Tetrahedron Letters 51 (2010) 6806–6809

Contents lists available at ScienceDirect

Tetrahedron Letters

journal homepage: www.elsevier.com/locate/tetlet

Decomplexation–nitroso Diels–Alder (NDA) approach to C,D-ring functionalisation for hippeastrine

G. Richard Stephenson *, Andrew M. Balfe, David L. Hughes, Richard D. Kelsey

School of Chemistry, University of East Anglia, Norwich NR4 7TJ, UK

ARTICLE INFO

Article history:
Received 3 August 2010
Revised 26 August 2010
Accepted 24 September 2010

Keywords:
Organoiron
Nitroso Diels–Alder
Tandem reactions
Deprotection
Hippeastrine

ABSTRACT

A tandem decomplexation–nitroso Diels–Alder (decomplexation–NDA) procedure has been shown to give the regiocontrol and stereocontrol needed for application in an organoiron-mediated synthesis of the alkaloid hippeastrine, using a selection of nitrosoarenes with functionality present to facilitate removal of the arene after the NDA step.

The nitroso Diels–Alder (NDA) reaction[1] has a long history[2] but is only recently becoming widely applied[3–6] as a general method for stereocontrolled organic synthesis. The intrinsic control of relative stereochemistry of C–N and C–O bond formation is a unique advantage of NDA reactions (Fig. 1) as exemplified, for example, in a recent application[4] in an approach to the synthesis of stenine (Fig. 1b),[6] which like our work towards hippeastine[7–9] (Fig. 1a) requires regioselective C–N bond formation next to an alkyl substituent (R: see Fig. 2).[10] For hippeastrine, we are developing an intermolecular NDA with nitroso reagents that give good regiocontrol and show compatibility with a novel one-pot decomplexation–NDA procedure[9] to allow tricarbonyliron complexes[11] to be employed directly as starting materials for the NDA step.[12]

In contrast to acylnitroso reagents,[13] we have shown[9] that arylNDA with 2-methylcyclohexa-1,3-diene gave the correct regiocontrol and with a model complex (**2**: R = Me, Ar = Ph) we successfully demonstrated good regio- and stereochemistry in the novel decomplexation–NDA procedure. This result has now been confirmed with a more advanced model complex [Fig. 2, box: R = CH_2CH_2OAc, Ar = $C_6H_3(OCH_2O)$] which gave the required cycloadduct **3** in 82% yield.

As an example with a removable aryl group, we chose 2-nitrosopyridine reagents[14] [dearylation is possible[15] by N-tosylation, quaternisation of the pyridine nitrogen and S_NAr displacement with methanolic NaOH(aq)] because the correct regiocontrol of the cycloaddition with 2-methylcyclohexa-1,3-diene is known from an X-ray study[15] of a single NDA product, which was obtained in 99% yield. Encouraged by the good prospects for efficient, regiocontrolled, high-yielding NDA cycloadditions, we have examined (Scheme 1) the compatibility of 2-nitrosopyridine **8** with our one-pot decomplexation–NDA method, using our initial model system (**2**: R = Me, Ar = Ph) to study the regiocontrol. The outcome was unexpected, as two regioisomeric products **5** and **6** were obtained in a 1:2 ratio in 60% yield. The major product proved (COSY ^{1}H NMR spectroscopy) to be **6**, the opposite regioisomer to that reported from 6-methyl-2-nitrosopyridine and 2-methylcyclohexa-1,3-diene[15] or from 2-nitrosopyridine and 2-(*n*-butyl)-cyclohexa-1,3-diene.[16]

We turned instead to a revised approach using 4-nitroarenes because the presence of the nitro group would also provide activation for removal of the arene by an S_NAr process. The cycload-

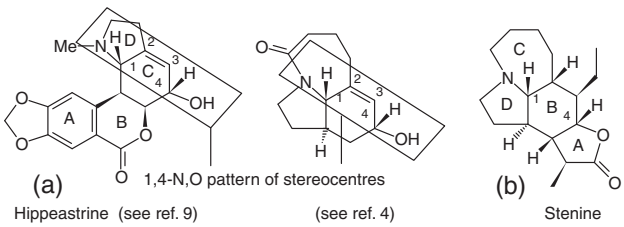


Figure 1. The 1,4-relationship between C–N and C–O bonds at key stereocentres in the C,D-rings of (a) hippeastrine and B,D rings of (b) stenine [for work towards stenine using an acylnitroso cycloaddition (acyl-NDA), see Shea and co-workers; Ref. 4].

* Corresponding author. Tel.: +44 1603 592019; fax: +44 1603 592003.
E-mail address: g.r.stephenson@uea.ac.uk (G.R. Stephenson).

0040-4039/$ - see front matter © 2010 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2010.09.118

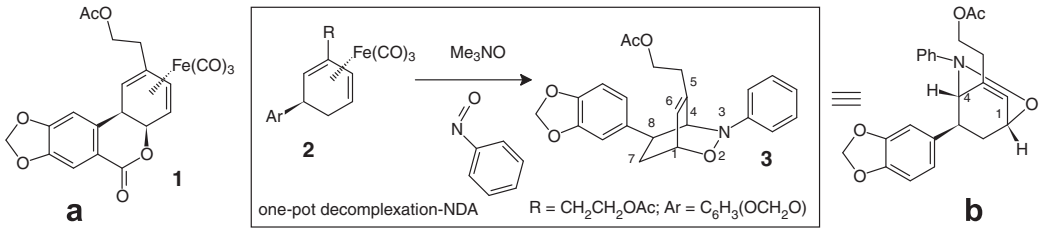
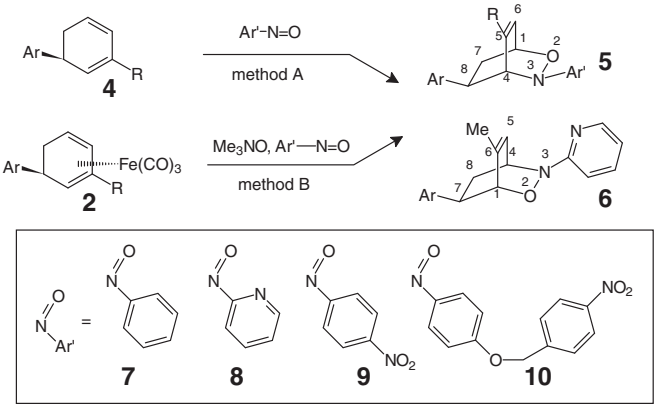


Figure 2. (a) Proposed advanced intermediate **1** for an organoiron route to hippeastrine; (b) NDA cycloadduct **3** with the correct regiochemistry of 1,4-difunctionalisation in a model system.



Scheme 1. Regio- and stereocontrol of NDA and tandem decomplexation–NDA reactions (see Table 1).

dition between 4-nitro-1-nitrosobenzene **9** and cyclohexa-1,3-diene has been described previously in 7% yield,[17] using an in situ generation of the nitroso reagent from 4-nitroaniline by oxidation[18] with H_2O_2 in the presence of a molybdenum catalyst, so we opted instead to generate 4-nitro-1-nitrosobenzene[19] by the standard procedure[20] converting 1,4-dinitrobenzene into the nitroso reagent via the aryl hydroxylamine. NDA reaction (Method A) gave **5** (Ar, R = H; Ar′ = 4-(C_6H_4)NO_2) in 92% yield (Table 1, entry 1). We obtained an X-ray structure[21] of this product (Fig. 3a) which showed the arene pointing outwards from the bicyclic system, equatorial with respect to the boat ring and *cis* to the alkene group of 2-oxa-3-aza-bicyclo[2.2.2]oct-5-ene. In the decomplexation–NDA reaction (Method B) with tricarbonyliron complex **2** (Ar, R = H), cycloadduct **5** (Ar, R = H; Ar′ = 4-(C_6H_4)NO_2) was obtained in 58% yield (entry 2). The cycloadduct was quaternised (Scheme 2) to form **11** as a 3:2 mixture of diastereoisomers, but attempted S_NAr with sodium methoxide gave 4-nitro-*N*-methylaniline[22] in 80% yield (Scheme 2), presumably formed by Hoffmann elimination, rearrangement and loss of phenol in the N–O bond-cleavage step.

Table 1
Nitroso Diels–Alder reactions of cyclohexa-1,3-dienes and their tricarbonyliron complexes (see Scheme 1)

Entry	Ar	R	Ar′	Method	Yield (%)
1	H	H	4-(C_6H_4)NO_2	A	92[a]
2	H	H	4-(C_6H_4)NO_2	B	58[a]
3	H	H	4-(C_6H_4)-X[b]	A	25[a]
4	H	H	4-(C_6H_4)-X[b]	B	19[a]
5	Ph	Me	4-(C_6H_4)NO_2	B	28[a]
6	Ph	Me	Ph	B	68[a,c]
7	Ph	Me	2-Py	B	60[d]
8	[e]	$(CH_2)_2$-OAc	Ph	B	82[f]

Method A: NDA reaction using the free diene in CH_2Cl_2 (−78 °C to rt, 16 h); method B: NDA reaction using the $Fe(CO)_3$ complex in the presence of Me_3NO in DMA (0 °C to rt, 16 h).
[a] Regioisomer **5**.
[b] X = OCH_2–$C_6H_4NO_2$.
[c] See Ref. 9.
[d] 2:1 mixture of regioisomers **6** and **5**.
[e] Ar = 3,4-(OCH_2O)–C_6H_3.
[f] Structure **3**.

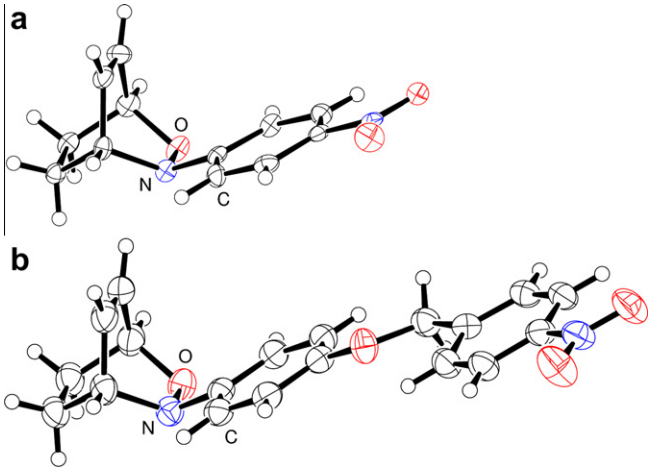
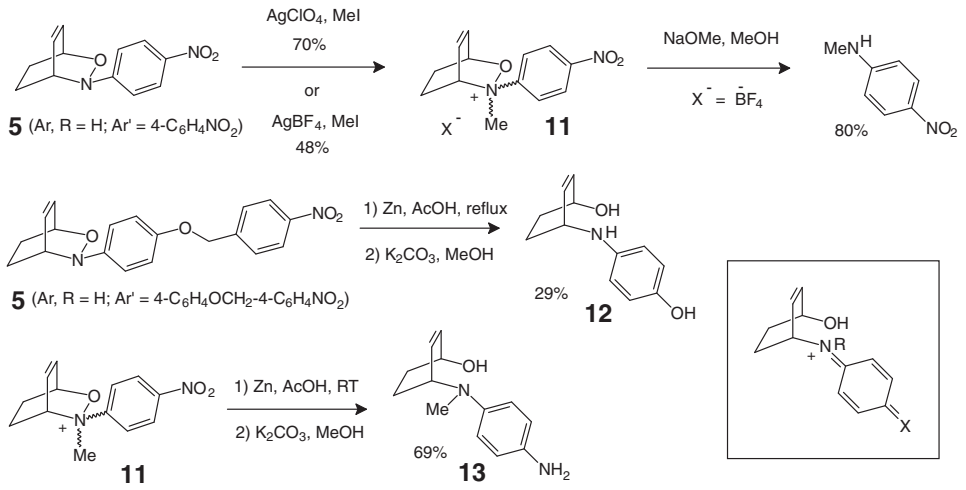


Figure 3. ORTEP drawings of (a): **5** [Ar, R = H; Ar′ = 4-(C_6H_4)NO_2] and (b): **5** [Ar, R = H; Ar′ = 4-(C_6H_4)–OCH_2-4-(C_6H_4)NO_2].

An alternative strategy for dearylation was explored using starting material **10**[23] [$\nu_{N=O}$ (Nujol) 1502 cm^{-1}] which was obtained by alkylation of phenol with 4-nitrobenzyl bromide and then reaction with nitrosonium tetrafluoroborate.[24] NDA reaction with cyclohexadiene (Table 1, entry 3) and its tricarbonyliron complex (entry 4), afforded in both cases the expected cycloadduct **5** (Ar, R = H; Ar′ = 4-(C_6H_4)–OCH_2-4-(C_6H_4)NO_2), though in low yields. The structure of this product **5** was also confirmed by X-ray crystallography (Fig. 3b), which showed the same general features as described above in the structure of **5** (Ar, R = H; Ar′ = 4-(C_6H_4)NO_2). In both cases, the configuration at the nitrogen atom places the arene nearer the CH=CH section of the hydrocarbon ring in preference to the CH_2–CH_2 side.[25] The cycloaddition product was reduced with zinc in acetic acid at room temperature to give the known 1-hydroxy-4-aminocyclohexadiene derivative which earlier this year was reported[26] as one of a series of products obtained by a different route from the simple nitrosobenzene-derived cycloadduct by an unusual indium triflate catalysed nucleophilic addition on the arene in a process combined with N–O bond-cleavage in the 2-oxa-3-aza-bicyclo[2.2.2]oct-5-ene.

Finally (Scheme 2), the reduction of **5** (Ar, R = H; Ar′ = 4-(C_6H_4)–OCH_2-4-(C_6H_4)NO_2) was repeated under more vigorous conditions (reflux in AcOH) to produce the deprotected phenol **12** in a single step. Reduction of the quaternised product **11** from 4-nitro-nitrosobenzene cycloaddition (RT in AcOH) was also examined, giving **13** in 69% yield. Both **12** and **13** would be suitable for an



Scheme 2. Studies of N–O bond-cleavage in the 2-oxa-3-aza-bicyclo[2.2.2]oct-5-ene products (box: proposed oxidation/hydrolysis strategy for dearylation).

investigation of an oxidation/hydrolysis method to remove the aryl group [e.g., via an iminium ion: see Scheme 2 (box)]. The reaction sequence using the quaternised product **11** is particularly attractive because of the more efficient reduction and the early introduction of the *N*-methyl group that is needed in the hippeastrine target molecule (Fig. 1a).

In conclusion, we have established that functionalised aryl nitroso reagents are compatible with the one-pot decomplexation–NDA process and show the correct regiocontrol with 2-alkyl substituted cyclohexadienes, placing the new C–N bond adjacent to the alkyl group. The approach via the 4-nitro-nitrosobenzene cycloaddition reaction is the most suitable and will be developed in future work with our more fully functionalised diene complex **2** [Fig. 2; R = CH_2CH_2OAc, Ar = $C_6H_3(OCH_2O)$], by methylation, reduction, conversion into the exocyclic iminium ion and hydrolysis to remove the arene. Other key features needed for an enantioselective synthesis of hippeastrine by this method (the formation of the ABC ring system[7] and access to key intermediates from enantiomerically pure arene *cis*-diols obtained[8] using *Pseudomonas putida* dioxygenation[27]) have already been established. The work described herein now places this strategy on a firm footing by defining the most suitable approach for the novel decomplexation–NDA step.

Crystallographic data (excluding structure factors) for the structures in this Letter have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication nos. CCDC 786977 [**5**: Ar, R = H; Ar′ = 4-(C_6H_4)NO_2] and CCDC 786978 [**5**: Ar, R = H; Ar′ = 4-(C_6H_4)–OCH_2-4-(C_6H_4)NO_2]. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK, (fax: +44-(0)1223-336033 or e-mail: deposit@ccdc.cam.ac.uk).

Acknowledgements

We thank the EPSRC for financial support (Ph.D. studentships to A.M.B. and R.D.K.) and the EPSRC National Mass Spectrometry Service, Swansea University, for high resolution mass spectrometric data. We thank Professor Claude Daul, University of Fribourg for access to computational facilities.

Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2010.09.118.

References and notes

1. Feature article: Yamamoto, H.; Momiyama, N. *Chem. Commun.* **2005**, 3514–3525; See also: Lu, P.-H.; Yang, C.-S.; Devendar, B.; Liao, C.-C. *Org. Lett.* **2010**, *12*, 2642–2645; Jones, A. L.; Snyder, J. K. *Org. Lett.* **2010**, *12*, 1592–1995; Barfoot, C.; Brooks, G.; Davis, D. T.; Elder, J.; Giordano, I.; Hennessy, A.; Jones, G.; Markwell, R.; McGuire, M.; Miles, T.; Pearson, N.; Spoors, G.; Sudini, R.; Wei, H.; Wood, J. *Tetrahedron Lett.* **2010**, *51*, 2846–2848; Bollans, L.; Basca, J.; O'Farrell, D. A.; Waterson, S.; Stachulski, A. V. *Tetrahedron Lett.* **2010**, *51*, 2160–2163; Monbaliu, J.-C.; Tinant, B.; Peeters, D.; Marchand-Brynaert, J. *Tetrahedron Lett.* **2010**, *51*, 1052–1055; Calvert, G.; Coote, S. C.; Blanchard, N.; Kouklovsky, C. *Tetrahedron* **2010**, *66*, 2969–2980; Yan, S.; Miller, M. J.; Werner, L.; Machara, A.; Hudlicky, T. *Adv. Synth. Catal.* **2010**, *352*, 195–200; Wencewicz, T. A.; Möllmann, U. *Bioorg. Med. Chem. Lett.* **2010**, *20*, 1302–1305.
2. Wichterle, O. *Collect. Czech. Chem. Commun.* **1947**, *12*, 292–304; Arbuzov, Y. A. *Dokl. Akad. Nauk SSSR* **1948**, *60*, 993–996; Kresze, G.; Firl, I. *Tetrahedron Lett.* **1965**, 1163–1170.
3. Anard, A.; Bhargava, G.; Kumar, V.; Mahajan, M. P. *Tetrahedron Lett.* **2010**, *51*, 2312–2315; Anand, A.; Bhargava, G.; Singh, P.; Mahajan, M. P. *Heterocycles* **2009**, *77*, 547–556; Lemos, A.; Lourcenco, J. P. *Tetrahedron Lett.* **2009**, *50*, 1311–1313; Lam, Y.; Hopkinson, M. N.; Stanway, S. J.; Gouverneur, V. *Synlett* **2007**, 3022–3026; Calvert, G.; Dussaussois, M.; Blanchard, N.; Kouklovsky, C. *Org. Lett.* **2004**, *6*, 2449–2451; Lightfoot, A. P.; Pritchard, R. G.; Wan, H.; Warren, J. E.; Whiting, A. *Chem. Commun.* **2002**, 2072–2073; Lee, J.; Chen, L.; West, A. H.; Richter-Addo, G. B. *Chem. Rev.* **2002**, *102*, 1019–1066.
4. Zhu, L.; Lauchli, R.; Loo, M.; Shea, K. J. *Org. Lett.* **2007**, *9*, 2269–2271.
5. A recent focus on catalytic enantioselective NDA reactions has increased the popularity of the method. See, for example: (a) Jana, C. K.; Grimme, S.; Struder, A. *Chem. Eur. J.* **2009**, *15*, 9078–9084; (b) Momiyama, N.; Yamamoto, Y.; Yamamoto, H. *J. Am. Chem. Soc.* **2007**, *129*, 1190–1195; (c) Jana, C. K.; Studer, A. *Angew. Chem., Int. Ed.* **2007**, *46*, 6542–6544; (d) Yamamoto, Y.; Yamamoto, H. *Angew. Chem., Int. Ed.* **2005**, *44*, 7082–7085; (e) Chow, C. P.; Shea, K. J. *J. Am. Chem. Soc.* **2005**, *127*, 3678–3679; (f) Ding, X.; Ukaji, Y.; Fujinami, S.; Inomata, K. *Chem. Lett.* **2003**, *32*, 582–583; (g) Flower, K. R.; Lightfoot, H.; Wan, H.; Whiting, A. *J. Chem. Soc., Perkin Trans. 1* **2002**, 2058–2064; For a review on asymmetric NDA reactions, see: Yamamoto, Y.; Yamamoto, H. *Eur. J. Org. Chem.* **2006**, *9*, 2031–2043.
6. For other examples in target molecule synthesis, see: Sancibrao, P.; Karila, D.; Kouklovsky, C.; Vincent, G. *J. Org. Chem.* **2010**, *75*, 4333–4336 (porantheridine); Dunn, T. B.; Ellis, J. M.; Kofimk, C. C.; Manning, J. R.; Overman, L. E. *Org. Lett.* **2009**, *11*, 5658–5661 (daphnicyclidins); Lin, W.; Virga, K. G.; Kim, K.-H.; Zajicek, J.; Mendel, D.; Miller, M. J. *J. Org. Chem.* **2009**, *74*, 5941–5946 (daphnipaxinin, spironoraristeromycin); Jana, C. K.; Studer, A. *Chem. Eur. J.* **2008**, *14*, 6326–6328 (*trans*-dihydronarciclasine); Shulka, K. H.; Boehmler, D. J.; Bogacyzk, S.; Duvall, B. R.; Peterson, W. A.; McElroy, W. T.; DeShong, P. *Org. Lett.* **2006**, *8*, 4183–4186 (pancratistatin analogue); Hudlicky, T.; Rinner, U.; Gonzalez, D.; Akgun, H.; Schilling, S.; Siengalewicz, P.; Martinot, T. A.; Pettit, G. R. *J. Org. Chem.* **2002**, *67*, 8726–8743 (narciclasine); Abe, H.; Aoyagi, S.; Kibayashi, C. *J. Am. Chem. Soc.* **2000**, *122*, 4583–4592 (fasicularine, lepadiformine); Hall, A.; Bailey, P. D.; Rees, D. C.; Rosair, G. M.; Wightman, R. H. *J. Chem. Soc., Perkin Trans. 1* **2000**, 329–342 (physoperuvine, epibatidine); Cabanal-Duvillard, I.; Berrien, J.-F.; Ghosez, L.; Husson, H.-P.; Royer, J. *Tetrahedron* **2000**, *56*, 3763–3769 (epibatidine); Faitg, T.; Soulie, J.; Lallemand, J.-L.; Ricard, L. *Tetrahedron: Asymmetry* **1999**, *10*, 2165–2174 (calystegine B2); Tolman, V.; Hanus, J.; Sedmera, P. *Czech. Chem. Commun.* **1999**, *64*, 696–702 (zeatin); Aoyagi, S.; Shishido, Y.; Kibayashi, C. *Tetrahedron Lett.* **1991**, *32*, 4325–4328 (nupharamine); For a classic example to control C–N

bond formation in alkaloid synthesis, see: Iida, H.; Watanabe, Y.; Kibayashi, C. *J. Org. Chem.* **1985**, *50*, 1818–1825.
7. Astley, S. T.; Stephenson, G. R. *Synlett* **1992**, 507–509.
8. Astley, S. T.; Meyer, M.; Stephenson, G. R. *Tetrahedron Lett.* **1993**, *34*, 2035–2038.
9. Anson, C. E.; Hartman, S.; Kelsey, R. D.; Stephenson, G. R. *Polyhedron* **2000**, *19*, 569–571.
10. The acylnitroso class of heterodienophiles does not naturally give this regioselectivity (see Ref. 13), but Shea's approach overcomes this difficulty by using an intramolecular cycloaddition strategy.
11. For other recent examples of tricarbonyliron complexes in organic synthesis, see: Pearson, A. J.; Kim, E. H. *Tetrahedron* **2010**, *66*, 4943–4946; Han, J.-L.; Liu, M.-C.; Ong, C.-W. *J. Org. Chem.* **2010**, *75*, 1637–1642; Roe, C.; Sandoe, E. J.; Stephenson, G. R. *Tetrahedron Lett.* **2010**, *51*, 591–595; Gone, J. R.; Wallock, N. J.; Lindeman, S.; Donaldson, W. A. *Tetrahedron Lett.* **2009**, *50*, 1023–1025; Knott, K. E.; Auschill, S.; Jäger, A.; Knölker, H.-J. *Chem. Commun.* **2009**, 1467–1469; Anson, C. E.; Malkov, A. V.; Roe, C.; Sandoe, E. J.; Stephenson, G. R. *Eur. J. Org. Chem.* **2008**, 196–213; Roe, C.; Sandoe, E. J.; Stephenson, G. R.; Anson, C. E. *Tetrahedron Lett.* **2008**, *49*, 650–653; Roe, C.; Stephenson, G. R. *Org. Lett.* **2008**, *10*, 189–192; Pearson, A. J.; Sun, H. *J. Org. Chem.* **2007**, *72*, 7693–7700; Williams, I.; Reeves, K.; Kariuki, B. M.; Cox, L. *Org. Biomol. Chem.* **2007**, *5*, 3325–3329; Pearson, A. J.; Sun, H.; Wang, X. *J. Org. Chem.* **2007**, *72*, 2547–2557; Owen, D. A.; Malkov, A. V.; Palotai, I. M.; Roe, C.; Sandoe, E. J.; Stephenson, G. R. *Chem. Eur. J.* **2007**, *13*, 4293–4311; Siddiquee, T. A.; Lukesh, J. M.; Lindeman, S.; Donaldson, W. A. *J. Org. Chem.* **2007**, *72*, 9802–9803; Pandey, R. K.; Lindeman, S.; Donaldson, W. A. *Eur. J. Org. Chem.* **2007**, 3829–3831; Choi, T. A.; Czerwonka, R.; Fröhner, W.; Krahl, M. P.; Reddy, K. R.; Franzzblau, S. G.; Knölker, H.-J. *ChemMedChem* **2006**, *1*, 812–815; Czerwonka, R.; Reddy, K. R.; Baum, E.; Knölker, H.-J. *Chem. Commun.* **2006**, 711–713; Chaudhury, S.; Danoaldson, W. A. *J. Am. Chem. Soc.* **2006**, *128*, 5984–5985; Pearson, A. J.; Wang, X. *Tetrahedron Lett.* **2005**, *46*, 4809–4811; Frank-Neumann, M.; Geoffrey, P.; Gassmann, D.; Winling, A. *Tetrahedron Lett.* **2004**, *45*, 5407–5410; Schobert, R.; Mangold, A.; Baumann, T.; Milius, W.; Hampel, F. *J. Organomet. Chem.* **2004**, *689*, 575–584; Stephenson, G. R. Polyfunctional Electrophilic Multihapto-organometallics for Organic Synthesis. In *Handbook of Functionalised Organometallics*; Knochel, P., Ed.; Wiley-VCH: Weinheim, 2005; pp 569–626 (ISBN 3-527-31131-9).
12. Tandem decomplexation/NDA is important because of the sensitive (see Ref. 9) lactone ring in this diene ligand (see Fig. 1a).
13. Howard, J. A. K.; Ilyashenko, G.; Sparkes, H. A.; Whiting, A.; Wright, A. R. *Adv. Synth. Catal.* **2008**, *350*, 869–882; Howard, J. A. K.; Ilyashenko, G.; Sparkes, H. A.; Whiting, A. *J. Chem. Soc., Dalton Trans.* **2007**, 2108–2111; Adamo, M. F. A.; Bruschi, S. *Targets Heterocycl. Syst.* **2007**, *11*, 396–430.
14. There has been considerable recent interest in applications of 2-nitrosopyridine reagents in MEND (Modular Enhancement of Nature's Diversity) procedures (Yang, B.; Zöllner, T.; Gebhard, P.; Möllmann, U.; Miller, M. J. *Org. Biomol. Chem.* **2010**, *8*, 691–697; Yang, B.; Miller, P. A.; Möllmann, U.; Miller, M. J. *Org. Lett.* **2009**, *11*, 2828–2831; Li, F.; Yang, B.; Miller, M. J.; Zajicek, J.; Noll, B. C.; Möllmann, U.; Dahse, H.-M.; Miller, P. A. *Org. Lett.* **2007**, *9*, 2923–2926) including polymer-supported examples: Krchnak, V.; Möllmann, U.; Dahse, H.-M.; Miller, M. J. *J. Comb. Chem.* **2008**, *10*, 112–117. This has provided many examples of high-yielding NDA reactions with this class of heterodienophile.
15. Yamamoto, Y.; Yamamoto, H. *J. Am. Chem. Soc.* **2004**, *126*, 4128–4129.
16. The reported regioselectivity may be a consequence of the Cu(I)-catalysis (see Refs. 14,5a) which is not compatible with the use of trimethylamine *N*-oxide in the tandem decomplexation/NDA procedure.
17. Møller, E.; Jørgensen, K. A. *J. Org. Chem.* **1996**, *61*, 5770–5778.
18. See also: Zhao, D.; Johansson, M.; Backvall, J.-E. *Eur. J. Org. Chem.* **2007**, 4431–4436.
19. Defoin, A.; Geoffroy, G.; le Nouen, D.; Spileers, D.; Streith, J. *Helv. Chim. Acta* **1989**, *72*, 1199–1215; For recent examples of the use of this nitroso reagent, see: (a) Tibiletti, F.; Simonetti, M.; Nicholas, K. M.; Palmisano, G.; Parravicini, M.; Imbesi, F.; Tollari, S.; Penoni, A. *Tetrahedron* **2010**, *66*, 1280–1288; (b) Rück-Braum, K.; Kempa, S.; Priewisch, B.; Richter, A.; Seedorff, S.; Wallach, L. *Synthesis* **2009**, 4256–4267; (c) Sakai, H.; Ding, X.; Yoshida, T.; Fujinami, S.; Ukaji, Y.; Inamata, K. *Heterocycles* **2008**, *76*, 1285–1300.
20. Davey, M. H.; Lee, Y. V.; Miller, R. D.; Marks, T. J. *J. Org. Chem.* **1999**, *64*, 4976–4979.
21. Møller's study (Ref. 17; 1996) also performed semiempirical AM1 calculations to identify the orientation of the aryl group. Our 2000 (Ref. 9) example and the two examples reported in this Letter show similar orientations of the aryl group in the solid state and support the earlier conclusions based on calculations. For a crystallographically defined pyridyl example, see Ref. 15. See also Ref. 25.
22. Katritzky, A.; Lourenzo, K. S. *J. Org. Chem.* **1988**, *53*, 3978–3982.
23. Attempts to nitrosylate the benzyl ether of phenol were unsuccessful, so we examined nitrobenzyl ether in the expectation that this would deactivate the benzyl arene and so improve selectivity for the phenyl ether ring.
24. The corresponding nitrosylations of anisole and 4-nitrophenyl phenyl ether are known: Atherton, J. H.; Modie, R. B.; Noble, D. R.; O'Sulivan, B. *J. Chem. Soc., Perkin Trans. 2* **1997**, 663–664; See also Ref. 19a.
25. Preliminary DFT calculations (GAUSSIAN03/B3LYP/6-31 g*) indicate that the more stable orientation has the arene lying over the CH=CH section of the hydrocarbon ring in preference to the CH_2–CH_2 side [energy differences with Ar = Ph: −0.0839497 Ha (220 kJ mol^{-1}); Ar = 4-NO_2–C_6H_4: −0.0033301 Ha (8.7 kJ mol^{-1}) in the gas phase].
26. Yang, B.; Miller, M. J. *Org. Lett.* **2010**, *12*, 392–395.
27. For a recent review, see: Hudlicky, T.; Reed, J. T. *Synlett* **2009**, 685–703; for *cis*-diol-derived dieneiron complexes, see: Howard, P. W.; Stephenson, G. R.; Taylor, S. C. *J. Organomet. Chem.* **1989**, *370*, 97–109; Howard, P. W.; Stephenson, G. R.; Taylor, S. C. *J. Organomet. Chem.* **1988**, *339*, C5–C8; related example (monool): Howard, P. W.; Stephenson, G. R.; Taylor, S. C. *Chem. Commun.* **1990**, 1182–1184.