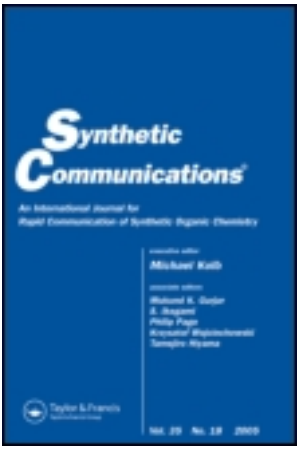


Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lsyc20

# SYNTHESIS OF $C_2$-SYMMETRIC BISTHIAZOLIDINE LIGANDS DERIVED FROM L-CYSTEINE

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Published online: 09 Nov 2006.

To cite this article: Sandra Díaz & Asensio González (2001) SYNTHESIS OF $C_2$-SYMMETRIC BISTHIAZOLIDINE LIGANDS DERIVED FROM L-CYSTEINE, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 31:11, 1697-1705, DOI: 10.1081/SCC-100103989

To link to this article: http://dx.doi.org/10.1081/SCC-100103989

SYNTHETIC COMMUNICATIONS, 31(11), 1697–1705 (2001)

# SYNTHESIS OF $C_2$-SYMMETRIC BISTHIAZOLIDINE LIGANDS DERIVED FROM L-CYSTEINE

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## ABSTRACT

Treatment of L-cysteine esters and thiazolidine-4-carboxylic esters with an excess of paraformaldehyde in the presence of trifluoroacetic acid provides $C_2$-symmetric $N,N'$-methylene-bisthiazolidines in good yield.

$C_2$-Symmetric compounds occupy a prominent position among chiral auxiliaries and ligands for asymmetric synthesis.[1] With important exceptions, there are only a few sulphur containing ligands derived from L-cysteine in spite of the relatively easy synthetic access to a wide variety of possible candidates.[2] As precedents for the potential of this type of ligand, it is important to cite the use of thiazolidine **1** as a ligand that allows the asymmetric hydrosilylation of carbonyl compounds as an alternative to the metal hydride reduction[3] and thiazolidine **2** used as catalyst for the asymmetric reduction of ketones using borane.[4]

Our interests lie in the preparation of new compounds derived from L-cysteine which might act as ligands in metal ion complexes.

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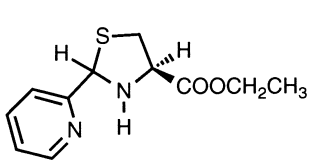

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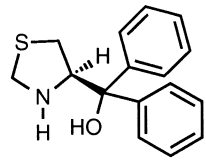

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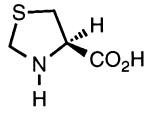
Particularly, we wish to exploit the reaction of the parent compound with formaldehyde, about which only a few papers have been published. Ratner and Clarke described that treatment of L-cysteine hydrochloride with 1.1 moles of *aqueous* formaldehyde, followed by the addition of pyridine, afforded (*R*)-thiazolidine-4-carboxylic acid **3**.[5] Armstrong and du Vigneaud showed that combination of 2 moles of L-cysteine with 1 mole of *aqueous* formaldehyde in strongly acidic solution afforded djenkolic acid **4**.[6] Ando and coworkers reported that treatment of L-cysteine with excess of *aqueous* formaldehyde in the presence of formic acid at 100°C provides a useful method of preparation of (*R*)-3-methylthiazolidine-4-carboxylic acid **5**.[7] In addition, we have recently described a simple experimental procedure that effectively allowed the preparation of the bicyclic thiazolidine **6** in quantitative yield using dichloromethane as solvent instead of water as the reaction medium and solid paraformaldehyde.[8]



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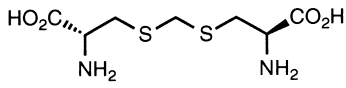

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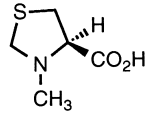

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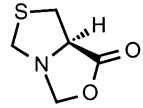
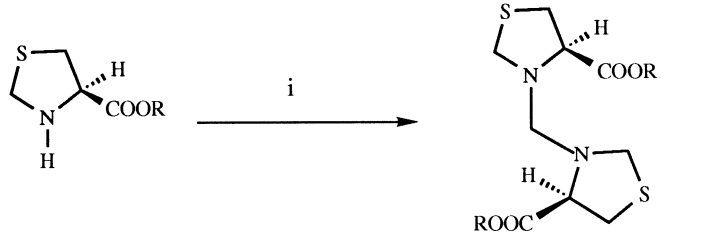


6

Finally, the synthesis of methylenebisoxazolidines by reaction of amino alcohols with aqueous formaldehyde in basic solution was reported very recently.[9] Continuing our studies on the reaction of L-cysteine derivatives with paraformaldehyde with regard to the synthesis of protected derivatives, we describe here the preparation of methylenebisthiazolidines **7**, **8**, and **9**, derived from L-cysteine using trifluoroacetic acid as the reaction solvent.

## RESULTS AND DISCUSSION

As illustrated in Scheme 1, our preparation of aminals starts either with L-cysteine ester derivatives, or with (*R*)-thiazolidine esters obtained from (*R*)-thiazolidine-4-carboxylic acid **3**. Our first experiments to arrive at aminals using up to five fold excess of paraformaldehyde in the presence of trifluoroacetic acid were not encouraging since the crude product contained variable proportions of thiazolidine ester and the corresponding aminal that could not be resolved by column chromatography. Subsequently, we proved that the hydrolysis of the aminal formed on silica was an additional difficulty. However, the use of twenty-fold excess of paraformaldehyde and trifluoroacetic acid (method A) was most satisfactory and the anticipated aminals were formed in good yields. In particular, *N*,*N*′-methylenebisthiazolidine dibenzyl ester **9** was isolated in 75% yield. $^{1}H$ and $^{13}C$ NMR spectra indicated the high symmetry of **9**, which could be crystallized from ethanol. On the other hand, attempts to prepare solid salts of aminals **7** and **8** under diverse conditions failed. With these results in hand, we synthesized *N*,*N*′-methylenebispenicillamine diethyl ester **10** from D-penicillamine ethyl ester which has the opposite configuration at the chiral center.




**7** R= $CH_3$-

**8** R= $CH_3$-$CH_2$-

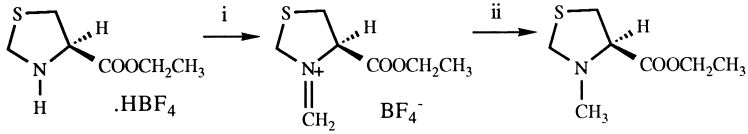
**9** R= $C_6H_5$-$CH_2$-

***Scheme 1.*** i) paraformaldehyde/$CF_3COOH$.

As an extention of the published conditions,[8] by treatment with paraformaldehyde in dichloromethane in the presence of anhydrous magnesium sulfate (method B), cysteamine was converted into *N*,*N*′-methylenebisthiazolidine **11**[10] in moderate yield instead of the simple monocyclic thiazolidine. When we applied these conditions to L-serine the reaction

did not proceed at all. The striking difference between L-cysteine (**6** was obtained quantitatively) and L-serine was attributed to the higher nucleophilic character of sulphur compared with oxygen atoms.

In contrast, treatment of ethyl (*R*)-thiazolidine-4-carboxylate hydrochloride with paraformaldehyde in dichloromethane in the presence of anhydrous magnesium sulfate (method B)[8,11] gave an iminium chloride in very good yield as an oil as shown by its $^{13}C$ NMR spectrum.[12] This result is not unexpected since it has been reported that the five-membered ring of pyrrolidine is by far the most reactive cyclic secondary amine in the formation of similar iminium salts.[13] Performing this reaction with the tetrafluoroborate salt of ethyl (*R*)-thiazolidine-4-carboxylate produced a high yield of the iminium tetrafluoroborate **12** as a solid of low melting point. The final proof of its constitution and the retention of configuration in this process[14] was determined by its conversion to ethyl (*R*)-*N*-methylthiazolidine-4-carboxylate **13** by reduction with $NaBH_4$ in ethanol which was correlated with the authentic compound obtained in one step by treatment of L-cysteine ethyl ester with aqueous formaldehyde in the presence of formic acid at 100°C.[7]




**12** **13**

***Scheme 2.*** i) paraformaldehyde/$CH_2Cl_2$/$MgSO_4$; ii) $NaBH_4$/$CH_3CH_2OH$.

Preliminary experiments of the complexation capabilities of ligand **8** with palladium(II) derivatives have been performed. When **8** was mixed with 1 equiv. of dichlorobis(benzonitrile)palladium (II) in dichloromethane, followed by a column chromatography on silylated silica gel[15] a yellow complex **14** was isolated. The microanalysis[16] confirmed the presence of two ligands and a trinuclear palladium complex with a molecular formula: $Pd_3(C_{13}H_{22}N_2O_4S_2)_2Cl_6$.

In a similar vein, when **8** was reacted with 0.5 equiv. of bis($\pi$-allylpalladium bromide), followed by a column chromatography on silylated silica gel[15] a brown complex **15** was isolated, whose microanalysis[17] indicated a complex with a molecular formula: $Pd_3(C_{13}H_{22}N_2O_4S_2)Br_6$. Moreover, the $^{13}C$ NMR of this complex showed that the allyl carbons are missing. This result suggests that a similar complex might be formed in both reactions.

There are various possibilities in the coordination mode of the ligand when they act as bidentate ones: N,N-, N,S- and S,S-type (where N and S indicate the nitrogen and sulfur atom of the thiazolidine rings, respectively). The S,S-coordination mode could be favored with ligand **8**, however in some cases it has been found that the chelation mode of certain ligands depends on the source of palladium.[18] Unfortunately, all our attempts to obtain good crystals of these complexes failed. A deeper investigation aimed at the determination of the structure of these complexes is now in progress.

In summary, we have described a simple procedure for the synthesis of $C_2$-symmetric *N*,*N*′-methylenebisthiazolidines derived from L-cysteine and D-penicillamine, using paraformaldehyde in the presence of trifluoroacetic acid, these compounds have potential as ligands in asymmetric catalysis. We are currently investigating the complexation capabilities of these ligands with transition metals and further applications of the stable iminium salt **12** and structurally related compounds in synthesis.



## EXPERIMENTAL

**General**. All solvents were dried by standard methods. All reagents were of commercial quality. Unless otherwise noted, $^1$H and $^{13}$C NMR spectra were recorded on a Varian Gemini 200 instrument at 200 and 50 MHz respectively. Chemical shifts are reported in ppm downfield (δ) from tetramethylsilane (TMS). The assignments of $^{13}$C NMR signals were made with the aid of DEPT sequence. IR spectra were recorded on a Nicolet 205 FT infrared spectrophotometer, and noteworthy absorptions are listed ($cm^{-1}$). Evaporation of solvents was accomplished with a rotatory evaporator. Microanalyses were performed by Centro de Investigación y Desarrollo (CSIC), Barcelona. Mass spectra were determined on a Hewlett-Packard 5930A mass spectrometer; ions are recorded as m/z with percentage abundances given in parentheses.

**Reactants**. Methyl (*R*)-thiazolidine-4-carboxylate hydrochloride and ethyl (*R*)-thiazolidine-4-carboxylate hydrochloride were synthesized from (*R*)-thiazolidine-4-carboxylic acid **3** according to literature procedures,[19,20] benzyl (*R*)-thiazolidine-4-carboxylate was obtained by esterification with benzyl alcohol and polyphosphoric acid[21] and (*S*)-penicillamine were used as starting materials for the preparation of the corresponding aminals, *i.e.* compounds **7**, **8**, **9** and **10** respectively. L-cysteine methyl ester hydrochloride and L-cysteine ethyl ester hydrochloride are commercially available.

**General Procedure for the Synthesis of *N*,*N*′-Methylenebisthiazolidines**. To a mixture of L-cysteine ester hydrochloride *or* (*R*)-thiazolidine-4-carboxylic ester hydrochloride *or* (*S*)-5,5-dimethylthiazolidine-4-carboxylic ester hydrochloride (8 mmoL) and paraformaldehyde (twenty fold excess), 15 mL of trifluoroacetic acid was added at 0°C with stirring. The resulting solution was stirred for 6 h at room temperature, the solvent was evaporated under reduced pressure at 45°C, and quenched with 50 mL of $H_2O$. The crude solution was neutralized with $NaHCO_3$, filtered to eliminate polymeric formaldehyde and the transparent solution was extracted with ether and dried. After filtration, the organic solvent was removed *in vacuo* affording pure *N*,*N*′-methylenebisthiazolidines.

**1,1-Bis[(*R*)-4-methoxycarbonylthiazolidin-3-yl]methane 7**. Yield: 0.95 g, 78% (oil). $[\alpha]^{22}D = -129$ (c = 0.25, $CHCl_3$). $^1H$ NMR ($CDCl_3$/TMS): δ 4.30 (dd, $J = 7.2$ and 3.2 Hz, 2H), 4.15 (m, 4H), 3.65 (s, 6H), 3,2–3.0 (m, 6H). $^{13}C$ NMR ($CDCl_3$): δ 171.4 (C = O), 73.1 ($CH_2$), 67.1 (CH), 57.4 ($CH_2$), 52.6 ($CH_3$), 32.6 ($CH_2$). IR (NaCl): 2954, 1735, 1448, 1372, 1286, 1221, 1193, 1079, 1031 $cm^{-1}$. MS m/z (%): 306 (3), 160 (100), 132 (66), 59 (36). Anal. calcd. for $C_{11}H_{18}N_2O_4S_2$ (306.39): C, 43.12%; H; 5.92%; N, 9.14%. Found: C, 43.40%; H; 5.78%; N, 9.38%.

**1,1-Bis[(*R*)-4-ethoxycarbonylthiazolidin-3-yl]methane 8**. Yield: 1.15 g, 86% (oil). $[\alpha]^{22}D = -134$ (c = 1, $CHCl_3$). $^1H$ NMR ($CDCl_3$/TMS): δ 4.36 (dd, $J = 7.8$ and 3.6 Hz, 2H), 4.23 (m, 8H), 3.3–3.1 (m, 6H), 1.28 (t, $J = 7.2$ Hz, 6H). $^{13}C$ NMR ($CDCl_3$): δ 170.8 (C = O), 73.0 ($CH_2$), 67.1 (CH), 61.3 ($CH_2$), 57.4 ($CH_2$), 32.6 ($CH_2$), 14.2 ($CH_3$). IR (NaCl): 2951, 1739, 1436, 1287, 1221, 1203, 1176, 1079 $cm^{-1}$. MS m/z (%): 334 (3), 174 (100), 146 (25), 59 (53). Anal. calcd. for $C_{13}H_{22}N_2O_4S_2$ (334.45): C, 46.69%; H; 6.63%; N, 8.38%. Found: C, 46.89%; H; 6.40%; N, 8.57%.

**1,1-Bis[(*R*)-4-benzyloxycarbonylthiazolidin-3-yl]methane 9**. Yield: 1.37 g, 75% mp = 80–81°C (EtOH). $[\alpha]^{22}D = -66$ (c = 1, $CHCl_3$). $^1H$ NMR ($CDCl_3$/TMS): δ 7.4–7.2 (m, 10H), 5.11 (s, 4H), 4.39 (dd, $J = 7.4$ and 3.4 Hz, 2H), 4.28 (m, 4H), 3.4–3.0 (m, 6H). $^{13}C$ NMR ($CDCl_3$): δ 170.6 (C = O), 135.3 (C), 128.6 (CH), 128.4 (CH), 128.1 (CH), 73.1 ($CH_2$), 67.2 (CH), 67.0 ($CH_2$), 57.3 ($CH_2$), 32.7 ($CH_2$). IR (KBr): 2944, 1734, 1455, 1387, 1292, 1223, 1192, 1067, 1009, 740 $cm^{-1}$. MS m/z (%): 458 (3), 236 (21), 91 (100). Anal. calcd for $C_{23}H_{26}N_2O_4S_2$ (458.59): C, 60.24%; H; 5.71%; N, 6.11%. Found: C, 60.51%; H; 5.60%; N, 6.33%.

**1,1-Bis[(*S*)-4-ethoxycarbonyl-5,5-dimethylthiazolidin-3-yl]methane 10**. Yield: 1.14 g, 73% (oil). $[\alpha]^{22}D = +126$ (c = 0.25, $CHCl_3$). $^1H$ NMR ($CDCl_3$/TMS): δ 4.48 (d, $J = 8.2$ Hz, 2H), 4.40 (dd, $J = 5.8$ and 3.6 Hz, 2H), 4.20 (q, $J = 7.0$ Hz, 4H), 4.08 (d, $J = 8.2$ Hz, 2H), 3.65 (s, 2H), 1.60 (s, 6H), 1.41 (s, 6H), 1.26 (t, $J = 7.0$ Hz, 6H). $^{13}C$ NMR ($CDCl_3$): δ 170.5 (C = O), 76.3 (CH), 73.2 ($CH_2$), 60.7 ($CH_2$), 54.8 ($CH_2$), 53.1 (C), 31.2 ($CH_3$), 26.8

($CH_3$), 14.4 ($CH_3$). IR (NaCl): 2978, 2931, 1746, 1460, 1387, 1368, 1298, 1261, 1179, 1081, 1032 $cm^{-1}$. Anal. calcd. for $C_{17}H_{30}N_2O_4S_2$ (390.56): C, 52.28%; H; 7.74%; N, 7.17%. Found: C, 52.51%; H; 7.96%; N, 7.39%.

**(*R*)-4-Ethoxycarbonyl-*N*-methylenethiazolidinium tetrafluoroborate 12**. Ethyl (*R*)-thiazolidine-4-carboxylate hydrochloride (1.97 g, 10 mmol) was basified at 0°C with 10% aqueous $Na_2CO_3$ solution, extracted with dichloromethane, dried and evaporated under reduced pressure to yield the free base (1.54 g, 96%). The resulting product was treated carefully with 50% aqueous $HBF_4$ and finally evaporated under vacuum to give the tetrafluoroborate salt as a viscous oil.

To a mixture of ethyl (*R*)-thiazolidine-4-carboxylate tetrafluoroborate (2.39 g, 9.56 mmol), anhydrous magnesium sulphate (3 g) in anhydrous dichloromethane (100 ml) at room temperature, paraformaldehyde (2 g) was added, and the suspension was stirred for 3 days. Another portion of anhydrous magnesium sulphate (1 g)/paraformaldehyde (2 g) was added and stirring was continued for 4 days. The suspension was filtered and removal of the solvent under reduced pressure afforded 2.41 g (93%) of **12** which was used without any purification in the next step.

$[\alpha]^{22}D = -59$ (c = 0.35, $CHCl_3$). $^1H$ NMR ($CDCl_3$/TMS): δ 8.2 (2H), 4.5 (d, $J = 9.4$ Hz), 4.25 (q, $J = 7$ Hz, 2H), 4.18 (d, $J = 9.4$ Hz, 1H), 4.0 (t, $J = 8$ Hz, 1H), 3.45 (dd, $J = 10$ and 8 Hz, 1H), 3.28 (dd, $J = 10$ and 8 Hz, 2H), 1.23 (t, $J = 7$ Hz, 3H). $^{13}C$ NMR (DMSO): δ 167.2 (C = O), 161.3 (C = N), 68.8 (CH), 62.5 ($CH_2$), 58.3 ($CH_2$), 31.2 ($CH_2$), 13.8 ($CH_3$). IR (NaCl): 2980, 2942, 1748, 1667, 1470, 1447, 1392, 1244, 1061, 1023 $cm^{-1}$.

**Ethyl (*R*)-*N*-methylthiazolidine-4-carboxylate 13**. To a solution of **12** (0.51 g, 1.96 mmol) in ethanol (25 ml), $NaBH_4$ (74 mg, 1.95 mmol) was added at 0°C under stirring. After 24 h the mixture was evaporated, quenched with water (40 ml), carefully neutralized with 2 M HCl and extracted with ether (3 × 15 ml). The combined extracts were dried ($Na_2SO_4$) and evaporated to give ethyl (*R*)-*N*-methylthiazolidine-4-carboxylate **13** (0.26 g, 76%). The absolute configuration of **13** was shown to be (*R*) by comparison of its rotatory power with that of sample of the authentic **13** prepared as reported.[7]

$[\alpha]^{22}D = -94$ (c = 0.35, $CHCl_3$) compared with that of authentic **13** $[\alpha]^{22}D = -90$ (c = 0.35, $CHCl_3$). $^1H$ NMR ($CDCl_3$/TMS): δ 4.30 (d, $J = 9.3$ Hz, 1H), 4.22 (q, $J = 7.0$ Hz, 2H), 4.0 (d, $J = 9.3$ Hz, 1H), 3.90 (dd, $J = 6.6$ and 4.4 Hz, 1H), 3.25 (m, 2H), 2.47 (s, 3H), 1.29 (t, $J = 7.0$ Hz, 3H). $^{13}C$ NMR ($CDCl_3$): δ 170.5 (C = O), 71.5 (CH), 61.4 ($CH_2$), 61.2 ($CH_2$), 41.8 ($CH_3$), 31.9 ($CH_2$), 14.2 ($CH_3$). IR (NaCl): 2982, 2956, 1739, 1681, 1448, 1374, 1288, 1215, 1191, 1135, 1027, 755 $cm^{-1}$. MS m/z (%): 175 (3), 161 (8), 142 (13), 116 (28), 102 (100), 86 (20), 59 (78).

## ACKNOWLEDGMENTS

We thank Dr. Jaume Granell for many helpful discussions and suggestions and Dr. David Amabilino for constructive criticism of the manuscript. Support for this research was provided by DGICYT through Grant PB97-0877 and UB-FEDER 2FD97-0293.

## REFERENCES AND NOTES

1. a) Whitesell, J.K., Chem. Rev. **1989**, *89*, 1581–1590; b) Seyden-Penne, J., *Chiral Auxiliaries and Ligands in Asymmetric Synthesis*, John Wiley & Sons, Inc.: New York, 1995; c) Eliel, E.L., Wilen, S.H., *Stereochemistry of Organic Compounds*, John Wiley & Sons, Inc., New York, 1994.
2. a) Blaser, H.U., Chem. Rev. **1992**, *92*, 935–952; b) Coppola, G.M., Shuster, H.F., *Asymmetric Synthesis*, John Wiley & Sons, Inc., New York, 1987; c) Braga, A.L., Appelt, H.R., Schneider, P.H., Silveira, C.C., Wessjohann, L.A., Tetrahedron: Asymmetry **1999**, *10*, 1733–1738; d) Kossenjans, M., Martens, J., Tetrahedron: Asymmetry **1998**, *9*, 1409–1417; e) Xingshu, L., Rugang, X., Tetrahedron: Asymmetry **1996**, *7*, 2779–2782; f) Christoffers, J., Mann, A., Pickardt, J. Tetrahedron **1999**, *55*, 5377–5388.
3. a) Brunner, H., Becker, R., Riepl, G. Organometallics **1984**, *3*, 1354; b) Ojima, I., Clos, N., Bastos, C. Tetrahedron **1989**, *45*, 6901–6939.
4. Trentmann, W; Mehler, T.; Martens, J. Tetrahedron: Asymmetry **1997**, *8*, 2033–2043.
5. Ratner, S.; Clarker, H.T., J. Am. Chem. Soc. **1937**, *59*, 200–206.
6. Armstrong, M.D.; duVigneaud, V. J. Biol. Chem. **1947**, *168*, 373–377.
7. Ando, W.; Takata, T.; Huang, L.; Tamura, Y. Synthesis **1986**, 139–140.
8. González, A.; Lavilla, R.; Piniella, J.F.; Alverez-Lerena, A. Tetrahedron **1995**, *51*, 3015–3024.
9. Bolm, C., Chuang, T.H., Raabe, G., Fang, J.M. Synthetic Commun. **1999**, *29*, 43–51.
10. Schimmelschmidt, K., Hoffmann, H., Mundlos, E. Chem. Ber. **1963**, *96*, 38–47.
11. a) Blaskovich, M.A., Kahn, M. Synthesis **1998**, 379–380; b) Böhme, H., Haake, M. Chem. Ber. **1972**, *105*, 2233–2236; c) Böhme, H., Hartke, K. Chem. Ber. **1960**, *93*, 1305–1309; d) Kossenjans, M., Martens, J. Tetrahedron: Asymmetry **1999**, *10*, 3409–3416; e) Grotjahn, D.B., Albers, R.J., Beckman, J. Synlett **2000**, 633–634; f) Armstrong, A.,

Ahmed, G., Garnett, I., Goacolou, K., Wailes, J.S. Tetrahedron **1999**, *55*, 2341–2352.
12. Examples of thiazolidineiminium salts are scarce, see for example: a) Aitken, R.A., Ali, K., Mesher, S.T.E. Tetrahedron Letters **1997**, 4179–4182; b) Cruz, A., Macías-Mendoza, D., Barragan-Rodriguez, E., Tlahuext, H., Nöth, H., Contreras, R. Tetrahedron: Asymmetry **1998**, *8*, 3903–3911.
13. a) Stanley, J.W., Beasley, J.G., Mathison, I.W. J. Org. Chem. **1972**, *37*, 3746–3748; b) Leonard, N.J., Paukstelis, J.V. J. Org. Chem. **1963**, *28*, 3021–3024.
14. Felluga, F., Pitacco, G., Visintin, C., Valentin, E. Helv. Chim. Acta. **1997**, *80*, 1457–1472.
15. Evans, M.B., Dale, A.D., Little, C.J. Chromatographia **1980**, *13*, 5–11.
16. Anal. calcd. for $Pd_3(C_{13}H_{22}N_2O_4S_2)_2Cl_6$ (1200.87); C, 26.00%; H, 3.69%; N, 4.66%. Found: C, 25.67%; H, 3.70%; N, 4.42%.
17. Anal. calcd. for $Pd_3(C_{13}H_{22}N_2O_4S_2)_2Br_6$ (1467.57); C, 21.28%; H, 3.02%; N, 3.81%. Found: C, 21.16%; H, 3.05%; N, 3.91%.
18. a) Lee, S., Lim, C.W., Song, C.E., Kim, K.M., Jun, C.H. J. Org. Chem. **1999**, *64*, 4445–4451; b) Wagner, B., Martens, J., Beck, W. Z. Naturforsch. **1992**, *47b*, 1343–1345; c) Kubiak, M., Glowiak, T. Acta Crystallogr. *Sect. B*, **1982**, *38*, 2031–2033.
19. Brenner, M., Huber, W. Helv. Chim. Acta. **1953**, *36*, 1109–1115.
20. Habermehl, G.; Ecsy, W. Heterocycles **1977**, *7*, 1027–1032.
21. Erlanger, B.F., Hall, R.M. J. Am. Chem. Soc. **1954**, *76*, 5281–5282.

Accepted in the Netherlands August 3, 2000