

- [10] A standard solution containing the same guest concentration was periodically checked with the same techniques employed for each experiment. To further show that the alcohol guests were included within the pores rather than on the crystal surface, the GC sample was filtered, washed with toluene, air dried, and then elemental microanalysis was performed to confirm the presence of alcohol.
- [11] *SAX Area-Detector Integration Program (SAINT)*, V4.024, Siemens Industrial Automation, Inc., Madison, WI, 1995.
- [12] *XPREF, V5.03*, is part of the program *SHELXTL Crystal Structure Determination*, Siemens Industrial Automation, Inc., Madison, WI, 1995.
- [13] *Siemens Area Detector ABSorption correction program (SADABS)*, G. Sheldrick, personal communication, 1996.

Stable Polymer-Bound Iodine Azide**

Andreas Kirschning,* Holger Monenschein, and Carsten Schmeck

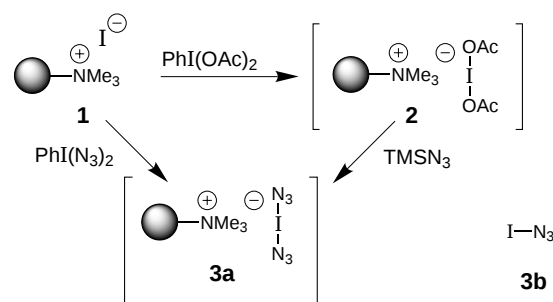
*Dedicated to Professor Armin de Meijere
on the occasion of his 60th birthday*

In addition to numerous methods for the syntheses of organic molecules on polymeric supports, there has been a recent upsurge in the interest in the use of polymer-bound reagents in organic chemistry.^[1] The intrinsic advantage of this hybrid solid-/solution-phase technique lies in the simple work-up and isolation of the reaction products combined with the flexibility of solution-phase chemistry. Furthermore, these reagents may be used in excess in order to drive the reaction to completion without making the isolation of the products more difficult. Although stoichiometric polymer-supported reagents have been employed in organic synthesis for many years, their application to the construction of small molecule libraries is a relative recent phenomenon. This can be ascribed to the fact that the number of readily available reagents of this type is still small. Important developments in this field are polymer-supported reductants,^[2] oxidants,^[3] solution-phase scavengers,^[4] chelating proton donors,^[5] carbodimide equivalents,^[6] or reagents that are capable of promoting C–C bond-forming reactions.^[7] However, polymer-bound reagents for 1,2-dihaloiodinations^[8, 9] of alkenes have not been described so far.^[10]

As an extension of our earlier work on ligand-transfer reactions from hypervalent iodine(III) reagents to halides in solution,^[11] we initiated a study on the development of the first stable electrophilic polymer-bound reagent that syntheti-

cally behaves like iodine azide (**3b**). Since the pioneering work of Hassner et al.^[12] azido-iodination of alkene double bonds has become a very useful procedure for introducing a nitrogen functionality into a carbon skeleton. Iodine azide (**3b**) has commonly been generated in situ from sodium azide and iodine chloride in polar solvents.^[12, 13] However, its explosive character is regarded to be a major disadvantage.

Our approach to iodine azide (**3b**) is based on the reaction of (diacetoxy)iodobenzene with polystyrene-bound iodide **1** in dichloromethane at room temperature, which presumably afforded polymer-bound di(acetyloxy)iodate(I) (**2**) (Scheme 1).^[14, 15] Treatment of **2** with trimethylsilylazide furnished a resin which synthetically acts like immobilized iodine azide (**3b**). However, extensive washing of the resin does not result in deactivation thus we propose that polymer-bound bis(azido)iodate(I) (**3a**) is the active species. Reagent



Scheme 1. Preparation of novel polymer-bound iodine azide. TMS = Me₃Si.

3a may also be generated by direct azido transfer after treatment of iodide **1** with (diazidoiodo)benzene. However, as PhI(N₃)₂ has to be prepared in situ from (diacetoxyiodo)benzene and trimethylsilylazide efficient azido transfer to **1** is hampered by the presence of trimethylsilyl acetate in solution. The IR spectrum of the new polymer **3a** shows a pair of strong bands at $\tilde{\nu}$ = 2010 and 1943 cm⁻¹, which confirm the presence of an azido group. It smoothly promotes azido-iodination of alkenes **4–18** to give the *anti* addition product (Table 1).^[16] Except for electron-deficient alkenes **5** and **11** and for methylenecyclopropane **17** (Table 1), sensitive β -iodo azides **19, 21–25**, and **27–33** are generated in good to excellent yield. They are conveniently purified by filtration and removal of the solvent.^[17] The regioselectivity of the 1,2-addition is governed by the more stable intermediate carbenium ion formed after electrophilic attack. Only when alkyl-substituted alkenes **15** and **16** were subjected to the azido-iodination conditions, were small amounts of the *anti*-Markovnikov 1,2-adducts formed. Remarkably, free hydroxy groups in allyl or homoallyl position, such as in alkenes **7, 13**, and **14**, are tolerated under the conditions employed. Addition to methylenecyclopropane **17** proceeded in a highly regioselective and stereoselective manner to furnish **32**. Rearrangement products which may have originated from the very stable intermediate cyclopropylmethyl cation^[18] were not isolated. The relative configuration of **32** was unequivocally assigned by nuclear Overhauser effect (NOE) experiments (Table 2). Finally, also 1,2-functionalization of carbohydrate-

[*] Dr. A. Kirschning, H. Monenschein
Institut für Organische Chemie der Technische Universität Clausthal
Leibnizstrasse 6, D-38678 Clausthal-Zellerfeld (Germany)
Fax: (+49) 5323-72-2858
E-mail: andreas.kirschning@tu-clausthal.de
Dr. C. Schmeck
Bayer AG, Business Group Pharma PH-R-CR, D-42096 Wuppertal
(Germany)

[**] This work was supported by the Fonds der Chemischen Industrie. We thank Bayer AG and particularly Dr. D. Häbich (Wuppertal) for financial and technical support.

Table 1. Azido-iodination of alkenes using polymer **3a**.

Alkene R ¹ , R ²	t, n(3) ^[a] [equiv]	Product	Yield ^[b] [%]
4 OMe, Me	16 h, 4	19	89 ^[c]
5 F, H	12 h, 4	20	38
6 H, Ph	20 h, 5	21	56 ^[d]
7 H, CH ₂ OH	2 d, 4	22	94
8	10 h, 5	23	74
9 Me, Me	12 h, 3	24	78
10 Bn, H	12 h, 3	25	74 ^[e]
11	14 h, 6	26	49
12	20 h, 5	27	78 ^[f]
13 OH	1.5 d, 6	28	98
14 CH ₂ OH	1.5 d, 6	29	91
15	2 d, 8	30	84 ^[g]
16	2 d, 8	31	86 ^[h]
17	2 d, 8	32	48
18	12 h, 4	33	82 ^[i]

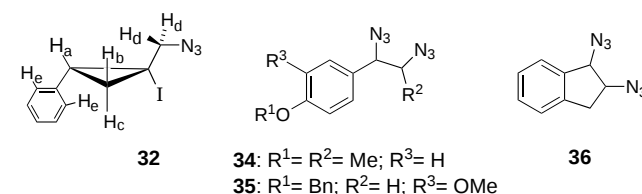
[a] The number of equivalents used refer to the amount of iodine in starting **1**. All reactions were carried out at room temperature. [b] Yield of isolated product after flash column chromatography. [c] Contains 30% of **34** (1:1 mixture). [d] Two stereoisomers (2:1). [e] Contains 5.3% of **35**. [f] Contains 11% of **36**. [g] Ratio of regioisomers 10:1. [h] Ratio of regioisomers 8:1. [i] Only β -galacto adduct shown; ratio of α -talo/ β -galacto isomers 1:9.

Table 2. NOE effects in **32**.

	rel. NOE effect [%] ^[a]
H _a /H _d	1.9, 2.1 (3.6)
H _a /H _c	2.0 (2.9)
H _e /H _c	4.4
H _e /H _d	— ^[b]
H _d /H _{d'}	16.0

[a] Values in parentheses refer to the reversed nuclear Overhauser experiment. [b] NOE not observed.

derived glycal **18** was achieved by the use of polymer **3a** to afford 2-deoxy-2-iodoglycosyl azides **33** with pronounced preference for the β -configured 1,2-diequatorial isomer.



Prolonged reaction times led to by-products **34–36** when styrenes **4** and **10** containing electron-donating aryl substituents as well as indene **12** were used as starting alkenes. Analytical support for the structures of these 1,2-diazides came from the analysis of the IR spectra, which revealed the presence of an azido functionality, and from the analysis of the chemical shifts of the former olefinic protons (δ = 4.32–4.81 and 3.39–4.26) and carbon atoms (δ = 67.4–70.7 and 61.4–58.3) in the ¹H and particularly the ¹³C NMR spectra, which clearly proved the absence of a C–I bond and the presence of two C–N bonds.

In conclusion, we have developed a new polymer-supported iodine azide source that can be employed for the azido-iodination of alkenes under very mild conditions and that allows easy product isolation. The reagent can be handled without the disadvantages associated with all known iodine azide reagents in solution. In addition, further chemical manipulations of the β -iodoazides allow the automated parallel synthesis of N-heterocycles.

Experimental Section

Preparation of 3a: A suspension of untreated polymer-bound iodide **1** (1 equiv; 2.9 mmol iodide per gram resin, Fluka) and PhI(OAc)₂ (1.8 equiv) in dry CH₂Cl₂ (2.5 mL mmol^{−1} iodide) under nitrogen was shaken at 300 rpm for 2 h at room temperature. During this time the brownish suspension was protected from light. The light yellow resin **2** was filtered, washed with dry CH₂Cl₂ (3 × ; 30 mL per gram resin), and dried in vacuo. A suspension of **2** (1 equiv with respect to **1**) protected from light in dry CH₂Cl₂ (4 mL mmol^{−1}) was treated with trimethylsilylazide (2.6 equiv) under nitrogen and was shaken at 300 rpm for 2 h. During this time the solution above the polymer had turned to red. Filtration and washing of the resin with CH₂Cl₂ (3 × ; 30 mL per gram resin) and drying in vacuo afforded the orange reagent **3a**. Resin **3a** can be prepared in this way on a 50 g scale. It does not tend to explode under mechanical stress or by heat (> 280 °C) or open flames. It can be stored for several weeks under nitrogen at −15 °C in the dark. The weight increase reproducibly served as an indicator for efficient ligand transfer onto polymer-bound iodide (−90% conversion with respect to theoretical iodide).

General procedure for the azido-iodination of alkenes: A mixture of alkene (1 equiv) and resin **3a** was shaken at 300 rpm under light protection in absolute CH_2Cl_2 (2 mL mmol⁻¹; the number of equivalents of **3a** is given in Table 1) at room temperature. Completion of the reaction was monitored by TLC (cyclohexane/ethyl acetate between 80/1 and 8/1) and was terminated by filtration. The resin was washed with CH_2Cl_2 (3 ×; 20 mL per gram resin) and the combined organic washings and filtrate were concentrated under reduced pressure. In some cases, for example for the separation of stereo- and regioisomers, additional purification of the products by flash chromatography on silica gel was necessary.

The structures of all addition products were elucidated by IR, ¹H NMR, and ¹³C NMR spectroscopy, and mass spectrometry (EI or DCI). ¹H, ¹³C-COSY and the distortionless enhancement by polarization transfer (DEPT) spectral editing technique were used to determine the regiochemistry of the 1,2-addition products. The ¹³C NMR shifts (in CDCl_3): δ = 58.0–64.7 ($\text{CH}_2\text{-N}_3$), 62.6–74.9 (CH-N_3), 62.8–63.8 (C-N_3 ; **28**, **29**), 7.8–8.4 ($\text{CH}_2\text{-I}$), 25.1–35.2 (CH-I), 16.1 (C-I ; **32**). Only the chemical ¹³C NMR shifts for the secondary iodide-bound carbon atoms in **7**, **13**, and **14** show a pronounced downfield shift (δ = 39.7–49.1) relative to all other examples. All new compounds gave either correct elementary analysis or were analyzed by high-resolution mass spectrometry in the CI-mode (reactant gas: isobutane).

Received: March 8, 1999 [Z13119IE]

German version: *Angew. Chem.* **1999**, *111*, 2720–2722

Keywords: alkenes • azides • electrophilic additions • polymer-supported reagents • synthetic methods

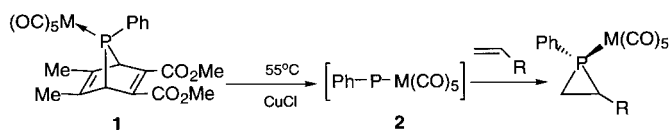
- [1] Reviews: S. J. Shuttleworth, S. M. Allin, P. K. Sharma, *Synthesis* **1998**, 1217–1239; S. W. Kaldor, M. G. Siegel, *Curr. Opin. Chem. Biol.* **1997**, *1*, 101–106; J. S. Früchtel, G. Jung, *Angew. Chem.* **1996**, *108*, 19–46; *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 17–42; P. Hodge, D. C. Sherrington in *Polymer-Supported Reaction in Organic Synthesis*, Wiley, New York, **1990**; P. Laszlo in *Preparative Chemistry using Supported Reagents*, Academic, San Diego, **1987**.
- [2] H. W. Gibson, F. C. Bailey, *J. Chem. Soc. Chem. Commun.* **1977**, 815–816; A. Nag, S. K. Sarkar, S. K. Palit, *Synth. Commun.* **1987**, *17*, 1007–1013.
- [3] B. Hinzen, S. V. Ley, *J. Chem. Soc., Perkin Trans. 1*, **1997**, 1907–1908; B. Tamani, M. Hattam, D. Mohadjer, *Polymer*, **1991**, *32*, 2666–2670; B. Tamani, N. Goudarzian, *Eur. Polym. J.* **1992**, *28*(9), 1035–1038.
- [4] R. J. Booth, J. C. Hodges, *J. Am. Chem. Soc.* **1997**, *119*, 4882–4886.
- [5] N. Krause, M. Mackenstedt, *Tetrahedron Lett.* **1998**, *39*, 9649–9650.
- [6] M. C. Desai, L. M. Stramiello, *Tetrahedron Lett.* **1993**, *34*, 7685–7688; M. Adamczyk, J. R. Fishpaugh, *Tetrahedron Lett.* **1996**, *37*, 4305–4308.
- [7] M. Bernhard, W. T. Ford, *J. Org. Chem.* **1983**, *48*, 326–332; I. Hughes, *Tetrahedron Lett.* **1996**, *37*, 7595–7598.
- [8] Reviews: E. Block, A. L. Schwan in *Comprehensive Organic Synthesis*, Vol. 4 (Eds.: B. M. Trost, I. Fleming, M. F. Semmelhack), Pergamon, Oxford, **1991**, pp. 329–362; J. Rodríguez, J.-P. Dulcère, *Synthesis* **1993**, 1177–1205.
- [9] M. Tiecco, L. Testaferri, A. Temperini, L. Bagnoli, F. Marini, C. Santi, *Synth. Commun.* **1998**, *28*, 2167–2179, and references therein.
- [10] G. A. Olah, X.-Y. Li, Q. Wang, G. K. S. Prakash, *Synthesis* **1993**, 693–699; B. Zajc, M. Zupan, *Tetrahedron* **1989**, *45*, 7869–7878.
- [11] A. Kirschning, C. Plumeier, L. Rose, *Chem. Commun.* **1998**, 33–34; A. Kirschning, A. Hashem, H. Monenschein, L. Rose, K.-U. Schöning, *J. Org. Chem.*, in press.
- [12] F. W. Fowler, A. Hassner, L. A. Levy, *J. Am. Chem. Soc.* **1967**, *89*, 2077–2082; A. Hassner, *Acc. Chem. Res.* **1971**, *4*, 9–16; A. Hassner, F. W. Fowler, *J. Org. Chem.* **1968**, *33*, 2686–2691.
- [13] G. O. Olah, Q. Wang, X.-Y. Li, G. K. S. Prakash, *Synlett* **1990**, 487–489.
- [14] The structures of iodate(i) complexes **2** and **3a** are proposed with reference to the analogous tetraalkylammonium salts: G. Doleschall, G. Tóth, *Tetrahedron* **1980**, *36*, 1649–1665; C. Szántay, G. Blaskó, M. Bárczai-Beke, P. Péchy, G. Dörmei, *Tetrahedron Lett.* **1980**, *21*, 3509–3512.

- [15] Polymer-bound iodate(i) complex **2** is also very useful for promoting iodoacetoxylation of alkenes: A. Kirschning, H. Monenschein, M. Jesberger, unpublished results.
- [16] Most β -iodoazides described in Table 1 were conveniently prepared by means of automated parallel synthesis.
- [17] In fact, in some cases we observed that aqueous work-up led to back reaction of the β -iodoazides to the starting alkenes, an obstacle which is completely avoided when employing our new polymer-bound reagent **3a**.
- [18] K. B. Wiberg, A. J. Ashen, *J. Am. Chem. Soc.* **1968**, *90*, 63–74.

Olefin Cycloadditions of the Electrophilic Phosphinidene Complex $[\text{iPr}_2\text{N-P=Fe}(\text{CO})_4]^*$

Jan B. M. Wit, Gerno T. van Eijkel, Franciscus J. J. de Kanter, Marius Schakel, Andreas W. Ehlers, Martin Lutz, Anthony L. Spek, and Koop Lammertsma*

Electrophilic phosphinidene complexes are known to display carbene-like properties.^[1] Through the pioneering work of Mathey et al.^[2] in the early 1980s these transient species became accessible through thermal decomposition of phosphinidene precursor **1** (Scheme 1). Even today this is



Scheme 1.

virtually the only route to $[\text{RPM}(\text{CO})_5]$ (**2**) ($\text{M} = \text{W}, \text{Mo}, \text{Cr}$; $\text{R} = \text{Ph}$),^[1a, 3] whereas the number of stable, isolable nucleophilic phosphinidene complexes continues to grow steadily.^[4] Unfortunately, access to **2** is hampered by the limited thermal window for cheletropic elimination from **1** (100–130 °C or ca. 55 °C in the presence CuCl) and by the laborious synthesis of **1**. In view of the rich chemistry of electrophilic phosphinidenes we sought alternative synthetic pathways.

Our attention was drawn to the work of King et al. in the late 1980s,^[5] in which dichlorophosphanes and Collman's salt were used to generate phosphorus–iron clusters such as **6** below 0 °C (Scheme 2). The formation of **6** was explained

- [*] Prof. Dr. K. Lammertsma, J. B. M. Wit, G. T. van Eijkel, Dr. F. J. J. de Kanter, Dr. M. Schakel, Dr. A. W. Ehlers
Department of Organic and Inorganic Chemistry
Faculty of Sciences, Vrije Universiteit
De Boelelaan 1083, NL-1081 HV Amsterdam (The Netherlands)
Fax: (+31)-20-4447488
E-mail: lammert@chem.vu.nl
Dr. M. Lutz, Dr. A. L. Spek
Bijvoet Center for Biomolecular Research
Crystal and Structural Chemistry
Utrecht University (The Netherlands)
- [**] This work was supported by the Council for Chemical Sciences of the Netherlands Organization for Scientific Research (CW-NOW).