

Mild chemo-selective hydration of terminal alkynes catalysed by AgSbF_6

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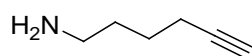
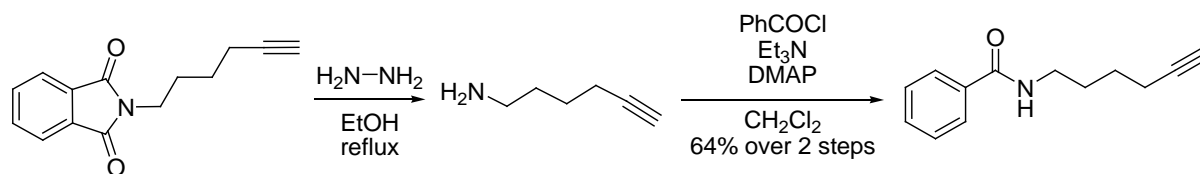
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1. General

All reagents were used as purchased from commercial suppliers without further purification. Flash column chromatography was performed with Merck silica gel 60, 0.040-0.063 mm (230-400 mesh). Merck aluminium backed plates pre-coated with silica gel 60 (UV₂₅₄) were used for thin layer chromatography and were visualized by staining with KMnO₄. ¹H, ¹³C, spectra were recorded on Bruker (400MHz/ 100MHz) or (300 MHz/ 75 MHz) spectrometers. Conditions are specified for each spectrum (temperature 25 °C). Splitting patterns are designated as s, singlet; d, doublet; t, triplet; q, quartet; quint, quintet; m, multiplet. Chemical shifts (δ) are given in ppm relative to the resonance of their respective residual solvent peak, CHCl₃ (7.27 ppm, ¹H; 77.16 ppm, the middle peak, ¹³C). Gas chromatography analyses were carried out on a Thermo Trace GC/DSQ II GC/MS. Infrared spectra were taken with a Nicolet 380 FT-IR. High resolution mass spectroscopy analyses were conducted by the *Institut Fédératif de Recherche 85* at the Université de Strasbourg. Melting points were determined on a Büchi Melting Point B-540 apparatus in open capillary tubes and are uncorrected.

2. Experimental procedures

Preparation of starting material

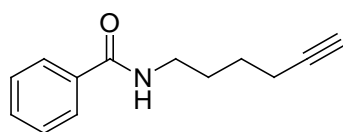


6-Amino-1-hexyne

Hydrazine hydrate (1.3 mL, 27.1 mmol) was added to a solution of 6-phthalimido-1-hexyne (1.76 g, 7.75 mmol) in ethanol. The mixture was stirred at reflux for 4 hours and then cooled to room temperature. The solvent was evaporated and an aqueous solution of NaOH 1M was added. The solution was extracted with diethyl ether, then the organic layers were combined, dried over Na_2SO_4 and concentrated to yield the desired product as a light yellow oil and was used without further purification.

$^1\text{H NMR}$ (CDCl_3 , 300MHz): $\delta = 2.75$ (t, 2 H, $^3J = 6.6$ Hz), 2.26-2.20 (m, 2H), 1.96 (t, 1H, $^3J = 2.8$ Hz), 1.93 (br, 2H), 1.61-1.57 (m, 4H).

The spectroscopic data are in agreement with those reported in the literature.¹



N-hex-5-ynylbenzamide

To a solution of benzoyl chloride (896 μL , 7.75 mmol) in 10 mL dichloromethane was added a solution of 6-amino-1-hexyne (751 mg, 7.75 mmol), triethylamine (1 mL, 7.75 mmol) and *N,N*-dimethylaminopyridine (19 mg, 0.15 mmol) in 5 mL of dichloromethane, at 0 °C. The reaction mixture was stirred at 0 °C for 30 minutes and at ambient temperature until the end of reaction (monitored by TLC). After hydrolysis, extraction of the aqueous phase with dichloromethane and drying of the organic phase with Na_2SO_4 , the crude product was purified by silica gel column chromatography (cyclohexane/ethyl acetate, 7:3) to give 1 g of *N*-hex-5-ynylbenzamide in 64% yield over 2 steps, as a white solid.

¹H NMR (CDCl₃, 300 MHz) : δ = 7.74 (d, 2H, ³J = 6.9 Hz), 7.53 (bs, 1H), 7.35 (t, 1H, ³J = 7.2 Hz), 7.25 (t, 2H, ³J = 7.2 Hz), 3.30 (td, 2H, ³J = 6.8 Hz), 2.07 (td, 2H, ³J = 7.0 Hz, ⁴J = 2.4 Hz), 1.91 (t, 1H, ⁴J = 2.4 Hz), 1.65-1.55 (m, 2H), 1.49-1.39 (m, 2H).

¹³C NMR (CDCl₃, 100 MHz) : δ = 167.7, 134.4, 130.9, 128.0, 126.8, 83.8, 68.6, 39.2, 28.3, 25.5, 17.8.

IR (neat): ν = 3302, 2939, 2863, 1633, 1537 cm⁻¹.

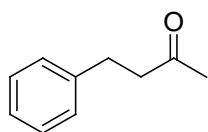
HRMS (ESI) calcd for C₁₃H₁₆NO (M + H)⁺ 202.1154, found 202.1158.

General procedure for the hydration of alkynes

To a solution of alkyne (1 mmol) in MeOH (1.5 mL) was added water (150 μ L) and AgSbF₆ (0.1 mmol). The reaction mixture was stirred for 24 hours at 75 °C, and then evaporated under reduced pressure. Ether was added and the organic phase was extracted with aqueous ammonia, dried over Na₂SO₄ and evaporated under reduced pressure. Column chromatography gave pure ketone.

Typical procedure for GC analysis

To a solution of alkyne (1 mmol) in MeOH (1.5 mL) was added water (150 μ L) and AgSbF₆ (0.1 mmol). The reaction mixture was stirred for 24 hours at 75 °C. An aliquot of the crude reaction mixture was taken, filtered on a small pad of celite and analysed by gas chromatography.

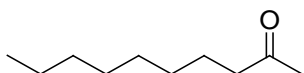


4-phenylbutan-2-one (entry 1) CAS #: [2550-26-7]

Yield: 93%; colorless oil.

¹H NMR (CDCl₃, 400 MHz) : δ = 7.33-7.28 (m, 2H), 7.24-7.20 (m, 3H), 2.92 (t, 2H, ³J = 7.6 Hz), 2.78 (t, 2H, ³J = 7.6 Hz), 2.16 (s, 3H).

¹³C NMR (CDCl₃, 100 MHz) : δ = 207.9, 141.0, 128.5, 128.3, 126.1, 45.2, 30.1, 29.8.

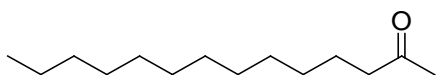


Decanone (entry 2) CAS #: [693-54-9]

Yield: 82%; colorless liquid.

$^1\text{H NMR}$ (CDCl_3 , 400 MHz) : δ = 2.41 (t, 2H, 3J = 7.6 Hz), 2.13 (s, 3H), 1.60-1.53 (m, 2H), 1.25 (bs, 10H), 0.88 (t, 3H, 3J = 7.0 Hz).

$^{13}\text{C NMR}$ (CDCl_3 , 100 MHz) : δ = 209.5, 43.9, 31.9, 29.9, 29.5, 29.3, 29.2, 24.0, 22.7, 14.2.



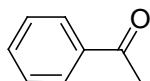
Tetradecan-2-one (entry 3)

Yield: 90%; white solid.

$^1\text{H NMR}$ (CDCl_3 , 400 MHz) : δ = 2.41 (t, 2H, 3J = 7.4 Hz), 2.13 (s, 3H), 1.60-1.53 (m, 2H), 1.25 (bs, 18H), 0.88 (t, 3H, 3J = 6.8 Hz).

$^{13}\text{C NMR}$ (CDCl_3 , 100 MHz) : δ = 209.3, 43.9, 32.0, 29.8, 29.7, 29.5, 29.5, 29.4, 29.2, 23.9, 22.7, 14.1.

The spectroscopic data are in agreement with those reported in the literature.²

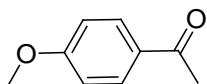


1-phenylethanone (entry 4) CAS #: [98-86-2]

Yield (GC): 90%; colorless liquid.

$^1\text{H NMR}$ (CDCl_3 , 400 MHz) : δ = 7.97 (d, 2H, 3J = 8.2 Hz), 7.57 (t, 1H, 3J = 7.4 Hz), 7.48 (t, 2H, 3J = 7.6 Hz), 2.61 (s, 3H).

$^{13}\text{C NMR}$ (CDCl_3 , 100 MHz) : δ = 198.0, 136.9, 133.0, 128.4, 128.2, 26.5.

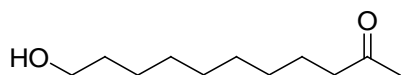


1-(4-methoxyphenyl)ethanone (entry 5) CAS #: [100-06-1]

Yield: 78%; white solid.

$^1\text{H NMR}$ (CDCl_3 , 300 MHz) : δ = 7.95 (d, 2H, 3J = 8.8 Hz), 6.94 (d, 2H, 3J = 8.8 Hz), 3.88 (s, 3H), 2.56 (s, 3H).

$^{13}\text{C NMR}$ (CDCl_3 , 100 MHz) : δ = 196.6, 163.4, 130.5, 130.2, 113.6, 57.3, 26.2.



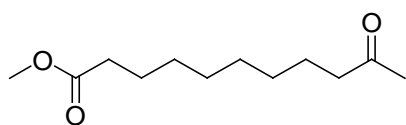
11-hydroxyundecan-2-one (entry 7)

Yield: 89%; white solid.

$^1\text{H NMR}$ (CDCl_3 , 300 MHz) : δ = 3.64 (t, 2H, 3J = 6.6 Hz), 2.42 (t, 2H, 3J = 7.3 Hz), 2.13 (s, 3H), 1.48-1.46 (m, 4H), 1.44 (bs, 1H), 1.37-1.25 (m, 10H).

$^{13}\text{C NMR}$ (CDCl_3 , 100 MHz) : δ = 209.7, 62.7, 43.7, 32.6, 29.7, 29.3, 29.2, 29.0, 25.6, 23.7.

The spectroscopic data are in agreement with those reported in the literature.³



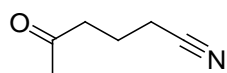
Methyl 10-oxoundecanoate (entry 8)

Yield: 93%; colorless oil.

$^1\text{H NMR}$ (CDCl_3 , 300 MHz) : δ = 3.66 (s, 3H), 2.41 (t, 2H, 3J = 7.3 Hz), 2.29 (t, 2H, 3J = 7.3 Hz), 2.13 (s, 3H), 1.63-1.53 (m, 4H), 1.29 (bs, 8H).

$^{13}\text{C NMR}$ (CDCl_3 , 100 MHz) : δ = 209.3, 174.3, 51.5, 43.8, 34.1, 29.9, 29.3, 29.3, 27.0, 27.0, 25.0, 23.9.

The spectroscopic data are in agreement with those reported in the literature.²

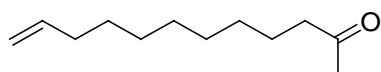


5-oxohexanenitrile (entry 9) CAS #: [10412-98-3]

Yield (GC): 92%; colorless liquid.

$^1\text{H NMR}$ (CDCl_3 , 300 MHz) : δ = 2.64 (t, 2H, 3J = 6.9 Hz), 2.43 (t, 2H, 3J = 6.9 Hz), 2.17 (s, 3H), 1.91 (quint, 2H, 3J = 6.9 Hz).

$^{13}\text{C NMR}$ (CDCl_3 , 100 MHz) : δ = 206.3, 119.2, 41.2, 30.1, 19.3, 16.4.



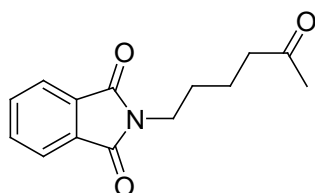
Dodec-11-en-2-one (entry 10)

Yield: 80%; colorless oil.

¹H NMR (CDCl₃, 400 MHz) : δ = 5.86-5.75 (m, 1H), 5.01-4.91 (m, 2H), 2.42 (t, 2H, ³J = 7.2 Hz), 2.13 (s, 3H), 2.03 (m, 2H, ³J = 6.8 Hz), 1.58-1.55 (m, 2H), 1.39-1.35 (m, 2H), 1.28 (bs, 8H).

¹³C NMR (CDCl₃, 100 MHz) : δ = 209.2, 139.1, 114.1, 43.8, 33.8, 29.8, 29.4, 29.3, 29.2, 29.1, 28.9, 23.9.

The spectroscopic data are in agreement with those reported in the literature.⁴



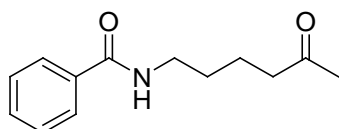
2-(5-oxohexyl)-1H-isoindole-1,3(2H)-dione (entry 11)

Yield: 88%; white solid.

¹H NMR (CDCl₃, 300 MHz) : δ = 7.78-7.75 (m, 2H), 7.67-7.64 (m, 2H), 3.63 (t, 2H, ³J = 6.9 Hz), 2.48 (t, 2H, ³J = 6.9 Hz), 2.08 (s, 3H), 1.67-1.55 (m, 4H).

¹³C NMR (CDCl₃, 100 MHz) : δ = 208.0, 168.0, 133.7, 131.8, 122.9, 42.6, 37.2, 29.7, 27.7, 20.6.

The spectroscopic data are in agreement with those reported in the literature.⁵



N-(5-oxohexyl)benzamide (entry 12)

Yield 94%; white solid.

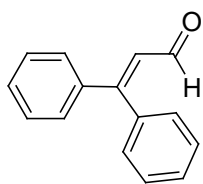
m.p.: 75.1-78 °C

¹H NMR (CDCl₃, 300 MHz) : δ = 7.77 (d, 2H, ³J = 8.1 Hz), 7.53-7.40 (m, 3H), 6.53 (bs, 1H), 3.44 (q, 2H, ³J = 6 Hz), 2.52 (t, 2H, ³J = 6.6 Hz), 2.16 (s, 3H), 1.72-1.58 (m, 4H).

¹³C NMR (CDCl₃, 100 MHz) : δ = 209.0, 167.6, 134.5, 131.1, 128.3, 126.9, 42.9, 39.4, 29.8, 28.7, 20.6.

IR (neat): ν = 3325, 2936, 1708, 1635, 1536 cm⁻¹.

HRMS (ESI) calcd for C₁₃H₁₈NO₂ (M + H)⁺ 220.1259, found 220.1263.

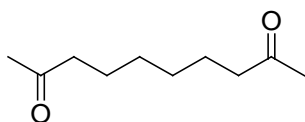


3,3-diphenylacrylaldehyde (entry 13) CAS #: [1210-39-5]

Yield: 82%; white solid.

$^1\text{H NMR}$ (CDCl_3 , 300 MHz) : δ = 9.54 (d, 1H, 3J = 7.6 Hz), 7.55-7.31 (m, 10H), 6.61 (d, 1H, 3J = 7.6 Hz).

$^{13}\text{C NMR}$ (CDCl_3 , 100 MHz) : δ = 193.3, 162.1, 139.6, 136.6, 130.6, 130.4, 129.4, 128.6, 128.5, 128.3, 127.2.



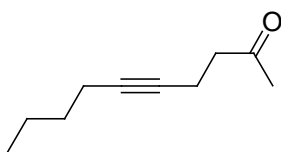
Decane-2,9-dione (entry 14)

Yield: 92%; white solid.

$^1\text{H NMR}$ (CDCl_3 , 400 MHz) : δ = 2.40 (t, 4H, 3J = 7.3 Hz), 2.12 (s, 6H), 1.58-1.52 (m, 4H), 1.30-1.26 (m, 4H).

$^{13}\text{C NMR}$ (CDCl_3 , 100 MHz) : δ = 209.1, 43.7, 29.9, 29.0, 23.7.

The spectroscopic data are in agreement with those reported in the literature.⁶



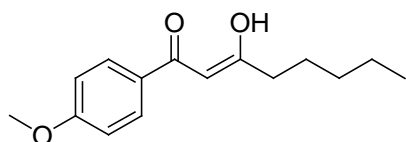
Dec-5-yn-2-one (entry 15)

Yield: 91%; colorless oil.

$^1\text{H NMR}$ (CDCl_3 , 400 MHz) : δ = 2.63 (t, 2H, 3J = 7.2 Hz), 2.43-2.39 (m, 2H), 2.17 (s, 3H), 2.14-2.10 (m, 2H), 1.48-1.33 (m, 4H), 0.91-0.88 (t, 3H, 3J = 7.2 Hz).

$^{13}\text{C NMR}$ (CDCl_3 , 100 MHz) : δ = 207.2, 81.0, 78.5, 43.1, 31.2, 30.0, 22.0, 18.5, 13.7, 13.6.

The spectroscopic data are in agreement with those reported in the literature.⁷



(2Z)-3-hydroxy-1-(4-methoxyphenyl)oct-2-en-1-one (entry 18)

Yield: 89%; light orange solid.

¹H NMR (CDCl₃, 300 MHz) : δ = 7.87 (d, 2H, ³J = 8.9 Hz), 6.94 (d, 2H, ³J = 8.9 Hz), 6.10 (s, 1H), 3.85 (s, 3H), 2.38 (d, 2H, ³J = 7.6 Hz), 1.68 (quint, 2H, ³J = 7.5 Hz), 1.37-1.32 (m, 4H), 0.91 (t, 3H, ³J = 6.4 Hz).

¹³C NMR (CDCl₃, 100 MHz) : δ = 194.9, 184.4, 163.1, 129.2, 127.9, 114.0, 95.2, 55.5, 38.8, 31.5, 25.8, 22.5, 14.

IR (neat): ν = 2952, 2931, 2869, 2837, 1601 cm⁻¹.

HRMS (ESI) calcd for C₁₃H₁₈NO₂ (M + H)⁺ 249.1412, found 249.1418.

3. References

- (1) D. I. Rozkiewicz; D. Jańczewski; W. Verboom; B. J. Ravoo; D. N. Reinhoudt, *Angew. Chem. Int. Ed.*, 2006, **45**, 5292.
- (2) K. Mitsudo, T. Kaide, E. Nakamoto, K. Yoshida, H. Tanaka, *J. Am. Chem. Soc.*, 2007, **129**, 2246.
- (3) T. Ooi, T. Miura, Y. Itagaki, H. Ichikawa, K. Maruoka, *Synthesis*, 2002, 279.
- (4) K. Sato, M. Aoki, J. Takagi, R. Noyori, *J. Am. Chem. Soc.*, 1997, **119**, 12386.
- (5) C.-H. Lee, J.-S. Lee, H.-K. Na, D.-W. Yoon, H. Miyaji, W.-S. Cho, J. L. Sessler, *J. Org. Chem.* 2005, **70**, 2067.
- (6) F. Aulenta, A. Hölemann, H. U. Reißig, *Eur. J. Org. Chem.*, 2006, 1733.
- (7) M. Picquet, C. Bruneau, P. H. Dixneuf, *Tetrahedron*, 1999, **55**, 3937.

4. ^1H and C^{13} NMR Spectra

