

Experimental Section

Full experimental details are in the Supporting Information. A representative procedure is as follows: to a flask purged with argon, a solution of [Fe(acac)₃] in toluene (0.025 M, 0.025 mmol, 1 mL), toluene (4 mL), and a substrate **1b** (0.5 mmol) were introduced. The flask was cooled to -40° C and a solution of butyllithium in hexane (1.5 M, 1.5 mmol) was added to the mixture. Reaction temperature was immediately raised to -20° C and the mixture was stirred at -20° C for 2 h. The reaction was quenched with 1N HCl. After the conventional workup and purification by chromatography on silica gel, a pure product **2b** was obtained in 97 % yield.

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- B. J. Wakefield in Organolithium Methods (Eds.: A. R. Katritzky, O. Meth-Cohn, C. W. Rees), Academic Press, London, 1988.
- [2] Zr: a) E. Negishi, T. Takahashi, Synthesis 1988, 1–19; Ti: b) D. C. Brown, S. A. Nichols, A. B. Gilpin, D. W. Thompson, J. Org. Chem. 1979, 44, 3457–3461; Cu: c) J. F. Normant, A. Alexakis, Synthesis 1981, 841–870; Zn: d) F. Bernadou, L. Miginiac, Tetrahedron Lett. 1976, 3083–3086; e) M. Bellassoued, Y. Frangin, Synthesis 1978, 838–840; Ni: f) B. B. Snider, R. S. E. Conn, M. Karras, Tetrahedron Lett. 1979, 1679–1682; See also: g) P. Knochel in Comprehensive Organic Synthesis, Vol. 4 (Eds.: B. M. Trost, I. Fleming, M. F. Semmelhack), Pergamon, Oxford, 1991, pp. 865–911.
- [3] a) J. E. Mulvaney, Z. G. Gardlund, S. L. Gardlund, J. Am. Chem. Soc. 1963, 85, 3897; b) J. E. Mulvaney, D. J. Newton, J. Org. Chem. 1969, 34, 1936–1939; c) W. Bauer, M. Feigel, G. Müller, P. von R. Schleyer, J. Am. Chem. Soc. 1988, 110, 6033–6046; d) L.-I. Olsson, A. Claesson, Tetrahedron Lett. 1974, 2161–2162.
- [4] In the absence of a catalyst, a complex mixture without a normal product 2b was produced.
- [5] a) M. Tamura, J. K. Kochi, J. Am. Chem. Soc. 1971, 93, 1487–1489;
 b) S. M. Neumann, J. K. Kochi, J. Org. Chem. 1975, 40, 599–606;
 c) R. S. Smith, J. K. Kochi, J. Org. Chem. 1976, 41, 502–509.
- [6] Conditions for all reactions reported here are not fully optimized. A sufficient amount of butyllithium per iron catalyst (5 mol %) seems to be required during the reaction for the successful carbolithiation. Therefore, 3 equivalents used in reactions are a large enough amount for the present carbolithiation, and, indeed, a reaction of 1b with 2 equivalents of butyllithium gave essentially the same result (95% of 2b, cf. Table 1, entry 6).
- [7] This product was possibly obtained by the addition of butyllithium to pent-1-en-3-yne, produced by the β-elimination of phenylpropanol from 1a. a) A. A. Petrov, V. A. Kormer, T. V. Yakovleva, *Zh. Obshch. Khim.* 1960, *30*, 2238; b) A. A. Petrov, Yu. I. Porfir'eva, V. A. Kormer, *Zh. Obshch. Khim.* 1961, *31*, 1518.
- [8] M. Nakamura, A. Hirai, E. Nakamura, J. Am. Chem. Soc. 2000, 122, 978–979.
- [9] BuMgBr was prepared in diethyl ether, and most of the solvent was replaced with toluene before use.

- [10] Only allylmagnesium bromide successfully added to 1b (in Et₂O at RT for 7 h using 20 mol % of [Fe(acac)₃]) and the corresponding allylated product was obtained in quantitative yield.
- [11] The produced vinyl anion seems to be unstable at room temperature. Yield of **2b** and its deuterium content were decreased to 90% and 82%-D, respectively when the reaction mixture was kept at ambient temperature for 3 h before quenching with DCl/D₂O, the reaction was conducted under the same conditions as in Equation (5).
- [12] Ethyllithium and hexyllithium were also added to 1b to afford alkenes in high yields (Et: 96%, Hex: 92%).

Radical Azidonation of Benzylic Positions with Iodonium Azide**

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We recently reported a procedure for the conversion of benzyloxy alcohols like **1** into benzylidene derivatives like **2** with *N*-iodosuccinimide (NIS) and light (Scheme 1).^[1] During



Scheme 1. The NIS-promoted transformation of benzyloxy alcohols into benzylidene derivatives and the effect of NaN_3 addition. Bn = benzyl.

the investigation of this reaction we noticed that **1** was transformed with excess NaN_3 very rapidly into a variety of products of which many had, according to mass spectrometry, one to three hydrogen atoms replaced with azido groups. When the analogous reaction was carried out on benzyl ethyl ether **3** [Eq. (1), light substituted with heat to avoid decomposition of azides] the monoazido derivative **4** was isolated in 65% yield together with small amounts of the by-products **5** and **6**.^[2]



Since this azidonation reaction appeared faster than the benzylidene derivative formation promoted by NIS alone and since the red color of the reaction mixture indicated that IN_3 was present, it was suggested that iodine azide was the reagent

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causing the reaction. Indeed if IN_3 was used, **3** could be transformed to **4** in 75% yield (Scheme 2).



Scheme 2. Reaction of various benzyl ethers with IN₃ in MeCN.

Some related chemistry has been reported in a series of papers by Magnus et al. They used PhIO/trimethylsilylazide (TMSN₃) at low temperature to azidonate a carbon atom α to amino and enol ether functionalities.^[3] It has also been reported that PhI(OAc)₂/NaN₃ can be used to generate carbon-centered radicals.^[4] Hassner et al. have pioneered and extensively studied the addition of IN₃ and other haloazides to alkenes normally follows an ionic mechanism, in certain cases, in particular when ClN₃ or BrN₃ is the reagent, the products of a radical addition to the alkene are obtained.^[5b] However, substitution of activated hydrogens by azido groups with IN₃ has not been carried out nor has the introduction of an azido group in a benzylic position.

As can be seen from Scheme 2 the reaction is highly efficient^[6] when carried out in refluxing acetonitrile: The yields of azides (Table 1) were 74–98%. The transformations $9 \rightarrow 10$, $11 \rightarrow 12$, and $13 \rightarrow 14$ show that the reaction tolerates other functionalities such as ester, epoxide, or acetal units. The reaction of 13 is more sluggish than the others requiring more reagent and time. The reason is presumably that the acetal functionality makes the benzylic position less reactive

Table 1. Analytical data of the azido compounds 4, 8, 10, 12, and 14.^[a] **4**: ¹H NMR: $\delta = 7.25 - 7.41$ (m, 5H), 5.38 (s, 1H), 3.85 (dqv, 1H, J = 7.0, 9.5 Hz), 3.58 (dqv, 1 H, J = 7.0, 9.5 Hz), 1.19–1.24 (t, 3 H, J = 7.0 Hz) 8: ¹H NMR: $\delta = 7.22 - 7.38$ (m, 5H), 5.24 (s, 1H), 3.43 (s, 3H) **10**: ¹H NMR (diasterometric ratio 1:1): $\delta = 7.25 - 7.50$ (m, 10H), 5.59 (s, 1 H), 5.42 (s, 1 H), 4.93 (m, 2 H), 3.82 (m, 2 H), 2.11 (s, 3 H), 2.30-1.90 (m, 4H), 1.82 (s, 3H), 1.68-1.84 (m, 4H), 1.25-1.49 (m, 8H); MS (EI): m/z: calcd (C15H19N3O3+Na) 312.1324, found 312.1322 12: ¹H NMR (diasterometric ratio 1:1): $\delta = 7.39 - 7.53$ (m, 10H), 5.72 (s, 1 H,), 5.70 (s, 1 H), 5.68 (s, 1 H), 5.67 (s, 1 H), 4.51 (t, 1 H, J = 4.4 Hz), 4.49 (t, 1 H, J = 4.4 Hz, 4.05 (br s, 2H), 3.72 (d, 2H, J = 4.4), 3.70 (d, 2H, J = 4.4), 3.48 (dd, 2H, J=3.7), 3.28 (br d, 1H, J=3.7), 3.16 (br d, 1H, J=3.7); MS (EI): m/z: calcd (C13H13N3O4+Na) 298.0804, found 298.0804 14: ¹H NMR (diasterometric ratio 1:1):^[b] $\delta = 7.40 - 7.50$ (m, 5H, 5H'), 5.64 (s, 1H'), 5.55 (s, 1H), 5.47 (d, 1H, J=3.50 Hz), 5.08 (d, 1H', J=3.50 Hz), 5.01 (dd, 1 H, J = 3.50, J = 8.1 Hz), 4.91 (dd, 1 H', J = 3.50 Hz, J = 7.7 Hz), 4.31-4.46 (m, 1H, 2H'), 4.17-4.25 (m, 1H, 1H'), 4.09 (d, 1H'), 3.99 (d, 1H, J = 13.6 Hz), 3.83 (dd, 1 H, J = 13.6, 2.9 Hz), 2.15 (s, 3 H), 2.03 (s, 3 H'), 1.56 (s, 3H), 1.53 (s, 3H'), 1.37 (s, 3H'), 1.20 (s, 3H); MS (EI): m/z: calcd (C17H21N3O6+Na) 386.1328, found 386.1329

[a] 200 MHz for all ¹H NMR spectra, in CDCl₃. [b] Primed protons refer to the second diasteromer.

because it is more electron withdrawing than a regular ether unit.

Strong support was found for the reaction to follow a radical mechanism: Compound 8 was not formed when 7 was allowed to react in the presence of the radical trap N-tertbutyl- α -phenylnitrone (Scheme 2).^[8] Substrate 7 and most of the radical trap (2 equiv) were recovered unconverted, which shows that capture of a small amount of radicals prevented the reaction. A certain electron-donating capacity is necessary at the benzylic position for the reaction to occur: When an ester is attached to this position as in benzyl benzoate no reaction is observed. Benzyl alcohol, on the other hand, is oxidized to benzaldehyde under the reaction conditions. Based on these results we suggest the following reaction course: Homolysis of IN₃ results in an azide radical that abstracts a hydrogen atom from the substrate to form a benzylic radical. This radical is oxidized by IN₃ or I₂ to a benzylic cation that combines with the azide ion to form the product.^[9]

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- a) J. Madsen, M. Bols, Angew. Chem. 1998, 110, 3348-3350; Angew. Chem. Int. Ed. 1998, 37, 3177-3178; b) J. Madsen, C. Viuf, M. Bols, Chem. Eur. J. 2000, 6, 1140-1146.
- [2] The by-products **5** and **6** were presumably formed from **4** through lightinduced decomposition of the latter to a nitrene followed by H and Ph migration, respectively.
- [3] a) P. Magnus, J. Lacour, J. Am. Chem. Soc. 1992, 114, 767-769; b) P. Magnus, J. Lacour, W. Weber, J. Am. Chem. Soc. 1993, 115, 9347-9348;
 c) P. Magnus, J. Lacour, P. A. Evans, P. Rigollier, H. Tobler, J. Am. Chem. Soc. 1998, 120, 12486-12499; d) P. Magnus, J. Lacour, W. Weber, Synthesis 1998, 547-551.
- [4] F. Fontana, F. Minisci, Y. M. Yan, L. Zhao, *Tetrahedron Lett.* 1993, 34, 2517–2520.
- [5] a) A. Hassner, Methoden Org. Chem. (Houben-Weyl) 4th ed. 1952-,
 Vol. E16a, 1990, pp. 1243-1290; b) A. Hassner, Acc. Chem. Res. 1971,
 4, 9-16; c) F. W. Fowler, A. Hassner, L. A. Levy, J. Am. Chem. Soc.
 1967, 89, 2077-2082.
- [6] General reaction conditions: A solution of $IN_3^{[7]}$ was prepared by mixing ICl (101 mg, 0.6 mmol) in MeCN (2 mL) with NaN₃ (107 mg,

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1.4 mmol) in MeCN (3 mL) at -10° C.^[5c] After 15 min the cooling bath was removed, and the ether compound (0.3 mmol) was added. The mixture was refluxed for between 0.4 and 5 h. Then CH₂Cl₂ (25 mL) was added, and the mixture was washed with 5% Na₂S₂O₃ solution (20 mL). The dried (MgSO₄) and evaporated organic phase was purified by flash chromatography.

- [7] IN_3 is an explosive substance, particularly as a solid (see ref. [5a]). We encountered no problems, but took care to remove IN_3 after the reaction by washing with $Na_2S_2O_3$ solution.
- [8] K. Yelekci, X. Lu, R. B. Silverman, J. Am. Chem. Soc. 1989, 111, 1138– 1140.
- [9] We have also investigated some amine substrates in order to compare IN_3 with the Magnus reagent PhIO/TMSN₃. Reaction of *N*,*N*-dimethylaniline with IN_3 gave several products, the major one being 4-iodo-*N*,*N*-dimethylaniline, while benzyldimethylamine led to a number of very labile products that on decomposition gave benzaldehyde and benzylmethylamine. This is in agreement with the formation of α -azidoamines like those obtained in the Magnus reaction. Magnus et al. could isolate such α -azidoamines by using nonaqeous work-up, but they are clearly much less stable than the α -azidoethers.

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