *65*, 1339−1344. (b) Woodward, R. B.; Brutcher, F. V., Jr. *J. Am. Chem. Soc.* **1958**, *80*, 209−211. (c) Cambie, R. C.; Gash, D. M.; Rutledge, P. S.; Woodgate, P. D. *J. Chem. Soc., Perkin Trans. 1* **1977**, 1157−1162. (d) Barluenga, J.; Rodriguez, M. A.; Campos, P. J.; Asenio, G. *J. Chem. Soc., Chem. Commun.* **1987**, 1491−1492. (e) Georgoulis, C.; Valery, J. *Bull. Soc. Chim. Fr.* **1975**, 1431−1432. (f) Trainor, R. W.; Deacon, G. B.; Jackson, W. R.; Giunta, N. *Aust. J. Chem.* **1992**, *45*, 1265−1280. (g) Bedekar, A. V.; Nair, K. B.; Soman, R. *Synth. Commun.* **1994**, *24*, 2299−2305.

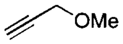
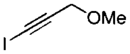
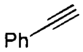
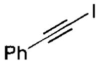
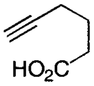
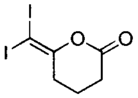
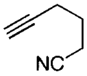
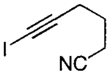
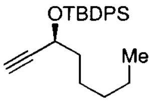
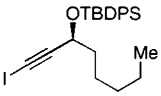
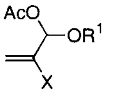
4-bromostyrene (**6**) gave the desired 1,2 -addition product **15** in moderate yield. In contrast, allyl chloride underwent nucleophilic substitution to furnish allyl acetate **25** as the major product. Importantly, hydroxy groups are tolerated under the reaction conditions employed. Thus, allyl alcohol **26** afforded acetate **28** in 91% yield, indicating that a Markovnikov-type addition to the alkenic double bond[13] is followed by an acyl migration to the terminal alcohol group (Scheme 2). In contrast, homoallyl alcohol **12** gave an intermediate cation which was intramolecularly trapped by the hydroxy group to furnish tetrahydrofuran **22**. Polymeric reagent **3a** is able to perform bromoacetoxylation of alkene **7**; however the transformation is accompanied by the formation of two more addition products, namely an isomeric mixture of 1,2-*syn*- and 1,2-*anti*-dibromides **23** along with bromohydrin **24** which was isolated as a single isomer (Table 1).

Scheme 2



All reagents are employed in excess with reference to the specified amount of halide in **1a** and **1b**.[7] This may be rationalized by assuming that only a proportional amount of immobilized halide was transformed into the hypervalent species or that only the most accessible haloate(I) anions are involved in the cohalogenation process. If acylated hypohalites are the active species after release from the polymer, their degradation prior to the reaction with alkenes may also contribute to the need for a formal excess of reagent. In most cases, filtration followed by removal of the solvent in vacuo afforded the 1,2-addition products. The position of iodine and thereby the regiochemistry of the addition process was unequivocally proven by chemical shift analysis of the adjacent carbon atom in the ^{13}C NMR spectra ($\delta = 48.6-24.2$ ppm for CHI, and $\delta = 7.8-7.2$ ppm for CH_2I). Vinyl halides, particularly vinyl iodides and 1-alkynyl halides, are of increasing importance as versatile building blocks in transition metal catalyzed cross-coupling reactions.[14] In this respect, the palladium-catalyzed Stille, Suzuki, and Heck reactions have become part of the organic chemist's daily methodological repertoire.[14,15]

Table 2. Haloacetoxylation of Alkynes and Alkoxyallenes

Alkyne, Allene, R^1	Reagent (equiv.)	Product[a] X		Yield %[b]
 **29**	**3b** (4)		**36**	70 (>95/85)
 **30**	**3b** (4)		**37**	82 (>95/90)
 **31**	**3b** (4)		**38**	57 (90/70)
 **32**	**3b** (4)		**39**	83 (>95/90)
 **33**	**3b** (4)		**40**	79 (>95/95)
 **34** Me	**3b** (3)	 X= I	**41**	79 (>95/>95)
35 Bn	**3a** (4)	X= Br	**42**	60 (>95/75)
Bn	**3b** (4)	X= I	**43**	67 (>95/80)

[a] For experimental details refer to ref 11. [b] All yields refer to isolated pure products. Values in parentheses refer to yields/purities of the crude products.

Therefore, we set up a second set of experiments using polymer-supported reagents **3a** and **3b** for the facile preparation of organic halides suitable for this synthetic purpose. As a consequence, alkynes as well as allenes were employed (Table 2).[16] In fact, methylated propargyl alcohol **29** afforded alkynyl iodide **36**[17] ($\delta = 6.2$ to -3.6 ppm for C-I) upon treatment with **3b**, presumably generated by electrophilic attack of the iodonium ion and formation of an intermediate

---

[11] **General Procedure for the 1,2-Cohalogenation of Alkenes:** A mixture of alkene (1 equiv) and resin (for number of equiv refer to Table 1) were shaken at 300 rpm under light protection in dry CH_2Cl_2 (1.5 mL/mmol) at room temperature. Completion of the reaction was monitored by TLC. Filtration terminated the reaction. The resin was washed with with CH_2Cl_2 (3×), and the combined organic washings and filtrate were concentrated under reduced pressure. In some cases, further purification by column chromatography was necessary. Finally, the polymer was recycled to the halide form **1** by treatment with concentrated HBr or HI for 1 h at room temperature.

[12] The assignment of the trans stereochemistry in **7**−**10** is based on the analogy to compounds **13** and **14** and the known preference for iodoacetoxylation of alkenes (see refs 9 and 10).

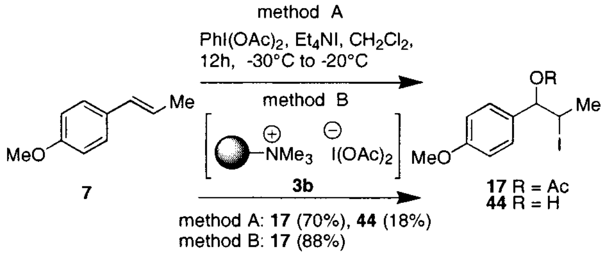
[13] Quantitative acyl migration from the primary addition product **27** to yield **28** occurred within 2 days in $CDCl_3$.

[14] Diederich, F.; Stang, P. J. In *Metal-catalyzed Cross-coupling Reactions*; Wiley-VCH: Weinheim, 1998.

vinyl cation followed by deprotonation. Likewise, alkynes **30**, **32**, and **33** were processed under reaction conditions similar to those of the corresponding alkynyl iodides **37**, **39**, and **40** in high yields.[18] Remarkably, the nitrile functionality in **32** is tolerated. A suitably oriented carboxyl group as in 5-hexynoic acid (**31**) afforded the unusual cyclization product **38**, containing a 1,2-diiodo-substituted exocyclic double bond. Formation of lactone **38** may be rationalized by electrophilic attack of a second equivalent of the iodonium ion onto the triple bond in the corresponding intermediate iodoalkyne and subsequent cyclization. Alternatively, initial ring closure would afford the monoiodo-substituted analogue of **38** followed by a second attack of the electrophilic reagent and deprotonation. It should be noted that the polymer-bound bromate(I) reagent **3a** does not promote bromination of alkynes under these reaction conditions. Thus, in the case of compound **33** the starting material was quantitatively recovered.

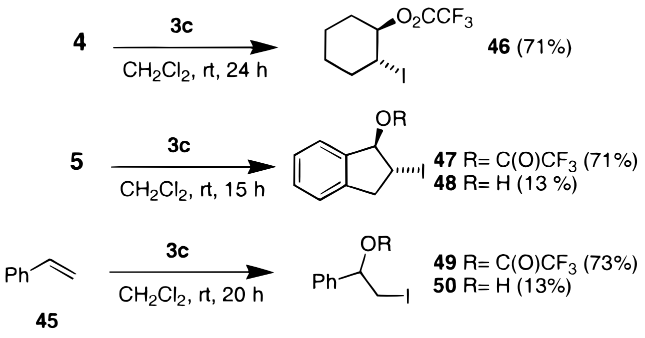
When comparing this polymer-supported technique with the solution variant using tetraethylammonium iodide and (diacetoxyiodo)benzene for the in situ preparation of $Et_4N\ I(OAc)_2$, we found that the isolated yield for the acetate is reduced as shown for alkene **7** (Scheme 3). Furthermore, the corresponding alcohol **44** was isolated as byproduct.

Scheme 3



In addition, 1,2-cohalogenation of alkenes with the trifluoroacetate containing polymer-supported reagent **3c** was investigated. Preliminary studies showed that cyclohexene **4**, indene **5**, and styrene **45** are transformed into the 2-iodo trifluoroacetates **46**, **47**, and **49** (Scheme 4). The simple workup procedure allows isolation of the labile products from which impurities **48** and **50** were removed by flash chromatography.

Scheme 4



In summary, we added a new family of electrophilic reagents to the rapidly growing class of polymer-supported reagents.[19] They efficiently promote haloacetoxylation of alkenes and alkoxyallenes under very mild conditions while alkynes are transformed into the corresponding iodoalkynes. They allow easy product isolation and hence are potentially useful for automated parallel synthesis.

Acknowledgment. This work was supported by the Fonds der Chemischen Industrie. Support by the Mary Stuart Rogers Foundation for K.S and T.O. is gratefully acknowledged.

Supporting Information Available: Spectra and detailed descriptions of experimental procedures. This material is available free of charge via the Internet at http://pubs.acs.org.

OL991149M

---

(15) (a) Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457−2483. (b) Negishi, E.; Copéret, C.; Ma., S.; Liou, S.-Y.; Liu, F. *Chem. Rev.* **1996**, *96*, 365−393. (c) Shibasaki, M.; Boden, C. O. J.; Kojima, A. *Tetrahedron* **1997**, *53*, 7371−7395. (d) Mitchell, T. N. *Synthesis* **1992**, 803−815. (e) Farina, V. *Pure Appl. Chem.* **1996**, *68*, 73−78.

(16) (a) Moriya, O.; Akawara, M.; Ueno, Y. *Chem Lett.* **1984**, 1437−1438. (b) Dulcère, J.-P.; Mihoubi, M. N.; Rodriguez, J. *J. Chem. Soc., Chem. Commun.* **1988**, 237−239.

(17) Alkynyl iodides can efficiently be transformed into the corresponding (*Z*)-vinyl iodides by diimine-promoted reduction: Mulzer, J., personal communication.

(18) Selected examples of 1-alkinyl halides in transition metal catalyzed cross coupling reactions: (a) Negishi, E.; Okukado, N.; King, A. O.; Van Horn, D. E.; Spiegel, B. L. *J. Am. Chem. Soc.* **1978**, *100*, 2254−2256. (b) Miyaura, N.; Yamada, K.; Suginome, H.; Suzuki, A. *J. Am. Chem. Soc.* **1985**, *107*, 972−980. (c) Shair, M. D.; Yoon, T.; Danishefsky, S. J. *J. Org. Chem.* **1994**, *59*, 3755−3757. (d) Yamanoi, S.; Matsumoto, T.; Suzuki, K. *Tetrahedron Lett.* **1999**, *40*, 2793−2796.

(19) Recently, polymer-supported (diacetoxyiodo)benzene was introduced by (a) Ley, S. V.; Thomas, A. W.; Finch, H. *J. Chem. Soc., Perkin Trans. 1* **1999**, 669−671. (b) Togo, H.; Nogami, G.; Yokoyama, M. *Synlett* **1998**, 534−536.