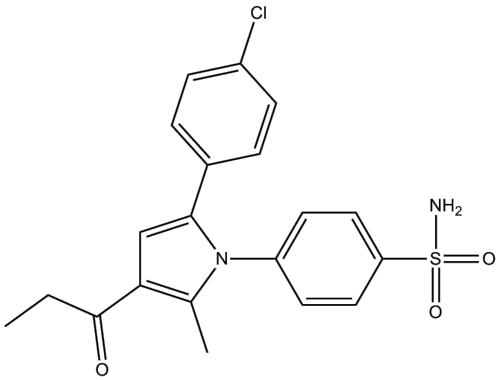
Product Data Sheet

Product Name: A-867744
Cat. No.: GC15014

Chemical Properties

Cas. No.	1000279-69-5		
Chemical Name	4-[5-(4-chlorophenyl)-2-methyl-3-propanoylpyrrol-1-yl]benzenesulfonamide		
SMILES	CCC(=O)C1=C(N(C(=C1)C2=CC=C(C=C2)Cl)C3=CC=C(C=C3)S(=O)(=O)N)C		
Formula	$C_{20}H_{19}ClN_2O_3S$	M.Wt	402.89
Solubility	DMF: 30 mg/ml,DMF:PBS (pH 7.2) (1:4): 0.20 mg/ml,DMSO: 10 mg/ml	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 °C and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20°C for several months.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		
Structure			

Background

Targeting α7 neuronal acetylcholine receptors (nAChRs) with selective agonists and positive allosteric modulators (PAMs) is considered a therapeutic approach for managing cognitive deficits in schizophrenia and Alzheimer's disease. A-867744 is a novel type II PAM with good potency and selectivity.
In vitro: In oocytes expressing α7 nAChRs, A-867744 potentiated acetylcholine (ACh)-evoked currents, with an EC50 value of about 1 μM. At highest concentrations of A-867744 tested, ACh-

evoked currents were essentially nondecaying. At lower concentrations, no evidence of a distinct secondary component was evident in contrast to 4-naphthalen-1-yl-3a,4,5,9b-tetrahydro -3H-cyclopent-a[c]quinoline-8-sulfonic acid amide (TQS), another type II α7 PAM [1].
In vivo: A-867744 was assessed for its PK properties in rat, dog, and monkey. The animal pharmacokinetic profile of A-867744 was characterized by relatively low plasma clearance values (1.1-2.5 L/h/kg) and volumes of distribution (1.7-4.6 L/kg) across species, with terminal elimination halflives in the 1.0-1.7 h. The bioavailability is 83% in rat and somewhat lower in dog (55%) and monkey (68%). These findings indicated that A-867744 showed acceptable pharmacokinetic profile across species and brain levels sufficient to modulate α7 nAChRs [2].
Clinical trial: A-867744 is currently in the preclinical developlent stage and no clinical data are available.

Reference:

[1] Malysz J, Grønlien JH, Anderson DJ, Håkerud M, Thorin-Hagene K, Ween H, Wetterstrand C, Briggs CA, Faghih R, Bunnelle WH, Gopalakrishnan M.
In vitro pharmacological characterization of a novel allosteric modulator of alpha 7 neuronal acetylcholine receptor, 4-(5-(4-chlorophenyl)-2-methyl-3-propionyl-1H-pyrrol-1-yl) (A-867744), exhibiting unique pharmacological profile. J Pharmacol Exp Ther. 2009;330(1):257-67.
[2] Faghih R, Gopalakrishnan SM, Gronlien JH, Malysz J, Briggs CA, Wetterstrand C, Ween H, Curtis MP, Sarris KA, Gfesser GA, El-Kouhen R, Robb HM, Radek RJ, Marsh KC, Bunnelle WH, Gopalakrishnan M. Discovery of 4-(5-(4-chlorophenyl)-2-methyl-3-propionyl-1H-pyrrol-1-yl) benzenesulfonamide (A-867744) as a novel positive allosteric modulator of the alpha7 nicotinic acetylcholine receptor. J Med Chem. 2009;52(10):3377-84.