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Stereochemistry of Consabatine from *Convolvulus sabatius* VIV. (Convolvulaceae)

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Abstract

The stereochemistry of consabatine, which was isolated from the roots of *Convolvulus sabatius* VIV. as a novel natural compound, has now been determined by the synthesis of its Mosher esters. Consabatine was found to be 1'*R*-configurated.

Keywords

Convolvulus sabatius • Convolvulaceae • Consabatine • 3α-Tropanol ester • Mosher esters

Introduction

Tropane alkaloids are one of the most important and widespread groups of secondary metabolites in the Convolvulaceae. From the roots of the Mediterranean *Convolvulus sabatius* VIV., consabatine was isolated as a new natural compound [1]. This extraordinary 3α-tropanol ester comprises an unusual isoprenylated cyclohexenylic acid as its acylic component. Mainly from the *Merremia* species, several related aromatic substances called merresectines – esters of 3α-tropanol with kurameric acid/nervogenic acid and derivatives – have been isolated as well [2]. Especially from the chemotaxonomic point of view, the identification of consabatine and the related merresectines is of significance, as they are specific to Convolvulaceae so far.

Results and Discussion

To clearly define a natural compound, the knowledge of not only its molecular structure, but also of its stereochemistry is essential. In order to determine the absolute configuration

of C-1' in the terpenoid moiety of consabatine, the advanced Mosher method was applied [3]. After preparation of the epimeric Mosher esters, *S*-MTPA-consabatine and *R*-MTPA-consabatine, they were submitted for ^{1}H-NMR spectroscopy. As described in [4], the differences in the protons' chemical shifts Δδ (*S* − *R*) between *S*-MTPA- and *R*-MTPA-consabatine were calculated (Fig. 1). According to [3], negative Δδ-values point to an orientation above the MTPA plane (L3), and positive values to an orientation below the MTPA plane (L2). As a consequence, consabatine shows a 1'*R*-configuration.

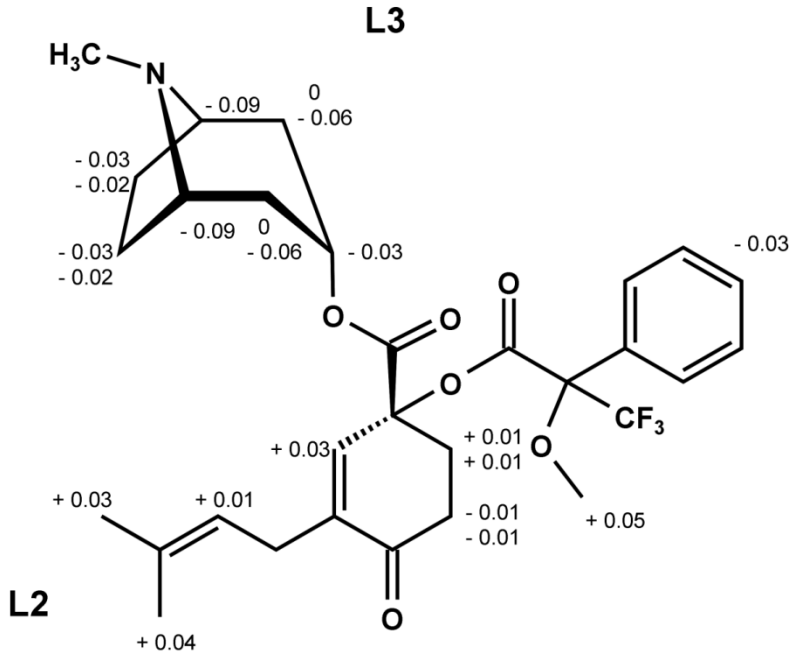

Fig. 1. MTPA-consabatine with differences Δδ (*S* − *R*) taken from the ^{1}H-NMR spectra of *S*-MTPA- and *R*-MTPA-consabatine

Experimental

General procedures

^{1}H-NMR and ^{1}H-^{1}H-COSY spectra were obtained on a Bruker AMX 400 MHz (TMS as internal standard). The EIMS was recorded on a Varian MAT 711 (70 eV).

Plant material

Several specimen of *Convolvulus sabatius* VIV. were bought at Gartencenter Pluta, Berlin. They were cultivated and harvested at the Berlin Botanical Garden.

Extraction and isolation of consabatine

The dried and ground roots of *Convolvulus sabatius* were extracted with methanol three times. After evaporation of the solvent, the residue was dissolved in 2% aqueous tartaric acid and extracted with petrolether, dichloromethane, and ethyl acetate. Then, the aqueous layer was alkalinized (pH 10) with 25% aqueous NH_3 and extracted with dichloromethane again. This alkaloidal extract was separated by means of preparative HPLC (0.5% aqueous H_3PO_4/MeOH 80:20 to 40:60 in 60 min) and preparative TLC

($CHCl_3$/MeOH/aq. NH_3conc. 80:20:2). Consabatine was verified by ^{1}H-NMR and EIMS measurements.

Consabatine (12.2 mg), (1*R*,3*r*,5*S*)-8-Methyl-8-azabicyclo[3.2.1]octan-3-yl (1*R*)-1-hydroxy-3-(3-methylbut-2-en-1-yl)-4-oxocyclohex-2-ene-1-carboxylate:
^{1}H-NMR (400 MHz, $CDCl_3$): δ 6.40 (1H, s, H-2'), 5.10 (2H, t, *J* = 5.0 Hz, H-3/H-2''), 3.14 (2H, br s, H-1/H-5), 2.96 (2H, br d, *J* = 7.0 Hz, CH_2-1''), 2.74 (1H, ddd, *J* = 5.5 Hz, 7.5 Hz, and 17.1 Hz, H-5'd), 2.62 (1H, ddd, *J* = 5.2 Hz, 8.9 Hz, and 17.1 Hz, H-5'u), 2.37 (1H, tt, *J* = 5.6 Hz, and 7.5 Hz, H-6'd), 2.30 (3H, s, N–CH_3), 2.24 (1H, dt, *J* = 5.3 Hz, and 8.7 Hz, H-6'u), 2.20 (2H, m, H-2ax/H-4ax), 2.02 (2H, m, H-6exo/H-7exo), 1.73 (3H, s, CH_3-4''), 1.72 (2H, m, H-2eq/H-4eq), 1.70 (2H, d, *J* = 8.1 Hz, H-6endo/H-7endo), 1.60 (3H, s, CH_3-5''); EIMS (70 eV): *m/z* (rel. int.) 347 (16), 330 (1), 223 (1), 141 (7), 140 (3), 125 (12), 124 (100), 97 (9), 96 (18), 95 (8), 94 (8), 83 (26), 82 (21).

Synthesis of the Mosher esters of consabatine

One-half of the consabatine obtained (6.1 mg) was dissolved in 0.5 mL anhydrous dichloromethane. Then 8.8 mg dimethylaminopyridine (DMAP), 3.7 µL triethylamine (TEA), and 6.6 µL (−)-α-methoxy-α-(trifluoromethyl)phenylacetic acid (MTPA) chloride were added under nitrogen atmosphere. The mixture was stirred overnight. To terminate the reaction, 4.34 µL 3-[(dimethylamino)propyl]amine (3-DMAPA) was added, and the mixture was stirred for 10 min. After evaporation of the solvent, the residue was applied to the preparative TLC ($CHCl_3$/MeOH/aq. NH_3 conc. 40:10:1) to give *S*-MTPA-consabatine.

S-MTPA-consabatine (4.2 mg): ^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.36–7.45 (5H, m, aromatic protons), 6.92 (1H, s, H-2'), 5.22 (1H, t, *J* = 4.4 Hz, H-3), 5.06 (1H, br t, *J* = 7.0 Hz, H-2''), 3.78 (1H, m, H-5'd), 3.76 (1H, m, H-5'u), 3.57 (3H, s, N–CH_3), 3.55 (3H, s, O–CH_3), 3.39 (2H, d, *J* = 7.3 Hz, H-2ax/H-4ax), 3.09 (2H, m, H-1/H-5), 2.95 (2H, br d, *J* = 7.4 Hz, CH_2-1''), 2.47 (2H, m, H-6exo/H-7exo), 2.29 (1H, m, H-6'd), 2.24 (1H, m, H-6'u), 2.12 (2H, br d, *J* = 16.1 Hz, H-6endo/H-7endo), 1.92 (2H, br d, *J* = 16.6 Hz, H-2eq/H-4eq), 1.76 (3H, s, CH_3-4''), 1.61 (3H, s, CH_3-5'').

The second half of consabatine (6.1 mg likewise) was treated in the same manner with (+)-MTPA chloride instead to give *R*-MTPA-consabatine.

R-MTPA-consabatine (3.7 mg): ^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.38–7.49 (5H, m, aromatic protons), 6.89 (1H, s, H-2'), 5.25 (1H, t, *J* = 5.1 Hz, H-3), 5.05 (1H, br t, *J* = 7.3 Hz, H-2''), 3.78 (1H, m, H-5'd), 3.75 (1H, m, H-5'u), 3.54 (3H, s, N–CH_3), 3.50 (3H, s, O–CH_3), 3.39 (2H, d, *J* = 7.2 Hz, H-2ax/H-4ax), 3.18 (2H, m, H-1/H-5), 2.96 (2H, br d, *J* = 7.0 Hz, CH_2-1''), 2.50 (2H, m, H-6exo/H-7exo), 2.30 (1H, m, H-6'd), 2.25 (1H, m, H-6'u), 2.14 (2H, br d, *J* = 15.8 Hz, H-6endo/H-7endo), 1.98 (2H, br d, *J* = 16.4 Hz, H-2eq/H-4eq), 1.73 (3H, s, CH_3-4''), 1.57 (3H, s, CH_3-5'').

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Authors' Statement

Competing Interests

The authors declare no conflict of interest.

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