Russian Journal of Organic Chemistry, Vol. 39, No. 3, 2003, pp. 403–407. Translated from Zhurnal Organicheskoi Khimii, Vol. 39, No. 3, 2003, pp. 433–436.

Dedicated to Full Member of the Russian Academy of Sciences I.P. Beletskaya on Her Jubilee

New Synthesis of β-Iodostyrenes

A. V. Shastin[1], V. N. Korotchenko[2], G. N. Varseev[2], V. G. Nenaidenko[2], and E. S. Balenkova[2]

[1] *Institute of Chemical Physics Problems, Russian Academy of Sciences, Chernogolovka, Moscow oblast, Russia*

[2] *Faculty of Chemistry, Moscow State University, Vorob'evy gory, Moscow, 119992 Russia e-mail: nen@acylium.chem.msu.ru*

Received November 6, 2002

Abstract—A general procedure for the synthesis of β-iodostyrenes is proposed. Aromatic aldehyde and ketone hydrazones are converted into the corresponding β-iodostyrenes by treatment with CHI_3 in the presence of a catalytic amount of CuCl.

Iodoalkenes are important reagents in palladium-catalyzed cross-coupling reactions [1]. Classical methods for preparation of iodoalkenes from carbonyl compounds are those based on the Wittig reaction [2] and reductive coupling of aldehydes and ketones with iodoform using $CrCl_2$ as reducing agent [3, 4]. These reactions usually lead to formation of iodoalkenes as mixtures of *E* and *Z* isomers. Stereochemically pure (*E*)- or (*Z*)-iodoalkenes are obtained via multistep procedures starting from acetylenes and involving vinylsilanes [5–7] or vinylboronic acids [8] as intermediates. In addition, (*E*)- or (*Z*)-iodoalkenes are available via oxidative halodecarboxylation of α,β-unsaturated carboxylic acids [9], elimination of hydrogen iodide from geminal diiodoalkanes [10], and exchange reaction of vinyl bromides with iodide ion [11]. The above procedures are generally laborious, and they utilize expensive reagents and anhydrous solvents.

We previously discovered a new catalytic olefination of carbonyl compounds [12, 13]. Hydrazones derived from aromatic aldehydes and ketones were found to react with halogenated compounds in the presence of a copper catalyst, affording substituted styrenes [12–16]. The corresponding aldehyde or ketone azines were formed as by-products. On the basis of the discovered reaction, we have developed radically new methods for olefination of carbonyl compounds with the use of CCl_4 [12–14], $CHBr_3$ [14, 15], CBr_4 [14, 16], and also CF_3CCl_3 and $CF_2ClCFCl_2$ [17] as C_1 and C_2 building blocks. The use of iodoform as C_1 synthon is expected to extend the scope of application of the catalytic olefination reaction. According to the general scheme, the reaction could lead to iodoalkenes [14]. The present communication reports on the results of our study of olefination of aromatic aldehyde and ketone hydrazones with CHI_3 as C_1 building block.

The activity of copper catalyst is strongly affected by the nature of solvent and base which are capable of forming complexes with copper [12, 13, 17]. Therefore, in the first step of our study we tried to optimize conditions for the reaction of iodoform with hydrazones **Ia**–**Ii**. The solvent and base effects were examined using 4-chlorobenzaldehyde hydrazone (**Ia**) as an example. The catalyst (CuCl) was taken in an amount of 10 mol %, and the amount of iodoform was 1.5 equiv with respect to hydrazone **Ia**. The following solvents were used: DMSO, ethanol, and acetonitrile, and the bases were aqueous ammonia, ethylenediamine, triethylamine *N*,*N*,*N*′,*N*′-tetramethylethylenediamine, K_2CO_3, and diazabicycloundecane (DBU). The greatest yield of the target β-iodostyrene (**IIa**) (40%) was obtained in DMSO as solvent with ammonia as base. Standard olefination conditions imply a 3–5-fold excess of polyhaloalkane [12–14]. In the case of iodoform, the use of such a large excess of the reagent was found to be unreasonable: The yield of β-iodostyrene did not change on raising the amount of CHI_3 from 1.5 to 5 equiv. However, in the reaction with equimolar amounts of the reactants, the

1070-4280/03/3903-0403 $25.00 © 2003 MAIK "Nauka / Interperiodica"

Synthesis of β-iodostyrenes **IIa**–**IIi**

Initial hydrazone	Yield of **II**, %	*E*:*Z* ratio[a]	Yield of **III**, %	Overall yield (**II** + **III**), %
Ia	40	4.2:1	55	95
Ib	28	3:1	58	86
Ic	21	2.8:1	69	90
Id	15	3.7:1	77	92
Ie	17	2:1	28	45
If	23	5.2:1	41	64
Ig	26	1.6:1	65	91
Ih	24	1.3:1	47	71
Ii	16	1.5:1	40	56

[a] According to the ^{1}H NMR data.

yield of iodostyrene **IIa** was considerably lower. Thus 1.5 equiv was the optimal amount of iodoform under the given conditions.

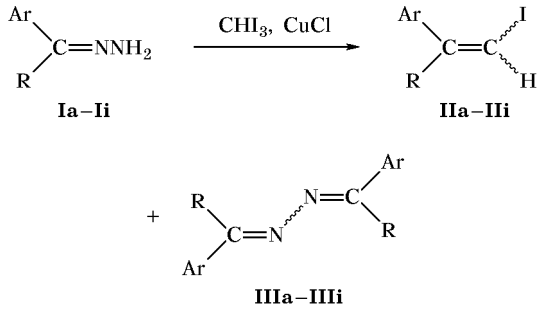
We encountered some problems while isolating the target products: it was difficult to purify iodoalkenes **IIa**–**IIi** from excess iodoform. Therefore, efforts were made to develop a procedure for purification of iodostyrenes. We have found that excess iodoform can be removed by treatment of the reaction mixture with hydrazine hydrate. Iodoform is thus reduced to methylene iodide and methyl iodide which are readily separated by simple distillation. The formation of methylene iodide and methyl iodide was proved by ^{1}H NMR spectroscopy. Presumably, this process is of general character, so that we plan to examine the reaction of polyhalogenated alkanes with hydrazine in the presence of copper catalyst.

$$CHI_3 \xrightarrow{N_2H_4\cdot H_2O,\ CuCl} CH_2I_2 + CH_3I + N_2$$

Hydrazones **Ia**–**Ii** derived from aromatic aldehydes and ketones were brought into reaction with iodoform under the optimal conditions found (Scheme 1).

Iodoalkenes **IIa**–**IIi** are formed in moderate yields (15–40%). The reaction is stereoselective, and it gives mainly the corresponding *E* isomers. In all cases, aldehyde and ketone azines **IIIa**–**IIIi** were isolated (see table). Our results show that the nature and position of substituent in the aromatic ring affects the yield of the final 2-iodostyrene, as well as the isomer ratio. The reactions with hydrazones derived from ketones are characterized by lower stereoselectivity than the reactions with aldehyde hydrazones. The presence of an *ortho*-substituent favors predominant formation of the corresponding *E* isomer. The steric

Scheme 1.



I–**III**, R = H, Ar = 4-ClC_6H_4 (**a**); R = H, Ar = 4-MeC_6H_4 (**b**); R = H, Ar = 2,6-$Cl_2C_6H_3$ (**c**); R = H, Ar = 4-$MeOC_6H_4$ (**d**); R = H, Ar = 4-$NO_2C_6H_4$ (**e**); R = H, Ar = 2-BrC_6H_4 (**f**); R = Me, Ar = 4-$NO_2C_6H_4$ (**g**); R = Me, Ar = 4-ClC_6H_4 (**h**); R = Me, Ar = 4-MeC_6H_4 (**i**).

configuration of iodostyrenes **IIg**–**IIi** was established on the basis of chemical shifts of the olefinic protons and their coupling constants with the methyl group protons; these data were compared with the corresponding parameters of analogous bromo derivatives whose structure was determined previously [14].

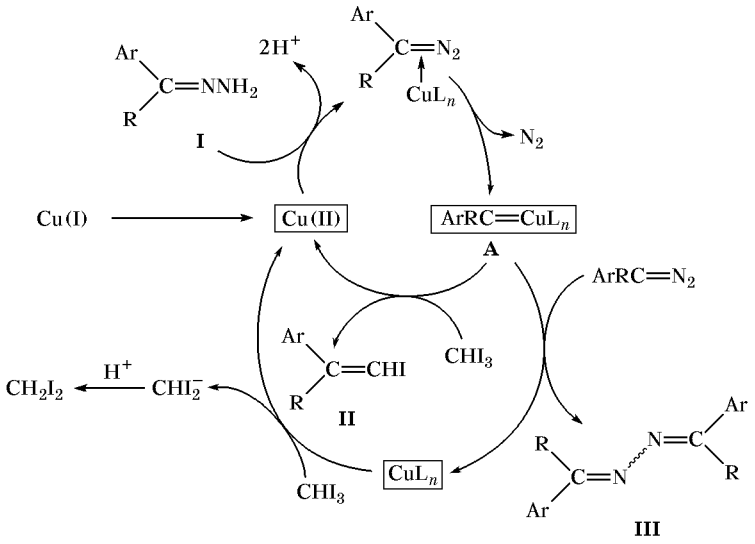
The obtained results are consistent with the mechanism proposed by us previously for catalytic olefination [12, 17] (Scheme 2). In the initial stage, copper(I) is oxidized to copper(II) with iodoform. Copper(II) reacts with hydrazone **I**, yielding copper–carbene complex **A** through intermediate formation of the corresponding diazoalkane. Complex **A** is analogous to metal–carbene complexes described in [18–20] and is the key intermediate in the reaction under study. Its subsequent reaction with CHI_3 gives β-iodostyrene **II** and regenerates Cu(II) which is recovered to the catalytic cycle. Concurrently, complex **A** reacts with diazoalkane to form the corresponding aldehyde or ketone azine **III**. Analysis of Scheme 2 allows us to explain relatively low yields of the target iodoalkenes. Hydrazones are oxidized by the action of Cu(II) which is also capable of oxidizing iodide ions to molecular iodine [21]:

$$Cu^{2+} + 3I^- \longrightarrow CuI + I_2$$

The yields of alkenes **IIa**–**IIi** and azines **IIIa**–**IIIi** as products of the catalytic reaction are reduced as a result of the occurrence of side hydrazone iodination process [22].

Thus we have developed a new general procedure for the synthesis of 2-iodostyrenes, which may be regarded as an alternative to the existing methods.

Scheme 2.



R = H, Me.

Advantages of the new procedure are its simplicity, accessibility of initial reactants, and mild reaction conditions.

EXPERIMENTAL

The IR spectra were recorded on a UR-20 spectrometer from samples prepared as thin films (liquid products) or suspensions in mineral oil (crystalline products). The ^{1}H and ^{13}C NMR spectra were obtained on a Varian VXR-400 instrument (400 and 100 MHz, respectively) using chloroform-*d* as solvent and tetramethylsilane as internal reference. Thin-layer chromatography was performed on Merck 60 F254 plates; silica gel (63–200 mesh, Merck) was used for column chromatography. Aromatic aldehyde and ketone hydrazones **Ia**–**Ii** were prepared by standard procedure from the corresponding commercially available aldehydes and ketones.

β-Iodostyrenes IIa–IIi (*general procedure*). To a solution of 5 mmol of freshly prepared hydrazone **Ia**–**Ii** in 5 ml of DMSO we added 1.2 ml of concentrated aqueous ammonia and 50 mg (0.5 mmol) of freshly purified copper(I) chloride [12]. A solution of 2.95 g (7.5 mmol) of iododform in 5 ml of DMSO was added dropwise over a period of 10 min, maintaining the mixture at room temperature. The mixture was stirred for 24 h, and 1 ml (20 mmol) of hydrazine hydrate was added dropwise (on cooling with a water bath) to remove excess iodoform. The mixture was stirred for 30 min at room temperature, treated with 500 ml of 0.1 M hydrochloric acid, and extracted with methylene chloride (3 × 50 ml). The combined extracts were dried over sodium sulfate, the solvent was evaporated, and the residue was separated by column chromatography using hexane as eluent. We failed to separate *E* and *Z* isomers of **II** in such a way.

1-(2-Iodovinyl)-4-chlorobenzene (IIa) [9]. Mixture of *E* and *Z* isomers (4.2 : 1), colorless crystals, R_f 0.6 (hexane). ^{1}H NMR spectrum, δ, ppm: *E* isomer: 6.74 d (1H, CHI, *J* = 14.9 Hz), 7.12 d (2H, H_{arom}, *J* = 8.5 Hz), 7.19 d (2H, H_{arom}, *J* = 8.5 Hz), 7.27 d (1H, CH=, *J* = 14.9 Hz); *Z* isomer: 6.51 d (1H, CHI, *J* = 8.8 Hz), 7.18 d (1H, CH=, *J* = 8.8 Hz), 7.25 d (2H, H_{arom}, *J* = 8.5 Hz), 7.47 d (2H, H_{arom}, *J* = 8.5 Hz).

1-(2-Iodovinyl)-4-methylbenzene (IIb) [9]. Mixture of *E* and *Z* isomers (3 : 1), colorless oily substance, R_f 0.65 (hexane). ^{1}H NMR spectrum, δ, ppm: *E* isomer: 2.33 s (3H, CH_3), 6.72 d (1H, CHI, *J* = 14.9 Hz), 7.11 d (2H, H_{arom}, *J* = 8.5 Hz), 7.18 d (2H, H_{arom}, *J* = 8.5 Hz), 7.38 d (1H, CHI, *J* = 14.9 Hz); *Z* isomer: 2.34 s (3H, CH_3), 6.48 d (1H, CHI, *J* = 8.8 Hz), 7.18 d (2H, H_{arom}, *J* = 8.5 Hz), 7.27 d (2H, H_{arom}, *J* = 8.5 Hz), 7.53 d (1H, CHI, *J* = 8.8 Hz).

1-(2-Iodovinyl)-2,6-dichlorobenzene (IIc). Mixture of *E* and *Z* isomers (2.8 : 1), colorless crystals, R_f = 0.6 (hexane). IR spectrum, ν, cm^{-1}: 1620 (C=C). ^{1}H NMR spectrum, δ, ppm: *E* isomer: 7.05 d (1H, CHI, *J* = 15.1 Hz), 7.30 d (2H, H_{arom}, *J* = 7.9 Hz), 7.35 t (1H, H_{arom}, *J* = 7.9 Hz), 7.47 d (1H, CHI, *J* = 15.1 Hz); *Z* isomer: 6.96 d (1H, CHI, *J* = 8.5 Hz), 7.30 d (2H, H_{arom}, *J* = 7.9 Hz), 7.35 t (1H, H_{arom}, *J* = 7.9 Hz), signals of the other protons are overlapped

by those of the major isomer. ^{13}C NMR spectrum (mixture of isomers), δ_C, ppm: 86.19 (CHI, *E* isomer), 89.59 (CHI, *Z* isomer), 127.93, 128.57, 128.83, 129.44, 133.77, 138.25. Found, %: C 32.01; H 1.65. $C_8H_5Cl_2I$. Calculated, %: C 32.14; H 1.69.

1-(2-Iodovinyl)-4-methoxybenzene (IId) [9]. Mixture of *E* and *Z* isomers (3.7 : 1), colorless oily substance, R_f 0.25 (hexane). ^1H NMR spectrum, δ, ppm: *E* isomer: 3.72 s (3H, CH_3), 6.51 d (1H, CHI, *J* = 14.9 Hz), 6.70 d (2H, H_{arom}, *J* = 8.2 Hz), 7.11 d (2H, H_{arom}, *J* = 8.2 Hz), 7.23 d (1H, CH=, *J* = 14.9 Hz); *Z* isomer: 3.70 s (3H, CH_3), the other signals are overlapped by those of the major isomer.

1-(2-Iodovinyl)-4-nitrobenzene (IIe). Mixture of *E* and *Z* isomers (2 : 1), yellow crystals, R_f 0.5 (hexane–CH_2Cl_2, 1 : 1). IR spectrum, ν, cm^{-1}: 1620 (C=C). ^1H NMR spectrum, δ, ppm: *E* isomer: 7.12 d (1H, CHI, *J* = 14.9 Hz), 7.37 d (2H, H_{arom}, *J* = 8.9 Hz), 7.45 d (1H, CH=, *J* = 14.9 Hz), 8.13 d (2H, H_{arom}, *J* = 8.9 Hz); *Z* isomer: 6.86 d (1H, CHI, *J* = 8.8 Hz), 7.30 d (1H, CH=, *J* = 8.8 Hz), signals of the aromatic protons are overlapped by those of the major isomer. ^{13}C NMR spectrum (mixture of isomers), δ_C, ppm: 86.42 (CHI), 123.74, 126.94, 142.28, 143.37, 144.50. Found, %: C 34.67; H 2.12. $C_8H_6INO_2$. Calculated, %: C 34.93; H 2.20.

1-(2-Iodovinyl)-2-bromobenzene (IIf). Mixture of *E* and *Z* isomers (5.2 : 1), colorless crystals, R_f 0.4 (hexane). IR spectrum, ν, cm^{-1}: 1610 (C=C). ^1H NMR spectrum, δ, ppm: *E* isomer: 6.84 d (1H, CHI, *J* = 14.9 Hz), 7.13 t (1H, H_{arom}, *J* = 7.9 Hz), 7.26 t (1H, H_{arom}, *J* = 7.9 Hz), 7.36 d (1H, H_{arom}, *J* = 7.9 Hz), 7.52 d (1H, H_{arom}, *J* = 7.9 Hz), 7.74 d (1H, CH=, *J* = 14.9 Hz); *Z* isomer: 6.72 d (1H, CHI, *J* = 8.5 Hz), signals of the other protons are overlapped by those of the major isomer. ^{13}C NMR spectrum (mixture of isomers), δ_C, ppm: 79.82 (CHI), 83.62 (CHI), 122.34, 127.01, 127.56, 129.56, 137.54, 143.70. Found, %: C 30.86; H 1.88. C_8H_6BrI. Calculated, %: C 31.10; H 1.96.

1-(2-Iodo-1-methylvinyl)-4-nitrobenzene (IIg). Mixture of *E* and *Z* isomers (1.6 : 1), yellow oily substance, R_f 0.6 (hexane–CH_2Cl_2, 1 : 1). IR spectrum, ν, cm^{-1}: 1615 (C=C). ^1H NMR spectrum, δ, ppm: *E* isomer: 2.24 d (3H, CH_3, *J* = 1.2 Hz), 6.73 q (1H, CHI, *J* = 1.2 Hz), 7.42 d (2H, H_{arom}, *J* = 8.8 Hz), 8.10 d (2H, H_{arom}, *J* = 8.8 Hz); *Z* isomer: 2.16 d (3H, CH_3, *J* = 1.5 Hz), 6.35 q (1H, CHI, *J* = 1.5 Hz), 7.42 d (2H, H_{arom}, *J* = 8.8 Hz), 8.10 d (2H, H_{arom}, *J* = 8.8 Hz). ^{13}C NMR spectrum (mixture of isomers), δ_C, ppm: 26.52 (CH_3), 28.28 (CH_3), 72.51 (CHI), 74.04 (CHI), 123.32, 123.75, 126.55, 128.71, 139.75, 146.88. Found, %: C 37.24; H 2.66. $C_9H_8INO_2$. Calculated, %: C 37.39; H 2.79.

1-(2-Iodo-1-methylvinyl)-4-chlorobenzene (IIh). Mixture of *E* and *Z* isomers (1.3 : 1), colorless oily substance, R_f 0.65 (hexane). IR spectrum, ν, cm^{-1}: 1610 (C=C). ^1H NMR spectrum, δ, ppm: *E* isomer: 2.24 d (3H, CH_3, *J* = 1.2 Hz), 6.52 q (1H, CHI, *J* = 1.2 Hz), 7.19 d (2H, H_{arom}, *J* = 8.5 Hz), 7.34 d (2H, H_{arom}, *J* = 8.5 Hz); *Z* isomer: 2.18 d (3H, CH_3, *J* = 1.5 Hz), 6.28 q (1H, CHI, *J* = 1.5 Hz), 7.19 d (2H, H_{arom}, *J* = 8.5 Hz), 7.34 d (2H, H_{arom}, *J* = 8.5 Hz). ^{13}C NMR spectrum (mixture of isomers), δ_C, ppm: 24.23 (CH_3), 26.35 (CH_3), 75.63 (CHI), 79.76 (CHI), 127.19, 128.53, 133.63, 139.70, 141.12, 145.95, 147.01. Found, %: C 38.56; H 2.75. C_9H_8ClI. Calculated, %: C 38.81; H 2.90.

1-(2-Iodo-1-methylvinyl)-4-methylbenzene (IIi). Mixture of *E* and *Z* isomers (1.5 : 1), colorless oily substance, R_f 0.7 (hexane). IR spectrum, ν, cm^{-1}: 1610 (C=C). ^1H NMR spectrum, δ, ppm: *E* isomer: 2.10 d (3H, CH_3, *J* = 1.3 Hz), 2.26 s (3H, CH_3, arom.), 6.32 q (1H, CHI, *J* = 1.3 Hz), 7.01–7.15 m (4H, H_{arom}); *Z* isomer: 2.00 d (3H, CH_3, *J* = 1.6 Hz), 2.24 d (3H, CH_3, arom.), 6.08 q (1H, CHI, *J* = 1.6 Hz), 7.01–7.15 m (4H, H_{arom}). ^{13}C NMR spectrum, δ_C, ppm: 21.25 (3H, CH_3, arom.), 21.35 (CH_3), 22.86 (CH_3), 75.33 (CHI), 78.18 (CHI), 125.83, 129.32, 134.96, 138.34, 139.39, 144.76. Found, %: C 46.31; H 4.23. $C_{10}H_{11}I$. Calculated, %: C 46.54; H 4.30.

This study was financially supported by the Russian Foundation for Basic Research (project nos. 00-03-32760, 00-03-32763, and 02-03-06142).

REFERENCES

1. Negishi, E., Kotora, M., and Xu, C., *J. Org. Chem.*, 1997, vol. 62, p. 8957.
2. Van Horn, D.E. and Negishi, E., *J. Am. Chem. Soc.*, 1978, vol. 100, p. 2252.
3. Castro, C.E. and Kray, W.C., *J. Am. Chem. Soc.*, 1966, vol. 88, p. 4447.
4. Takai, K., Nitta, K., and Utimoto, K., *J. Am. Chem. Soc.*, 1986, vol. 108, p. 7408.
5. Miller, R.B. and Reichenbach, T., *Tetrahedron Lett.*, 1974, p. 543.
6. On, H.P., Lewis, W., and Zweifel, G., *Synthesis*, 1981, p. 999.
7. Barluenga, J., Alvares-Garcia, L.J., and Gonzalez, J.M., *Tetrahedron Lett.*, 1995, p. 2153.
8. Petasis, N.A. and Zavialov, I.A., *Tetrahedron Lett.*, 1996, p. 567.

9. Graven, A., Jorgensen, K.A., Dahl, S., and Stanczak, A., *J. Org. Chem.*, 1994, vol. 59, p. 3543.
10. Martinez, A.G., Alvares, R.M., Gonzalez, S.M., Subramanian, L.R., and Conrad, M., *Tetrahedron Lett.*, 1992, p. 2043.
11. Suzuki, H., Aihara, M., Yamamoto, H., Takamoto, Y., and Ogawa, T., *Synthesis*, 1988, p. 236.
12. Shastin, A.V., Korotchenko, V.N., Nenajdenko, V.G., and Balenkova, E.S., *Tetrahedron*, 2000, vol. 56, p. 6557.
13. Shastin, A.V., Korotchenko, V.N., Nenaidenko, V.G., and Balenkova, E.S., *Izv. Ross. Akad. Nauk, Ser. Khim.*, 1999, p. 2210.
14. Korotchenko, V.N., Shastin, A.V., Nenajdenko, V.G., and Balenkova, E.S., *J. Chem. Soc., Perkin Trans. 1*, 2002, p. 883.
15. Shastin, A.V., Korotchenko, V.N., Nenaidenko, V.G., and Balenkova, E.S., *Izv. Ross. Akad. Nauk, Ser. Khim.*, 2001, p. 1003.
16. Shastin, A.V., Korotchenko, V.N., Nenajdenko, V.G., and Balenkova, E.S., *Synthesis*, 2001, p. 2081.
17. Korotchenko, V.N., Shastin, A.V., Nenajdenko, V.G., and Balenkova, E.S., *Tetrahedron*, 2001, vol. 57, p. 7519.
18. Dakin, L.A., Schaus, S.E., Jacobsen, E.N., and Panek, J.S., *Tetrahedron Lett.*, 1998, vol. 39, p. 8947.
19. Gettwert, V., Krebs, F., and Maas, G., *Eur. J. Org. Chem.*, 1999, p. 1213.
20. Aggarwal, V.K., Ford, J.G., Jones, R.V., and Fieldhouse, R.H., *Tetrahedron: Asymmetry*, 1998, vol. 9, p. 1801.
21. Latimer, W.M., *The Oxidation States of the Elements and Their Potentials in Aqueous Solutions*, New York: Prentice-Hall, 1952, 2nd ed.
22. Barton, D.H., Bashiardes, R.G., and Fourrey, J.L., *Tetrahedron*, 1988, vol. 44, p. 147.