University of Groningen

Reduction of Carbon-Carbon Double Bonds Using Organocatalytically Generated Diimide

Smit, Christian; Fraaije, Marco W.; Minnaard, Adriaan J.

Published in:
Journal of Organic Chemistry

DOI:
[10.1021/jo801588d](https://doi.org/10.1021/jo801588d)

IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.

Document Version
Publisher's PDF, also known as Version of record

Publication date:
2008

[Link to publication in University of Groningen/UMCG research database](#)

Citation for published version (APA):

Smit, C., Fraaije, M. W., & Minnaard, A. J. (2008). Reduction of Carbon-Carbon Double Bonds Using Organocatalytically Generated Diimide. *Journal of Organic Chemistry*, 73(23), 9482-9485.
<https://doi.org/10.1021/jo801588d>

Copyright

Other than for strictly personal use, it is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), unless the work is under an open content license (like Creative Commons).

The publication may also be distributed here under the terms of Article 25fa of the Dutch Copyright Act, indicated by the "Taverne" license. More information can be found on the University of Groningen website: <https://www.rug.nl/library/open-access/self-archiving-pure/taverne-amendment>.

Take-down policy

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

Downloaded from the University of Groningen/UMCG research database (Pure): <http://www.rug.nl/research/portal>. For technical reasons the number of authors shown on this cover page is limited to 10 maximum.

Reduction of Carbon-Carbon Double Bonds using Organocatalytically Generated Diimide

Christian Smit¹, Marco W. Fraaije² and Adriaan J., Minnaard^{1*}

1. Stratingh Institute for Chemistry, Nijenborgh 4, 9747 AG , Groningen, The Netherlands
2. Laboratory of Biochemistry, Groningen Biomolecular Sciences and Biotechnology Institute, Nijenborgh 4, 9747 AG , Groningen, The Netherlands

A.J.Minnaard@rug.nl

Supporting Information

Contents:

General Experimental.....	S-2
Hydrogenation of olefins.....	S-3
UV spectra of flavin catalyst 1a.....	S-6
UV spectrum of Riboflavin.....	S-7
Mass Spec of flavin catalysts.....	S-8
NMR of flavin catalyst 1b.....	S-9
NMR of Products	S-9
References.....	S-16

General: ^1H -NMR spectra were recorded at 300 or 400 MHz with CDCl_3 as solvent. Progress and conversion of the reactions was determined by GC-MS equipped with an HP1 column.

Materials: Riboflavin, acetaldehyde, palladium (10%) on activated carbon, $\text{H}_2\text{NNH}_2 \cdot \text{H}_2\text{O}$, methyl-*p*-tolylsulfide, 1-decene, 1,6-heptadien-4-ol, norbornylene, cis-cyclooctene, 1-(1-ethynyl)-1-cyclohexene, styrene, 4-allyl-2-methoxyphenol (eugenol), 2-vinylpyridine, allyl phenyl sulfide, trans-stilbene, 3,7-dimethyl-6-octadien-3-ol (linalool), geraniol, (+)- and (-)-limonene, 10-undecen-1-ol and chlorotrityl chloride polymer resin were commercially available and used without further purification. (-)-(((S)-2-methylbut-3-enyloxy)methyl)benzene (**18a**) was generously donated by A.W. van Zijl,¹ benzyl diallylcarbamate was prepared according to a literature procedure.²

The products decane, propyl phenyl sulfide and dihydrolinalool have been previously described (see appropriate references in the following pages) following a similar reaction procedure. The hydrogenation of the olefins was followed by GC-MS, conversion was calculated based on disappearance of the signal of the substrate and appearance of a signal corresponding to the product(s). Both the GC-MS library and observed mass were used to confirm the identity of the products. The volatile products 4-heptanol, norbornane, and cyclooctene were not isolated. The products 1-ethyl cyclohexene, 2-methoxy-4-propylphenol, 2-ethylpyridine, citronellol, 3,7-dimethyl-1-hydroxy-2-octene, 3,7-dimethyl-1-octanol, *N*-(benzyloxycarbonyl)dipropylamine, (+) and (-)-1-ethyl-4-isopropylcyclohexene and 1-undecanol afforded ^1H NMR spectra indentical to literature.

Note: GC-MS analysis was carried out on samples passed through a short plug of MgSO_4 to remove hydrazine, diimide and water.

Typical Procedure for the hydrogenation of an olefin with 20 equiv of hydrazine monohydrate and 5 mol% of flavin catalyst 1a.

A mixture of olefin (0.5 mmol), flavin catalyst **1a** (10.0 mg, 0.025 mmol), and $\text{NH}_2\text{NH}_2\cdot\text{H}_2\text{O}$ (0.5 g, 11 mmol) in ethanol (4.0 mL) was stirred vigorously at 25 °C under air. Samples of 200 μL were eluted with ethanol over a short MgSO_4 column and subjected to GC-MS analysis.

4-heptanol (5b): conversion and purity (>95%) based on GC-MS analysis after 4 h. No side products were observed.

cyclooctane (3b): conversion and purity (>95%) based on GC-MS analysis after 4 h. No side products were observed.

1-ethylcyclohexene(7b)³: conversion and purity (>95%) based on GC-MS analysis after 4 h. No side products were observed.

Ethylbenzene (8b)⁴: conversion and purity (>95%) based on GC-MS analysis after 4 h. No side products were observed.

n-Butylbenzene (9b)⁵: Purification by extraction with 4x 5 ml pentane followed by washing of the organic layer with brine and evaporation of the solvent afforded a yellow oil. (99% yield) $^1\text{H-NMR}$ δ 7.05-7.35 (m, 5H), 5.5 (t, 2H), 1.05-1.80 (m, 4H), 0.9 (t, 3H). >95% (GC-MS).

2-methoxy-4-propylphenol (10b)⁶: Purification by extraction with 4x 5 ml pentane followed by washing the organic layer with brine and evaporation of the solvent afforded a yellow oil. [78% yield] $^1\text{H-NMR}$ δ 6.83 (m, 1H), 6.67 (m, 2H), 5.52 (s, 1H), 3.86 (s, 3H), 2.57 (t, J = 7.61 Hz, 2H), 1.61 (m, 2H), 0.92 (m, 3H); $^{13}\text{C-NMR}$ δ 146.5 (C), 143.8 (C), 134.9 (C), 121.2 (CH), 114.3 (CH), 111.3 (C), 56.1 (CH_3), 38.0 (CH_2), 25.1 (CH_2), 14.0 (CH_3). >95% (GC-MS). HRMS calcd for $\text{C}_{10}\text{H}_{15}\text{O}_2$ 167.1066, found 167.1069

2-ethylpyridine(11b)⁷: Purification by extraction with 4x 5 ml pentane followed by washing the organic layer with brine and evaporation of the solvent afforded a yellow oil. [73% yield] $^1\text{H-NMR}$ δ 8.52 (d, J = 4.8 Hz, 1H), 7.59 (m, 1H), 7.16 (d, J = 4.8 Hz, 1H), 7.09 (m, 1H), 2.83 (q, J = 7.6 Hz, 2H), 1.31 (m, 3H); $^{13}\text{C-NMR}$ δ 165.3 (C), 149.4 (CH), 136.6 (CH), 122.2 (CH), 121.1 (CH), 31.6 (CH_2), 14.1 (CH_3). >95% (GC-MS). HRMS calcd for $\text{C}_7\text{H}_{10}\text{N}$ 108.0807, found 108.0817

propyl phenyl sulfide(12b): Purification by extraction with 4x 5 ml pentane followed by washing the organic layer with brine and evaporation of the solvent afforded a yellow oil (99 % yield, >95% (GC-MS)).

Citronellol (15b)^{8a} /3,7-dimethyl-1-hydroxy-2-octene (15c): Conversion based on GC-MS data. Except for the expected 3,7-dimethyl-1-hydroxy-2-octene, no other products were observed.

3,7-dimethyl-1-octanol (15d)^{8b}: Conversion based on GC-MS data. Except for the expected 3,7-dimethyl-1-octanol, no other products were observed.

Benzenepropanoic acid, β -methyl-, ethyl ester (16b)⁹: Conversion based on GC-MS data.

N-(Benzyloxycarbonyl)dipropylamine (17b)¹⁰: Purification by extraction with 4x 5 ml ethyl acetate followed by washing the organic layer with brine and evaporation of the solvent afforded a yellow oil. (90% yield) $^1\text{H-NMR}$ δ 7.30 (m, 5H), 5.11 (s, 2H), 3.18 (br s, 4H), 1.54 (br s, 4H), 0.85 (br, 6H); $^{13}\text{C-NMR}$ δ 137.6 (C), 128.9 (CH), 128.2 (CH), 128.1 (CH), 110.3 (CO), 67.2 (CH_2), 49.7 (CH_2), 49.1 (CH_2), 22.3 (CH_2), 21.8 (CH_2), 11.7 (CH_3). HRMS calcd for $\text{C}_{14}\text{H}_{22}\text{NO}_2$ 236.1666, found 236.1645.

(-)-(((S)-2-methylbutoxy)methyl)benzene(18b): Starting from (-)-(((S)-2-methylbut-3-enyloxy)methyl)benzene (**18a**) with an ee of 92%. Purification by extraction with 4x 5 ml pentane followed by washing the organic layer with brine and evaporation of the solvent afforded a yellow oil. (99% yield):

¹H-NMR δ 7.34 (d, *J* = 4.5 Hz, 4H), 7.32-7.23 (m, 1H), 4.53 (s, 2H), 3.36 (m, 1H), 3.28 (m, 1H), 1.72 (m, 1H), 1.51 (m, 1H), 1.18 (m, 1H), 0.94 (m, 6H); ¹³C-NMR δ 139.1 (C), 128.5 (CH), 127.7 (CH), 127.6 (CH), 76.0 (CH₂), 73.2 (CH₂), 35.3 (CH), 26.5 (CH₂), 16.9 (CH₃), 11.6 (CH₃); HRMS [M+ NH₄⁺] calcd for C₁₂H₁₉O₆ 196.1701, found 196.1695. Enantioselectivity was determined by chiral HPLC analysis, Chiralcel OD-H (99.75% heptane/ 0.25% i-PrOH), 40 °C, retention times (min): 9.7 (major) and 9.9 (minor).

Racemic ((2-methylbutoxy)methyl)benzene(17c): was obtained by reduction of racemic ((2-methylbut-3-enyloxy)methyl)benzene following the same procedure as for **17b**. Purification by extraction with 4x 5 ml pentane followed by washing of the organic layer with brine and evaporation of the solvent afforded a yellow oil. (99% yield)

(+)-1-ethyl-4-isopropylcyclohexene (19b)¹¹: starting from (+)-limonene with an ee of 87%. Purification by extraction with 4x 5 ml pentane followed by washing the organic layer with brine and evaporation of the solvent afforded a yellow oil. (72% yield, 90% ee) ¹H-NMR δ 5.32 (s, 1H), 4.79-1.08 (m, 8H), 1.64 (s, 3H), 0.99-0.72 (m, 6H); ¹³C-NMR δ 133.6 (C), 120.7 (CH), 39.7 (CH), 32.0 (CH), 30.5 (CH₂), 28.6 (CH₂), 26.2 (CH), 23.1 (CH₃), 19.7 (CH₃), 19.4 (CH₃); The ee was determined using GC with a Chiraldex B-PM column, 50 °C for 5 min followed by heating to 150 °C in 10 min. After 15 min at 150 °C cooling to 50 °C in 15 min.

(-)-1-ethyl-4-isopropylcyclohexene (20b)¹¹: starting from (-)-limonene with an ee of 99+%. Purification by extraction with 4x 5 ml pentane followed by washing the organic layer with brine and evaporation of the solvent afforded a yellow oil. (89% yield, 99+% ee). ¹H-NMR δ 5.32 (s, 1H), 4.79-1.08 (m, 8H), 1.64 (s, 3H), 0.99-0.72 (m, 6H); ¹³C-NMR δ 133.6 (C), 120.7 (CH), 39.7 (CH), 32.0 (CH), 30.5 (CH₂), 28.6 (CH₂), 26.2 (CH), 23.1 (CH₃), 19.7 (CH₃), 19.4 (CH₃). The ee was determined using GC with a Chiraldex B-PM column, 50 °C for 5 min followed by heating to 150 °C in 10 min. After 15 min at 150 °C cooling to 50 °C in 15 min.

10-undecen-1-ol coupled to 2-chlorotrityl chloride polymer resin. To 0.5 gram of 2-chlorotrityl chloride polymer resin (0.5-0.7 mmol Cl per gram) in 5 ml dry THF was added 119 mg undecanol (0.7 mmol) and 110 mg pyridine (1.4 mmol). The mixture was shaken for 6 hours at 60 °C after which the resin was filtered and washed 3 times with DCM/MeOH/DIEA (17/2/1), 3 times with DCM, 3 times with DMF and 3 times with methanol. After drying in vacuum over KOH, 450 mg of product was obtained.

Cleavage of 10-undecen-1-ol from 2-chlorotrityl polymer resin

To 150 mg of the resin loaded with 10-undecen-1-ol was added 3 ml CDCl₃ and 0.01 ml TFA. The mixture was shaken for two hours. The resin was filtered and the amount of undecanol was determined by ¹H NMR to be 0.26 mmol per gram, by applying TMS as an internal standard.

Reduction of 10-undecen-1-ol coupled to 2-chlorotrityl chloride polymer resin. To 500 mg of resin was added 3.5 ml EtOH, 0.5 ml hydrazine hydrate, and 10 mg 5-ethyl-riboflavin catalyst **1a**. The reaction vessel was shaken for 24 hours under an O₂ atmosphere (balloon). Afterwards, the resin was filtered and washed 3 times with dichloromethane and three times with MeOH.

Cleavage of 10-undecanol from 2-chlorotrityl chloride polymer resin

To 150 mg of resin was added 3 ml CDCl₃ and 0.01 ml TFA. The mixture was shaken for two hours. The resin was filtered and the yield of the product was determined by ¹H NMR by addition of 10 μL TMS (72.5 μmol) as internal standard. 90% yield, >95% (GC-MS), no remaining undecanol was observed.

Oxidation of 4-methylphenylmethyl sulfoxide (2a) with flavin catalyst 1a

In a NMR tube with 600 μL methanol-*d*₄ was added 1.58 mg **1a** (4 μmol) and 30 μL methyl-*p*-tolyl sulfide (2.2 mmol). 40 μL H₂O₂ (30% in H₂O, 3.5 mmol) was added and the reaction was followed in time using ¹H-NMR¹² (See Figure 1)

Figure 1: Conversion of 4-methylphenyl methyl sulfide into 4-methylphenyl methyl sulfoxide

UV spectra of **1a** and **1b**:

The nomenclature of the spectra is derived from the work of Bruice et al.¹³ Catalyst **1a** and **1b** show the same UV-spectra, measured with 1.9 mg catalyst/10 ml in H₂O (0.47 mM). the catalyst can be found in a number of different distinct states:

- 1) "Blue colored radical" (semiquinone species) (0.47 mM catalyst in pure H₂O)

- 2) "Pink protonated radical" (0.47 mM catalyst in H₂O + 16.6 μ L 6N HCl)

3) "Red Flavinium cation" (0.47 mM catalyst in H₂O + 16.6 μ L 6N HCl + 50 μ L 30% H₂O₂)

4) Riboflavin (starting material)

Due to the volatile nature of this compound, not all the pentane could be removed

Due to the volatile nature of this compound, not all pentane could be removed

19b

19b

- [1] van Zijl, A. W.; Lopez, F.; Minnaard, A.J.; Feringa, B.L. *J. Org. Chem.* **2007**, *72*, 2558-2563.
- [2] Mori, A.; Mizusaki, T.; Miyakawa, Y.; Ohashi, E.; Haga, T.; Maegawa, T.; Monguchi, Y.; Sajiki, H. *Tetrahedron* **2006**, *62*, 11925-11932.
- [3] Barluenga, J.; Yus, M.; Concellon, J. M.; Bernad, P. *J. Chem. Res., Synopsis* **1980**, *2*, 41.
- [4] SciFinder[®], CC-01-H_NMR-1716.
- [5] Brown, A.C.; *J. Org. Chem.* **1985**, *50*, 1749-1750
- [6] Brunel, J. M. *Tetrahedron* **2007**, *63*, 3899–3906.
- [7] Chelucci, G.; Gladiali, S.; Marchetti, M. *J. Heterocycl. Chem.* **1988**, *25*, 1761-1765.
- [8a] Savoia, D. *J. Org. Chem.* **1981**, *26*, 5344-5348, (SDBS No. 2184HSP-03-357)
- [8b] Savoia, D. *J. Org. Chem.* **1981**, *26*, 5344-5348 (SDBS No. 6855HSP-01-967)
- [9] Piccolo, O. *J. Org. Chem.* **1991**, *1*, 183-187.
- [10] Hattori, K.; Sajiki, H.; Hirota, K. *Tetrahedron* **2000**, *56*, 8433.
- [11] Schneider, D. F.; *Tetrahedron* **2002**, *26*, 5307-5315.
- [12] Imada, Y.; Iida, H.; Murahashi, S-I.; Naota, T. *Angew. Chem. Int. Ed.* **2005**, *44*, 1704 –1706
- [13] Kemal C.; Chan T.W.; Bruice T.C. *Proc. Natl. Acad. Sci. USA* **1977**, *74*, 405-409.