ELSEVIER

# Preliminary communication

# A unique $Li_{12}$-aggregate containing both $-NLi_2$ and $-CHLi \sim NLi$ units

Sarah C. Ball, James Cobb, Robert P. Davies, Paul R. Raithby, Gregory P. Shields, Ronald Snaith *

*Department of Chemistry, University of Cambridge, Lensfield Road, Cambridge CB2 1EW, UK*

## Abstract

Dilithiation of 2-methylpyridine followed by PhCN insertion affords the complex $\{[C_5H_4N \cdot CHC(Ph)N]^{2-} \cdot 2Li^+\}_6 \cdot (THF)_4$, 5. The crystal structure of 5 reveals an unusual $Li_{12}$ aggregate containing four types of $Li^+$ cation and two types of dianionic ligand which bond to the metal centres via exclusively N–Li interactions or via combinations of C–Li and N–Li coordinations.

*Keywords:* Lithium; Reaction mechanisms; Dilithiated molecules; X-ray structure; Pyridine; Imide
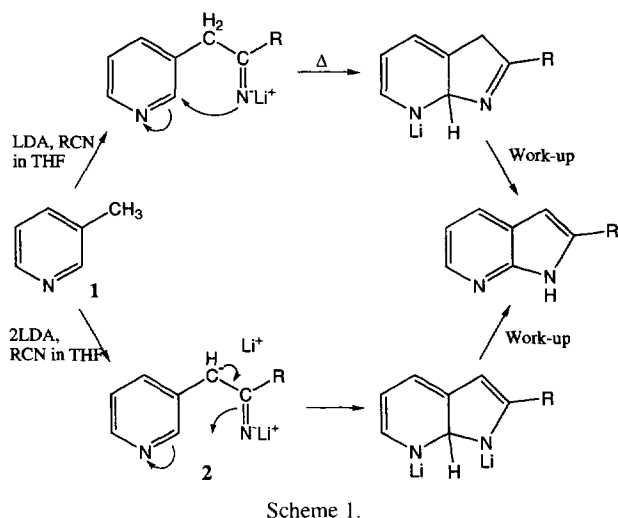
Our recent work has concentrated on isolating and characterising lithium intermediates which occur during 'one-pot' organic syntheses involving lithiations [1–3]. Of particular interest has been the intermediacy or otherwise of *di*lithiated organic molecules. Although such species are often proposed to be present prior to work-up in numerous organic syntheses, we have failed to obtain solid dilithiated compounds from our examinations thus far of a series of such syntheses: the α-lithiation of lithium carbamates leading to the specific α-substitution of NH-containing heterocycles [1,4], the dilithiation and $CS_2$ insertion reactions of $R_2CH_2$ precursors leading to ketene dithioacetals [2,5], and the carboxamide-directed lithiations of lithium azoenolates [3,6]. Possible explanations of this discrepancy — the clear inference, given the final organic product gained after work-up, that dilithiation has occurred and yet the failure to isolate such a species — have included: (i) a dilithium compound is formed but only in trace amounts, the equilibrium between the mono- and dilithiated compounds then being driven forward by reaction between the latter and the added electrophile, and (ii) the second equivalent of the lithiating reagent joins with the monolithium derivative to form a quasi-dianion complex (QUADAC) [7] which then behaves like a true dianionic species on addition of electrophile.

Here we describe results related to a further organic protocol suggested to involve dilithiated intermediates

[8]. In this, lithiation of β-methylazines (pyridines, quinolines, pyrazines, quinoxalines, pyrimidines) followed by insertion of a nitrile can lead to ring closure reactions, as illustrated in Scheme 1 (top equation) for 3-methylpyridine, **1**. Although reactions of this type give only modest yields of the cyclisation products and require harsh conditions, it was found that higher yields could be gained under milder conditions by using an excess of the lithiating reagent (Scheme 1, bottom equation). It was suggested that removal of a second methyl proton, so giving a dilithium intermediate of type **2**, aids the cyclisation process. In our present study, we describe the isolation and solid-state structure of a complex related to **2**. Synthesised from reaction of 2-methylpyridine **3** with LDA (two equivalents) and PhCN, the product is a highly complicated aggregate of genuinely (non-QUADAC) dilithiated organic molecules and consists of six dianions, 12 $Li^+$ cations and four THF molecules. However, the six dianions are not all equivalent but rather they (with their $Li^+$ cations) are of two types which can be represented by **4** and **4'**.
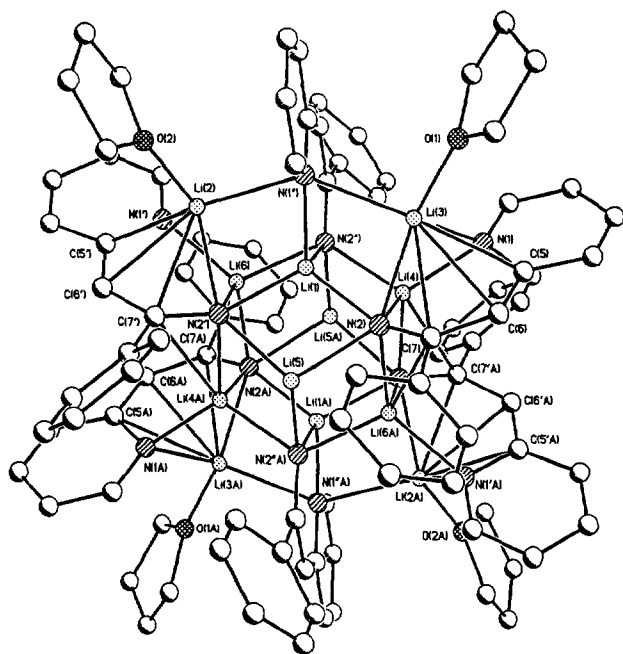


* Corresponding author.

Scheme 1.



Fig. 1. Molecular structure of **5** (hydrogen atoms, toluene solvent molecules, and the disorder among the THF molecules are omitted for clarity).
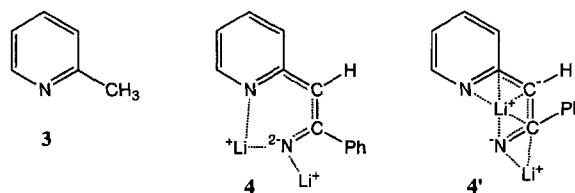
Reaction of 3-methylpyridine **1** in THF with two equivalents of LDA and PhCN (Scheme 1, bottom equation) failed to afford any crystalline dilithiated material. Accordingly, we switched to the analogous reaction of the more acidic precursor 2-methylpyridine **3**. This gave a red solution; removal of most of the THF led to precipitation of an orange powder. Crystallisation of this from toluene gave orange-red crystals **5** in good yield; no other crystalline substance could be isolated. Complex **5** was partly characterised by elemental analysis and by $^1$H, $^{13}$C NMR spectroscopy. In particular the spectra showed the presence of an aliphatic CH unit and not of a $CH_2$ unit, implying that dilithiation has occurred to give $[C_5H_4N \cdot CHC(Ph)N]^{2-} \cdot 2Li^+$. [1] Furthermore, they indicated the presence of THF and toluene solvate molecules, approximately a half and a third of a molecule respectively per formula unit of the dilithium species. The solid-state structure of **5** was then

solved by X-ray crystallography, [2] revealing it to be $\{[C_5H_4N \cdot CHC(Ph)N]^{2-} \cdot 2Li^+\}_6 \cdot (THF)_4 \cdot (toluene)_2$. The molecular structure (excluding toluene solvent molecules and H atoms) and pertinent atom numbering system for **5** are shown in Fig. 1. Fig. 2 depicts only the 12 $Li^+$ cations, the six imide and six pyridyl N atoms of the dianions, and the O atoms of the four THF molecules. At first glance it seems that there are three types of $Li^+$

---

[1] Synthesis and characterisation of **5**: 2-methylpyridine (0.47 g, 5 mmol) was added to a chilled solution of LDA ($^iPr_2NLi$, 1.07 g, 10 mmol) in THF (8 ml). The resulting orange-red solution was warmed to room temperature prior to addition of PhCN (0.52 g, 5 mmol). The then dark red solution precipitated an orange micro-crystalline solid on almost total removal of solvent. Dissolution of this in toluene (13 ml) and subsequent refrigeration of the solution over 1 day afforded orange-red crystals of **5**, $\{[C_5H_4N \cdot CHC(Ph)N]^{2-} \cdot 2Li^+\}_6 \cdot (THF)_4 \cdot (toluene)_2$. First batch yield, 0.80 g (56%); continued refrigeration of the solution gave further crystals of **5** (summed yield ca. 75% after 3 days). Anal. for **5**, $C_{108}H_{108}Li_{12}N_{12}O_4$. Found: C, 74.8; H, 6.4; Li, 4.5; N, 10.3%. Calc.: C, 75.3; H, 6.3; Li, 4.9; N, 9.8%. In the $^1$H NMR spectrum (250 MHz, DMSO) the CH proton appears at $\delta$4.60 (s, 1H by integration relative to the $C_5H_4N$ and Ph resonances). In the $^{13}$C NMR spectrum (100.6 MHz, DMSO) the CH carbon resonance is at $\delta$86.5 (H odd by ATP scans).

[2] Crystallographic data for **5**: $C_{108}H_{108}Li_{12}N_{12}O_4$; $M = 1721.34$, transparent block, crystal dimensions $0.26 \times 0.33 \times 0.40\,mm^3$, triclinic, $P\bar{1}$ (No. 2), $a = 13.652(3)$, $b = 13.964(3)$, $c = 14.799(3)$ Å, $\alpha = 103.29(3)$, $\beta = 112.95(3)$, $\gamma = 103.48(3)°$; $V = 2358.7(8)$ Å$^3$, $D_{calc} = 1.212\,Mg\,m^{-3}$, $Z = 1$, $F(000) = 908$, $Mo\,K\alpha$ radiation, $\lambda = 0.71073$ Å, $\mu(Mo\,K\alpha) = 0.072\,mm^{-1}$, $T = 153(2)$ K. Data were collected on a Stoe four-circle diffractometer equipped with an Oxford Cryostream crystal cooling apparatus. A total of 10 127 reflections (8276 independent) were collected in the range $4.07 \le \theta \le 25.00°$. Structure solved by direct methods (SHELXTL-PLUS) and refined with all non-hydrogen atoms anisotropic by full-matrix least squares based on $F^2$ (SHELXL-93); H-atoms were included in idealised positions. The four THF molecules were each positionally disordered over two different sites and were refined with partial occupancies. The final cycle of refinement included 654 parameters with unweighted $R_1 = 0.0730$ on 4904 data with $I > 2\sigma(I)$ and weighted $wR_2 = 0.2016$ on all data. G.o.f. = 1.059, weighting scheme $w^{-1} = [\sigma^2(F^2) + (0.0589P)^2 + 3.04P]$ where $P = 2F_c^2/3$. Highest peak in final difference map $0.288\,e\,\text{Å}^{-3}$. Atomic coordinates, bond lengths and angles, and vibrational parameters have been deposited at the Cambridge Crystallographic Data Centre. This information may be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK.
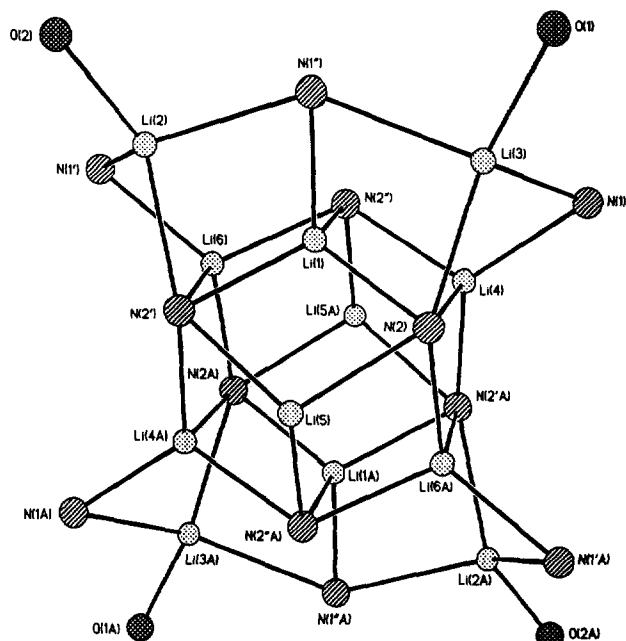
Fig. 2. The 12 $Li^+$ cations, six imide and six pyridyl N atoms, and four O atoms (of THF) found in the structure of 5.

cation present. Six of these form a double hexagonal core with the six imide N atoms. This core could be viewed (Fig. 2) as being comprised of two stacked six-membered $N_3Li_3$ rings, Li(1)N(2)Li(6A)N(2″A)Li(4A)N(2′) on top joined via imide N–Li inter-ring bonds to their symmetry-related atoms below. Such stacked-ring arrangements are well known, in particular for a series of hexameric imidolithium compounds (RR′C=NLi)₆ (see Ref. [9] and for reviews of organonitrogen–lithium compounds see Ref. [10]). However, while their $N_3Li_3$ rings are somewhat puckered (typically, summed internal ring angles are about 695°) in 5 this distortion is much more severe (sum of angles 664.4°). In part, this seems to be to allow accommodation of the second type of $Li^+$ cation, Li(5) which sits above the top ring and Li(5A) which sits below the bottom one. The remaining cations [Li(2), Li(3) and symmetry-related] are found outside this capped core and each is complexed by a THF molecule. In fact, however, closer inspection of Fig. 2 shows that the $Li^+$ cations of the $N_6Li_6$ core are not identical: two of them [Li(1), Li(1A)] are attached to pyridyl N atoms which are each involved with two *exo* $Li^+$ cations whereas the remaining four $Li^+$ cations are coordinated to pyridyl N atoms each of which is bonded to just one *exo* $Li^+$ centre. Overall, therefore, the structure of 5 contains four distinctive types of $Li^+$ cation.

A more detailed analysis of the structure of 5 allows assignment of $Li^+$ cations as being essentially N-attached or C-attached (or, for some cations, both) and thereby clarifies the natures of the dianionic ligands. Four of the 12 metal cations are clearly exclusively

N-attached. Those found capping the $N_6Li_6$ core [Li(5), Li(5A)] are bonded only to three imide N atoms [Li(5)–N(2″A) 2.020(7), Li(5)–N(2) 2.097(7), Li(5)–N(2′) 2.095(7) Å]. Two of the $Li^+$ centres of the core [Li(1), Li(1A)] are also exclusively N-attached but now four-coordinate, with bonds to three imide N atoms [Li(1)–N(2″) 2.041(6), Li(1)–N(2) 1.954(7), Li(1)–N(2′) 2.008(6) Å] and to one pyridyl N atom [Li(1)–N(1″) 1.988(6) Å]. These four cations can be assigned to two dianions: Li(1) and Li(5A) to that containing imide N(2″), and Li(1A) and Li(5) to that containing imide N(2″A). Inspection of Fig. 1 makes it clear that these two dianions exhibit no C–Li contacts whatsoever. They and their $Li^+$ cations can be considered as $[C_5H_4N \cdot CHC(Ph)N]^{2-} \cdot 2Li^+$ units, 4. In fact, such formally *geminal* dilithium species are extremely rare, the only known structure of a dilithiated primary amine being that of $(NaphthylNLi_2)_{10} \cdot 7Et_2O$ which has an $N_{10}Li_{14}$ core [11]. More recently the first dilithiated phosphane and arsane species of types $(RPLi_2)_8 \cdot Li_2O$ and $(RAsLi_2)_{12} \cdot Li_2O$ have been structurally characterised [12]. A $Li_{12}$ species as such — though with a very different molecular framework from that in 5 — has also been found for a THF complex of dilithioacetylacetone [13].

The other four dianions of 5 engage in both N–Li and C–Li bonding. Each dianion can be assigned formally to one of the remaining $Li^+$ cations of the $N_6Li_6$ core [Li(4), Li(6) and their symmetry-related atoms] and to one of the cations exo the core [Li(2), Li(3) and their symmetry-related atoms]. Each core $Li^+$ bonds to three imide N atoms [Li(4)–N(2″) 2.048(7), Li(4)–N(2′A) 2.137(7), Li(4)–N(2) 2.082(7); Li(6)–N(2A) 2.116(7), Li(6)–N(2″) 2.061(7), Li(6)–N(2′) 2.129(7) Å] and to one pyridyl N atom [Li(4)–N(1) 2.035(7); Li(6)–N(1′) 2.028(7) Å]. In addition, each cation has a long contact to an imide C atom [Li(4)–C(7′A) 2.618(7); Li(6)–C(7A) 2.625(7) Å]. Much more striking are the coordinations of the exo $Li^+$ cations, each having no fewer than seven attachments of significance (Fig. 1). These are to an imide N atom of the core [Li(2)–N(2′) 2.154(7); Li(3)–N(2) 2.195(7) Å], to two pyridyl N atoms [Li(2)–N(1′) 2.146(7), Li(2)–N(1″) 2.392(8); Li(3)–N(1) 2.137(7), Li(3) – N(1″) 2.334(8) Å], to an O atom of a THF molecule [Li(2)–O(2) 1.907(7); Li(3)–O(1) 1.936(7) Å], and, most significantly, to three C atoms: the $\alpha$C of the pyridyl ring [Li(2)–C(5′) 2.575(8); Li(3)–C(5) 2.515(8) Å], the CH unit of the dianion [Li(2)–C(6′) 2.568(8); Li(3)–C(6) 2.524(8) Å], and the imide C [Li(2)–C(7′) 2.341(8); Li(3)–C(7) 2.392(8) Å]. Consideration of these coordinations allows assignments of specific dianions to specific pairs of $Li^+$ cations: Li(2) and Li(4A) to the dianion containing imide N(2′) and pyridyl N(1′), Li(3) and Li(6A) to that containing imide N(2) and pyridyl N(1). Taking just the former set, it can be seen (Fig. 1) that Li(4A) bridges the imide

C=N unit [C(7')–N(2') 1.323(4) Å] although the long Li–C contact [2.618(7) Å] suggests that Li(4A) is near-exclusively N-attached [distance 2.137(7) Å]. In contrast, Li(2) interacts much more extensively with its dianion, contacting the pyridyl N, the $\alpha$C of the pyridyl ring, the CH unit produced by the dilithiation of the original $CH_3$ group, the imide C, and the imide N (relevant distances noted above). A somewhat similar profundity of Li...C and Li...N interactions has been found in one or two other dilithiated molecules, the closest structural analogy being perhaps with the $Li_8$ aggregate $(o\text{-}LiC_6H_4CH_2NLiCH_2CH_2NMe_2)_4$ [14]. However, in 5 the Li–imide + C distances especially [e.g. Li(2)–C(7') 2.341(8) Å] are remarkably short (given that each such $Li^+$ is seven-coordinate), being similar to Li–C distances found in simple alkyllithium species, e.g. 2.31, 2.37 Å in $[(MeLi)_4]_\infty$ [15]. Overall, the four dianions which are each involved with a core $Li^+$ and with an *exo* $Li^+$ can be considered as $[C_5H_4N \cdot CH^-C(Ph)N^-]$ ligands within 4'. There is, of course, considerable charge delocalisation over the whole ligand framework {as there is for the other two dianions, formally of type $[C_5H_4N \cdot CHC(Ph)N^{2-}$, shown in 4} and this is reflected in the C=C and C=N distances.

In conclusion, the structure of 5 can best be formulated as $[C_5H_4N \cdot CHC(Ph)N^{2-} \cdot 2Li^+]_2 \cdot [C_5H_4N \cdot CH^-(Li \cdot THF)C(Ph)N^-Li^+]_4$. Its relevance to the mechanism of the cyclisation reaction which first prompted this study (Scheme 1) is strictly limited. Most pertinently, the structure of any dilithium species 2 derived from 3-methylpyridine 1 could not, from simple geometry, be totally analogous to that of 5, derived from 2-methylpyridine 3. Furthermore, the dianions found in 5 will be much more stabilised than any dianions produced by double deprotonation and RCN insertion of 3-methylpyridine. It may be, therefore, that a genuine dilithium species of type 2 is not produced at all in this latter system but rather that a QUADAC is formed: note, however, that we have been unable to isolate *any* dilithium species from this system. Despite these critical comments regarding the specific relevance of structure 5, it does give some interesting general pointers concerning proposed mechanisms which implicate dilithiated intermediates. The first is that it is unrealistic to represent such species as unsolvated monomers. The very complicated structure of 5 illustrates well that dilithiated organic molecules will be large aggregates: $Li^+$ cations will inevitably interact with several negative centres of several delocalised dianionic ligands, especially so when these ligands contain heteroatoms. In addition, such species — or, rather, at least some of their $Li^+$ cations — will invariably be complexed since polar solvents (ethers especially) are usually the reaction media employed. The detailed structure of 5 also raises the possibility that not all of the dianions within a dilithiated aggregate will be of the

same type. Such a prospect might be kept in mind since it could presumably be relevant to the reduced yields of single products anticipated (given the proposed mechanisms) and/or, related to this, to the occurrence of by-products. The final point is that it is really the *solution* nature of a species such as 5 that is relevant to the mechanism of any reaction involving it. It might be argued that the $Li_{12}$-aggregate found for 5 in the solid is present in solution as an $Li_2$-dianion formula unit/'monomer', as would be presented in an organic reaction scheme. However, this is unlikely on two counts. Firstly, aggregated 5 is obtained from THF solution and it is discrete, with no significant inter-aggregate contacts: lattice effects are minimal. Secondly, the sheer number of interlocking contacts within 5 — it contains for example $Li^+$ cations which are variously 3-, 4-, 5-, or 7-coordinate and imide N atoms which bond to four or five $Li^+$ centres — makes it improbable that the structure will be markedly deaggregated in solution. Nonetheless it may be somewhat amended: showing how, and to what, is not a trivial task, although it is one we are working on. A final daunting thought is that it may not after all be the solution structure of a species such as 5 which is relevant to a mechanism, but rather what such a species *becomes* (transiently, prior to the final product) once an electrophile is added (with, by definition, an accompanying nucleophile which may act as a Lewis base towards $Li^+$).

## References

[1] S.C. Ball, I. Cragg-Hine, M.G. Davidson, R.P. Davies, A.J. Edwards, I. Lopez-Solera, P.R. Raithby and R. Snaith, *Angew. Chem. Int. Ed. Engl.*, 34 (1995) 921.

[2] S.C. Ball, I. Cragg-Hine, M.G. Davidson, R.P. Davies, P.R. Raithby and R. Snaith, *J. Chem. Soc. Chem. Commun.*, (1996) 1581.

[3] M.G. Davidson, R.P. Davies, P.R. Raithby and R. Snaith, *J. Chem. Soc. Chem. Commun.*, (1996) 1695.

[4] A.R. Katritzky and K. Akutagawa, *Tetrahedron Lett.*, 26 (1985) 5935. A.R. Katritzky, L.M. Vazquez de Miguel and G.W. Rewcastle, *Synthesis*, (1988) 215.

[5] J.A. Goodwin, I. Kwok and B.J. Wakefield, *Synthesis*, (1990) 991.

[6] J.A. Turner, *J. Org. Chem.*, 48 (1983) 3401. A. Plant and D.J. Chadwick, *Synthesis*, (1990) 915.

[7] P.J. Crowley, M.R. Leach, O. Meth-Cohn and B.J. Wakefield, *Tetrahedron Lett.*, 27 (1986) 2909. W. Zarges, M. Marsch, K. Harms and G. Boche, *Angew. Chem. Int. Ed. Engl.*, 28 (1989) 1392. G. Boche, *Angew. Chem. Int. Ed. Engl.*, 28 (1989) 277.

[8] M.L. Davis, B.J. Wakefield and J.A. Wardell, *Tetrahedron, 48* (1992) 939.

[9] D. Barr, R. Snaith, W. Clegg, R.E. Mulvey and K. Wade, *J. Chem. Soc. Dalton Trans.*, (1987) 1071.

[10] R.E. Mulvey, *Chem. Soc. Rev.*, 20 (1991) 167. K. Gregory, P.v.R. Schleyer and R. Snaith, *Adv. Inorg. Chem.*, 37 (1991) 47.

[11] D.R. Armstrong, D. Barr, W. Clegg, S.R. Drake, R.J. Singer, R.

Snaith, D. Stalke and D.S. Wright, *Angew. Chem. Int. Ed. Engl.*, 30 (1991) 1707.

[12] M. Driess, H. Pritzkow, S. Martin, S. Rell, D. Fenske and G. Baum, *Angew. Chem. Int. Ed. Engl.*, 35 (1996) 986.

[13] W. Clegg, L. Horsburgh, R.E. Mulvey and M.J. Ross, *Angew. Chem. Int. Ed. Engl.*, 34 (1995) 1233.

[14] D. Barr, R. Snaith, D.S. Wright, R.E. Mulvey, K. Jeffrey and D. Reed, *J. Organomet. Chem.*, 325 (1987) C1. D. Barr, W. Clegg, S.M. Hodgson, R.E. Mulvey, D. Reed, R. Snaith and D.S. Wright, *J. Chem. Soc. Chem. Commun.*, (1988) 367.

[15] E. Weiss and G. Hencken, *J. Organomet. Chem.*, 21 (1970) 265.