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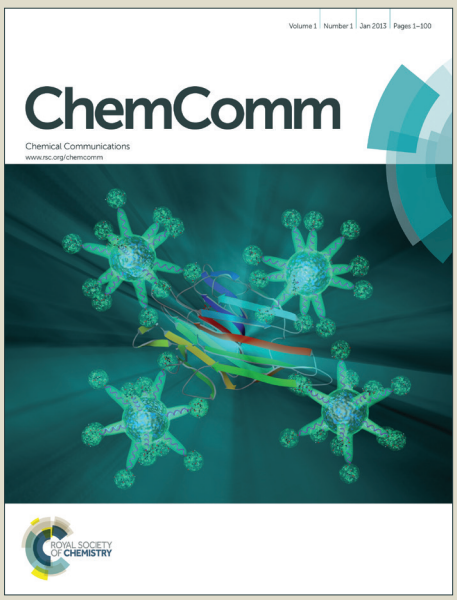

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ARTICLE TYPE

2-Arylcyclopropylmethanol as a substitute for homoallyl aryl alcohol in the construction of *cis*-2,6-disubstituted tetrahydropyran. Synthesis of (±)-centrolobine

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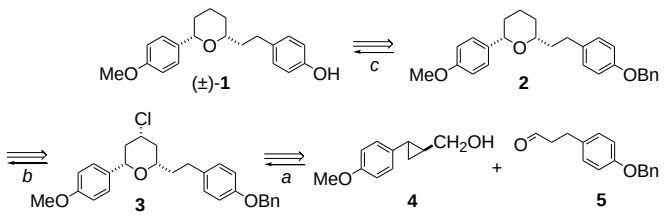
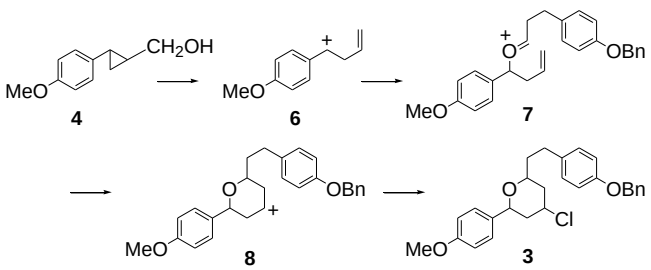
The application of 2-arylcyclopropylmethanols as a substitute to homoallyl aryl alcohols and their reactions with aliphatic aldehydes in the presence of $SnCl_4$ in CH_2Cl_2 leads to an efficient Prins cyclization to generate *cis*-2,6-disubstituted tetrahydropyrans in high yields. The reaction is free from 2-oxonia-Cope rearrangement. This protocol was used to synthesize (±)-centrolobine in an overall 84% yield over three steps. The protocol holds promise for scaffold generation for medicinal chemistry exploitation.

The Prins cyclization is a versatile method for construction of the tetrahydropyran ring[1] which is featured in a variety of biologically active natural products.[2] It involves the union of a homoallyl aryl alcohol and a carbonyl compound in the presence of a Lewis acid. We have previously reported the reaction of 2-*tert*-butyldiphenylsilylmethyl-1-phenylcyclopropyl methanol with carbonyl species in the presence of CF_3CO_2H in Prins fashion to generate trifluoroacetates which hydrolyzed to the corresponding alcohols during the aqueous workup and resulted in the formation of *cis*-2,6-disubstituted 4-hydroxytetrahydropyrans.[3] We noticed an excellent opportunity in this protocol to construct centrolobine **1** and the associated analogs. (-)-Centrolobine is a crystalline antibiotic isolated from the heartwood of *Centrolobium robustum*[4] and stem of *Brosinum potabile*[5] found in the Amazon forest. Its absolute configuration was elucidated as 2(*S*),6(*R*) from its first enantioselective total synthesis.[6] Since then, several enantioselective and racemic syntheses of centrolobine have appeared.[7] (-)-Centrolobine shows activity against *Leishmania amazonensis promastigotes* which has been identified as a major health risk in Brazil.

We considered replacing CF_3CO_2H by $SnCl_4$ in the hope that this will introduce a chlorine atom in place of the trifluoroacetoxy group which could be removed by reductive dechlorination. The retrosynthetic analysis of our synthetic plan is shown in Scheme 1. Indeed, the union of *trans*-2-(*p*-mehoxyphenyl)cyclopropyl methanol **4**[8] and 3-(*p*-benzyloxyphenyl)propanal **5**[7g,9] in dry CH_2Cl_2 in the presence of $SnCl_4$ at 0 °C generated the 4-chlorotetrahydropyran derivative **3** in 95% yield. Reductive dechlorination on reflux with *n*-Bu_3SnH in toluene furnished **2** in 95% yield. Finally, debenzylation of **2** under hydrogenation conditions produced the racemic centrolobine in 98% yield. The physical and spectroscopic data obtained for (±)-**1** were in full agreement with the literature.[5,7a] Thus, we achieved a facile synthesis of (±)-centrolobine in 84% yield over three steps in commencing from the cyclopropyl methanol **4** and the aldehyde **5**. The equatorial orientation of the chlorine atom in **3** was ascertained spectroscopically from the observation that the proton on C4 exhibited a coupling constant of 11.6 Hz due to axial-axial coupling. This was confirmed further from a single crystal X-ray structure of **3** (see ESI).



Scheme 1. Retrosynthesis of (±)-centrolobine. Reagents and reaction conditions: (*a*) $SnCl_4$, CH_2Cl_2, 0 °C, 60 min, 95%. (*b*) *n*-Bu_3SnH, AIBN, toluene, reflux, 2 h, 95%. (*c*) H_2, 5 mol% Pd-C, MeOH, 2 h, 98%.

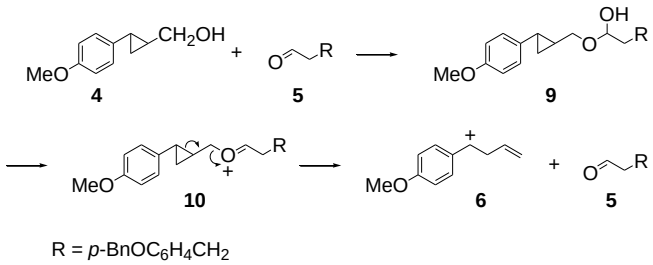


Scheme 2. The stepwise progress of the Prins cyclization

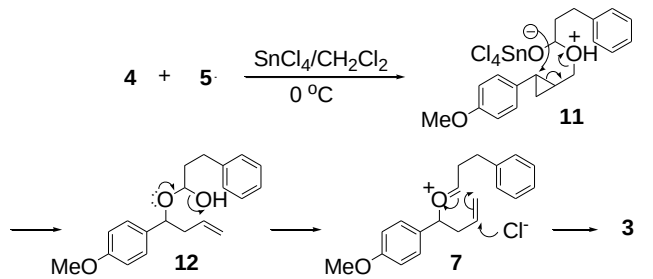
The overall reaction is likely to proceed through the stable benzylic cation **6** which is formed from **4** under the Lewis acid action of $SnCl_4$.[3,10] A combination of this cation with 3-(*p*-benzyloxyphenyl)propanal **5** will be expected to generate the oxocarbemium ion **7** which undergoes Prins cyclization followed by capture of the resultant cyclohexyl cation **8** by $SnCl_4$-derived chloride ion to form the 4-chloro-2,6-disubstituted tetrahydropyran species **3**. The entire process is shown in a stepwise manner in Scheme 2.

Alternatively, **4** may combine with **5** in the presence of $SnCl_4$ to generate the hemiacetal **9**, as shown in Scheme 3. The hemiacetal

9 can then dehydrate and generate the oxocarbenium ion **10**. Cleavage of the cyclopropane's $\sigma_{C\text{-}C}$ bond in **10** under the strong electron-withdrawing effect of the oxocarbenium ion may now lead to the formation of the cation **6**, and the aldehyde **5** is regenerated but only to react again with **6** in the manner as outlined in Scheme 2. This pathway entails dual role of the aldehyde: (a) activation of $\sigma_{C\text{-}C}$ bond in cyclopropyl methanol for its smooth cleavage and (b) reaction with the cation **6** to form the Prins product.



Scheme 3. An alternate pathway for the formation of cation **6** required for the Prins cyclization

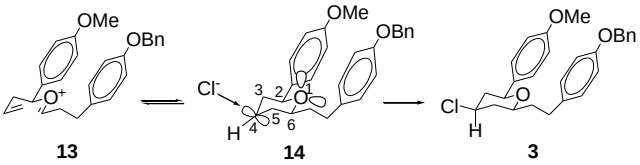


Scheme 4. Another pathway for the Prins cyclization involving cleavage of the cyclopropane bond under intramolecular S_N2 attack by oxy anion

In yet another approach, the reaction may be considered to proceed by following the steps shown in Scheme 4. The combination of **4** and **5** may generate **11** under the Lewis acid action. Intramolecular reorganization, including cleavage of the cyclopropane bond under nucleophilic attack of the oxy anion, as shown, will generate the hemiacetal **12**. This hemiacetal may then dehydrate under the acidic conditions of the reaction to form the key oxocarbenium species **7** required for the Prins cyclization and generate **3** as shown in Scheme 2. Obviously, this pathway offers an excellent scope to generate chiral tetrahydropyrans from chiral cyclopropyl methanol substrates.

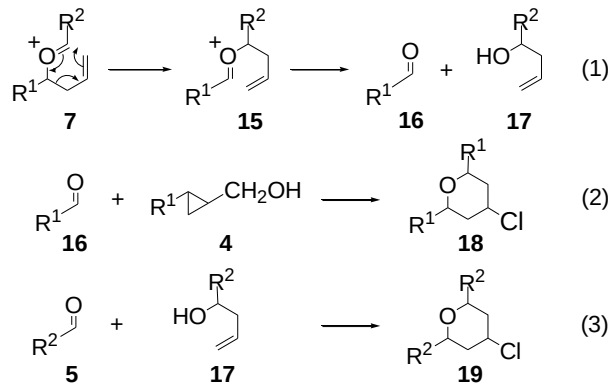
In the event that an 82:18 enantiomeric mixture of the cyclopropyl methanol **4**[11] was reacted with **5**, a racemic mixture of **3** was obtained. Clearly, the reaction did not follow the pathway shown in Scheme 4. The pathways shown in Schemes 2 and 3 are, therefore, the obvious pathways for the present Prins reaction. The enantiomeric compositions of both **3** and **4** were ascertained by chiral HPLC.[12]

The factors that control the stereochemical outcome of the above Prins reaction are two-fold. The intramolecular ring closure of an alkene onto an oxocarbenium ion proceeds through a chair transition state resembling **13**, as shown in Scheme 5, wherein (i) the C2 substituent occupies a favorable equatorial position and the (*E*)-oxocarbenium ion geometry is preferred over the (*Z*)-oxocarbenium ion geometry,[13] leading to the tetrahydropyranyl cation **14** and (ii) the stereocenter formed at C4 is controlled by an extensive orbital overlap[14] which places the hydrogen at C4 in the pseudoaxial position and allows a nucleophilic attack along the equatorial trajectory to deliver the observed tetrahydropyran **3**. In **14**, the equatorial electron pair orbital on the ring oxygen is antiperiplanar to $\sigma_{C2\text{-}C3}$ and $\sigma_{C5\text{-}C6}$ that are rendered electron-deficient for the positive charge on C4. This premise results in electron-donation from the electron pair orbital on oxygen to the above two ring σ bonds to enable them to stabilize the equatorially disposed empty orbital on C4.[15]



Scheme 5. The stereochemical course of the Prins cyclization

The oxocarbenium ion **7** may alternatively be expected to rearrange in 2-oxonia-Cope fashion[7a,16] to generate yet another oxocarbenium ion **15** which, on hydrolysis, will lead to the formation of *p*-methoxybenzaldehyde **16** and 1-(*p*-benzyloxyphenylethyl)-3-buten-1-ol **17**, as shown in eqn 1. Now, the reaction of **16** with the cyclopropyl alcohol **4** in the manner as in Scheme 2 will be expected to generate the symmetrical tetrahydropyran derivative **18**, as depicted in eqn 2. Likewise, the reaction of 3-(*p*-benzyloxyphenyl)propanal **5** with the above generated 1-(*p*-benzyloxyphenylethyl)-3-buten-1-ol **17** will lead to the formation of yet another symmetrical tetrahydropyran derivative **19**, as expressed in eqn 3.



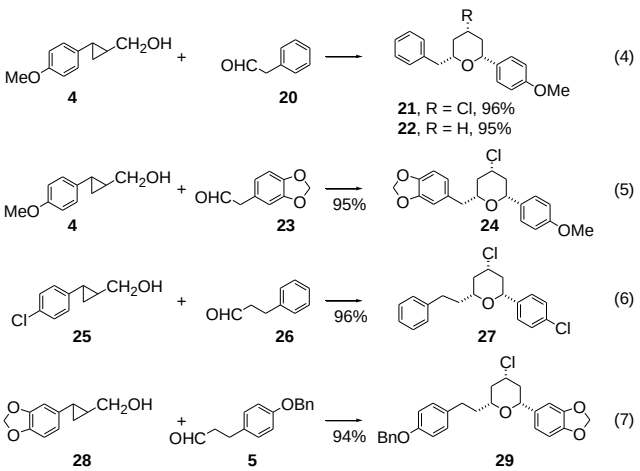
Scheme 6. The 2-oxonia-Cope rearrangement leading to the formation of symmetrical tetrahydropyran products

To our pleasant surprise, **18** and **19** were not formed. Thus, the present protocol to generate the tetrahydropyran skeleton from 2-arylcyclopropyl methanol is free from 2-oxonia-Cope rearrangement which has previously been demonstrated to have plagued many efforts in assembling the said skeleton via the Prins pathway by using a homoallyl aryl alcohol as the starting substrate.[7a,7d,17] The 2-oxonia-Cope rearrangement has been known to be facilitated by electron-donating substituents, such as the methoxy group in the present instance, on the aryl ring.[7a] The genesis of the observed reaction selectivity which excludes completely the 2-oxonia-Cope rearrangement is not understood at the present.

Other researchers have previously used the Prins cyclization of

homoallyl aryl alcohols,[7b,18] cross metathesis-cum-reductive etherification,[7b,c] diastereoselective ring rearrangement metathesis,[19] hetero-Diels-Alder reaction[20] and acid-catalyzed[21] or oxidative[7g,22] intramolecular etherification as the key steps in the synthesis of molecules with tetrahydropyran as the core skeleton. The use of a 2-aryl-substituted cyclopropyl carbinol as an *in situ* substitute for the corresponding homoallyl aryl alcohol required for the Prins cyclization is a new approach which offers great promise for the synthesis of a diverse scaffold of compounds containing tetrahydropyran as the core skeleton for medicinal chemistry exploitation.

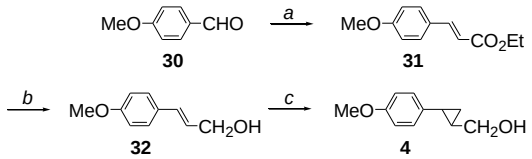
In a rapid deployment of the present methodology, we have reacted the alcohol **4** with α-phenylacetaldehyde **20** and isolated the 4-chlorotetrahydropyran derivative **21** in 96% yield, eq 4. Reductive removal of the chlorine atom furnished **22** in 95% yield. The alcohol **4** was also reacted with α-(3,4-methylenedioxyphenyl)acetaldehyde **23** to isolate the tetrahydropyran derivative **24** in 95% yield, eq 5. In efforts to vary the aryl substituent on the cyclopropane ring, the alcohols **25**[8c] and **28** were reacted with the aldehydes **26** and **5** to isolate **27** and **29** in 96% and 94% yields, respectively, eqs 6 and 7.



The present protocol, however, is not applicable to aromatic and vinylogously aromatic aldehydes such as benzaldehyde, cinnamaldehyde and their *p*-methoxy derivatives. In all these instances, the aldehydes were recovered and, in no instance, the fate of 2-(*p*-methoxyphenyl)cyclopropyl methanol **4** could be ascertained for the complex nature of the product mixture. The cause of this failure is also not understood at the present.

Conclusions

We have used 2-arylcyclopropyl methanol as an *in situ* precursor to aryl-substituted homoallyl alcohol for reaction with aliphatic aldehydes in Prins manner to generate *cis*-2,4,6-trisubstituted tetrahydropyran derivatives in high yields. The strategy was successfully used for the synthesis of (±)-centrolobine in 84% yield over three steps. The substrate **4** was prepared by following the reactions given in Scheme 7 in 80% overall yield. Horner-Wadsworth-Emmons olefination of the commercially available *p*-anisaldehyde **30** furnished the ester **31** in 94% yield.[23] The ester function in **31** was reduced to the corresponding alcohol **32** on reaction with DIBAL in 95% yield.[24] Finally, cyclopropanation using CH_2I_2 and Et_2Zn furnished the required substrate **4** in 90% yield.[8c] Thus, commencing from the commercially available *p*-anisaldehyde, we have achieved the synthesis of (±)-centrolobine in 67% yield over six steps in all.



Scheme 7. Reagents and reaction conditions: (a) $(EtO)_2POCH_2CO_2Et$, NaH, THF, 0–30 °C, 2 h, 94%. (b) DIBAL, toluene, -78–0 °C, 3 h, 95%. (c) CH_2I_2, Et_2Zn, CH_2Cl_2, -23 °C, 5 h, 90%.

In application of the Prins cyclization pathway, the following syntheses are notable. In a successful attempt to prevent the 2-oxonia-Cope rearrangement, Rychnovsky commenced with *p*-tosyloxybenzaldehyde and synthesized (–)-centrolobine over seven steps in 30% overall yield.[7a] Lee and Loh have commenced from 3-(*p*-hydroxyphenyl)propanol and synthesized (–)-centrolobine in 27% overall yield over six steps.[7e] The synthesis involved asymmetric allylation. Dziedzic and Furman used *p*-tosyloxybenzaldehyde and 4-(*p*-benzyloxy)butene as the reactants and synthesized (–)-centrolobine in 10% yield over nine steps.[7h] The synthesis used Sharpless asymmetric dihydroxylation and hydrostannylation as the key steps. Zhou and Loh have synthesized (±)-centrolobine in 58% yield over three steps.[18b] The synthesis employed the reaction of 4-hydroxy-6-(*p*-hydroxyphenyl)hexene with *p*-$MeOC_6H_5CHO$ in the presence of TMSBr to generate the 4-bromo derivative of (±)-centrolobine. Reductive removal of bromine with the use of $NaBH_4$-$InBr_3$ generated (±)-centrolobine. Thus, in comparison, the present synthetic protocol is better than most previously known syntheses using the Prins cyclization strategy. Additionally, the present protocol avoids the undesirable 2-oxonia-Cope rearrangement which makes isolation of the pure desired product very simple.

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Notes and references

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† Electronic Supplementary Information (ESI) available: Experimental details, sectroscopic data, ^1H and ^{13}C NMR spectra, HPLC traces for the enantio-enriched **4** and the product **3** derived from it and the ORTEP of the crystal struture of (±)-**3**. See DOI: 10.1039/b000000x/

‡ *A typical procedure for the synthesis of (±)-centrolobine*. A solution of 2-(*p*-methoxyphenyl)cyclopropyl methanol **4** (0.178 g, 1.0 mmol) and 3-*p*-benzyloxyphenylpropanal **5** (0.288g, 1.2 mmol) in dry CH_2Cl_2 (10 mL) was cooled to 0 °C and mixed with neat $SnCl_4$ (260 μL, 2.2 mmol). The reaction mixture turned dark red instantaneously. The content was stirred at 0 °C for 60 min before the quench by saturated aqueous $NaHCO_3$ (10 mL) and stirred for an additional 15 min. The organic layer was separated from the aqueous layer and the aqueous layer was extracted by CH_2Cl_2 (3 x 5 mL). The combined organic solution was washed by brine (1 x 5 mL), dried by anhydrous Na_2SO_4 and concentrated. Purification by silica gel column chromatography using mixtures of EtOAc and hexanes as the eluant yielded **3**, 0.33 g, solid, mp 80 °C, 95% yield. ^1H NMR (400 MHz, $CDCl_3$): δ 7.36–7.28 (4H, m), 7.26–7.20 (3H, m), 7.01 (2H, d, J = 8.5 Hz), 6.82 (4H, d, J = 8.7 Hz), 4.96 (2H, s), 4.21 (1H, bd, J = 11.2 Hz), 4.08–4.01 (1H, m), 3.73 (3H, s), 3.40–3.32 (1H, m), 2.72–2.56 (m, 2H),

2.32–2.60 (1H, m), 2.14–2.08 (m, 1H), 1.92–1.83 (1H, m), 1.75 (1H, dd, *J* = 23.7, 11.7 Hz), 1.73–1.66 (1H, m), 1.59 (1H, dd, *J* = 23.7, 11.5 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.4, 149.6, 138.5, 134.0, 129.5, 128.7, 128.0, 127.6, 127.2, 114.8, 113.9, 78.1, 75.6, 70.1, 56.0, 55.4, 44.1, 42.3, 37.6, 30.7. IR: ν_{max} cm^{-1} 1612, 1512, 1455, 1247, 1176, 1070, 1035, 828, 740. Calculated *m/z* for $[M + NH_4]^+$ = 454.2149, observed *m/z* = 454.2151.

1 (a) B. B. Snider, In *The Prins Reaction Carbonyl Ene Reactions*; Trost, B. M.; Fleming, I.; Heathcock, C. H. Eds.; Pergamon Press: Oxford, U.K., 1991; Vol. 2, pp 527-561. (b) L. E. Overman and L. D. Pennington, *J. Org. Chem.*, 2003, **68**, 7143.

2 For examples of polyether antibiotics, see: (a) D. Faulkner, *J. Nat. Prod. Rep.*, 2002, **19**, 1. For examples of polysubstituted tetrahydropyrans, see: (b) S. R. Angle and N. A. El-Said, *J. Am. Chem. Soc.*, 1999, **121**, 10211. (c) H. Huang and J. S. Panek, *J. Am. Chem. Soc.*, 2000, **122**, 9836.

3 V. K. Yadav and V. K. Naganaboina, *J. Am. Chem. Soc.*, 2004, **126**, 8652.

4 (a) I. L. de Albuquerque, C. Galeffi, C. G. Casinovi and G. B. Marini-Bettólo, *Gazz. Chim. Ital.*, 1964, **94**, 287. (b) C. Galeffi, C. G. Casinovi and G. B. Marini-Bettolo, *Gazz. Chim. Ital.*, 1965, **95**, 95. (c) A. A. Craveiro and O. R. Gottlieb, *An. Acad. Brasil. Cienc.*, 1968, **40**, 39. (d) A. A. Craveiro, A. da C. Prado, O. R. Gottleib and P. C. W. de Albuquerque, *Phytochemistry*, 1970, **9**, 1869.

5 A. F. de C. Alcantara, M. R. Souza and D. Piló-Veloso, *Fitoterapia*, 2000, **71**, 613.

6 F. Colobert, R. D. Mazery, G. Solladié and M. C. Carreño, *Org. Lett.*, 2002, **4**, 1723.

7 (a) S. Marumoto, J. J. Jaber, J. P. Vitale and S. D. Rychnovsky, *Org. Lett.*, 2002, **4**, 3919. (b) P. A. Evans, J. Cui and S. J. Gharpure, *Org. Lett.*, 2003, **5**, 3883. (c) L. Boulard, S. Bouzbouz, J. Cossy, X. Franck and B. Figadere, *Tetrahedron Lett.*, 2004, **45**, 6603. (d) S. Chandrasekhar, S. J. Prakash and T. Shyamsunder, *Tetrahedron Lett.*, 2005, **46**, 6651. (e) C.-H. A. Lee and T.-P. Loh, *Tetrahedron Lett.*, 2006, **47**, 1641. (f) V. Böhrsch and S. Blechert, *Chem. Commun.*, 2006, **42**, 1968. (g) K. R. Prasad and P. Anbarasan, *Tetrahedron*, 2006, **63**, 1089. (h) M. Dziedzic and B. Furman, *Tetrahedron Lett.*, 2008, **49**, 678. (i) T. Takeuchi, M. Matsuhashi and T. Nakata, *Tetrahedron Lett.*, 2008, **49**, 6462. (j) M. Pham, A. Allatabakhsh and T. G. Mineham, *J. Org. Chem.*, 2008, **73**, 741. (k) A. He, N. Sutivisedsak and C. D. Spilling, *Org. Lett.*, 2009, **11**, 3124. (l) F. Rogano and P. Rüedi, *Helv. Chim. Acta*, 2010, **93**, 1281. (m) W. Chaladaj, R. Kowalczyk and J. Jurczak, *J. Org. Chem.*, 2010, **75**, 1740. (n) D. K. Mohapatra, R. Pal, H. Rahaman and M. K. Gurjar, *Heterocycles*, 2010, **80**, 219. (o) H. Fujioka, K. Yahata, O. Kubo, Y. Sawama, T. Hamada and T. Maegawa, *Angew. Chem. Int. Ed.*, 2011, **50**, 12232. (p) M. Iqbal, N. Mistry and P. A. Clarke, *Tetrahedron*, 2011, **67**, 4960. (q) C. R. Reddy, P. P. Madhavi and S. Chandrasekhar, *Synthesis*, 2011, 123. (r) S. Kasireddy and A. P. Singh, *Eur. J. Org. Chem.*, 2013, 2298. For the synthesis of (±)-centrolobine, see: (s) G. Sabitha, K. B. Reddy, G. S. K. K. Reddy, N. Fatima and J. S. Yadav, *Synlett*, 2005, 2347. (t) H. Fuwa, K. Noto and M. Sasaki, *Heterocycles*, 2010, **82**, 641. (u) Y.-K. Jeong, D.-Y. Kim; Y.-S. Choi and J.-S. Ryu, *Org. Bio. Chem.*, 2011, **9**, 374. (v) J.-H. Xie, L.-C. Guo, X-H. Yang, L.-X. Wang and Q.-L. Zhou, *Org. Lett.*, 2012, **14**, 4758. (w) J. Zheng, Y. J. Tan, J. Ma, M. L. Leow, D. Tirtorahardjo and X.-W. Liu, *Chem.–Eur. J.*, 2014, **20**, 405.

8 (a) S. Gharaati, M. Moghadamb, S. Tangestaninejad, V. Mirkhani, I. Mohammadpoor-Baltork, B. Barati and F. Sadegh, *J. Organomet. Chem.*, 2013, **741-742**, 78. (b) J. Pietruszka, A. C. M. Rieche, T. Wilhelm and A. Witt, *Adv. Synth. Cat.*, 2003, **345**, 1273. (c) A. B. Charette, C. Molinaro and C. Brochu, *J. Am. Chem. Soc.*, 2001, **123**, 12168. (d) T. Ikeno, M. Sato and T. Yamada, *Chem. Lett.*, 1999, 1345. (e) M. Newcomb, S.-Y. Choi and P. H. Toy, *Can. J. Chem.*, 1999, **77**, 1123. (f) H. Kitajima, K. Ito, Y. Aoki and T. Katsuki, *Bull. Chem. Soc. Jpn.*, 1997, **70**, 207.

9 C. G. Frost and B. C. Hartley, *J. Org. Chem.*, 2009, **74**, 3599.

10 (a) V. K. Yadav, V. K. Naganaboina and M. Parvez, *Chem. Commun.*, 2007, **43**, 2281. (b) V. K. Yadav and R. Balamurugan, *Chem. Commun.*, 2002, **38**, 514.

11 H. Takahasi, M. Yoshioka, M. Shibasaki, M. Ohno, N. Imai and S. Kobayashi, *Tetrahedron*, **1995**, *44*, 12013. We have used bis-*o*-nitrobenzenesulfonamide of (1*R*,2*R*)-(–)-1,2-diaminocyclohexane as the chiral catalyst.

12 CHIRALCEL OD-H column (Daicel Chemical Ind. Ltd.) was used to ascertain the enantiomeric compositions of **4** and **3**. **4**: 4% IPA in hexane, 0.5 ml/min; T_R = 39.17 min (minor) and 46.58 min (major). **3**: 3% IPA in hexane, 0.5 ml/min, T_R = 43.29 min and 52.88 min.

13 D. Cremer, J. Gauss, R. F. Childs and C. Blackburn, *J. Am. Chem. Soc.*, 1985, **107**, 2435.

14 (a) R. W. Alder, J. N. Harvey and M. T. Oakley, *J. Am. Chem. Soc.*, 2002, **124**, 4960. (b) R. Jasti and S. D. Rychnovsky, *Org. Lett.*, 2006, **8**, 2175.

15 P. Deslongchamps, In *Stereoelectronic Effects in Organic Chemistry*, Pergamon Press, 1983.

16 (a) S.-I. Sumida, M. Ohga, J. Mitani and J. Nokami, *J. Am. Chem. Soc.*, 2000, **122**, 1310. (b) C.-L. K. Lee; C.-H. A. Lee, K.-T. Tan and T.-P. Loh, *Org. Lett.* , 2004, **6**, 1281. (c) Y.-H. Chen and F. E. McDonald, *J. Am. Chem. Soc.*, 2006, **128**, 4568.

17 (a) L. D. M. Lolkema, C. Semeyn, L. Ashek, H. Hiemstra and W. N. Speckamp, *Tetrahedron*, **1994**, *50*, 7129. (b) S. R. Crosby, J. R. Harding, C. D. King, G. D. Parker and C. L. Willis, *Org. Lett.*, 2002, **4**, 3407. (c) D. J. Hart and C. E. Bennet, *Org. Lett.*, 2003, **5**, 1499. (d) C. S. Barry, N. Bushby, J. R. Harding, R. A. Hughes, G. D. Parker, R. Roe and C. L. Willis, *Chem. Commun.*, 2005, **41**, 3727. (e) R. Jasti, C. D. Anderson and S. D. Rychnovsky, *J. Am. Chem. Soc.*, 2005, **127**, 9939. (f) R. Jasti and S. D. Rychnovsky, *J. Am. Chem. Soc.*, 2006, **128**, 13640.

18 (a) K.-P. Chan and T.-P. Loh, *Org. Lett.*, 2005, **7**, 4491. (b) H. Zhou and T.-P. Loh, *Tetrahedron Lett.*, 2009, **50**, 4368.

19 V. Böhrsch and S. Blechert, *Chem. Commun.*, 2006, **42**, 1968.

20 T. Washio, R. Yamaguchi, T. Abe, H. Nambu, M. Anada and S. Hashimoto, *Tetrahedron*, 2007, **63**, 12037.

21 C. R. Reddy, P. P. Madhavi and S. Chandrasekhar, *Synthesis*, 2008, 2939.

22 F. Rogano, G. Froidevaux and P. Ruedi, *Helv. Chim. Acta*, 2010, **93**, 1299.

23 (a) T. Jiang, T. Livinghouse and H. M. Lovick, *Chem. Commun.*, 2011, **47**, 12861. (b) T. Jiang and T. Livinghouse, *Org. Lett.*, 2010, **12**, 4271.

24 D. Gärtner, H. Konnerth and A. J. von Wangelin, *Catal. Sci. Technol.*, 2013, **3**, 2541.