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Practical Approach to Structurally Diverse Monoimine Salts and Nonsymmetrical Metallosalphen Complexes

Eduardo C. Escudero-Adán,[†] Marta Martínez Belmonte,[†] Jordi Benet-Buchholz,[†] and Arjan W. Kleij*[,†,‡]

*Institute of Chemical Research of Catalonia (ICIQ), Av. Països Catalans 16,
43007 Tarragona, Spain, and Institució Catalana de Recerca i Estudis Avançats
(ICREA), Pg. Lluís Companys 23, 08010 Barcelona, Spain*

akleij@iciq.es

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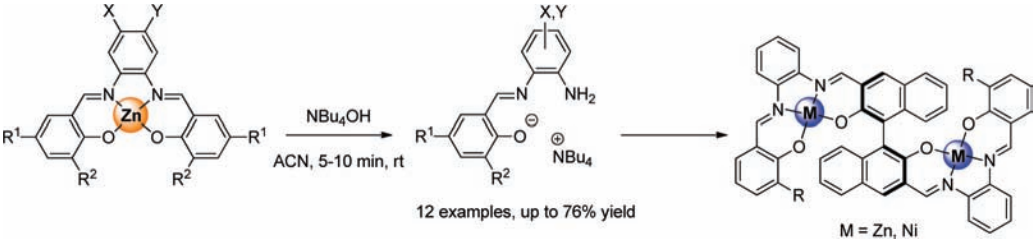
ABSTRACT



A practical approach toward the synthesis of monoimine NBu_4 salts derived from Zn(salphen) complexes is described. The method involves nucleophilic addition of the hydroxide anion to the imine bond followed by hydrolysis. These monoimines provide accessible and useful reagents for the synthesis of (chiral) metallosalens with fine-tunable properties.

Salen complexes are widely applied as versatile catalyst systems[1] and components of materials with interesting supramolecular and photophysical properties.[2] These properties may be altered by changing the substitution pattern on the aromatic rings of the (symmetrical) salen ligand, thereby creating options to fine tune electronic and steric effects.[3] Another less utilized route departs from desymmetrization of the salen structure by introduction of different groups on both salicylideneimine fragments.[4] This latter strategy is complicated by the difficulty to induce high selectivity when the diamine reagent is treated with two separate salicylaldehydes and usually gives a mixture of products that need to be separated by chromatographic methods.[5] In the past decade, various methods have been reported that focus on the selective formation of nonsymmetrical salen ligands/complexes.[6] One of these methods involves monoimine formation from diamine reagents by choosing appropriate

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[†] ICIQ.

[‡] ICREA.

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reaction stoichiometries and conditions to allow selective crystallization of the monoimine product from solution.[7] These monoimines can, in a second metal-templated condensation step, give easy access to nonsymmetrical complexes without scrambling of the imine bonds.[8] However, monoimine reagents with electron-withdrawing substituents are still difficult to prepare since the corresponding bis-Schiff base products cocrystallize with the desired monoimine, making isolation a tedious process. We recently set out to explore the synthesis of these electron-poor imines and report here a general method that allows easy formation of these reagents under very mild conditions. These compounds create new and extended possibilities for the electronic and steric fine-tuning of new push−pull systems,[9] salen complexes with predesigned electronic features to accommodate or improve catalytic conversions,[10] and new, conjugated macromolecular salen compounds.[11]

Scheme 1. Nucleophilic Addition of NBu_4OH to Zn(salphen) **1a** Giving Monoimine NBu_4 Salt **1b**

Our initial focus was on Zn(salphen) complex **1a** (Scheme 1, salphen = *N*,*N*′-bis[salicylideneimine]-1,2-phenylenediamine) which was treated with a methanolic solution of NBu_4OH (1 M) in CH_3CN at room temperature; we hypothesized that nucleophilic attack of the OH anion on the imine bond should allow for imine hydrolysis. It should be noted that complex **1a**, as for most of the Zn(salphen) complexes in this work, is virtually insoluble in CH_3CN as a result of strong self-dimerization and $\pi-\pi$ stacking interactions.[12] We recently reported that the axial position in the Zn(salphen) complex can be coordinated by various anions giving rise to stable assembled structures.[13] In the present case, addition of NBu_4OH to a suspension of **1a** in CH_3CN immediately provoked full dissolution of the solid material, and concomitantly a strong color change from orange to deep red was observed. After simple workup of the crude mixture (see Supporting Information), a crystalline red solid was isolated.

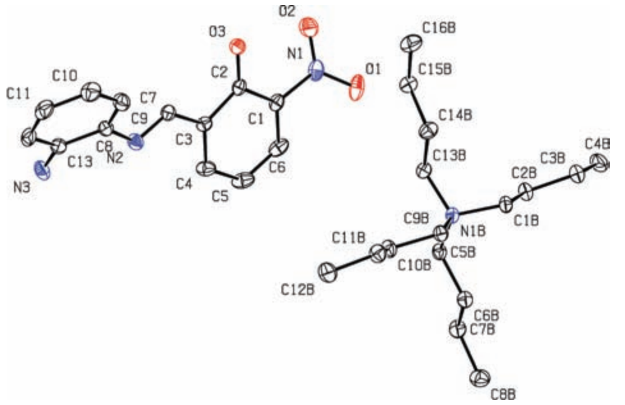

Figure 1. X-ray molecular structure of monoimine NBu_4 salt **1b**. H-atoms are omitted for clarity. Please note that the phenolic O-atom (O3) is anionic.

These crystals were first analyzed by ^1H NMR (DMSO-d_6) and revealed the presence of a product with a characteristic peak at 4.95 ppm (NH_2 group) and four distinct resonances that can be ascribed to a NBu fragment. X-ray diffraction then unambiguously determined the nature of this product, and the result is reported in Figure 1.[14] The structure comprises a monoimine salt (the phenolic position is deprotonated) with a NBu_4 counterion. In line with the NMR data, a "free" amine is present which should be the result of the hydrolysis of one of the imine bonds in **1a**. Upon analysis of the crude reaction mixture, we found further evidence for this assumption since the presence of 3-nitro-salicylaldehyde was confirmed by comparing the NMR characteristics with those of an authentic sample. It is therefore reasonable to consider a mechanism where nucleophilic addition of the OH anion to the imine bond[15,16] is mediated by initial OH coordination to **1a**.[13] This produces a homogeneous reaction mixture following addition of another OH anion with subsequent proton abstraction from (adventitious) water present in the medium. To further confirm that the OH anion

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(12) Zinc-based salphen complexes with groups that are sterically not sufficiently large enough give rise to dimer formation through μ-oxo bridges where one O-atom of each salphen ligand acts as an axial ligand. For recent work on this subject: (a) Martínez Belmonte, M.; Wezenberg, S. J.; Haak, R. M.; Anselmo, D.; Escudero-Adán, E. C.; Benet-Buchholz, J.; Kleij, A. W. *Dalton Trans.* **2010**, *39*, 4541. (b) Elemans, J. A. A. W.; Wezenberg, S. J.; Escudero-Adán, E. C.; Benet-Buchholz, J.; den Boer, D.; Coenen, M. J. J.; Speller, S.; Kleij, A. W.; De Feyter, S. *Chem. Commun.* **2010**, *46*, 2548.

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(14) Crystallographic summary: Formula $C_{29}H_{46}N_4O_3$, Fw 498.70, orthorhombic, *P*na2(1), $a = 16.092$ Å, $b = 13.971$ Å, $c = 12.527$ Å, $a = b = g = 90°$, $V = 2816.3$ Å^3, $Z = 4$, $r_{calc} = 1.176$ mg/M3, F(000) = 1088, θ (min/max) = 1.9/32.3°, total reflections = 6612, unique = 5796 (R_{int} = 0.050), GoF = 1.021, $R1/wR1 = 0.0458/0.1132$ [$I > 2s(I)$], $R1/wR1 = 0.0542/0.1197$ (all data), flack parameter = −0.7(9), res. electr. dens. 0.342 and −0.239 e•Å^{-3}.

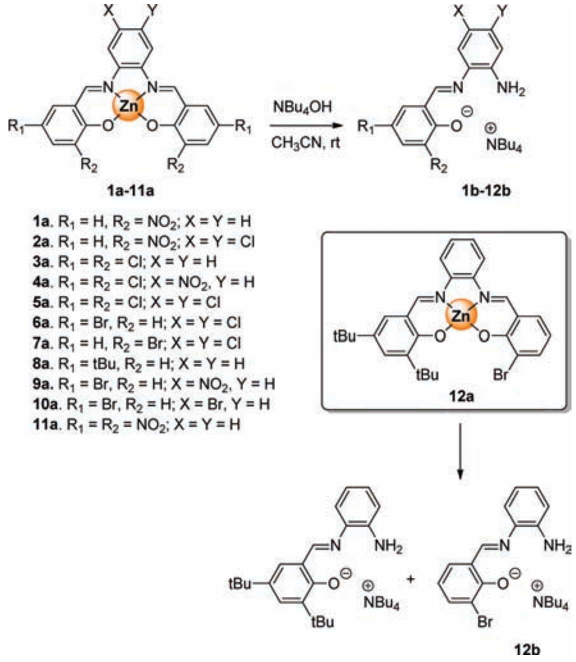
plays a dominant role in this conversion, complex **1a** was also treated under similar conditions with NaOH in a separate reaction. Although a heterogeneous mixture was retained, a clear color change from orange to red (as in the reaction with NBu_4OH) was observed for the reaction mixture. Analysis of the solid material by ^1H NMR revealed the presence of both the monoimine product (presumably as the sodium salt) as well as the liberated salicylaldehyde. Hence, the use of NBu_4OH is clearly advantageous as it gives rise to a homogeneous mixture and facilitates product isolation by means of crystallization (Supporting Information).

The scope of this new protocol was then tested with a series of Zn(salphen) complexes having various (electron-withdrawing) peripheral groups (i.e., **1a**−**12a**, Scheme 1). We were delighted to find that monoimine salts **1b**−**12b** could be readily obtained. In all cases, the monoimine NBu_4 salts were produced in moderate to good yields (Table 1); the ionic nature was easily revealed by ESI(−)-MS; and the structures of **2b** and **10b** were also supported by X-ray diffraction studies (Supporting Information). Notably, compounds **1b**−**12b** were produced under very mild conditions (rt, CH_3N as medium) and very short reaction times (≤5−10 min). Although the reaction works very efficiently with those Zn complexes having electron-withdrawing groups, we found that Zn(salphens) having donating groups (Table 1, entry 8) can also be converted into the monoimine salt. Interestingly, when nonsymmetrical Zn(salphen)s were utilized (Table 1, entries 4, 9, and 10), high selectivity was observed for breaking of only one of the two imine bonds.[17] While for compounds **4b** and **9b** the isolated materials showed virtually a single compound in the ^1H NMR spectra, for **10b** two isomeric structures were observed in an approximate 7:3 ratio (Supporting Information). We also probed complex **12a** since it constitutes two imine bonds with potentially different reactivity. Under the conditions used for the preparation of **1b**−**11b**, we found that no genuine selectivity could be observed for scission of only one of the imine bonds. A small amount of pure **12b** (8%) was isolated, but subsequent fractions of product that were collected contained both possible monoimine derivatives. Apparently, complex **12a** is hydrolyzed at both imine bonds under these experimental conditions, and cocrystallization prevents isolation of either product in high yield.

We then used monoimine salts **1b** and **5b** as reagents for metallosalen structures that are not (easily) accessible through the known synthetic routes (Scheme 2). Thus, treatment of **1b**/**5b** with a (substituted) salicylaldehyde and metal acetate in a one-pot procedure[7b] gave access to metallosalen structures **13**−**15**. The synthesis of the Zn(salphen) complex **14** represents an example of a desymmetrization protocol where first the symmetrical complex **1a** is converted into monoimine salt **1b** followed by a condensation step that allows for the presence of different ring substituents in the second aldimine fragment. We then also focused on the preparation of chiral metallosalens (**16** and **17**) using a known binaphthyl-based dialdehyde (Supporting Information).[18]

These types of bismetallosalen derivatives have recently attracted much attention in the polymerization of epoxides.[19] Compounds **16** and **17** were easily prepared

Table 1. Synthesis of Monoimine NBu_4 Salts **1b**−**12b** Using Complexes **1a**−**12a**[a]



entry	product	R¹	R²	X	Y	yield (%)[b]
1	**1b**	H	NO_2	H	H	51
2	**2b**	H	NO_2	Cl	Cl	58
3	**3b**	Cl	Cl	H	H	40
4	**4b**	Cl	Cl	NO_2[c]	H	49
5	**5b**	Cl	Cl	Cl	Cl	76
6	**6b**	Br	H	Cl	Cl	59
7	**7b**	H	Br	Cl	Cl	67
8	**8b**	tBu	H	H	H	44
9	**9b**	Br	H	NO_2[c]	H	53
10	**10b**	Br	H	H	Br[c,d]	41
11	**11b**	NO_2	NO_2	H	H	55
12	**12b**	H	Br	H	H	8

[a] All reactions carried out on a 0.24−0.40 mmol scale based on the Zn(salphen) except for entries 1 (0.61 mmol) and 8 (0.83 mmol). [b] Isolated yield. [c] Structure supported by NMR predictive simulations using gNMR from IvorySoft and ^1H−COSY measurements. [d] Structure of the major isomer supported by X-ray crystallography; see Supporting Information.

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(15) Similar nucleophilic additions to imine bonds in metallosalen structures have been reported: (a) Cametti, M.; Dalla Cort, A.; Colapietro, M.; Portalone, G.; Russo, L.; Rissanen, K. *Inorg. Chem.* **2007**, *46*, 9057. (b) Wang, Y.; Parkin, S.; Atwood, D. *Inorg. Chem.* **2002**, *41*, 558. (c) Paris, S. I. M.; Laskay, Ü.; Liang, S.; Pavlyuk, O.; Tschirschwitz, S.; Lönnecke, P.; McMills, Ü. C.; Jackson, Ü. P.; Petersen, Ü. L.; Hey-Hawkins, E.; Jensen, Ü. P. *Inorg. Chim. Acta* **2010**, doi: 10.1016/j.ica.2010.06.041.

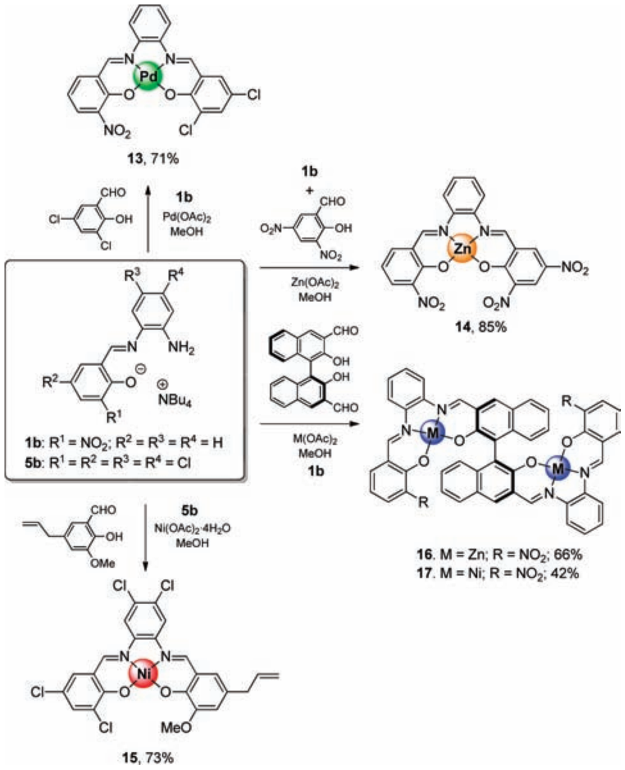
(16) Note that the use of NBu_4X (X = Cl, I) did not provoke hydrolysis of the imine bond in **1**; in these cases, unreacted **1** was isolated as the only product.

(17) Note that this is the case for the isolated product.

(18) Belokon, Y. N.; Chusov, D.; Borkin, D. A.; Yashkina, L. V.; Bolotov, P.; Skrupskaya, T.; North, M. *Tetrahedron: Asymmetry* **2008**, *19*, 459.

(19) (a) Hirahata, W.; Thomas, R. M.; Lobkovsky, E. B.; Coates, G. W. *J. Am. Chem. Soc.* **2008**, *130*, 17658. (b) Widger, P. C. B.; Ahmed, S. M.; Hirahata, W.; Thomas, R. M.; Lobkovsky, E. B.; Coates, G. W. *Chem. Commun.* **2010**, *46*, 2935.

Scheme 2. Synthesis of Nonsymmetrical Metallosalen Complexes **13**−**17** Using Monoimine Salt **1b** and **5b** as Reagents



using monoamine **1b**, and simple variation of the electronic features in these structures through the use of different monoimine reagents can thus provide a new series of (polymerization) catalysts.[10b,19]

In summary, we described a new, mild, and easy method for the synthesis of a series of monoimine salts derived from Zn-centered salphen complexes. This new methodology is based on a selective imine bond hydrolysis provoked by addition of an OH nucleophile. The nucleophilic addition of the hydroxide anion is likely facilitated by the presence of a highly Lewis acidic Zn center[20] that increases the reactivity of the imine bond.[21] The reported protocol is advantageous in terms of reaction conditions, isolation, and scope using easily accessible Zn(salphen) complexes as substrates. These monoimine salts are not (easily) accessible via other methods and thus create new potential for the fine-tuning of steric and electronic features of metallosalen structures (cf., Scheme 2) useful in various applications including homogeneous catalysis and as molecular building blocks in supramolecular chemistry.[22] Our future plans focus on the application of this new reactivity for the fabrication of larger, multinuclear metallosalen architectures.

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Supporting Information Available: Synthetic and complete analytical data for all new compounds, copies of NMR spectra, and crystallographic data for **1b**, **2b**, and **10b** in CIF format. This material is available free of charge via the Internet at http://pubs.acs.org.

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(20) For recent contributions demonstrating the high Lewis acid character of the Zn ion in these salphen complexes, see: (a) San Felices, L.; Escudero-Adán, E. C.; Benet-Buchholz, J.; Kleij, A. W. *Inorg. Chem.* **2009**, *48*, 846. (b) Martínez Belmonte, M.; Escudero-Adán, E. C.; Benet-Buchholz, J.; Kleij, A. W. *Eur. J. Inorg. Chem.* **2009**, 5307. (c) Escudero-Adán, E. C.; Benet-Buchholz, J.; Kleij, A. W. *Eur. J. Inorg. Chem.* **2009**, 3562.

(21) We also examined the use of the chiral Zn complex based on *N*,*N*′-bis[3,5-di-*tert*-butylsalicylidene-1,2-diaminocyclohexane] and a nonmetalated salphen ligand as substrates: in the first case, no reaction was observed, while in the latter case, only some hydrolysis was noted in the isolated, impure product. See for details the Supporting Information. The results imply the importance of the presence of a salphen backbone in combination with Zn to have sufficient reactivity/selectivity.

(22) For a recent example: Wezenberg, S. J.; Escudero-Adán, E. C.; Benet-Buchholz, J.; Kleij, A. W. *Inorg. Chem.* **2008**, *47*, 2925.