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Use of *cis*-dichloro[(*S*)-α-methylbenzylamine](ethylene)Pt(II) as a chiral derivatizing agent for the determination by ^{195}Pt-NMR of the enantiomeric composition of unsaturated ethers or alcohols having a quaternary chiral carbon atom

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Abstract

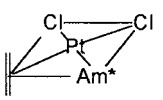
cis-Dichloro[(*S*)-α-methylbenzylamine](ethylene)platinum(II) is an efficient chiral derivatizing agent for the determination, by ^{195}Pt-NMR spectroscopy, of the enantiomeric composition of unsaturated ethers and alcohols having a quaternary chiral carbon atom.

Keywords: Chiral derivatizing agent; NMR; Enantiomeric purity; Unsaturated ethers; Unsaturated alcohols

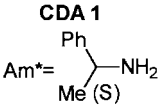
1. Introduction

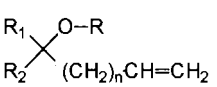
One of the most common and valuable direct methods for the determination of the enantiomeric composition involves the use of chiral derivatizing agents (CDAs) [1] to convert enantiomeric pairs into diastereoisomeric mixtures, which can be detected by NMR.

The inherent simplicity of the method led to the development of a variety of such effective chiral auxiliaries [1]. Among them, some organometallic CDAs [1a,2] have the unique feature to involve the coordination of π-moieties of the analytes in the derivatization reaction and platinum complexes, in particular, also add the attractive opportunity of making possible the detection of the diastereoisomeric mixtures by ^{195}Pt-NMR. Some years ago we had suggested the use of *cis*-dichloro[(*S*)-α-methylbenzylamine](ethylene)Pt(II) (**1**) (see below), already reported as a resolving agent for chiral unsaturated compounds [3], as CDA [2e] for the ^{195}Pt-NMR analyses of unsaturated ethers or alcohols having a tertiary allylic chiral carbon atom (CH_2=CHCHROR$_1$, R_1 = H, Me). The corresponding *trans*-complexes were employed for the analyses of trisubstituted allenes (RR_1C=C=CR_2H) [2f–g].



CDA 1





2

	R	R_1	R_2	**2**
	Me	Ph	Me	**a**
n = 0	Me	Bu^t	Me	**b**
	H	Ph	Me	**c**
	H	Ph	Pr^i	**d**
	H	Ph	Me	**e**
n = 1	H	Ph	Pr^i	**f**
	Me	Ph	Pr^i	**g**

In the present paper we will show that **1** is a CDA, having general applicability also for the determination of the enantiomeric composition of unsaturated ethers

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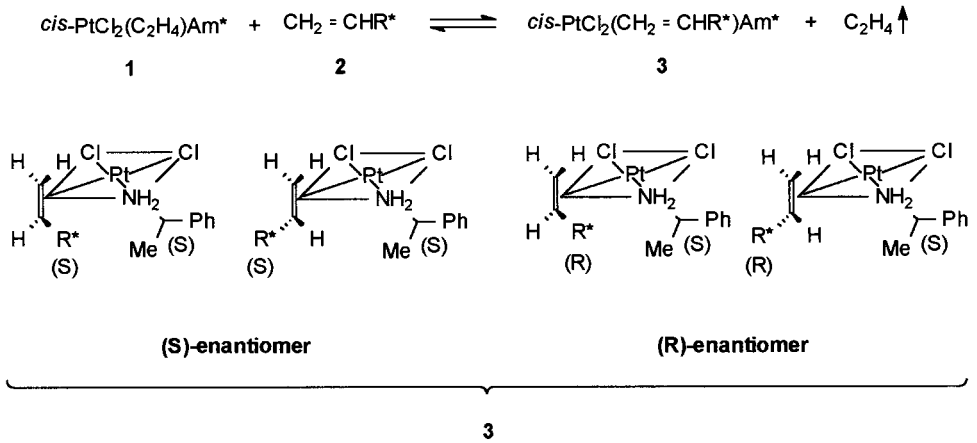

Scheme 1.

and alcohols having a quaternary allylic or homoallylic chiral carbon atom (see above, compounds **2**).

2. Results and discussion

The use of complex **1** as chiral derivatizing agent is especially practical as the derivatization process simply involves the exchange of its coordinated ethylene by the enantiomeric mixtures to be analyzed, to produce complexes **3** (Scheme 1). This reaction can be suitably carried out by mixing the two components, **1** and **2**, in the deuterated solvent ($CDCl_3$) (**1**/**2** = 1:0.8–0.6). As the formation of the diastereoisomeric mixtures is quantitative and fast and can be performed directly in the NMR tube, the ^{195}Pt-NMR spectroscopy constitutes an ease way to their analysis. In fact, the spectral characteristics of the nucleus involved (^{195}Pt, I = 1/2, 33% natural abundance) make possible their detection in short instrumental times (about 5–10 min) by using standard pulse sequences, for solutions containing about 100 mg of substances in 0.5 ml of deuterated solvent and the analysis of the diastereoisomers is not complicated by splittings due to *J* coupling (at least in this kind of complexes). Finally, the same equilibrium reaction (Scheme 1), which is employed to obtain the diastereoisomeric mixture, can be used to recover both the CDA and the complexed unsaturated substrate, by treating with an excess of ethylene. The coordination of the two prochiral faces of the double bond of each enantiomer of the unsaturated analyte produces two diastereoisomers whose ratio depends on its structure (Scheme 1). Therefore, complexes **3** are constituted by a maximum number of four diastereoisomers in solution. As, in principle, each of them can originate a single ^{195}Pt resonance, the determination of the enantiomeric composition can be simply performed by comparing the areas of the signals originated by each enantiomer.

In the ^{195}Pt-NMR spectra of mixtures **3**, obtained by coordination of substrates **2**, we always detected separate absorptions (Table 1) for the diastereoisomers produced by each enantiomer. In the simplest case, as for racemic allyl ether **2a**, the ^{195}Pt-NMR spectrum of the diastereoisomeric mixture showed only two well re-

Table 1
^{195}Pt-NMR spectrum (64.3 MHz, $CDCl_3$, 25°C, Na_2PtCl_6 external standard) of diastereoisomeric complexes containing compounds **2**

Complex	δ (ppm)
3a	−2715, −2693
3b	−2742, −2713, −2653, −2636
3c	−2714, −2700, −2695, −2678
3d	−2692, −2670
3e	−2731, −2724, −2710, −2701
3f	−2727, −2708, −2700
3g	−2726, −2722

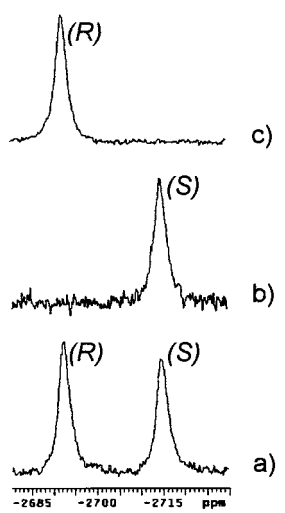

Fig. 1. ^{195}Pt-NMR spectrum (64.3 MHz, $CDCl_3$, 25°C, Na_2PtCl_6 external standard) of complex *cis*-dichloro[(*S*)-α-methylbenzylamine](**2a**)Pt(II): (a) (*R*)(*S*)-**2a**; (b) (*S*)-**2a**; (c) (*R*)-**2a**.

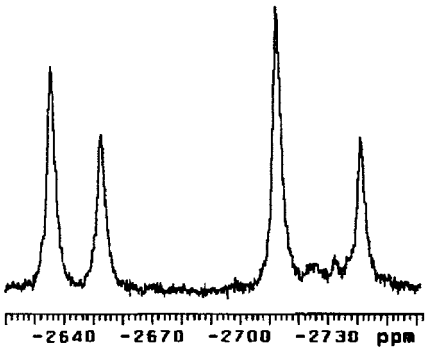

Fig. 2. ^{195}Pt-NMR spectrum (64.3 MHz, $CDCl_3$, 25°C, Na_2PtCl_6 external standard) of complex *cis*-dichloro[(*S*)-α-methylbenzylamine][(*R*)(*S*)-**2b**]Pt(II).

solved resonances at −2715 and −2693 ppm, having equal intensities (Fig. 1a). The comparison of this spectrum with those of the complexes prepared from the single enantiomers (Fig. 1b, c) allowed us to assign the two resonances to the complexed (*S*)- and (*R*)-enantiomers, respectively.

The mixture arising from the complexation of racemic **2b** gives rise to two pairs of sharp signals having different intensities, each due to a single enantiomer (Fig. 2). Therefore, in the case of **2b**, having two alkyl substituents at the quaternary chiral center, each enantiomer originates different amounts of two diastereoisomers which are all detected: probably the coordination of the prochiral face bringing the sterically hindered ^{t}Bu group in proximity of the platinum is less favorable than the coordination of the other prochiral face bringing the Me group towards the metal. It is noted that in the above case of **2a**, leading a phenyl and an alkyl group, where only two signals were detected, the complexation of each enantiomer proceeds with total diastereoselectivity or ^{195}Pt-NMR cannot distinguish the complexation of the two prochiral faces of each enantiomer.

For allyl alcohol **2c**, structurally analogous to **2a**, four absorptions are observed (Table 1) corresponding to the complexation of the two enantiofaces of the two enantiomers, whereas in the case of **2d**, having an isopropyl group in place of the methyl one, only two signals are observed.

Also homoallylic systems are discriminated in the ^{195}Pt-NMR spectra of the corresponding complexes (Table 1), however the chemical shift differences are lower than they are for allylic compounds, probably due to the minor rigidity of the coordinated unsaturated substrate in the former, relatively to the latter ones, as observed for the structurally analogous **2c** and **2e**. The introduction of a more hindered isopropyl group in **2f** diminishes the chemical shift differences of the prevailing stereoisomers, which originate two partially superimposed resonances, whereas the two minor isomers are still differentiated. The coordination of the ether **2g**, analogous of **2f**, proceeds with total stereoselectivity originating only two signals.

However, the important fact is that for all cases, the relative amounts of the two enantiomers can be measured or directly comparing the areas of the two signals (**2a**, **2d**, **2g**) or the sum of the areas of the two signals originated by each enantiomer (**2b**, **2c**, **2e**, **2f**).

3. Conclusions

In conclusion, complex **1** represents an efficient CDA for NMR spectroscopy having a widespread applicability to the analyses of unsaturated ethers or alcohols containing an allylic or homoallylic quaternary chiral carbon atom. To this regard we wish to focus that, overall in the case of ethers, no alternative general direct methods of analyses have been reported. Taking into account that efficiency of CDA **1** in the enantiomeric purity determination of analogous allylic ethers and alcohols having a tertiary chiral carbon atom had been already proved [2e], it affords one of the most general direct methods for the analyses of this kind of compounds. Previous investigations [4] on complexes containing a primary amine *cis* to a chiral allyl ether demonstrated the occurrence of a hydrogen bond interaction NH···O, which imposes different proximity constraints between the platinum nucleus and the groups bound to the chiral carbon atom of the coordinated unsaturated ether, as well as between it and the amine ligand. Reasonably, these interactions are responsible for the different deshielding effects on the metal nucleus, thus leading to the possibility of differentiating between the ^{195}Pt absorptions of the diastereoisomeric species.

4. Experimental

4.1. General

^{195}Pt-NMR spectra were recorded in $CDCl_3$ at 64.3 MHz. All ^{195}Pt-NMR chemical shifts are referenced to Na_2PtCl_6 as external standard and the ^{195}Pt resonance of *cis*-dichloro[(*S*)-α-methylbenzylamine](ethylene)-Pt(II) (**1**) is at lower frequencies (−2780 ppm) than the absorptions due to complexes containing substrates **2**. Standard pulse sequences have been employed for ^{195}Pt-NMR measurements.

4.2. Materials

Carbonyl compounds were purchased from Fluka A.G. Co., Buchs. Tetrahydrofuran (THF) was distilled from $LiAlH_4$ prior to use. Grignard reagents were

prepared in THF and standardized by titration methods. Alcohols were prepared by addition of Grignard reagents to carbonyl compounds [5]. Racemic **2c** was resolved by crystallization of brucine salts of its hydrogenphtalate [6]. The methyl ethers were prepared from the corresponding alcohols first with sodium hydride and then with methyl iodide [7]. *cis*-Dichloro[(*S*)-α-methylbenzylamine](ethylene)platinum(II) (**1**) has been prepared according to literature procedure [8].

2a: 60% yield; b.p. 45°C (1 mmHg); ^{1}H-NMR $\delta =$ 1.59 (3H, s, CH_3), 3.18 (3H, s, OCH_3), 5.23 (1H, dd, $J = 17.4$ Hz, $J = 1.2$ Hz, C=CH_2), 5.25(1H, dd, $J = 10.6$ Hz, $J = 1.2$ Hz, C=CH_2), 6.01 (1H, dd, $J = 17.4$ Hz, $J = 10.6$ Hz, C*H*=CH_2), 7.19–7.44 (5H, m, Ph); ^{13}C-NMR $\delta = 23.9$, 50.7, 114.4, 126.2, 127.0, 128.1, 142.7, 144.5. Anal. Calc. for $C_{11}H_{14}O$: C, 81.44; H, 8.70. Found: C, 81.41; H, 8.66%.

2b: 57% yield; b.p. 120–121°C; ^{1}H-NMR $\delta = 0.91$ (9H, s, ^{t}Bu), 1.18 (3H, s, CH_3), 3.12 (3H, s, OCH_3), 5.06 (1H, dd, $J = 17.3$ Hz, $J = 1.6$ Hz, C=CH_2), 5.23 (1H, dd, $J = 10.7$ Hz, $J = 1.6$ Hz, C=CH_2), 5.81 (1H, dd, $J = 17.3$ Hz, $J = 10.7$ Hz, C*H*=CH_2). Anal. Calc. for $C_9H_{18}O$: C, 76.00; H, 12.75. Found: C, 76.08; H, 12.73%.

2c: 63% yield; b.p. 72°C (1 mmHg) [lit. [5a] b.p. 73–74°C (1 mmHg)]; ^{1}H-NMR $\delta = 1.64$ (3H, s, CH_3), 2.29 (1H, bs, OH), 5.13 (1H, dd, $J = 10.5$ Hz, $J = 1.1$ Hz, C=CH_2), 5.28 (1H, dd, $J = 17.1$ Hz, $J = 1.1$ Hz, C=CH_2), 6.16 (1H, dd, $J = 17.1$ Hz, $J = 10.5$ Hz, C*H*=CH_2), 7.20–7.51 (5H, m, Ph); ^{13}C-NMR $\delta = 29.3$, 112.3, 125.1, 127.0, 128.2, 144.9, 146.4. Anal. Calc. for $C_{10}H_{12}O$: C, 81.04; H, 8.16. Found: C, 81.08; H, 8.18%.

2d: 94% yield; b.p. 122°C (17 mmHg) [lit. [5b] b.p. 119–120°C (18 mmHg)]; ^{1}H-NMR $\delta = 0.77$ (3H, d, $J = 6.9$ Hz, CH_3), 0.89 (3H, d, $J = 6.9$ Hz, CH_3), 1.77 (1H, bs, OH), 2.17 (1H, dq, $J = 6.9$ Hz, CH), 5.17 (1H, dd, $J = 10.7$ Hz, $J = 1.2$ Hz, C=CH_2), 5.31 (1H, dd, $J = 17.2$ Hz, $J = 1.2$ Hz, C=CH_2), 6.28 (1H, dd, $J =$ 17.2 Hz, $J = 10.7$ Hz, C*H*=CH_2), 7.17–7.49 (5H, m, Ph); ^{13}C-NMR $\delta = 16.7$, 17.1, 37.3, 112.7, 125.5, 126.6, 128.0, 143.2, 145.7. Anal. Calc. for $C_{12}H_{16}O$: C, 81.77; H, 9.15. Found: C, 81.75; H, 9.19%.

2e: 96% yield; b.p. 100°C (17 mmHg) [lit. [5c] 98–112°C (15 mmHg)]; ^{1}H-NMR $\delta = 1.53$ (3H, s, CH_3), 2.18 (1H, bs, OH), 2.48 (1H, ddt, $J = 13.8$ Hz, $J = 8.3$ Hz, $J = 1.0$ Hz, CH_2), 2.67 (1H, ddt, $J = 13.8$ Hz, $J = 6.4$ Hz, $J = 1.0$ Hz, CH_2), 5.09 (1H, ddt, $J = 10.3$ Hz, $J = 2.3$ Hz, $J = 1.0$ Hz, C=CH_2), 5.11 (1H, ddt, $J = 16.8$ Hz, $J = 2.3$ Hz, $J = 1.0$ Hz, C=CH_2), 5.61 (1H, m, CH=CH_2), 7.15–7.50 (5H, m, Ph); ^{13}C-NMR $\delta =$ 29.9, 48.5, 119.3, 124.7, 126.6, 128.1, 133.7, 147.7. Anal. Calc. for $C_{11}H_{14}O$: C, 81.44; H, 8.70. Found: C, 81.40; H, 8.73%.

2f: 94% yield; b.p. 120°C (17 mmHg) [lit. [5d] b.p. 118–124°C (17 mmHg)]; ^{1}H-NMR $\delta = 0.75$ (3H, d, $J = 6.9$ Hz, CH_3), 0.93 (3H, d, $J = 6.9$ Hz, CH_3), 1.92 (1H, bs, OH), 1.99 (1H, dq, $J = 6.9$ Hz, CH), 2.52 (1H, dd, $J = 13.8$ Hz, $J = 8.9$ Hz, CH_2), 2.79 (1H, ddt, $J = 13.8$ Hz, $J = 5.5$ Hz, $J = 1.2$ Hz, CH_2), 5.05 (1H, dd, $J = 9.9$ Hz, $J = 1.2$ Hz, C=CH_2), 5.11 (1H, ddt, $J = 16.9$ Hz, $J = 1.2$ Hz, $J = 1.2$ Hz, C=CH_2), 5.46 (1H, m, C*H*=CH_2), 7.16–7.45 (5H, m, Ph); ^{13}C-NMR $\delta =$ 16.8, 17.5, 37.9, 43.9, 119.4, 126.0, 126.3, 127.7, 134.0, 140.3. Anal. Calc. for $C_{13}H_{18}O$: C, 82.06; H, 9.53. Found: C, 82.03; H, 9.50%.

2g: 73% yield; b.p. 70–71°C (1 mmHg); ^{1}H-NMR $\delta = 0.71$ (3H, d, $J = 6.7$ Hz, CH_3), 0.74 (3H, d, $J = 6.7$ Hz, CH_3), 2.10 (1H, dq, $J = 6.7$ Hz, CH), 2.74 (1H, ddt, $J = 15.6$ Hz, $J = 5.4$ Hz, $J = 1.8$ Hz, CH_2), 2.89 (1H, ddt, $J = 15.6$ Hz, $J = 8.3$ Hz, $J = 1.1$ Hz, CH_2), 3.17 (3H, s, OCH_3), 5.12 (1H, ddt, $J = 10.1$ Hz, $J = 1.4$ Hz, $J = 1.1$ Hz, C=CH_2), 5.18 (1H, ddt, $J = 17.1$ Hz, $J = 1.8$ Hz, $J = 1.4$ Hz, C=CH_2), 5.89 (1H, m, C*H*=CH_2), 7.18–7.42 (5H, m, Ph); ^{13}C-NMR $\delta = 16.7$, 17.8, 34.8, 36.5, 50.3, 117.4, 126.0, 126.5, 127.3, 127.9, 134.0, 140.4. Anal. Calc. for $C_{14}H_{20}O$: C, 82.30; H, 9.87. Found: C, 82.33; H, 9.83%.

4.3. General procedure

4.3.1. Enantiomeric composition determination

The complex **1** (50 mg) is suspended in 0.5 ml of $CDCl_3$ into the NMR tube and added by **2** (molar ratio **1**/**2** = 1:0.8–0.6). The sample is then analyzed by ^{195}Pt-NMR.

4.3.2. Preparation and purification of cis-dichloro-[(S)-α-methylbenzylamine](2)platinum(II) (3)

On treatment of **1** (50–210 mg) in CH_2Cl_2 solution (5 ml) with **2** (molar ratio **1**/**2** = 1:1), the ethylene was immediately displaced. Removal of the solvent under vacuum afforded **3** quantitatively as a pale yellow microcrystalline solid. The crude product was purified (60–70% yield) by crystallization at room temperature from $CHCl_3$–pentane (1:2). Elemental analyses and melting points of the crystallized complexes **3** are as follows.

3a: m.p. 145–147°C. Anal. Calc. for $C_{19}H_{25}Cl_2NOPt$: C, 41.54; H, 4.59; N, 2.55. Found: C, 41.27; H, 4.36; N, 2.87%.

3b: m.p. 107–109°C. Anal. Calc. for $C_{17}H_{29}Cl_2NOPt$: C, 38.57; H, 5.52; N, 2.65. Found: C, 38.45; H, 5.68; N, 2.47%.

3c: m.p. 167–169°C. Anal. Calc. for $C_{18}H_{23}Cl_2NOPt$: C, 40.38; H, 4.33; N, 2.62. Found: C, 39.77; H, 4.63; N, 2.36%.

3d: m.p. 145–146°C. Anal. Calc. for $C_{20}H_{27}Cl_2NOPt$: C, 42.64; H, 4.83; N, 2.49. Found: C, 43.49; H, 5.01; N, 2.31%.

3e: m.p. 103–105°C. Anal. Calc. for $C_{19}H_{25}Cl_2NOPt$: C, 41.54; H, 4.59; N, 2.55. Found: C, 40.65; H, 4.69; N, 2.14%.

3f: m.p. 99–101°C. Anal. Calc. for $C_{21}H_{29}Cl_2NOPt$: C, 43.68; H, 5.06; N, 2.43. Found: C, 43.54; H, 5.14; N, 1.92%.

3g: m.p. 117–119°C. Anal. Calc. for $C_{22}H_{31}Cl_2NOPt$: C, 44.67; H, 5.28; N, 2.37. Found: C, 44.32; H, 5.41; N, 2.48%.

Acknowledgements

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References

[1] (a) D. Parker, Chem. Rev. 91 (1991) 1441. (b) S. Yamaguchi, in: J.D. Morrison (Ed.), Asymmetric Synthesis, vol. 1, Academic, New York, 1983, p. 125–149. (c) R. Hulst, R.M. Kellogg, B.L. Feringa, Recl. Trav. Chim. Pays-Bas 114 (1995) 115.

[2] (a) D. Parker, R.J. Taylor, Tetrahedron 44 (1988) 2241. (b) D. Parker, R.J. Taylor, J. Chem. Soc. Chem. Commun. (1987) 1781. (c) S.Y.M. Chooi, P. Leung, C.C. Lim, K.F. Mok, G.H. Quek, K.Y. Sim, M.K. Tan, Tetrahedron Asymm. 3 (1992) 529. (d) J.M. Buriak, J.A. Osborn, J. Chem. Soc. Chem. Commun. (1995) 689. (e) P. Salvadori, G. Uccello-Barretta, S. Bertozzi, R. Settambolo, R. Lazzaroni, J. Org. Chem. 53 (1988) 5768. (f) P. Salvadori, G. Uccello-Barretta, R. Lazzaroni, A.M. Caporusso, J. Chem. Soc. Chem. Commun. (1990) 1121. (g) G. Uccello-Barretta, F. Balzano, P Salvadori, R. Lazzaroni, A.M. Caporusso, R. Menicagli, Enantiomer 1 (1996) 365. (h) V.V. Dunina, L.G. Kuz'mina, M. Yu. Kazakova, Yu. K. Grishin, Yu. A. Veits, E.I. Kazakova, Tetrahedron Asymm. 8 (1997) 2537. (i) B. Staubach, J. Buddrus, Angew. Chem. Int. Ed. Engl. 35 (1996) 1344. (j) J. Albert, J. Granell, G. Muller, D. Sainz, M. Font-Bardia, X. Solans, Tetrahedron Asymm. 6 (1995) 325. (k) J. Klein, S. Neels, R. Borsdorf, J. Chem. Soc. Perkin Trans 2 (1994) 2523. (l) D.B. Grotjahn, C. Joubran, Tetrahedron Asymm. 6 (1995) 745.

[3] (a) R. Lazzaroni, P. Salvadori, P. Pino, Tetrahedron Lett. (1968) 2507. (b) R. Lazzaroni, G. Uccello-Barretta, D. Pini, S. Pucci, P. Salvadori, J. Chem. Res. (S) (1983) 286.

[4] G. Uccello-Barretta, R. Lazzaroni, C. Bertucci, P. Salvadori, Organometallics 6 (1987) 550.

[5] (a) C.S. Marvel, G.R. Woolford, J. Org. Chem. 23 (1958) 1658. (b) J. Cologne, J.-C. Brunie, Bull. Soc. Chim. Fr. 1 (1963) 42. (c) V.R. Skvarchenko, W.-L. Ling, N.V. Sedykh, R. Ya. Levina, Zh. Obshch. Khim. 32 (1962) 217. (d) K. Maruyama, K. Murakami, Bull. Chem. Soc. Jpn. 41 (1968) 1401.

[6] R.J.D. Evans, S.R. Landor, J. Chem. Soc. (1965) 2553.

[7] C.A. Brown, D. Barton, Synthesis (1974) 434.

[8] A. Panunzi, G. Paiaro, J. Am. Chem. Soc. 88 (1966) 4843.