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PAPER

Reduction of hydrazines to amines with aqueous solution of titanium(III) trichloride†

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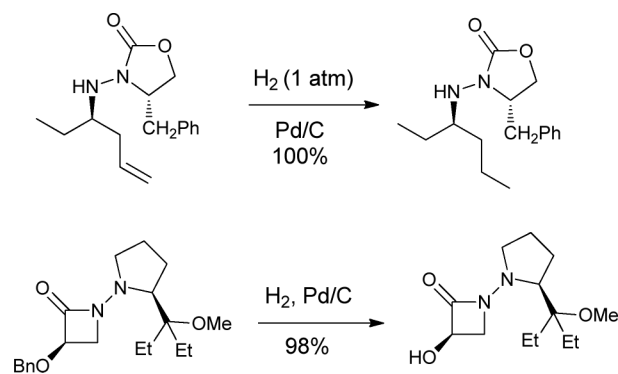
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N–N bond cleavage in hydrazines is widely used in the preparation of amines and thus occupies a significant place in organic synthesis. In this paper, we report a new method for the reductive cleavage of N–N bonds in hydrazines by commercially available and cheap aqueous titanium(III) trichloride. The reaction proceeds smoothly under a broad pH range from acidic to neutral and basic conditions to afford amines in good yields. This method is compatible with substrates containing functionalities such as C–C double bonds, benzyl–nitrogen bonds, benzyloxy and acyl groups.

Introduction

Amines are present in numerous natural products, synthetic materials (for example, ligands), and biologically active compounds as important pharmacophores, and have been greatly touted in the area of drug discovery.¹ Among various methods for the synthesis of amines, hydrazines are common intermediates.² Remarkable recent examples are the anionic^{2g,3} or radical⁴ additions to the C=N bond of hydrazones, the electroreductive coupling of ketones with hydrazones,⁵ the addition of carbon nucleophiles to acylhydrazonium salts,⁶ the addition of *N*-aminolactams to Michael acceptors,^{2i,7} the aza-Michael addition of hydrazines to electrophilic alkenes,⁸ the radical cyclization of *N*-allyl- α -perchlorohydrazides,⁹ and the 1,3-dipolar cycloaddition of azoethine imines to dipolarophiles.¹⁰ These examples clearly show that the N–N bond cleavage in hydrazines occupies a significant place in organic synthesis. The most widely used methods for N–N bond cleavage are: (1) Zn/H⁺ reduction,^{2j} where acidic conditions are required, (2) reduction with trivalent molybdenum, which is unstable and requires *in situ* preparation by reduction of molybdenum pentachloride with zinc powder,¹¹ (3) catalytic hydrogenolysis by RANEY®-Ni,^{2a,3a,9a,12} PtO₂,¹³ and Pd-based catalysts,^{2e,2g,3d,4d,14} where hydrogenation of double bonds and hydrogenolysis of benzyloxy protecting groups may take place as side reactions prior to the reductive cleavage of hydrazine N–N bonds (Scheme 1),^{2e,2g} (4) dissolving metal reduction such as Na (Li)/NH₃,^{2c,15} where strong basic conditions are generated, (5) hydroboration using BH₃·THF,¹⁶ which is obviously incompatible with C–C double bonds, (6) reduction with samarium(II) iodide (SmI₂),^{2g,21} where an activating acyl group on one of the nitrogens of the hydrazine is



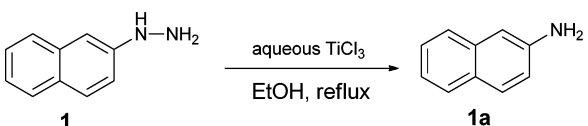
Scheme 1

usually needed to promote the reaction, (7) the recently developed novel oxidative cleavage with magnesium monoperoxyphthalate or *meta*-chloroperbenzoic acid,^{2e,2f} which is usually restricted to *N*-acyl-*N,N'*-disubstituted hydrazines, (8) our newly found reaction of *N,N*-disubstituted hydrazines with 2-naphthanol.¹⁷ Although these above-mentioned methods are frequently used, there are limitations and difficulties, mainly related with the harsh acidic or basic reaction conditions, incompatible with a number of functionalities and protecting groups, and the lack of reactivity in some cases.^{2e} Therefore, developing new efficient and general preparative methods for amines from hydrazines is of promising interest.

Titanium(III) trichloride, usually as a 15%–25% aqueous solution, is one of the common reducing agents. It is cheap and stable, and has been shown to serve as a powerful reductant for a variety of organic substrates such as nitro-compounds, nitrosamines, oximes, carbonyl compounds, and azides *etc.*, often under exceptionally mild conditions.¹⁸ As far as we know, this reagent has not been employed for the reductive cleavage of N–N bonds in hydrazines to produce amines. In this paper, we describe a new method for the readily reductive cleavage of N–N bonds in hydrazines by aqueous titanium(III) trichloride under a broad pH range from

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† Electronic supplementary information (ESI) available: Experimental details, characterization data including ¹H NMR and ¹³C NMR spectra for starting materials and products. See DOI: 10.1039/c1ob05328k

Table 1 Reduction of 2-naphthylhydrazine by aqueous solution of TiCl_3 ^a


| Entry | TiCl_3 /hydrazine (mol) | Yield (%) ^b |
|-------|----------------------------------|------------------------|
| 1 | 2 : 1 | 44 |
| 2 | 3 : 1 | 59 |
| 3 | 4 : 1 | 91 |
| 4 | 5 : 1 | 87 |
| 5 | 6 : 1 | 86 |

^a Reaction conditions: aqueous TiCl_3 , EtOH as co-solvent, reflux for 4 h under argon. ^b Average isolated yield of two runs.

acidic to neutral and basic conditions, and which is compatible with C–C double bonds, benzyl–nitrogen bonds, benzyloxy and acyl protecting groups, and does not need any activating group attached to the hydrazine nitrogen.

Results and discussion

The hydrazines used in this study were prepared following the literature procedures (see ESI†). The reduction of hydrazines by aqueous titanium(III) trichloride was explored using 2-naphthylhydrazine as a model substrate for the optimization of reaction conditions. Due to the strong reducing ability and possible air oxidation, the reduction of hydrazine with aqueous titanium(III) trichlorides was performed under an argon atmosphere. The reaction was easily carried out by adding the commercially available aqueous solution of titanium(III) trichloride to an ethanol solution of 2-naphthylhydrazine and refluxing the mixture for several hours. We found that the molar ratio of titanium(III) trichloride to 2-naphthylhydrazine affected the product yield significantly. The reaction was tested with ratios of TiCl_3 to 2-naphthylhydrazine from 2 : 1 to 6 : 1, and the results are shown in Table 1. It was found whatever ratio was used, the corresponding 2-naphthylamine could be obtained. The ratio of 4 : 1 was found to afford the highest yield of 2-naphthylamine (entry 3, Table 1). With lower ratios of TiCl_3 to 2-naphthylhydrazine (entries 1 and 2, Table 1), 2-naphthylhydrazine was not completely converted (TLC monitoring) and lower product yields were obtained. Increasing the ratio of TiCl_3 to 2-naphthylhydrazine did not further improve the product yields (entries 4 and 5, Table 1).

Having optimized the reaction conditions, we next investigated the scope of the reaction with respect to hydrazines. In addition to ethanol, the co-solvents could be tetrahydrofuran (THF), or *N,N*-dimethylformamide (DMF) according to the solubility of hydrazines. As shown in Table 2, all types of substituted hydrazines, monosubstituted hydrazines (entries 1–6, Table 2), *N,N*-disubstituted hydrazines (entries 7–17, Table 2), symmetrical and unsymmetrical *N,N'*-disubstituted hydrazines (entries 18–23, Table 2), *N,N,N'*-trisubstituted hydrazines (entries 24–28, Table 2), and *N,N,N',N'*-tetrasubstituted hydrazines (entries 29–32, Table 2) could be reductively dissociated to the corresponding primary and secondary amines by an aqueous solution of titanium(III) trichloride under the reaction conditions, and the yields were generally good. It was noted that C–C double bonds (entries

20, 28, 32, Table 2) and benzyloxy group (entry 22, Table 2), which are usually susceptible to hydrogenation and hydroboration reactions, were inert in the reaction. The reaction also tolerated benzyl–nitrogen bonds (entries 10, 19, 26, 27, 30, Table 2), halogen (entries 4 and 5, Table 2), methoxy (entry 3, Table 2), and acyl groups (entries 14, 21–23, Table 2).

The commercially available aqueous titanium(III) trichloride is a strongly acidic solution containing HCl (3%), which may restrict the application of this method to some acid-sensitive hydrazines. We then explored the reaction under neutral and basic conditions (Table 3). Thus, the aqueous solution of titanium(III) trichloride was basified with aqueous sodium hydroxide or 25% ammonia to around pH 10, or adjusted to around pH 7 before the addition of the hydrazine solution. The reaction proceeded as well as in acidic conditions and completed after refluxing the mixture for 4–6 h under argon. Comparable yields of amines were obtained under these neutral or basic conditions. Functionalities such as C–C double bonds, benzyl–nitrogen bonds, halogen, methoxy, benzyloxy and acyl groups were also compatible with the reaction conditions.

Conclusions

In conclusion, we have disclosed a new method for the reductive cleavage of N–N bonds in hydrazines to generate amines. This method allows the use of a commercially available and cheap aqueous solution of TiCl_3 as the reducing agent, and offers good results for various types of substituted hydrazines. The reactions proceed smoothly within a wide pH range from acidic, neutral to basic by refluxing the reaction mixture under argon for several hours. Functionalities such as C–C double bond, benzyl–nitrogen bond, and benzyloxy groups, which are usually susceptible to hydrogenation and hydroboration reactions, are sustainable in this reaction. An acyl group attached to one of the nitrogens of hydrazine, which is needed as an activating group in the SmI_2 -reduction, is inert in and not necessary for the present reaction. With these features, this method offers an important complement to some other methods, and may find potential application in organic synthesis.

Experimental

General

All reagents and solvents were obtained from commercial sources and were used without further purification. Hydrazines used in this study were prepared following the literature procedures (see ESI†). Column chromatography was performed with silica gel (300–400 mesh). Thin layer chromatography was carried out using Merck silica gel GF254 plates. NMR spectroscopy was performed on a Bruker (400 MHz or 600 MHz) spectrometer using TMS as internal standard. HRMS analyses were made on a Bruker Daltonics Bio TOF-Q Mass Spectrometer using ESI or MALDI–TOF ionization. Infrared spectra were measured on a Perkin-Elmer FT-IR spectrometer, using KBr pellet technique for solid compounds and liquid film technique for oils. GC–MS were made on an Agilent Technologies 6890-5973N GC–MS spectrometer. Products were characterized by comparison of ^1H and ^{13}C NMR spectroscopic data with those reported in the literature.

Table 2 Reduction of various hydrazines by aqueous titanium(III) trichloride^a

$$\begin{array}{c} \text{R}^1 \quad \text{R}^3 \\ \diagdown \quad / \\ \text{N} - \text{N} \\ / \quad \diagdown \\ \text{R}^2 \quad \text{R}^4 \end{array} \xrightarrow[\text{reflux}]{\text{TiCl}_3} \begin{array}{c} \text{R}^1 \\ | \\ \text{NH} \\ | \\ \text{R}^2 \end{array} + \begin{array}{c} \text{R}^3 \\ | \\ \text{NH} \\ | \\ \text{R}^4 \end{array}$$

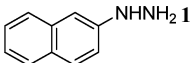
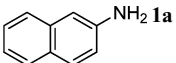
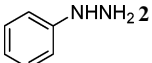
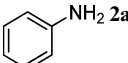
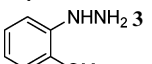
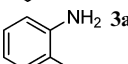
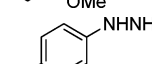
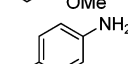
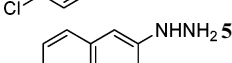
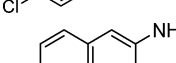
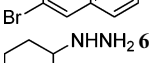
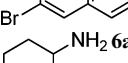
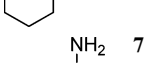
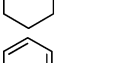
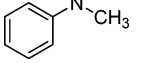
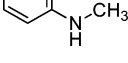
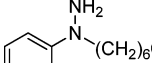
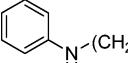
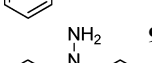
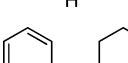
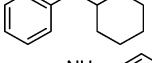
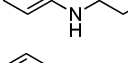
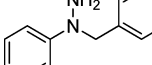
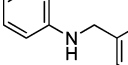
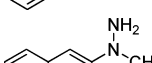
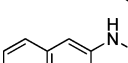
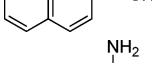
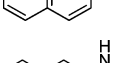
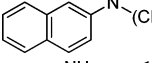
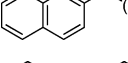
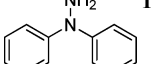
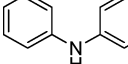
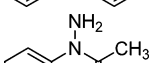
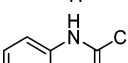
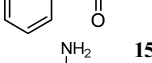
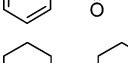
| Entry | Hydrazine | Amine a | Yield (%) ^b | Amine b | Yield (%) ^b |
|-------|---|---|------------------------|-----------------|------------------------|
| 1 |  |  | 91 | NH ₃ | — ^c |
| 2 |  |  | 90 | NH ₃ | — ^c |
| 3 |  |  | 86 | NH ₃ | — ^c |
| 4 |  |  | 88 | NH ₃ | — ^c |
| 5 |  |  | 90 | NH ₃ | — ^c |
| 6 |  |  | 75 | NH ₃ | — ^c |
| 7 |  |  | 78 | NH ₃ | — ^c |
| 8 |  |  | 80 | NH ₃ | — ^c |
| 9 |  |  | 79 | NH ₃ | — ^c |
| 10 |  |  | 76 | NH ₃ | — ^c |
| 11 |  |  | 80 | NH ₃ | — ^c |
| 12 |  |  | 81 | NH ₃ | — ^c |
| 13 |  |  | 84 | NH ₃ | — ^c |
| 14 |  |  | 82 | NH ₃ | — ^c |
| 15 |  |  | 70 | NH ₃ | — ^c |
| 16 |  |  | 61 | NH ₃ | — ^c |
| 17 |  |  | 74 | NH ₃ | — ^c |
| 18 |  |  | 78 | | |

Table 2 (Contd.)

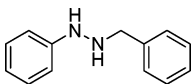
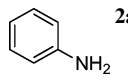
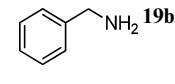
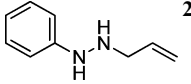
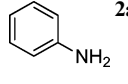
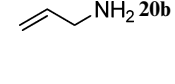
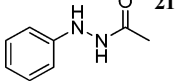
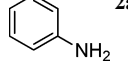
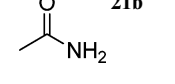
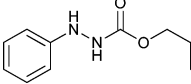
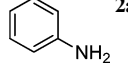
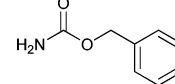
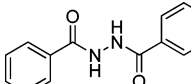
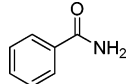
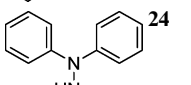
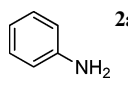
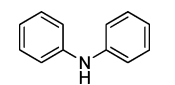
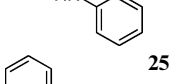
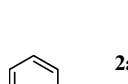
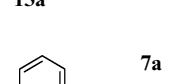
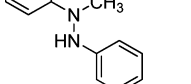
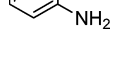
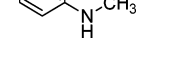
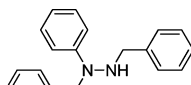
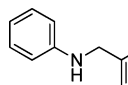
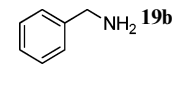
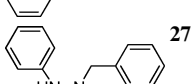
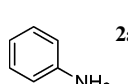
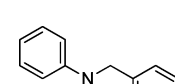
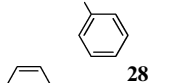
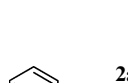
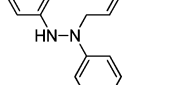
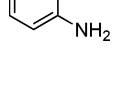
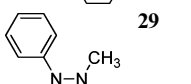
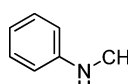
| $\begin{array}{c} \text{R}^1 \quad \text{R}^3 \\ \diagdown \quad / \\ \text{N}-\text{N} \\ / \quad \diagdown \\ \text{R}^2 \quad \text{R}^4 \end{array} \xrightarrow[\text{reflux}]{\text{TiCl}_3} \begin{array}{c} \text{R}^1 \\ \\ \text{NH} \\ \\ \text{R}^2 \end{array} + \begin{array}{c} \text{R}^3 \\ \\ \text{NH} \\ \\ \text{R}^4 \end{array}$ | | | | | |
|---|---|--|------------------------|--|------------------------|
| Entry | Hydrazine | Amine a | Yield (%) ^b | Amine b | Yield (%) ^b |
| 19 |  19 |  2a | 78 |  19b | 71 |
| 20 |  20 |  2a | 74 |  20b | 70 |
| 21 |  21 |  2a | 72 |  21b | 65 |
| 22 |  22 |  2a | 75 |  22b | 73 |
| 23 |  23 |  23a | 75 | | |
| 24 |  24 |  2a | 78 |  13a | 81 |
| 25 |  25 |  2a | 82 |  7a | 85 |
| 26 |  26 |  10a | 69 |  19b | 73 |
| 27 |  27 |  2a | 74 |  10a | 70 |
| 28 |  28 |  2a | 81 |  28b | 77 |
| 29 |  29 |  7a | 84 | | |
| 30 |  30 |  10a | 77 | | |
| 31 |  31 |  13a | 85 | | |

Table 2 (Contd.)

Hydrazine $\xrightarrow[\text{reflux}]{\text{TiCl}_3}$ Amine a + Amine b

| Entry | Hydrazine | Amine a | Yield (%) ^b | Amine b | Yield (%) ^b |
|-------|-----------|---------|------------------------|---------|------------------------|
| 32 | | | 77 | | 81 |

^a Reaction conditions: aqueous TiCl₃, EtOH or THF or DMF as co-solvent, reflux for 4–6 h under argon. ^b Yield of isolated product. ^c The yield of NH₃ was not determined.

Table 3 Reduction of hydrazines under basic or neutral conditions^a

Hydrazine $\xrightarrow[\text{reflux}]{\text{aqueous TiCl}_3, \text{pH 7 or pH 10}}$ Amine a + Amine b

| Hydrazine | pH 10 | | pH 7 | |
|-----------|---------------------------------|---------------------------------|---------------------------------|---------------------------------|
| | Amine a, Yield (%) ^b | Amine b, Yield (%) ^b | Amine a, Yield (%) ^b | Amine b, Yield (%) ^b |
| 1 | 1a, 85 | NH ₃ ^c | 1a, 90 | NH ₃ ^c |
| 2 | 2a, 88 | NH ₃ ^c | 2a, 82 | NH ₃ ^c |
| 3 | 3a, 86 | NH ₃ ^c | 3a, 82 | NH ₃ ^c |
| 4 | 4a, 85 | NH ₃ ^c | 4a, 84 | NH ₃ ^c |
| 5 | 5a, 86 | NH ₃ ^c | 5a, 82 | NH ₃ ^c |
| 6 | 6a, 76 | NH ₃ ^c | 6a, 72 | NH ₃ ^c |
| 7 | 7a, 80 | NH ₃ ^c | 7a, 83 | NH ₃ ^c |
| 8 | 8a, 84 | NH ₃ ^c | 8a, 80 | NH ₃ ^c |
| 9 | 9a, 82 | NH ₃ ^c | 9a, 76 | NH ₃ ^c |
| 10 | 10a, 78 | NH ₃ ^c | 10a, 80 | NH ₃ ^c |
| 11 | 11a, 84 | NH ₃ ^c | 11a, 82 | NH ₃ ^c |
| 12 | 12a, 86 | NH ₃ ^c | 12a, 78 | NH ₃ ^c |
| 13 | 13a, 85 | NH ₃ ^c | 13a, 87 | NH ₃ ^c |
| 14 | 14a, 84 | NH ₃ ^c | 14a, 79 | NH ₃ ^c |
| 15 | 15a, 72 | NH ₃ ^c | 15a, 76 | NH ₃ ^c |
| 16 | 16a, 65 | NH ₃ ^c | 16a, 55 | NH ₃ ^c |
| 17 | 17a, 75 | NH ₃ ^c | 17a, 73 | NH ₃ ^c |
| 18 | 2a, 80 | | 2a, 82 | |
| 19 | 2a, 80 | 19b, 78 | 2a, 75 | 19b, 70 |
| 20 | 2a, 78 | 20b, 82 | 2a, 77 | 20b, 80 |
| 21 | 2a, 78 | 21b, 70 | 2a, 70 | 21b, 68 |
| 22 | 2a, 76 | 22b, 75 | 2a, 77 | 22b, 75 |
| 23 | 23a, 77 | | 23a, 80 | |
| 24 | 2a, 76 | 13a, 81 | 2a, 80 | 13a, 84 |
| 25 | 2a, 76 | 7a, 78 | 2a, 74 | 7a, 79 |
| 26 | 10a, 72 | 19b, 75 | 10a, 70 | 19b, 78 |
| 27 | 2a, 76 | 10a, 79 | 2a, 74 | 10a, 75 |
| 28 | 2a, 82 | 28b, 85 | 2a, 80 | 28b, 82 |
| 29 | 7a, 88 | | 7a, 86 | |
| 30 | 10a, 70 | | 10a, 65 | |
| 31 | 13a, 81 | | 13a, 80 | |
| 32 | 7a, 79 | 28b, 83 | 7a, 80 | 28b, 79 |

^a Reaction conditions: aqueous solution of TiCl₃ basified or neutralized with aqueous NaOH or concentrated NH₃·H₂O, EtOH or THF or DMF as co-solvent, reflux for 4–6 h under argon. ^b Yield of isolated product. ^c The yield of NH₃ was not determined.

General procedure for N–N bond cleavage of hydrazines under acidic conditions

Hydrazines (10 mmol) were dissolved in EtOH, THF or DMF (10 mL) according to their solubility. Then an aqueous solution of

titanium(III) trichloride (40 mmol, 30 mL, 18% aqueous solution) was added and the mixture was refluxed for 4–6 h under argon with stirring. After cooling to room temperature, the reaction mixture was basified, while cooling in an ice-bath, with an aqueous solution of NaOH (20%) to pH >10. The solvents were removed

under reduced pressure. The residue was extracted with CH_2Cl_2 repeatedly. In cases where the amine products might be distilled out, the distillate was also extracted with CH_2Cl_2 . The organic phases were combined. The solvent was evaporated and the residue was purified by column chromatography on silica gel to give the amines.

General procedure for N–N bond cleavage of hydrazines under basic conditions

The aqueous solution of titanium(III) trichloride (40 mmol, 30 mL, 18% aqueous solution) was basified by an aqueous solution of NaOH (20%) or ammonia (25%) to about pH 10. Then hydrazine (10 mmol) in organic solvent (EtOH, THF or DMF, 10 mL) was added and the mixture was stirred for 4–6 h under reflux. After cooling to room temperature, the solvents were removed under reduced pressure. The residue was extracted with CH_2Cl_2 repeatedly. In cases where the amine products might be distilled, the distillate was also extracted with CH_2Cl_2 . The organic phases were combined. The solvent was evaporated and the residue was purified by column chromatography on silica gel to give the amines.

General procedure for N–N bond cleavage of hydrazines under neutral conditions

The aqueous solution of titanium(III) trichloride (40 mmol, 30 mL, 18% aqueous solution) was adjusted to about pH 7 via aqueous solution of NaOH (20%) or ammonia (25%). Then hydrazine (10 mmol) in organic solvent (EtOH, THF or DMF, 10 mL) was added and the mixture was stirred for 4–6 h under reflux. After cooling to room temperature, the reaction mixture was basified, while cooling in an ice-bath, with an aqueous solution of NaOH (20%) to pH >10. The solvents were removed under reduced pressure. The residue was extracted with CH_2Cl_2 repeatedly. In cases where the amine products might be distilled out, the distillate was also extracted with CH_2Cl_2 . The organic phases were combined. The solvent was evaporated and the residue was purified by column chromatography on silica gel to give the amines.

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Notes and References

- (a) S. Inaf and D. Witiak, *Synthesis*, 1999, 435; (b) R. N. Salvatore, C. H. Yoon and K. W. Jung, *Tetrahedron*, 2001, **57**, 7785; (c) M. Kienle, S. R. Dubbaka, K. Brade and P. Knochel, *Eur. J. Org. Chem.*, 2007, 4166; (d) J. Bradshaw, K. Krakowiak and R. Izatt, *Tetrahedron*, 1992, **48**, 4475; (e) I. Blagbrough, S. Carrington and A. Geall, *Pharm. Sci.*, 1997, **3**, 223; (f) R. Bergeron, Y. Feng, W. Weimer, J. McManis, H. Dimova, C. Porter, B. Raisler and O. Phanstiel, *J. Med. Chem.*, 1997, **40**, 1475.
- Selected examples of N–N bond cleavage in hydrazines: (a) R. L. Hinman, *J. Org. Chem.*, 1957, **22**, 148; (b) H. Feuer and F. Jr. Brown, *J. Org. Chem.*, 1970, **35**, 1468; (c) S. E. Denmark, O. Nicaise and J. P. Edwards, *J. Org. Chem.*, 1990, **55**, 6219; (d) F. Alonso, G. Radivoy and M. Yus, *Tetrahedron*, 2000, **56**, 8673; (e) R. Fernández, A. Ferrete, J. M. Lassaletta, J. M. Llera and A. Monge, *Angew. Chem., Int. Ed.*, 2000, **39**, 2893; (f) R. Fernández, A. Ferrete, J. M. Llera, A. Magriz, E. Martín-Zamora, E. Díez and J. M. Lassaletta, *Chem.–Eur. J.*, 2004, **10**, 737; (g) G. K. Friestad and H. Ding, *Angew. Chem., Int. Ed.*, 2001, **40**, 4491; (h) D. Enders and K. Funabiki, *Org. Lett.*, 2001, **3**, 1575; (i) H. Ding and G. K. Friestad, *Org. Lett.*, 2004, **6**, 637; (j) I. Sapountzis and P. Knochel, *Angew. Chem., Int. Ed.*, 2004, **43**, 897; (k) P. Sinha, C. C. Kofink and P. Knochel, *Org. Lett.*, 2006, **8**, 3741.
- (a) D. Enders, H. Schubert and C. Nubling, *Angew. Chem., Int. Ed. Engl.*, 1986, **25**, 1109; (b) S. E. Denmark, T. Weber and D. W. Piotrowski, *J. Am. Chem. Soc.*, 1987, **109**, 2224; (c) A. Alexakis, N. Lensen, J. P. Tranchier, P. Mangeney, J. Feneau-Dupont and J. P. Declercq, *Synthesis*, 1995, 1038; (d) Y. H. Kim and J. Y. Choi, *Tetrahedron Lett.*, 1996, **37**, 5543; (e) S. Kobayashi, T. Furuta and H. Oyamada, *Synlett*, 1998, 1019; (f) P. Bataille, M. Paterne and E. Brown, *Tetrahedron: Asymmetry*, 1999, **10**, 1579.
- (a) C. F. Sturino and A. G. Fallis, *J. Am. Chem. Soc.*, 1994, **116**, 7447; (b) W. R. Bowman, P. T. tephenson, N. K. Terrett and A. R. Young, *Tetrahedron Lett.*, 1994, **35**, 6369; (c) J. Marco-Contelles, G. Balme, D. Bouyssi, C. Destabel, C. D. Henriët-Bernard, J. Grimaldi and J. M. Hatem, *J. Org. Chem.*, 1997, **62**, 1202; (d) D. L. J. Clive, J. Zhang, R. Subedi, V. Boutard, S. Hiebert and R. Ewanuk, *J. Org. Chem.*, 2001, **66**, 1233; (e) D. Ribber, R. Hazell and T. Skrydstrup, *J. Org. Chem.*, 2000, **65**, 5382; (f) G. K. Friestad, *Org. Lett.*, 1999, **1**, 1499; (g) L. Kaim, A. Gacon and A. Perroux, *Tetrahedron Lett.*, 1998, **39**, 371; (h) O. Miyata, M. Muroya, J. Koide and T. Naito, *Synlett*, 1998, 271; (i) H. Miyabe, M. Ueda and T. Naito, *J. Org. Chem.*, 2000, **65**, 5043; (j) G. K. Friestad and J. Qin, *J. Am. Chem. Soc.*, 2001, **123**, 9922; (k) H. Miyabe, M. Ueda, A. Nishimura and T. Naito, *Org. Lett.*, 2002, **4**, 131.
- T. Shono, N. Kise, T. Fujimoto, A. Yamanani and R. Nomura, *J. Org. Chem.*, 1994, **59**, 1730.
- (a) H. Suzuki, S. Aoyagi and C. Kibayashi, *Tetrahedron Lett.*, 1994, **35**, 6119; (b) H. Suzuki, S. Aoyagi and C. Kibayashi, *J. Org. Chem.*, 1995, **60**, 6114; (c) E. Deniau and D. Enders, *Tetrahedron*, 2001, **57**, 2581; (d) N. M. Teerhuis, H. Hiemstra and W. N. Speckamp, *Tetrahedron Lett.*, 1997, **38**, 155; (e) N. M. Teerhuis, H. Hiemstra and W. N. Speckamp, *Tetrahedron Lett.*, 1997, **38**, 159.
- D. Enders, P. Teschner and G. Raabe, *Heterocycles*, 2000, **52**, 733.
- (a) D. Enders, H. Wahl and W. Bettray, *Angew. Chem., Int. Ed.*, 1995, **34**, 453; (b) D. Enders and J. Wiedemann, *Synthesis*, 1996, 1443; (c) D. Enders, S. F. Muller and G. Raabe, *Angew. Chem., Int. Ed.*, 1999, **38**, 195; (d) D. Enders and S. Wallert, *Synlett*, 2002, 304.
- (a) F. Gheli and A. Parsons, *J. Org. Chem.*, 2000, **65**, 6249; (b) M. Casarini, F. Gheli, E. Libertini, U. Pagnoni and A. Parsons, *Tetrahedron*, 2002, **58**, 7925.
- (a) A. Chaveau, T. Martens, M. Bonin, L. Micouin and H. P. Husson, *Synthesis*, 2002, 1885; (b) F. Roussi, A. Chaveau, M. Bonin, L. Micouin and H. Husson, *Synthesis*, 2000, 1170; (c) F. Roussi, M. Bonin, A. Chiaroni, L. Micouin, C. Riche and H. Husson, *Tetrahedron Lett.*, 1999, **40**, 3727.
- S. Polanc, B. Stanovnik and M. Tisler, *Synthesis*, 1980, 830.
- (a) D. Evans, T. Britton, R. Dorow and J. Dellaria, *J. Am. Chem. Soc.*, 1986, **108**, 6397; (b) A. Alexakis, N. Lensen and P. Mangeney, *Synlett*, 1991, 625; (c) O. Nicaise and S. Denmark, *Bull. Soc. Chim. Fr.*, 1997, **134**, 395; (d) Y. Hsieh, G. Lee, Y. Wang and T. Luh, *J. Org. Chem.*, 1998, **63**, 1484; (e) S. Martin and R. Hom, *Tetrahedron Lett.*, 1999, **40**, 2887; (f) V. Breuil-Desvergnès, P. Compain, J. Vatele and J. Gore, *Tetrahedron Lett.*, 1999, **40**, 5009.
- (a) C. Genari, L. Colombo and G. Bertolini, *J. Am. Chem. Soc.*, 1986, **108**, 6394; (b) F. M. Guerra, M. R. Mish and E. M. Carreira, *Org. Lett.*, 2000, **2**, 4265.
- (a) S. Chandrasekhar, C. Reddy and R. Rao, *Synlett*, 2001, 1561; (b) P. Bataille, M. Paterne and E. Brown, *Tetrahedron: Asymmetry*, 1998, **9**, 2181.
- (a) D. Enders and C. Lriverend, *Tetrahedron: Asymmetry*, 1997, **8**, 2787; (b) D. Enders and E. Díez, *J. Org. Chem.*, 1999, **64**, 6329.
- N. Yamazaki and C. Kibayashi, *Tetrahedron Lett.*, 1997, **38**, 4623.
- Q. Tang, C. Zhang and M. Luo, *J. Am. Chem. Soc.*, 2008, **130**, 5840.
- (a) J. E. McMurry, *Acc. Chem. Res.*, 1974, **7**, 281; (b) G. Lunn and E. B. Sansone, *J. Org. Chem.*, 1984, **49**, 3470; (c) G. H. Timms and E. Wildsmith, *Tetrahedron Lett.*, 1971, **12**, 195; (d) E. E. Van Tاملen and M. A. Schwartz, *J. Am. Chem. Soc.*, 1965, **87**, 3277; (e) B. Stanovnik, M. Tisler, S. Polanc and M. Gracner, *Synthesis*, 1978, 65.