J. of Supercritical Fluids 109 (2016) 35–42

Contents lists available at ScienceDirect

The Journal of Supercritical Fluids

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

Asymmetric catalytic synthesis of functionalized tetrahydroquinolines in supercritical fluids

Evgeniya V. Filatova[a], Olga V. Turova[a], Ilya V. Kuchurov[a], Alexey A. Kostenko[b], Albert G. Nigmatov[a], Sergei G. Zlotin[a,*]

[a] N. D. Zelinsky Institute of Organic Chemistry, Russian Academy of Sciences, 47 Leninsky prospect, 119991, Moscow, Russia
[b] D. I. Mendeleev University of Chemical Technology, 9 Miusskaya square, 125047, Moscow, Russia

ARTICLE INFO

Article history:
Received 16 September 2015
Received in revised form 3 November 2015
Accepted 4 November 2015
Available online 11 November 2015

Keywords:
Green chemistry
Supercritical fluids
Asymmetric organocatalysis
Michael reactions
Cascade reactions
Tetrahydroquinolines

ABSTRACT

Bifunctional tertiary amine-catalysed Michael-initiated asymmetric domino-reactions are accomplished for the first time in supercritical fluids (sc-CO_2 and sc-CHF_3). In the proposed conditions, o-N-tosylaminophenyl α,β-unsaturated ketones react with α-nitroalkenes to afford valuable to pharmacology densely functionalized chiral tetrahydroquinolines in moderate to high yields and with very high diastereo- (*dr* > 99:1) and enantioselectivity (up to 98% *ee*).

1. Introduction

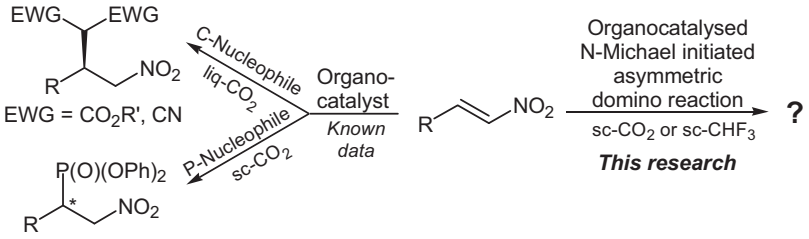
Environment protection is one of the main challenges faced by humanity in the 21st century. The acute global pollution is caused by a variety of anthropogenic factors among which are the rapidly increasing generation of industrial waste and the excessive combustion of fossil fuels emitting greenhouse gases, primarily carbon dioxide. The most perspective but so-far hardly achievable way to reduce this emission is a radical replacement of fossilized hydrocarbons with alternative renewable energy sources [1]. A less radical and more realistic approach to reduce the consumption of hydrocarbons as solvents and auxiliary materials for industrial and particularly chemical technologies is based on their partial substitution with liquefied or converted to supercritical (sc) state carbon dioxide already present in the Earth atmosphere [2].

Today, CO_2 is extensively used for extraction of natural compounds from plants [3,4], as an advanced eluent in chromatography [4], and an easily removable solvent (anti-solvent) for the formation of micro- and nano-sized particles of various materials [5]. It has a significant and far from being exhausted potential in organic synthesis. Transition metal catalysed hydrogenation [6], hydroformylation [7], polymerization [8], and a number of other catalytic reactions have been successfully performed in the sc-CO_2 medium [9]. Some of these reactions [9a,c] are considered a perspective platform for the development of new chemical technologies which are not associated with non-renewable hydrocarbons. However, to the best of our knowledge, there is just scarce data on the use of liquefied or sc-CO_2 as neoteric solvent for highly selective, especially enantioselective reactions, in the presence of organocatalysts.

Over the past decade, this type of catalysis has become a powerful tool for the synthesis of enantiomerically enriched organic compounds [10]. Unlike organometal catalysts, organocatalysts do not contaminate products with toxic heavy metals, which is important for their pharmacological applications [11]. Organocatalysis is considered a green-chemistry method, as all atoms presented in starting compounds may be incorporated into final products in such a way [12]. Particularly attractive are recently developed 'atom economical' organocatalytic domino-reactions, which allow enantioselective synthesis of complex organic molecules from two or more simple achiral precursors in one experimental step (one pot) [13]. Among most efficient catalysts of these reactions are bifunctional tertiary amines, bearing squaramide [14] or (thio)urea

* Corresponding author. Tel.: +7 499 137 13 53; fax: +7 499 135 53 28.
E-mail address: zlotin@ioc.ac.ru (S.G. Zlotin).

http://dx.doi.org/10.1016/j.supflu.2015.11.004
0896-8446/



Scheme 1. Research strategy.

fragments [15], which properly locate reagents in transition states by means of hydrogen bonds [16] and promote high enantioselectivity of reactions. Commonly, domino-reactions are carried out in conventional hydrocarbon-derived organic solvents which efficiently solvate polar intermediates.

Recently, our research group has discovered that chiral tertiary amine-catalysed asymmetric additions of C- or P-nucleophiles to α-nitro alkenes effectively proceed in liquid or sc-CO_2 [17,18]. Herein, we report the first application of this solvent along with trifluoromethane in supercritical state to enantioselective catalytic domino-reactions (Scheme 1).

2. Experimental

2.1. General remarks

The ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ and DMSO-d_6 with a Bruker AM 300 spectrometer. ^{1}D ROE NMR spectra were registered by Bruker AV600. Chemical shifts of ^{1}H and ^{13}C were measured relative to Me_4Si or $CDCl_3$, respectively. The high-resolution mass spectra (HRMS) were measured on Bruker microTOF II spectrometer using electrospray ionization (ESI). The measurements were done in a positive ion mode (interface capillary voltage 4500 V) or in the negative ion mode (3200 V) in the mass range of m/z = 50–3000 Da; external or internal calibration was done with Electrospray Calibrant Solution (Fluka). A syringe injection was used for solutions in acetonitrile, methanol (flow rate 3 μL/min). Nitrogen was applied as a dry gas; interface temperature was set at 180 °C. Specific optical rotations $[\alpha]_D^{20}$ were measured with a Jasco DIP-360 instrument at 589 nm. Silica gels 0.060–0.200 and 0.035–0.070 nm (Acros) were used for column chromatography. Enantiomeric excess values (*ee*) of products were determined by HPLC (Stayer-A, 250 mm × 4.6 mm Chiralpak AD-H column, *n*-hexane/*i*-PrOH = 80:20 unless otherwise specified, 1 ml/min, 254 nm, 30 °C). Solvents and H-bonding additives for catalytic reactions were purified by standard methods. Solvents of "For chromatography" grade were purchased and used for HPLC-analysis as they are.

2.2. General procedure for asymmetric domino aza-Michael–Michael reaction of o-N-tosylaminophenyl α, β-unsaturated ketones 1 with α-nitroalkenes **2**

Chalcone **1** (0.100 mmol), α-nitroalkene **2** (0.150 mmol) and a catalyst (0.005 mmol) were placed in a stainless steel autoclave (V = 2 mL) equipped with a magnetic stirring bar. The autoclave was filled with CHF_3 or CO_2 by means of a syringe-press to a total pressure of 30 bar and heated to a selected temperature. Then, an additional amount of corresponding sc-fluid was added to the final pressure and the reaction mixture was stirred in the specified conditions for the required time (see Tables 1–3). The autoclave was slowly depressurized, the residue was recovered by rinsing with EtOAc and purified by column chromatography on silica gel (eluent *n*-hexane/EtOAc = 4:1) to afford compound **3**.

2-((2*R*,3*S*,4*R*)-1-[(4-Methylphenyl)sulfonyl]-3-nitro-2-phenyl-1,2,3,4-tetrahydroquinolin-4-yl)-1-phenylethanone (3aa) Colorless solid, mp 177–178 °C (mp^{lit} 180–181 °C [14i], 186–188 °C [15e]). $[\alpha]_D^{20}$ + 13.8 (*c* 0.73, $CHCl_3$), 98.4% *ee*. HPLC (*n*-hexane/*i*-propanol = 90:10): t_{minor} = 19.96 min, t_{major} = 35.37 min.

2-((2*R*,3*S*,4*R*)-2-(2-Chlorophenyl)-1-[(4-methylphenyl) sulfonyl]-3-nitro-1,2,3,4-tetrahydroquinolin-4-yl)-1-phenylethanone (3ab) Colorless solid, mp 210–211 °C (mp^{lit} 211–213 °C [15e]). $[\alpha]_D^{20}$ – 19.6 (*c* 1.15, $CHCl_3$), 95% *ee*. HPLC (*n*-hexane/*i*-propanol = 70:30): t_{minor} = 8.73 min, t_{major} = 9.68 min.

2-((2*R*,3*S*,4*R*)-2-(4-Chlorophenyl)-1-[(4-methylphenyl) sulfonyl]-3-nitro-1,2,3,4-tetrahydroquinolin-4-yl)-1-phenylethanone (3ac) Colorless solid, mp 135–136 °C, $[\alpha]_D^{20}$ + 17.2 (*c* 4.10, $CHCl_3$), 96% *ee*. HPLC (*n*-hexane/*i*-propanol = 70/30): t_{minor} = 9.80 min, t_{major} = 13.57 min.

2-((2*R*,3*S*,4*R*)-2-(2,4-Dichlorophenyl)-1-[(4-methylphenyl) sulfonyl]-3-nitro-1,2,3,4-tetrahydroquinolin-4-yl)-1-phenylethanone (3ad) Yellow solid, mp 82–83 °C. $[\alpha]_D^{20}$ – 7.8 (*c* 4.00, $CHCl_3$), 90% *ee*. ^{1}H NMR (300 MHz, $CDCl_3$): 7.92–7.80 (*m*, 4H), 7.67–7.59 (*m*, 4H), 7.51–7.33 (*m*, 6H), 7.24–7.15 (*m*, 2H), 6.84 (*d*, *J* = 6.8 Hz, 1H), 6.34 (*d*, *J* = 7.3 Hz, 1H), 4.95 (dd, J_1 = 8.6 Hz, J_2 = 8.2 Hz, 1H), 3.28 (dd, J_1 = 17.9 Hz, J_2 = 7.7 Hz, 1H), 3.19–3.10 (*m*, 1H), 2.98–2.88 (*m*, 1H), 2.46 (*s*, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): 195.19, 144.97, 136.14, 136.06, 135.93, 135.16, 134.68, 133.80, 133.22, 130.48, 130.06, 128.84, 128.77, 128.62, 128.06, 127.91, 127.38, 127.07, 126.80, 126.06, 92.04, 59.46, 37.05, 35.79, 29.70, 21.70. HRMS (ESI): calcd for $C_{30}H_{24}Cl_2N_2NaO_5S$ $[M+Na]^+$: 618.4832. Found: 617.0675. HPLC: t_{minor} = 10.15 min, t_{major} = 14.05 min.

2-((2*R*,3*S*,4*R*)-2-(2-Bromoophenyl)-1-[(4-methylphenyl) sulfonyl]-3-nitro-1,2,3,4-tetrahydroquinolin-4-yl)-1-phenylethanone (3ae) Colorless solid, mp 199–200 °C (mp^{lit} 198–201 °C [15e]). $[\alpha]_D^{20}$ – 25.0 (*c* 2.49, $CHCl_3$), 97% *ee*. HPLC: t_{minor} = 13.96 min, t_{major} = 15.17 min.

2-((2*R*,3*S*,4*R*)-2-(4-Bromophenyl)-1-[(4-methylphenyl) sulfonyl]-3-nitro-1,2,3,4-tetrahydroquinolin-4-yl)-1-phenylethanone (3af) Colorless solid, mp 153–154 °C. $[\alpha]_D^{20}$ + 18.5 (*c* 5.35, $CHCl_3$), 94% *ee*. ^{1}H NMR (300 MHz, $CDCl_3$): 7.86 (*d*, *J* = 7.8 Hz, 1H), 7.85 (*d*, *J* = 7.3 Hz, 2H), 7.63–7.55 (*m*, 3H), 7.50–7.36 (*m*, 5H), 7.30 (*d*, *J* = 8.2 Hz, 2H), 7.19 (*t*, *J* = 7.8 Hz, 1H), 7.13 (*d*, *J* = 8.7 Hz, 2H), 6.81 (*d*, *J* = 7.8 Hz, 1H), 6.02 (*d*, *J* = 6.9 Hz, 1H), 4.84 (dd, J_1 = 10.3 Hz, J_2 = 7.1 Hz, 1H), 3.29 (dd, J_1 = 18.0 Hz, J_2 = 7.8 Hz, 1H), 3.02 (dt, J_1 = 9.2 Hz, J_2 = 3.5 Hz, 1H), 2.89 (dd, J_1 = 18.3 Hz, J_2 = 3.6 Hz, 1H), 2.43 (*s*, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): 195.10, 144.84, 138.79, 135.92, 135.53, 135.10, 133.80, 132.31, 131.31, 130.01, 128.84, 128.60, 128.03, 127.91, 127.29, 127.21, 125.78, 122.61, 94.17, 62.19, 36.69, 35.86, 21.67. HRMS (ESI): calcd for $C_{30}H_{25}BrN_2NaO_5S$ $[M+Na]^+$: 628.4897. Found: 629.0541. HPLC: t_{minor} = 14.19 min, t_{major} = 20.33 min.

2-((2*R*,3*S*,4*R*)-2-(2-Methoxyphenyl)-1-[(4-methylphenyl) sulfonyl]-3-nitro-1,2,3,4-tetrahydroquinolin-4-yl)-1-phenylethanone (3ag) Colorless solid, mp 195–196 °C (mp^{lit} 214–216 °C [15e]). $[\alpha]_D^{20}$ – 42.1 (*c* 1.88, $CHCl_3$), 86% *ee*. HPLC: t_{minor} = 15.15 min, t_{major} = 23.52 min.