A novel reductive cyclization of arylmethylidenemalononitrile promoted by samarium diiodide

Longhu Zhou † and Yongmin Zhang *

Department of Chemistry, Hangzhou University, Hangzhou, 310028, P.R. China

The intermolecular and intramolecular reductive coupling reactions of arylmethylidenemalononitriles induced by SmI$_2$ have been studied. The configuration of the cyclodimerization products, 4,5-*trans*-isomers of 2-amino-1,3,3-tricyano-4,5-diarylcyclopentenes, has been confirmed by X-ray analysis and a possible reaction mechanism is proposed.

Carbon–carbon bond formation is the essence of organic synthesis and the reductive dimerization of carbonyl derivatives is a most valuable method for establishing carbon–carbon bonds. Since the time Kagan demonstrated a simple preparation of samarium diiodide from samarium metal and 1,2-diiodo-ethane,[1] SmI$_2$ has been developed as a mild, neutral and versatile single electron transfer reductant. It has been widely used in synthetic reactions, and is especially useful for ring closure reactions, carbon–carbon bond formation and in reaction stereocontrol.[2] The reactivity of samarium diiodide towards various nitrogen compounds including nitro compounds,[3] azocompounds,[4] hydrazones,[3b,5] oximes,[3b] imines,[3b] azides[6] and hydroxylamines[7] has been examined.

Nitro groups are known to be easily reduced by samarium diiodide. The cyano group however, is relatively more stable to samarium diiodide than a nitro group and could not be reduced by this reagent. Souppe and Kagan[8] reported that aromatic and aliphatic nitriles are inert in the presence of SmI$_2$ and *m*- or *p*-nitrobenzonitrile could be selectively reduced to the corresponding cyanoanilines in almost quantitative yields. Kang and Hong[9] reported the decyanation of α-cyano substituted nitrile derivatives by samarium diiodide. However, no cyclization products were observed. It has been known that α,β-unsaturated carboxylic acid derivatives are reduced with SmI$_2$ to the corresponding saturated compounds.[10] Recently, Yacovan and Hoz[11] reported that 1,1-diphenyl-2,2-dicyanoethylene can be quantitatively reduced to (diphenylmethyl)malononitrile without any dimeric products or reduction products of the cyano group. To the best of our

knowledge, no literature examples for the reduction of a cyano group to give an amine have been reported with this reagent. Here, we wish to describe our preliminary results on novel intermolecular reductive cyclodimerization and intramolecular reductive cyclizations of arylmethylidenemalononitriles by SmI$_2$, which differ from substituted malononitriles,[9] diphenylmethylidenemalononitrile[11] and nitrobenzonitrile[10] to give substituted cyclopentamines or 2-aminoquinoline derivatives respectively.

When arylmethylidenemalononitriles **1** were treated with SmI$_2$ in THF, the intermolecular reductively coupled cyclization products, the 4,5-*trans*-isomers of 2-amino-1,3,3-tricyano-4,5-diarylcyclopentenes **2**, were formed (Scheme 1).
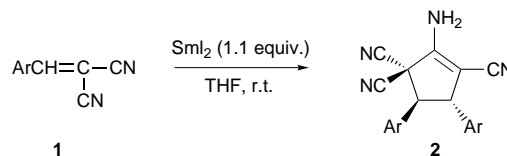
Scheme 1

Table 1 summarizes our results on the cyclodimerization of a number of substrates. In the reactions, the cleavage takes place at the carbon–nitrogen triple bond and the carbon–carbon double bond. The chloro, bromo and alkoxy groups of the substrates could not be reduced under the reaction conditions and have no influence on the rate of cyclodimerization. All the reactions were completed rapidly within a few minutes and afforded the corresponding substituted cyclopentenes in good yields. The effect of HMPA (hexamethylphosphoramide) to promote the reaction of various organic compounds with

---

† *Permanent address*: Department of Chemistry, Xuzhou Normal University, Jiangsu, 221009, China.

Table 1 Cyclodimerization of arylmethylidenemalononitriles induced by SmI$_2$

| | | | Yield (%)[a] | |
Entry	Ar	Reaction time/min	In THF[b]	In THF–HMPA[c]
a	4-ClC$_6$H$_4$	5	84	86
b	4-CH$_3$OC$_6$H$_4$	5	83	82
c	4-CH$_3$C$_6$H$_4$	5	80	84
d	4-BrC$_6$H$_4$	5	78	76
e	3-BrC$_6$H$_4$	5	73	73
f	C$_6$H$_5$	5	68	67
g	3,4-OCH$_2$OC$_6$H$_3$	5	70	72
h	2-furyl	10	67	69
i	3,4-(OCH$_3$)$_2$C$_6$H$_3$	5	75	77

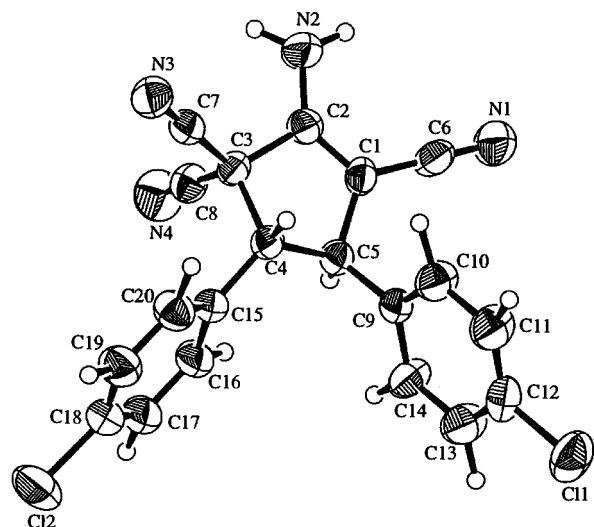[a] Isolated yield. [b] 10 ml THF was used. [c] 10 ml THF and 1 ml HMPA were used.

Fig. 1 Molecular structure of **2a** showing the atom numbering scheme

SmI$_2$, is well known.[12] However, in this case, the reactivity of the starting materials and the yields of the reaction were the same either in the presence of HMPA or without HMPA. As shown in Table 1, the reactions are very stereoselective, as only one isomer was obtained and careful analysis of the reaction mixture indicated the absence of any other stereoisomer. This was confirmed by an X-ray crystal structure analysis of a single crystal of **2a·EtOH·H$_2$O**, which clearly illustrates the *trans*-stereochemistry of the product (Fig. 1).

Though the detailed mechanism of the above cyclodimerization has not been clarified yet, the cyclopentene formation can be explained by the possible mechanism presented in Scheme 2.
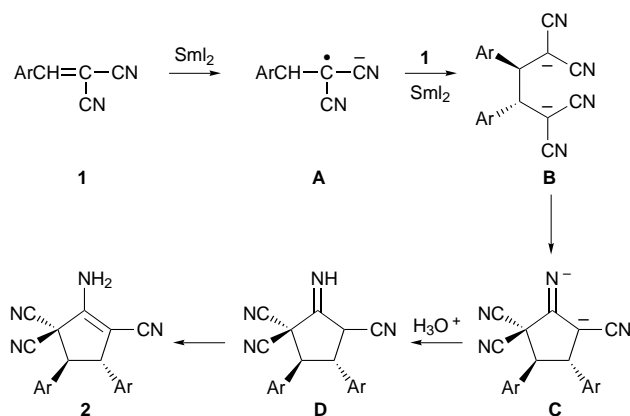
Scheme 2

In the initial step, an electron is transferred from SmI$_2$ to substrate **1** to form radical anion **A**, which then attacks another molecule of substrate to form a carbon–carbon bond and generate intermediate **B**. Intermediate **B** then reacts intramolecularly to result in the formation of a new carbon–carbon bond and produce intermediate **C**. Then **C** is converted to **D** which isomerizes to give product **2**.

However, the reductive cyclization process is even more surprising when contrasted with the reaction of substrate **3** with SmI$_2$ in THF. When a solution of 1 equiv. of substrate **3** in anhydrous THF was allowed to react with 6 equiv. of SmI$_2$ in dry THF under the same reaction conditions, an entirely different type of intramolecular reductive cyclization took place and afforded the 2-aminoquinoline derivative **4** (Scheme 3). The cyclodimerization product **2** was not detected.
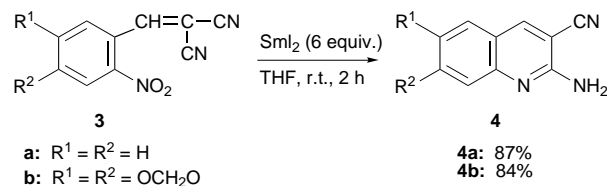
Scheme 3

In summary, SmI$_2$ promotes a novel reductive cyclization of arylmethylidenemalononitriles, which has not been achieved previously by other reductants. Further studies to develop other new reactions using SmI$_2$ are now in progress.

Experimental

General details

Tetrahydrofuran (THF) was distilled from sodium–benzophenone immediately prior to use. All reactions were conducted under a nitrogen atmosphere. Melting points are uncorrected. Infrared spectra were recorded on Perkin-Elmer 683 spectrometers in KBr with absorptions in cm^{-1}. ^{1}H NMR Spectra were determined on Bruker AC-80 or JEOL PMX-60 spectrometers as CDCl$_3$ solutions. J Values are in hertz. Chemical shifts are expressed in ppm downfield from internal tetramethylsilane. Mass spectra were recorded on HP 5989A or Finnigan MAT GC–MS spectrometers. Microanalyses were carried out on a Perkin-Elmer 240C instrument.

General procedure for the cyclodimerization reactions

A solution of arylmethylidenemalononitrile **1** (1 mmol) in anhydrous THF (3 ml) was added to a solution of SmI$_2$ (1.1 mmol) in THF (10 ml) at room temperature under a dry nitrogen atmosphere. The reaction was completed in a few minutes and the deep blue green colour of samarium diiodide changed to a brownish yellow. The reaction was quenched with dilute HCl (1 M, 1 ml) and extracted with diethyl ether (3 × 40 ml). The combined extracts were washed with saturated aqueous Na$_2$S$_2$O$_3$ (15 ml), saturated aqueous NaCl (15 ml), and dried over anhydrous Na$_2$SO$_4$. After evaporating the solvent under reduced pressure, the crude product was purified by preparative thin layer chromatography [eluent, ethyl acetate–light petroleum (bp 30–60 °C) (1:2)].

Compound 2a. Mp 158–160 °C; v_{max}(KBr)/cm^{-1} 3370, 3200, 2220, 1680, 1630 and 1500; δ_H 3.74 (1H, d, J 9.5, ArCH), 4.51 (1H, d, J 9.5, ArCH), 5.30 (2H, br s, NH$_2$), 6.85–7.40 (8H, m, 2 × ArH); m/z 382 (M + 4, 12.1%), 380 (M + 2, 62.6), 378 (M$^+$, 84.6), 377 (42.7), 343 (85.3), 308 (22.3), 278 (16.9), 189 (18.4), 155 (100) (Found: C, 63.12; H, 3.08; N, 14.83. C$_{20}$H$_{12}$N$_4$Cl$_2$ requires C, 63.33; H, 3.19; N, 14.77%).

Crystal data and structure refinement for 2a·C$_2$H$_5$OH·H$_2$O. Crystals suitable for X-ray analysis were obtained by slow evaporation of an ethanol solution of **2a**. C$_{22}$H$_{20}$O$_2$N$_4$Cl$_2$, M = 443.33, triclinic, space group $P\bar{1}$, a = 11.033(4), b = 12.199(3), c = 10.732(3) Å, a = 114.46(2), β = 118.33(3), γ = 81.56(3)°, V = 1155.1(7) Å^3, Z = 2, D_c = 1.275 g cm^{-3}, F(000) = 460.00, μ(Mo-Kα) = 3.05 cm^{-1}, colorless prismatic crystals, crystal size 0.20 × 0.20 × 0.30 mm.

Intensity data were collected at 293 K on a Rigaku AFC7R diffractometer with graphite-monochromated Mo-Kα radiation (λ = 0.701 69 Å): 3033 independent reflections were collected using $\omega - 2\theta$ scan mode in the range of 6° < 2θ < 49.4°, of which 2063 intensity data with [$I > 2\sigma(I)$] were observed. The corrections for Lp factors were applied. The structure was solved by direct methods[13] and expanded using Fourier techniques.[14] Some non-hydrogen atoms were refined anisotropically, while the rest were refined isotropically. Hydrogen atoms were included in F value calculations but fixed during the structural refinement. A full-matrix least-squares

Table 2 Selected bond lengths (Å) and angles (°)

Cl1–C12	1.752(6)	C2–C1–C6	123.2(5)
Cl2–C18	1.757(6)	C5–C1–C6	122.5(5)
N1–C6	1.141(8)	N2–C2–C1	133.1(6)
N2–C2	1.338(7)	N2–C2–C3	118.9(5)
N3–C7	1.133(7)	C1–C2–C3	108.1(5)
N4–C8	1.137(7)	C2–C3–C4	101.4(4)
C1–C2	1.332(7)	C2–C3–C7	114.7(4)
C1–C5	1.514(8)	C2–C3–C8	107.8(5)
C1–C6	1.436(9)	C4–C3–C7	112.3(4)
C2–C3	1.539(8)	C4–C3–C8	111.7(4)
C3–C4	1.570(7)	C7–C3–C8	108.9(4)
C3–C7	1.472(8)	C3–C4–C5	103.1(4)
C3–C8	1.470(8)	C1–C5–C4	100.2(4)
C4–C5	1.531(7)	N1–C6–C1	178.8(7)
		N3–C7–C3	176.9(6)
C2–C1–C5	114.1(5)	N4–C8–C3	177.3(7)

refinement gave final $R = 0.082$ and $R_w = 0.098$ with $w = 1/\sigma^2(F_0)$, $S = 2.81$. The maximum peak in the final difference Fourier map is 0.42 e Å^{-3} and the minimum peak is -0.52 e Å^{-3}. In the final circle refinement the largest parameter shift $(\Delta/\sigma)_{max}$ is 0.04. All calculations were performed using the TEXSAN program package.[15] Selected bond lengths and angles are shown in Table 2.‡

Compound 2b. Mp 95–97 °C; ν_{max}(KBr)/cm^{-1} 3380, 3240, 2210, 1670, 1620 and 1520; δ_H 3.68 (3H, s, OCH$_3$), 3.74 (3H, s, OCH$_3$), 4.17 (1H, d, J 9.5, ArCH), 4.50 (1H, d, J 9.5, ArCH), 5.40 (2H, br s, NH$_2$), 6.70–7.48 (8H, m, 2 × ArH); m/z 371 (M + 1, 30.3%), 370 (M$^+$, 100), 369 (35.2), 355 (21.3), 339 (35), 225 (16.4), 199 (31.7), 184 (32.5), 171 (68.6), 155 (50.4), 142 (31.4), 114 (35.5) (Found: C, 71.62; H, 4.71; N, 15.30. C$_{22}$H$_{18}$N$_4$O$_2$ requires C, 71.34; H, 4.90; N, 15.13%).

Compound 2c. Mp 190–192 °C; ν_{max}(KBr)/cm^{-1} 3375, 3240, 2210, 1670, 1620 and 1520; δ_H 2.23 (3H, s, CH$_3$), 2.30 (3H, s, CH$_3$), 3.77 (1H, d, J 9.5, ArCH), 4.51 (1H, d, J 9.5, ArCH), 5.35 (2H, br s, NH$_2$), 6.95–7.35 (8H, m, 2 × ArH); m/z 339 (M + 1, 15.1%), 338 (M$^+$, 100), 325 (15.6), 324 (28.8), 155 (15), 91 (10.4) (Found: C, 77.97; H, 5.21; N, 16.73. C$_{22}$H$_{18}$N$_4$ requires C, 78.08; H, 5.36; N, 16.56%).

Compound 2d. Mp 145–147 °C; ν_{max}(KBr)/cm^{-1} 3380, 3215, 2210, 1680, 1630 and 1500; δ_H 3.70 (1H, d, J 9.0, ArCH), 4.54 (1H, d, J 9.0, ArCH), 5.41 (2, br s, NH$_2$), 6.97–7.63 (8H, m, 2 × ArH); m/z 470 (M + 4, 48.3%), 468 (M + 2, 100), 466 (M$^+$, 51.3), 391 (23.1), 390 (36.5), 389 (74.2), 388 (30.4), 309 (35.2), 308 (47.1), 155 (43.9) (Found: C, 51.49; H, 2.77; N, 11.70. C$_{20}$H$_{12}$Br$_2$N$_4$ requires C, 51.31; H, 2.58; N, 11.97%).

Compound 2e. Mp 116–118 °C; ν_{max}(KBr)/cm^{-1} 3380, 3210, 2210, 1670, 1630, 1600 and 1580; δ_H 3.60 (1H, d, J 9.2, ArCH), 4.50 (1H, d, J 9.2, ArCH), 5.33 (2H, br s, NH$_2$), 6.78–7.60 (8H, m, 2 × ArH); m/z 470 (M + 4, 46.2%), 468 (M + 2, 100), 466 (M$^+$, 50.3), 390 (20.3), 389 (49.1), 388 (32.6), 308 (27.3), 155 (15.4), 154 (41.7) (Found: C, 51.61; H, 2.31; N, 12.26. C$_{20}$H$_{12}$Br$_2$N$_4$ requires C, 51.31; H, 2.58; N, 11.97%).

Compound 2f. Mp 128–130 °C; ν_{max}(KBr)/cm^{-1} 3380, 3200, 2210, 1670, 1630 and 1505; δ_H 3.80 (1H, d, J 9.2, ArCH), 4.58 (1H, d, J 9.2, ArCH), 5.20 (2H, br s, NH$_2$), 7.10–7.70 (10H, m, 2 × ArH); m/z 311 (M + 1, 21.5%), 310 (M$^+$, 100), 283 (15.3), 156 (15.1), 155 (41.4), 128 (18.4) (Found: C, 77.57; H, 4.38; N, 18.20. C$_{20}$H$_{14}$N$_4$ requires C, 77.40; H, 4.55; N, 18.05%).

Compound 2g. Mp 166–168 °C; ν_{max}(KBr)/cm^{-1} 3380, 3240, 2210, 1675, 1620 and 1510; δ_H 4.26 (1H, d, J 8.8, ArCH), 4.43 (1H, d, J 8.8, ArCH), 5.27 (2H, br s, NH$_2$), 5.98 (4H, s, 2 × OCH$_2$O), 6.30–6.93 (6H, m, 2 × ArH); m/z 399 (M + 1, 15.4%), 398 (M$^+$, 100), 371 (16.5), 155 (43.5), 154 (26.7) (Found: C, 66.52; H, 3.78; N, 13.82. C$_{22}$H$_{14}$N$_4$O$_4$ requires C, 66.33; H, 3.54; N, 14.06%).

Compound 2h. Mp 125–127 °C; ν_{max}(KBr)/cm^{-1} 3360, 3240, 2210, 1680, 1630 and 1510; δ_H 4.23 (1H, d, J 9.0, ArCH), 4.60 (1H, d, J 9.0, ArCH), 5.61 (2H, br s, NH$_2$), 6.23–7.53 (6H, m, 2 × furan-H); m/z 291 (M + 1, 21.3%), 290 (M$^+$, 100), 263 (15.5), 155 (37.4) (Found: C, 66.43; H, 3.61; N, 19.41. C$_{16}$H$_{10}$N$_4$O$_2$ requires C, 66.20; H, 3.47; N, 19.30%).

Compound 2i. Mp 138–140 °C; ν_{max}(KBr)/cm^{-1} 3360, 3220, 2220, 1670, 1620 and 1525; δ_H 3.74 (1H, d, J 9.5, ArCH), 3.80 (6H, s, 2 × OCH$_3$), 3.88 (6H, s, 2 × OCH$_3$), 4.48 (1H, d, J 9.5, ArCH), 5.40 (2H, br s, NH$_2$), 6.60–7.15 (6H, m, 2 × ArH); m/z 431 (M + 1, 15.2%), 430 (M$^+$, 100), 403 (25.7), 293 (21.3), 266 (19.3), 156 (18.4), 155 (13.2) (Found: C, 67.21; H, 5.01; N, 13.20. C$_{24}$H$_{22}$N$_4$O$_4$ requires C, 66.97; H, 5.15; N, 13.02%).

General procedure for the intramolecular reductive cyclization reactions

A solution of nitro cyano olefins **3** (1 mmol) in anhydrous THF (3 ml) was added to a solution of SmI$_2$ (6 mmol) in THF (40 ml) at room temperature under a dry nitrogen atmosphere. The mixture was stirred under these conditions until the reaction was complete. The reaction mixture was poured into 10% aqueous K$_2$CO$_3$ (50 ml) and extracted with diethyl ether (4 × 30 ml). After usual work-up, the crude product was purified by preparative thin layer chromatography [eluent, ethyl acetate–cyclohexane (1 : 1)].

Compound 4a. Mp 226–227 °C; ν_{max}(KBr)/cm^{-1} 3400, 3160 and 2230; δ_H 5.46 (2H, br s, NH$_2$), 7.32–7.71 (4H, m, ArH), 8.30 (1H, s, hetero-ArH); m/z 170 (M + 1, 21.5%), 169 (M$^+$, 100), 144 (73.2), 143 (33.5), 117 (20.3), 116 (32.5) (Found: C, 70.86; H, 4.36; N, 24.78. C$_{10}$H$_7$N$_3$ requires C, 70.99; H, 4.14; N, 24.84%).

Compound 4b. Mp 280 °C (decomp.); ν_{max}(KBr)/cm^{-1} 3400, 3160 and 2230; δ_H 6.14 (2H, s, OCH$_2$O), 6.66 (2H, br s, NH$_2$), 6.91 (1H, s, ArH), 7.12 (1H, s, ArH), 8.37 (1H, s, hetero-ArH) (Found: C, 62.21; H, 3.15; N, 19.50. C$_{11}$H$_7$N$_3$O$_2$ requires C, 61.97; H, 3.31; N, 19.71%).

References

1 P. Girard, J. L. Namy and H. B. Kagan, *J. Am. Chem. Soc.*, 1980, **102**, 2693.
2 For reviews see: G. A. Molander and C. R. Harris, *Chem. Rev.*, 1996, **96**, 307; F. Matsuda, *Synth. Org. Chem. Jpn.*, 1995, **53**, 987; G. A. Molander, *Org. React.*, 1994, **46**, 221; T. Imamota, *Lanthanides in Organic Synthesis*, Academic Press, London, 1994, ch. 4; M. Shibasaki and H. Sasai, *Synth. Org. Chem. Jpn.*, 1993, **51**, 972; G. A. Molander, *Chem. Rev.*, 1992, **92**, 29; D. P. Curran, T. L. Fevig, C. P. Jasperse and M. J. Totleben, *Synlett*, 1992, 943; J. A. Soderquist, *Aldrichim. Acta*, 1991, **24**, 15; G. A. Molander, *Comprehensive Organic Synthesis*, eds. B. M. Trost and I. Fleming, Pergamon, Oxford, vol. 1, 1991, 251; H. B. Kagan, *New. J. Chem.*, 1990, **14**, 453; G. A. Molander, in *Chemistry of the Metal-Carbon Bond*, ed. F. R. Hartly, Wiley, Chichester, 1989, vol. 5, ch. 8; H. B. Kagan, M. Sasaki and J. Collin, *Pure Appl. Chem.*, 1988, **60**, 1725; H. B. Kagan and J. L. Namy, *Tetrahedron*, 1986, **42**, 6573.

‡ Full crystallographic details, excluding structure factor tables, have been deposited at the Cambridge Crystallographic Data Centre (CCDC). For details of the deposition scheme, see 'Instructions for Authors', *J. Chem. Soc., Perkin Trans. 1*, available *via* the RSC Web page (http://www.rsc.org/authors). Any request to the CCDC for this material should quote the full literature citation and the reference number 207/234.

3 Y. Zhang and R. Lin, *Synth. Commun.*, 1987, **17**, 329; J. Souppe, L. Danon, J. L. Namy and H. B. Kagan, *J. Organomet. Chem.*, 1983, **250**, 227; T. Mukaiyama, K. Yoyozu, K. Kato and T. Yamada, *Chem. Lett.*, 1992, 181.
4 A. S. Kende and J. S. Mendoza, *Tetrahedron Lett.*, 1991, **32**, 1699.
5 M. J. Burk and J. E. Feaster, *J. Am. Chem. Soc.*, 1992, **114**, 6266.
6 N. R. Natale, *Tetrahedron Lett.*, 1982, **23**, 5009; L. Benati, P. C. Monievecohi, D. Nanni, P. Spagnolo and M. Volta, *Tetrahedron Lett.*, 1995, **36**, 7313; C. Goulaouic-Dubois and M. Hesse, *Tetrahedron Lett.*, 1995, **36**, 7427.
7 G. E. Keck, S. F. McHardy and T. T. Wager, *Tetrahedron Lett.*, 1995, **36**, 7419.
8 J. Souppe, L. Danon, J. L. Namy and H. B. Kagan, *J. Organomet. Chem.*, 1983, **250**, 227.
9 H. Y. Kang and W. S. Hong, *Tetrahedron Lett.*, 1995, **36**, 7661.
10 P. Girard, J. L. Namy and H. B. Kagan, *J. Am. Chem. Soc.*, 1980, **102**, 2693; J. Inanaga, *Rev. Heteroat. Chem.*, 1990, **3**, 75.
11 A. Yacovan and S. Hoz, *J. Org. Chem.*, 1997, **62**, 771; A. Yacovan and S. Hoz, *J. Am. Chem. Soc.*, 1996, **118**, 261.
12 T. L. Fevig, R. L. Elliott and D. P. Curran, *J. Am. Chem. Soc.*, 1988, **110**, 5064; E. Hasegawa and D. P. Curran, *Tetrahedron Lett.*, 1993, **34**, 1717; M. Murakami, M. Hayashi and Y. Ito, *J. Org. Chem.*, 1992, **57**, 793.
13 C. J. Gilmore, *J. Appl. Crystallogr.*, 1984, **17**, 42.
14 P. T. Beurskens, G. Admiraal, G. Beurskens, W. P. Bosman, S. Garcia, R. Granda, O. Gould, J. M. M. Smits and C. Smykalla, The DIRDIF program System Technical Report of the Crystallography Laboratory, University of Nijmegen, The Netherlands, 1992.
15 TEXSAN: Crystal Structure Analysis Packages, Molecular Structure Corporation (1985 and 1992).