Supporting Information

Synthesis of novel sulfonamide azoles *via* C–N cleavage of sulfonamides by azole ring and relational antimicrobial study

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1. Experimental protocol

All chemicals and solvents were commercially available, and used without further purification. All fluorescence spectra were recorded on F-7000 Spectrofluorimeter (Hitachi, Tokyo, Japan) equipped with 1.0 cm quartz cells, the widths of both the excitation and emission slit were set as 2.5 nm, and the excitation wavelength was 295 nm. The UV spectrum was recorded at room temperature on a TU-2450 spectrophotometer (Puxi Analytic Instrument Ltd. of Beijing, China) equipped with 1.0 cm quartz cells.

The stock solution of compound **9d** was prepared in DMF. Calf thymus DNA (Sigma Chemical Co., St. Louis, MO) was used without further purification, and its stock solution was prepared by dissolving an appropriate amount of DNA in doubly distilled water. The solution was allowed to stand overnight and store at 4 ^{o}C in the dark for about a week. The concentration of DNA in stock solution was determined by UV absorption at 260 nm using a molar absorption coefficient ξ_{260} = 6600 L mol^{-1} cm^{-1} (expressed as molarity of phosphate groups) by Bouguer-Lambert-Beer law. The purity of DNA was checked by monitoring the ratio of the absorbance at 260 nm to that at 280 nm. The solution gave a ratio of > 1.8 at A260/A280, which indicates that DNA was sufficiently free from protein. NR stock solution (2.0×10^{-3} mol/L) was prepared by dissolving its solid (Sigma Chemical Co.) in doubly distilled water and was kept in a cool and dark place. All the solutions were adjusted with Tris(hydroxymethyl)aminomethane (Tris)-HCl buffer solution (pH = 7.4), which was prepared by mixing and diluting Tris solution with HCl solution. All chemicals were of analytical reagent grade, and doubly distilled water was used throughout.

Human serum albumin (HSA) was obtained from Sigma-Aldrich (St. Louis, MO, USA). Tris, sodium chloride and hydrochloric acid were analytical purity. Sample masses were weighed on a microbalance with a resolution of 0.1 mg. All other chemicals and solvents were commercially available, and used without further purification. All fluorescence spectra were recorded at 298, 303, 310 K in the range of 300–450 nm on F-7000 Spectrofluorimeter (Hitachi, Tokyo, Japan) equipped with 1.0 cm quartz cells, the widths of both the excitation and emission slit were set as 2.5 nm, and the excitation wavelength was 295 nm. UV spectra were recorded at room temperature on a TU-2450 spectrophotometer (Puxi Analytic Instrument Ltd. of Beijing, China) equipped with 1.0 cm quartz cells.

2. Biological assay procedures

Minimal inhibitory concentration (MIC, μg/mL) is defined as the lowest concentration of the new compounds that completely inhibited the growth of bacteria, by means of standard two folds serial dilution method in 96-well microtest plates according to the National Committee for Clinical Laboratory Standards (NCCLS). The tested microorganism strains were provided by the School of Pharmaceutical Sciences, Southwest University and the College of Pharmacy, Third Military Medical University. Chloromycin, Norfloxacin and Fluconazole were used as control drugs. To ensure that the solvent had no effect on bacterial growth, a control test was performed with test medium supplemented with DMSO at the same dilutions as used in the experiment. All the bacteria and fungi growth was monitored visually and spectrophotometrically. The lowest concentration (highest dilution) required to arrest the growth of bacteria was regarded as minimal inhibitory concentration (MIC).

2.1. Antibacterial Assays

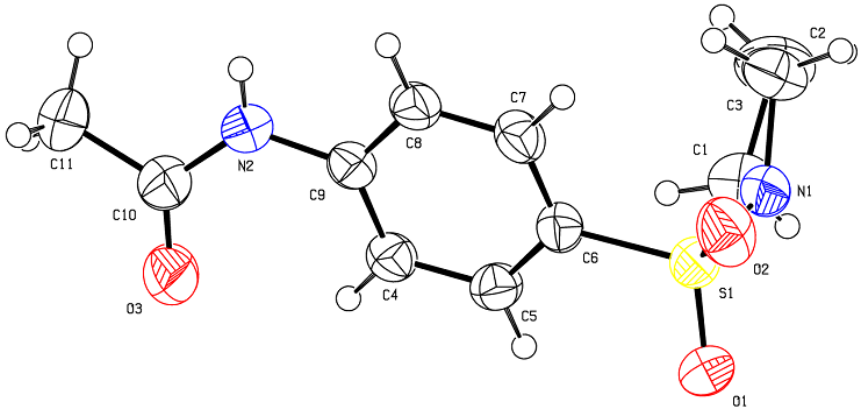
The prepared compounds **4**–**13** were evaluated for their antibacterial activities against Gram-positive bacteria (*S. aureus* ATCC 6538, *Methicillin-resistant Staphylococcus aureus* N315 (MRSA), *M. luteus* ATCC4698 and *B. subtilis* ATCC 21216), Gram-negative bacteria (*E. coli* ATCC 8099, *P. aeruginosa* ATCC 27853, *B. typhi* and *B. proteus* ATCC 13315). The bacterial suspension was adjusted with sterile saline to a concentration of 1×10^5 CFU. Initially the compounds were dissolved in DMSO to prepare the stock solutions, then the tested compounds and reference drugs were prepared in Mueller–Hinton broth (Guangdong huaikai microbial sci. & tech co., Ltd, Guangzhou, Guangdong, China) to obtain the required concentrations of 512, 256, 128, 64, 32, 16, 8, 4, 2, 1, 0.5 μg/mL. These dilutions were inoculated and incubated at 37 ºC for 24 h.

2.2. Antifungal Assays

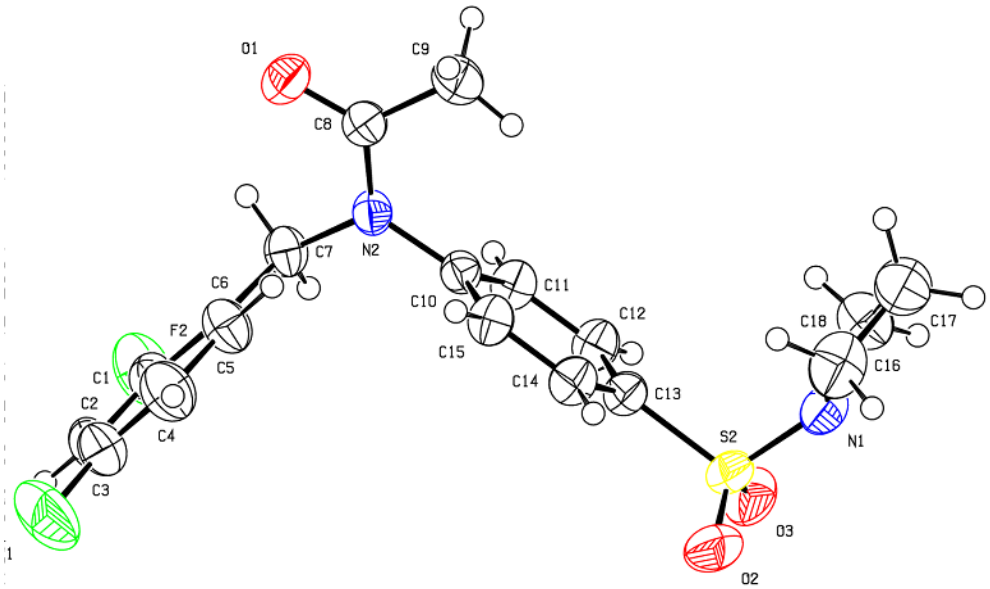
The newly synthesized compounds **4**–**13** were evaluated for their antifungal activities against *C. albicans* ATCC 76615, *C. mycoderma*, *C. utilis*, *S. cerevisia* and *A. fumigatus* ATCC 96918. A spore suspension in sterile distilled water was prepared from 1-day old culture of the fungi growing on Sabouraud agar (SA) media. The final spore concentration was $1-5 \times 10^3$ spore mL^{-1}. From the stock solutions of the tested compounds and reference antifungal drug Fluconazole, dilutions in sterile RPMI 1640 medium (Neuronbc Laboraton Technology CO., Ltd, Beijing, China) were made resulting in eleven wanted concentrations (0.5 to 512 μg/mL) of each tested compound. These dilutions were inoculated and incubated at 35 ºC for 24 hours.

3. X-Ray single-crystal structure of sulfonamides

X-Ray single-crystal structure of compound **4b**



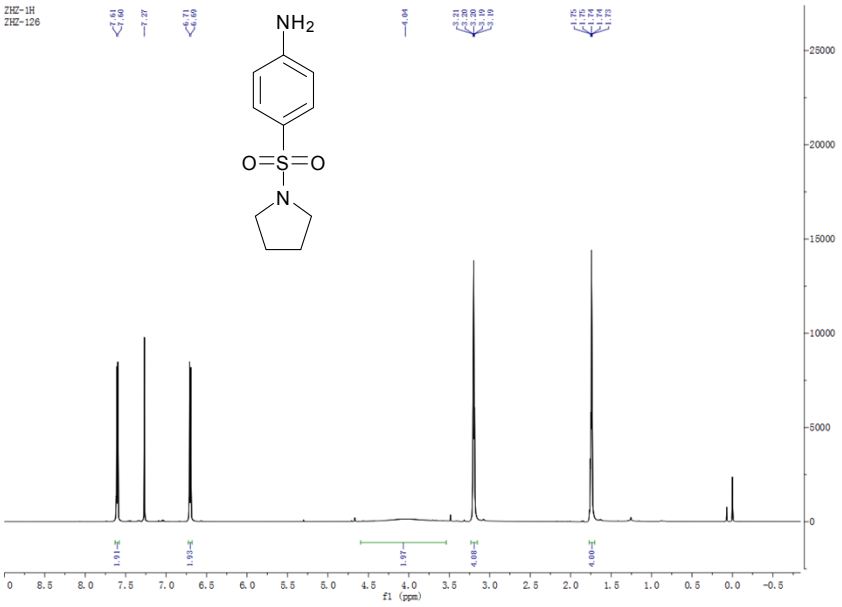
X-Ray single-crystal structure of compound **6g**



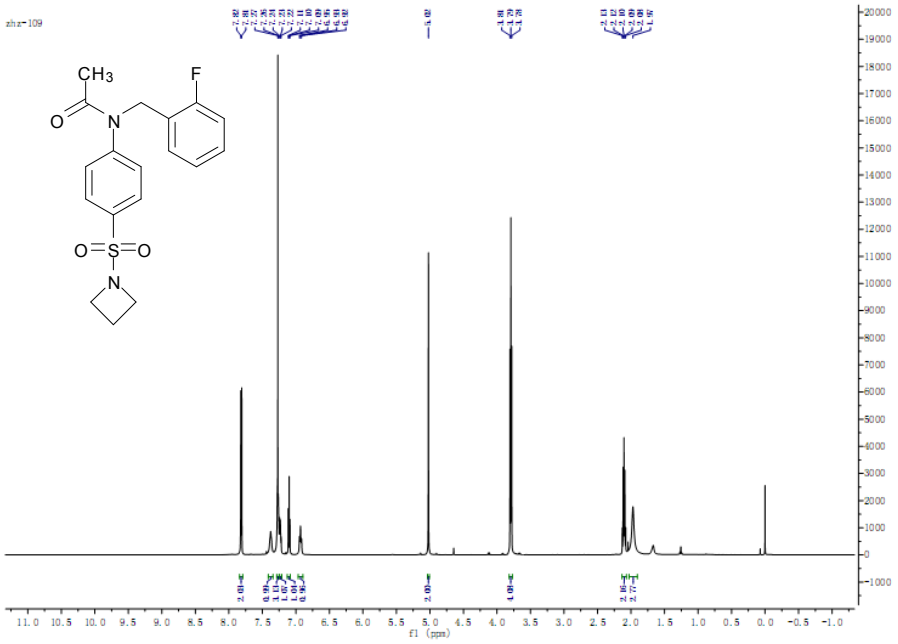
4. Spectra for some sulfonamide compounds

^{1}H NMR Spectrum of N-(4-(pyrrolidin-1-ylsulfonyl)phenyl)acetamide (**4c**)

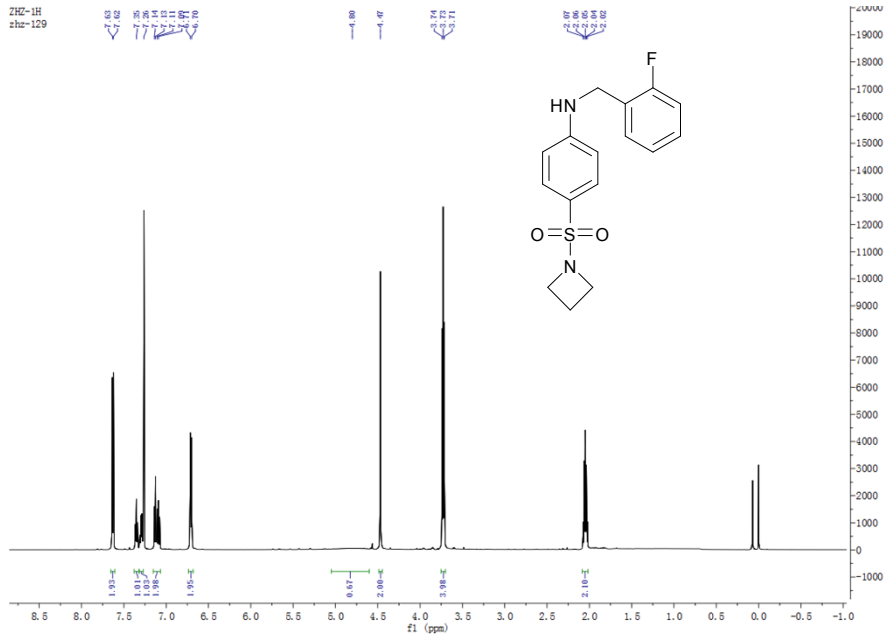
^{1}H NMR Spectrum of 4-(pyrrolidin-1-ylsulfonyl)aniline (**5b**)



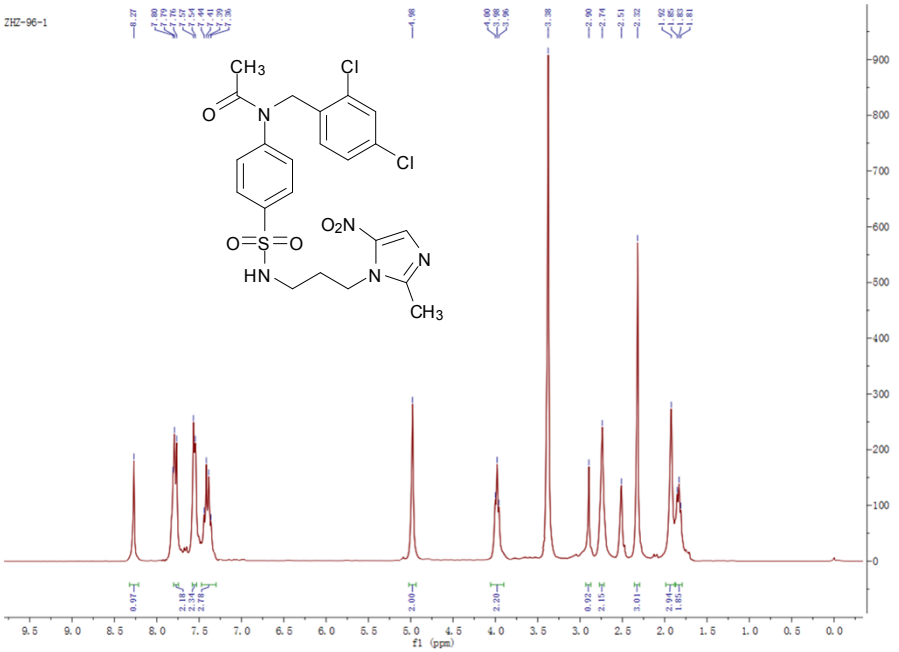
^{1}H NMR Spectrum of N-(4-(azetidin-1-ylsulfonyl)phenyl)-N-(2-fluorobenzyl)acetamide (**6c**)



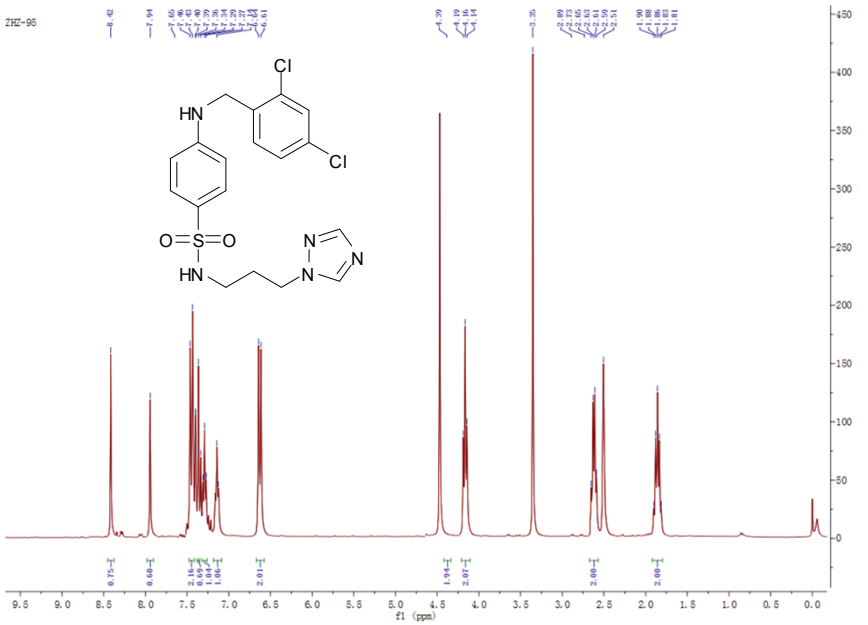
^{1}H NMR Spectrum of 4-(azetidin-1-ylsulfonyl)-N-(2-fluorobenzyl)aniline (**7c**)



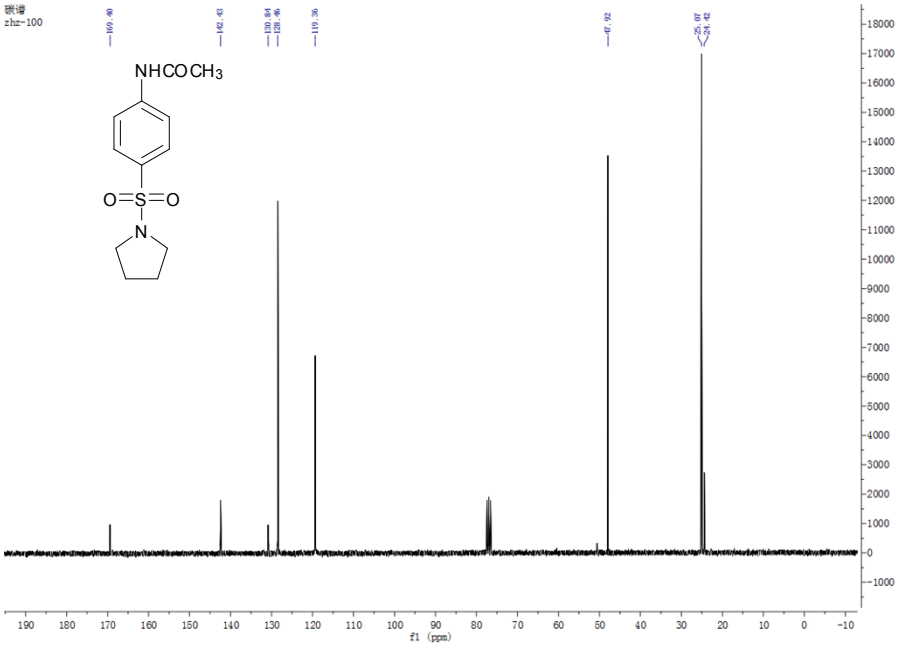
^{1}H NMR Spectrum of N-(2,4-dichlorobenzyl)-N-(4-(N-(3-(2-methyl-5-nitro-1H-imidazol-1-yl) propyl)sulfamoyl)phenyl)acetamide (**8d**)



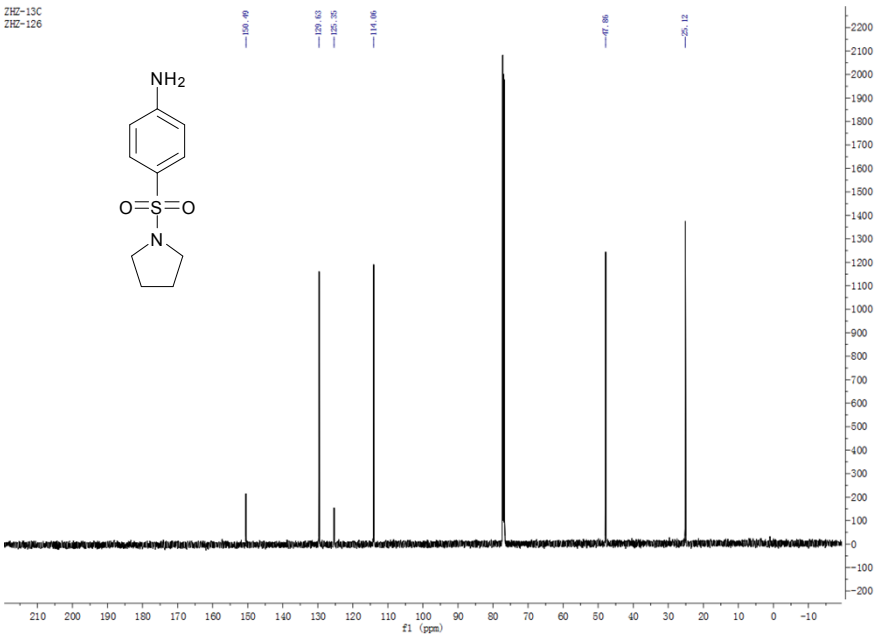
^{1}H NMR Spectrum of N-(3-(1H-1,2,4-triazol-1-yl)propyl)-4-(2,4-dichlorobenzylamino)benzenesulfanilamide (**9c**)



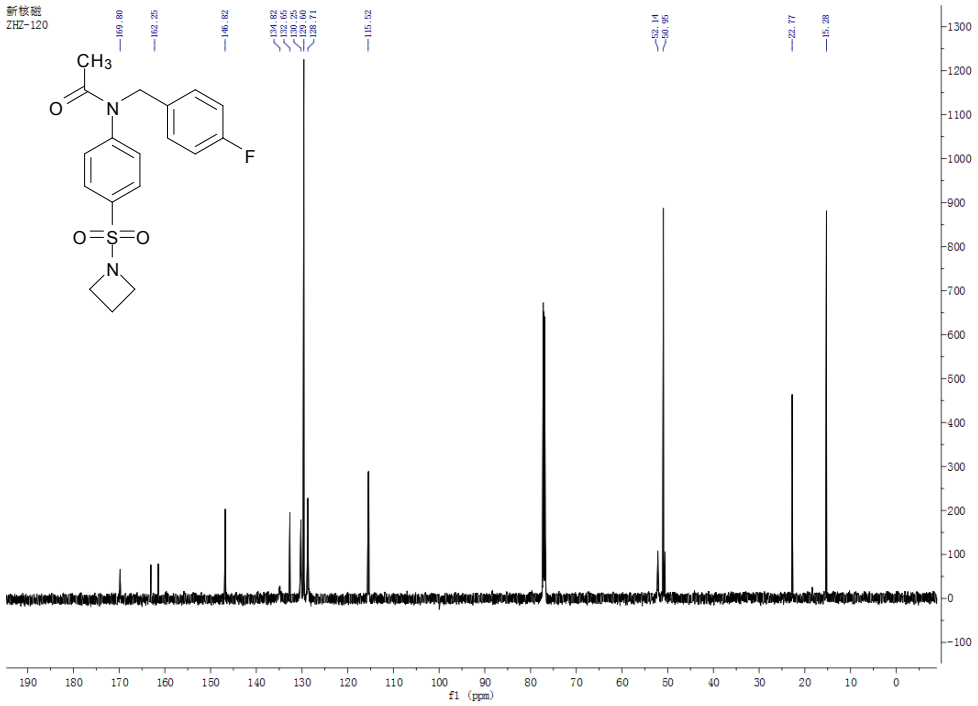
^{13}C NMR Spectrum of N-(4-(pyrrolidin-1-ylsulfonyl)phenyl)acetamide (**4c**)



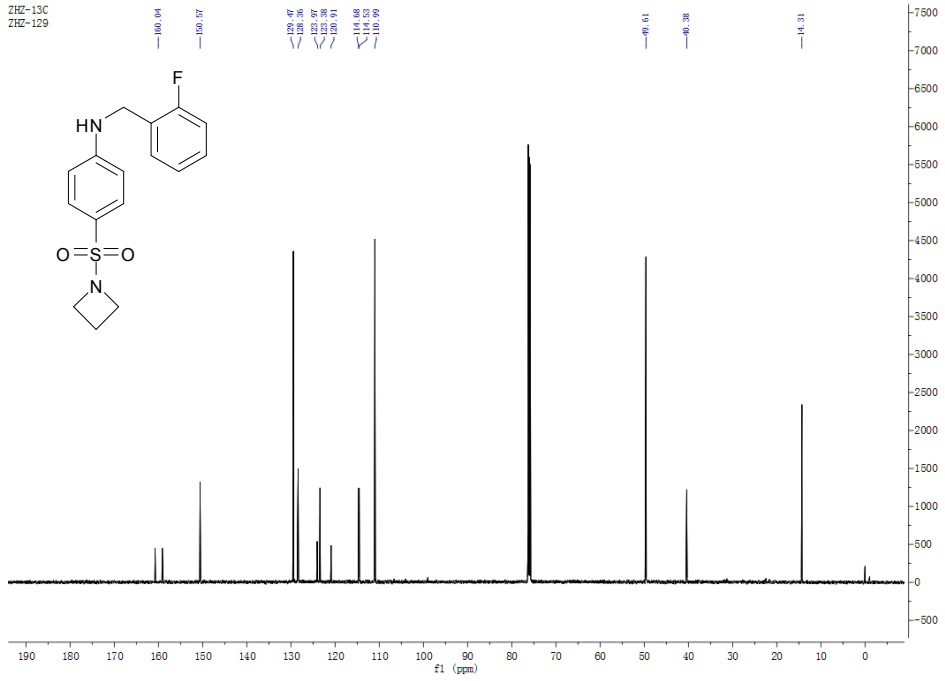
^{13}C NMR Spectrum of 4-(pyrrolidin-1-ylsulfonyl)aniline (**5b**)



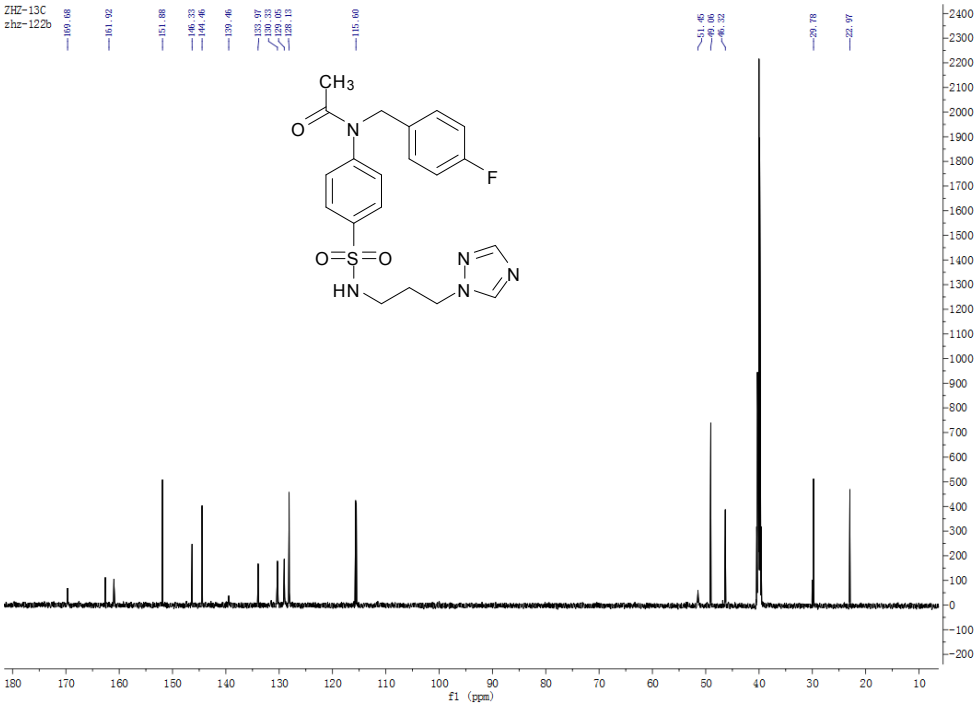
^{13}C NMR Spectrum of N-(4-(azetidin-1-ylsulfonyl)phenyl)-N-(4-fluorobenzyl)acetamide (**6f**)



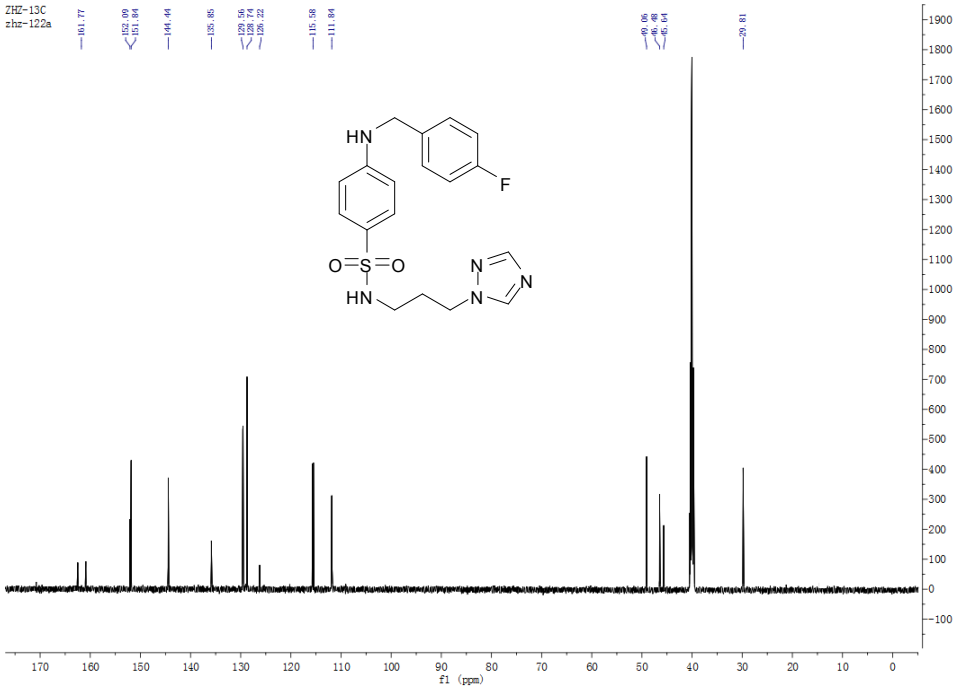
^{13}C NMR Spectrum of 4-(azetidin-1-ylsulfonyl)-N-(2-fluorobenzyl)aniline (**7c**)



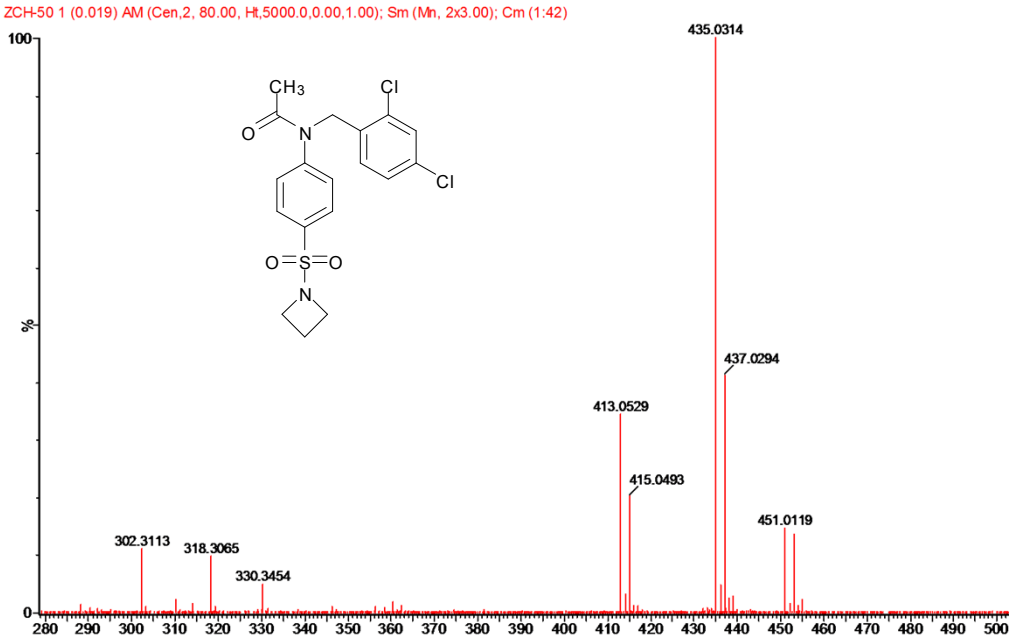
^{13}C NMR Spectrum of N-(4-(N-(3-(1H-1,2,4-triazol-1-yl)propyl)sulfamoyl)phenyl)-N-(4-fluorobenzyl)acetamide (**8b**)



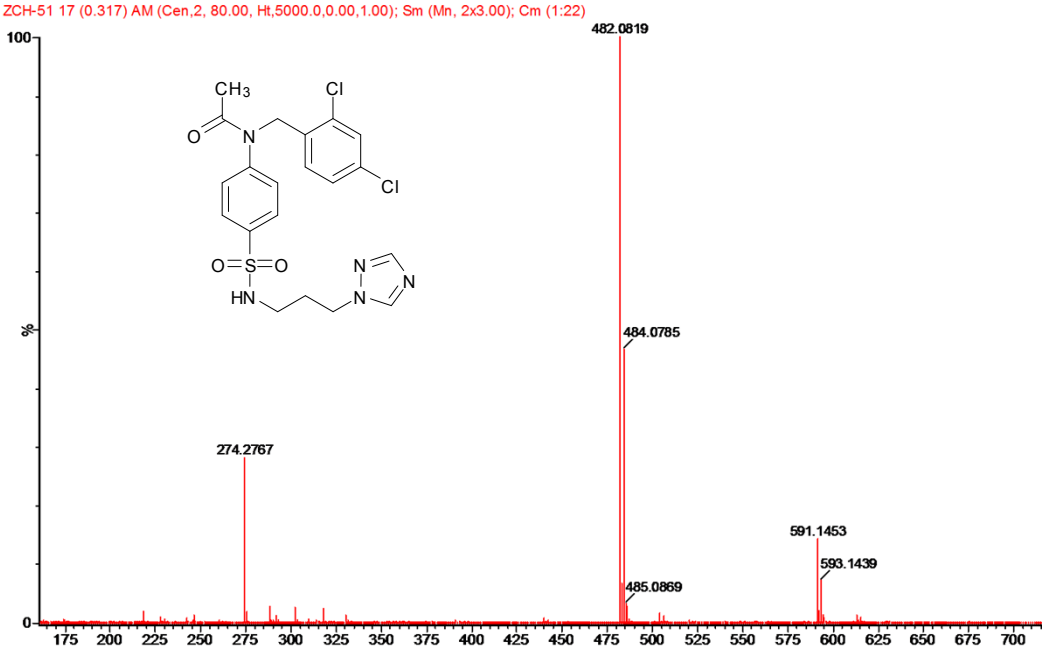
^{13}C NMR Spectrum of N-(3-(1H-1,2,4-triazol-1-yl)propyl)-4-(4-fluorobenzylamino)benzenesulfanilamide (**9b**)



Mass Spectrum of N-(4-(azetidin-1-ylsulfonyl)phenyl)-N-(2,4-dichlorobenzyl)acetamide (**6h**)



Mass Spectrum of N-(4-(N-(3-(1H-1,2,4-triazol-1-yl)propyl)sulfamoyl)phenyl)-N-(2,4-dichlorobenzyl)acetamide (**8c**)



Mass Spectrum of N-(3-(1H-benzo[d]imidazol-1-yl)propyl)-4-(2,4-dichlorobenzylamino) benzenesulfanilamide (**13a**)