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The synthesis of furazano- and thiadiazolopyrazine steroids and their antiproliferative activity

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SUPPLEMENTARY INFORMATION

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1. Experimental Section

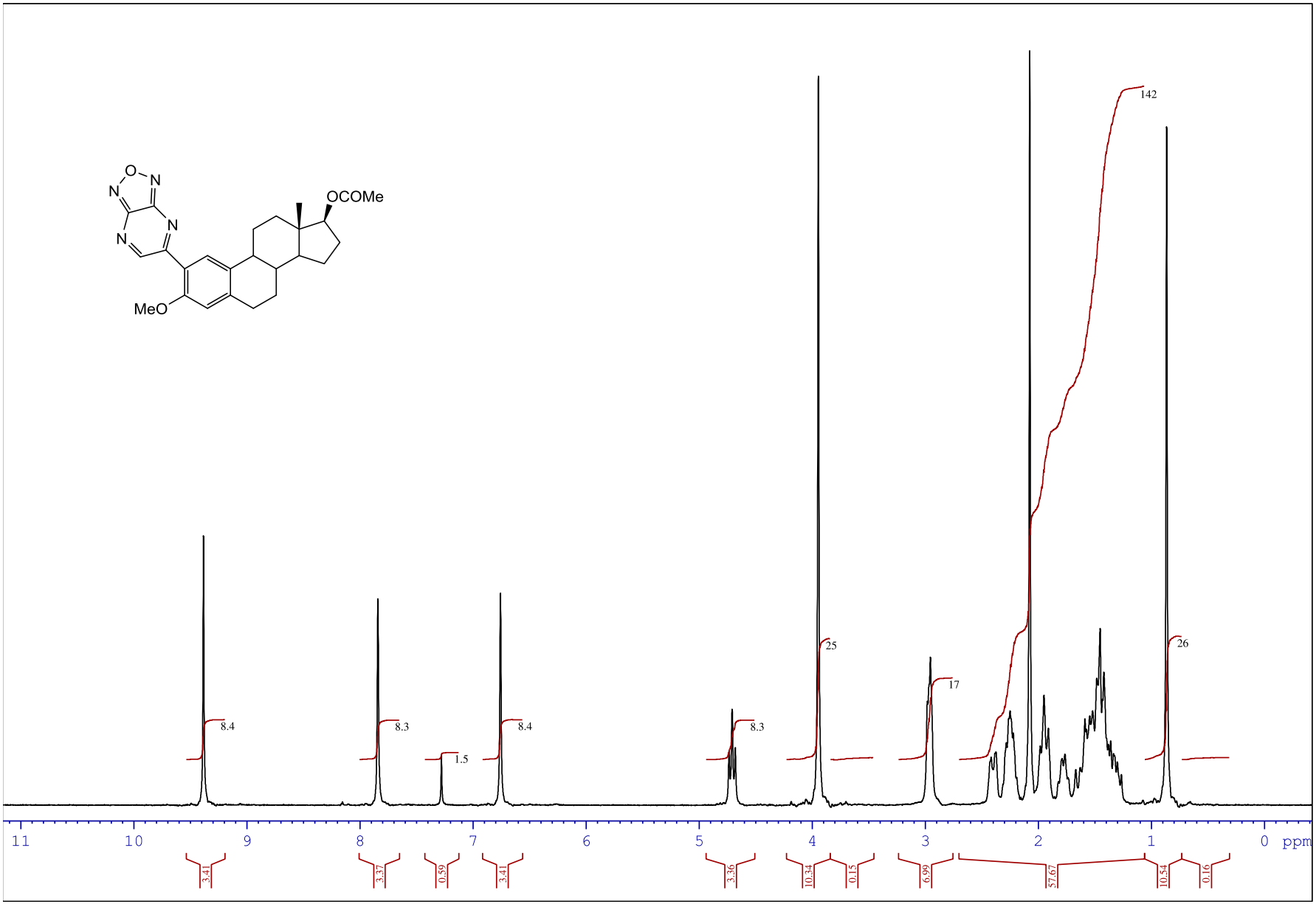
^{1}H, ^{13}C NMR experiments were recorded on Bruker AM-300 (300 and 75 MHz, respectively). The chemical shifts (δ) were expressed in ppm and referenced to $CDCl_3$ (7.27 ppm for ^{1}H and 77.0 ppm for ^{13}C). High-resolution mass spectra were obtained on a Bruker MicroTOF mass spectrometer by electrospray ionization (ESI) using Q-TOF detection. The melting points were determined on a Kofler hot stage apparatus and are uncorrected. TLC was performed using Silicagel 60 F254 plates. The chromatograms were visualized with an UV lamp (254 and 365 nm) and [$Ce(SO_4)_2/H_2SO_4$] developing solution. Commercial reagents were used without further purification. All reactions were carried out using freshly distilled solvents.

X-ray diffraction data for **1** and **2** were collected at 100K on a Bruker Quest D8 diffractometer equipped with a Photon-III area-detector (shutterless φ- and ω-scan technique), using graphite-monochromatized Mo K_α-radiation. The intensity data were integrated with the SAINT program and were semi-empirically corrected for absorption and decay from equivalent reflections by multi-scan methods with SADABS. The structures were solved by direct methods using SHELXT and refined by the full-matrix least-squares minimization method on F^2 using *SHELXL*-2018. All non-hydrogen atoms were refined with anisotropic displacement parameters. Hydrogen atoms were placed in ideal calculated positions and refined as riding atoms with relative isotropic displacement parameters. A rotating group model was applied for methyl groups. Absolute structure parameters for both structures were determined by the Parsons quotient method. Crystal data, data collection and structure refinement details for **1** and **2** are summarized in Table S1. The structures have been deposited at the Cambridge Crystallographic Data Center with the reference CCDC numbers 2335159 and 2335160, correspondingly; they also contain the supplementary crystallographic data. These data can be obtained free of charge from the CCDC *via* https://www.ccdc.cam.ac.uk/structures/

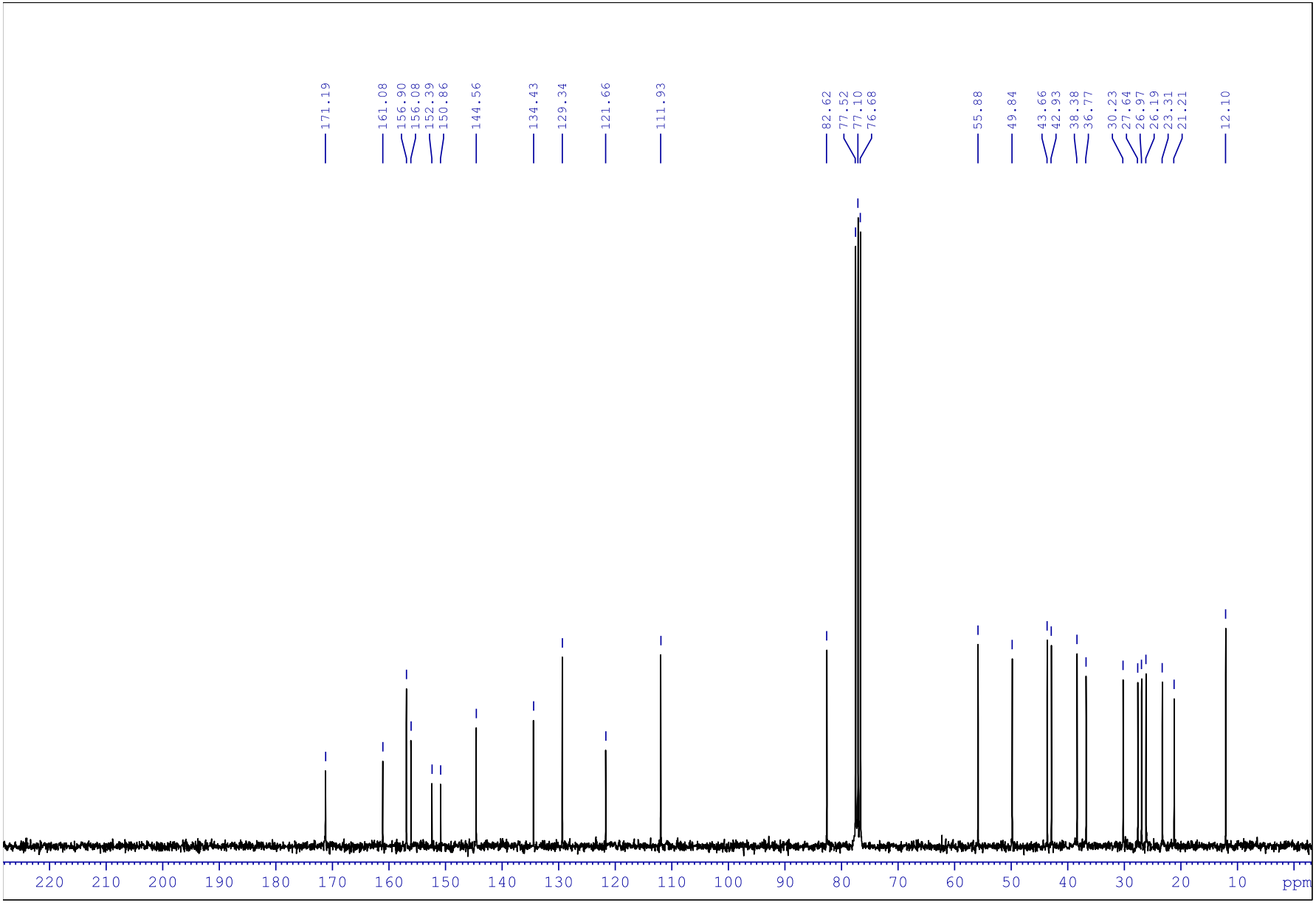
Table S1. Crystal data, data collection and structure refinement details for **1** and **2**

Code	**1**	**2**
Chemical formula	$C_{25}H_{28}N_4O_4$	$C_{25}H_{28}N_4O_3S$
Formula weight	448.51	464.57
Temperature, K	100(2)	100(2)
Wavelength, Å	0.71073	0.71073
Crystal system	Monoclinic	Monoclinic
Space group	$P2_1$	$P2_1$
Unit cell parameters		
a, Å	8.8859(2)	9.0759(3)
b, Å	6.67640(10)	6.6412(2)
c, Å	18.9053(4)	18.7515(6)
β, °	95.9540(10)	97.1860(10)
Volume, $Å^3$	1115.52(4)	1121.37(6)
Z	2	2
Calculated density, $g \cdot cm^{-3}$	1.335	1.376
Absorption coefficient (μ), mm^{-1}	0.092	0.181
F(000)	476	492
Crystal size, mm	0.46×0.13×0.09	0.59×0.13×0.04
Θ_{min} / Θ_{max}, °	2.166 / 34.979	2.189 / 34.983
Index ranges	-14≤h≤14, -10≤k≤10, -30≤l≤30	-14≤h≤14, -10≤k≤10, -30≤l≤30
Number of reflections		
Collected	69480	69216
Independent [R_{int}]	9778 [0.0353]	9853 [0.0563]
Observed with I>σ(I)	8707	8132
Completeness to Θ_{full} / Θ_{max}	0.997 / 0.998	0.999 / 0.999
T_{max} / T_{min}	0.8625 / 0.7794	0.8022 / 0.7024
Data / restraints / parameters	9778 / 1 / 301	9853 / 1 / 301
Goodness-of-fit on F^2	1.054	1.069
R1 / wR2 for reflections with I>σ(I)	0.0399 / 0.1011	0.0518 / 0.1137
R1 / wR2 for all data	0.0483 / 0.1080	0.0726 / 0.1283
Absolute structure parameter	0.01(19)	0.00(4)
Residual electron density ($\Delta\rho_{max}$ / $\Delta\rho_{min}$), $\bar{e} \cdot Å^{-3}$	0.391 / -0.210	0.541 / -0.444

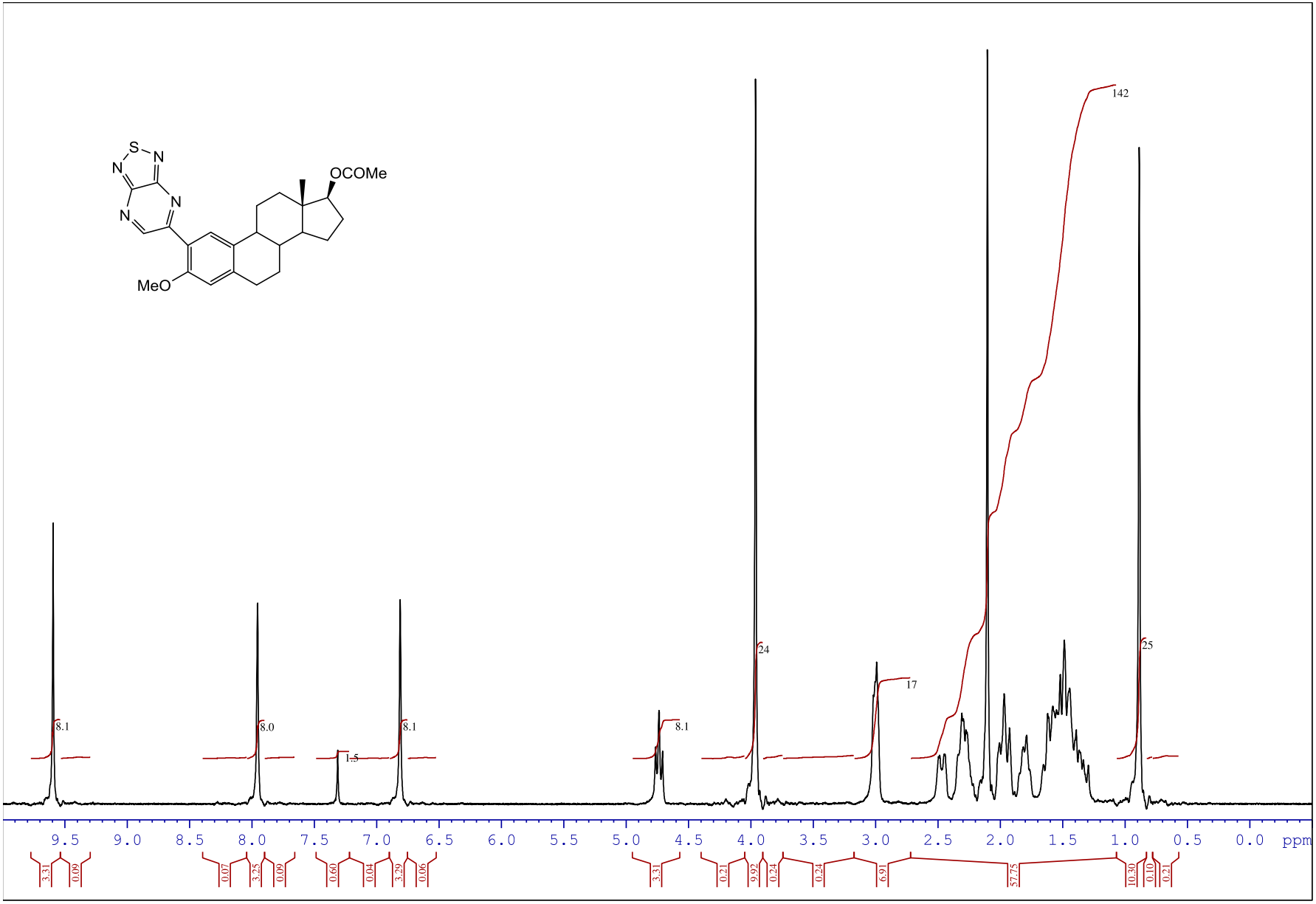
1. NMR spectra



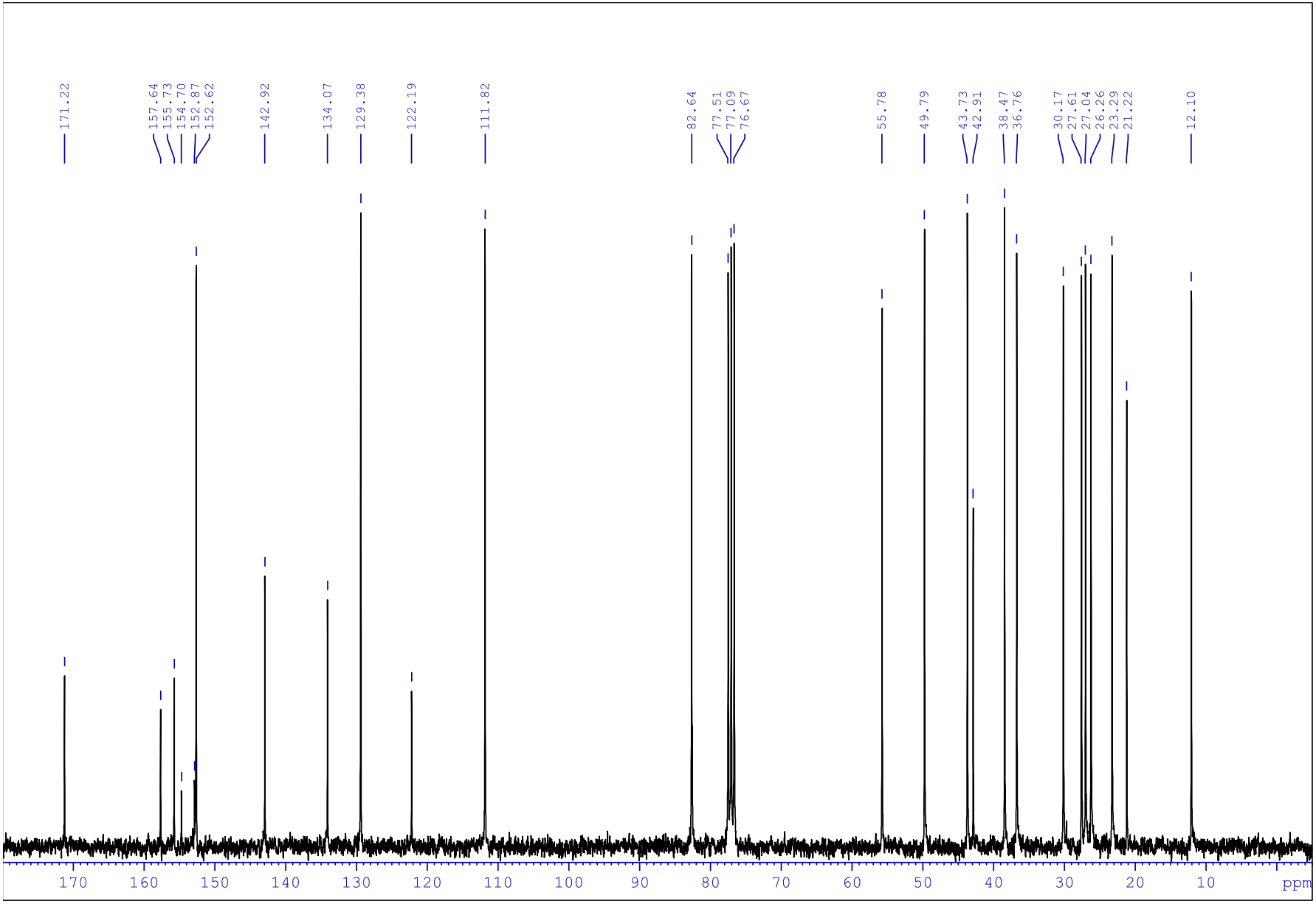
^{1}H NMR spectrum of **1**.



^{13}C NMR spectrum of **1**.



^{1}H NMR spectrum of **2**.



^{13}C NMR spectrum of **2**.

4. Mass spectra

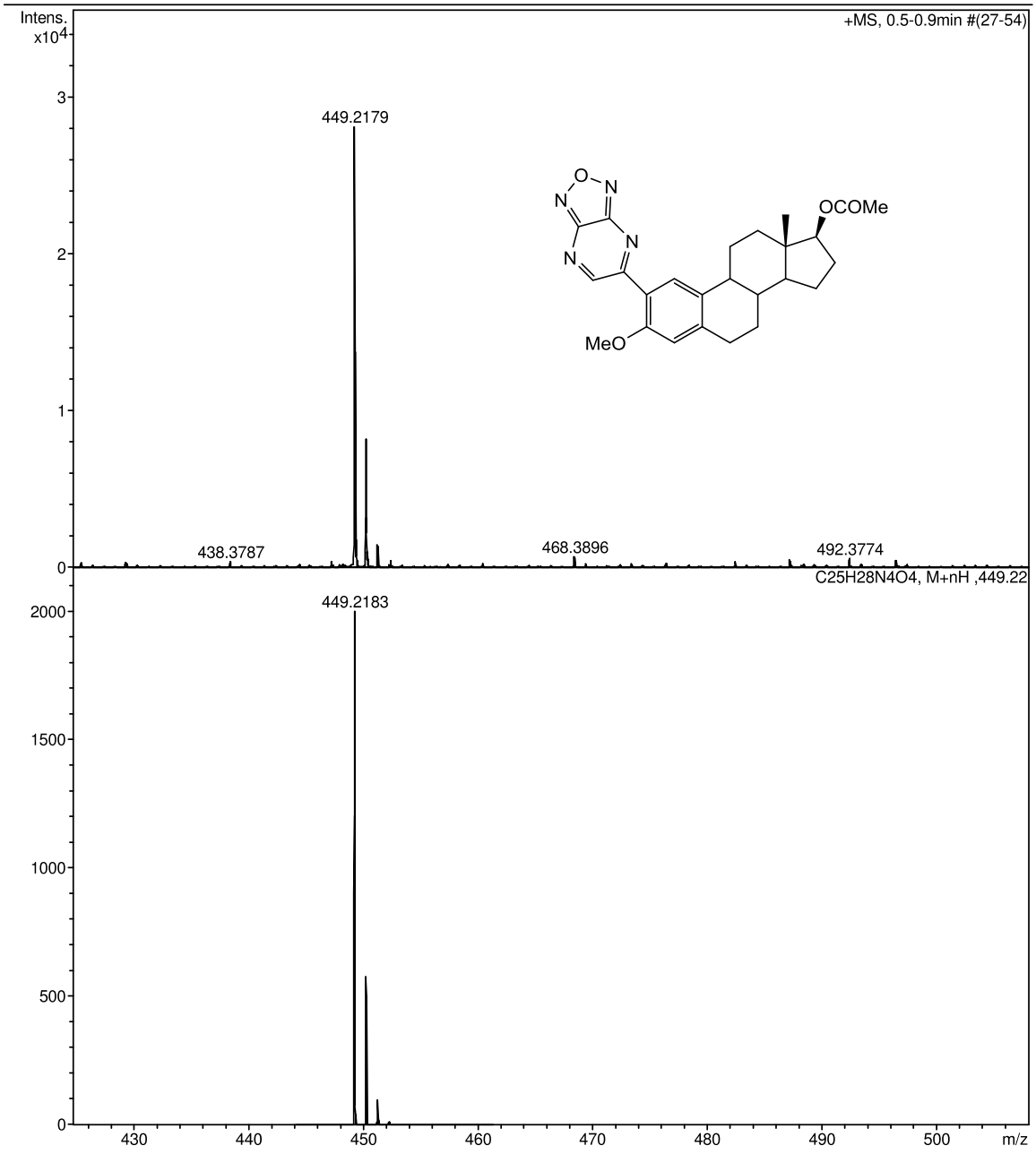
Display Report

Analysis Info Acquisition Date

Method	tune_50-1600.m	Operator	BDAL@DE
		Instrument / Ser#	micrOTOF 10248
Comment	C25H28N4O4 mH 449.2183 calibrant added CH3CN		

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	1.0 Bar
Focus	Not active			Set Dry Heater	200 °C
Scan Begin	50 m/z	Set Capillary	4500 V	Set Dry Gas	4.0 l/min
Scan End	1600 m/z	Set End Plate Offset	-500 V	Set Divert Valve	Waste



Mass-spectra of **1**.

Display Report

Analysis Info

Acquisition Date

Method

Operator BDAL@DE

Instrument / Ser# micrOTOF 10248

Comment C25H28N4O3S mH 465.1954 calibrant added CH3CN

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	1.0 Bar
Focus	Not active			Set Dry Heater	200 °C
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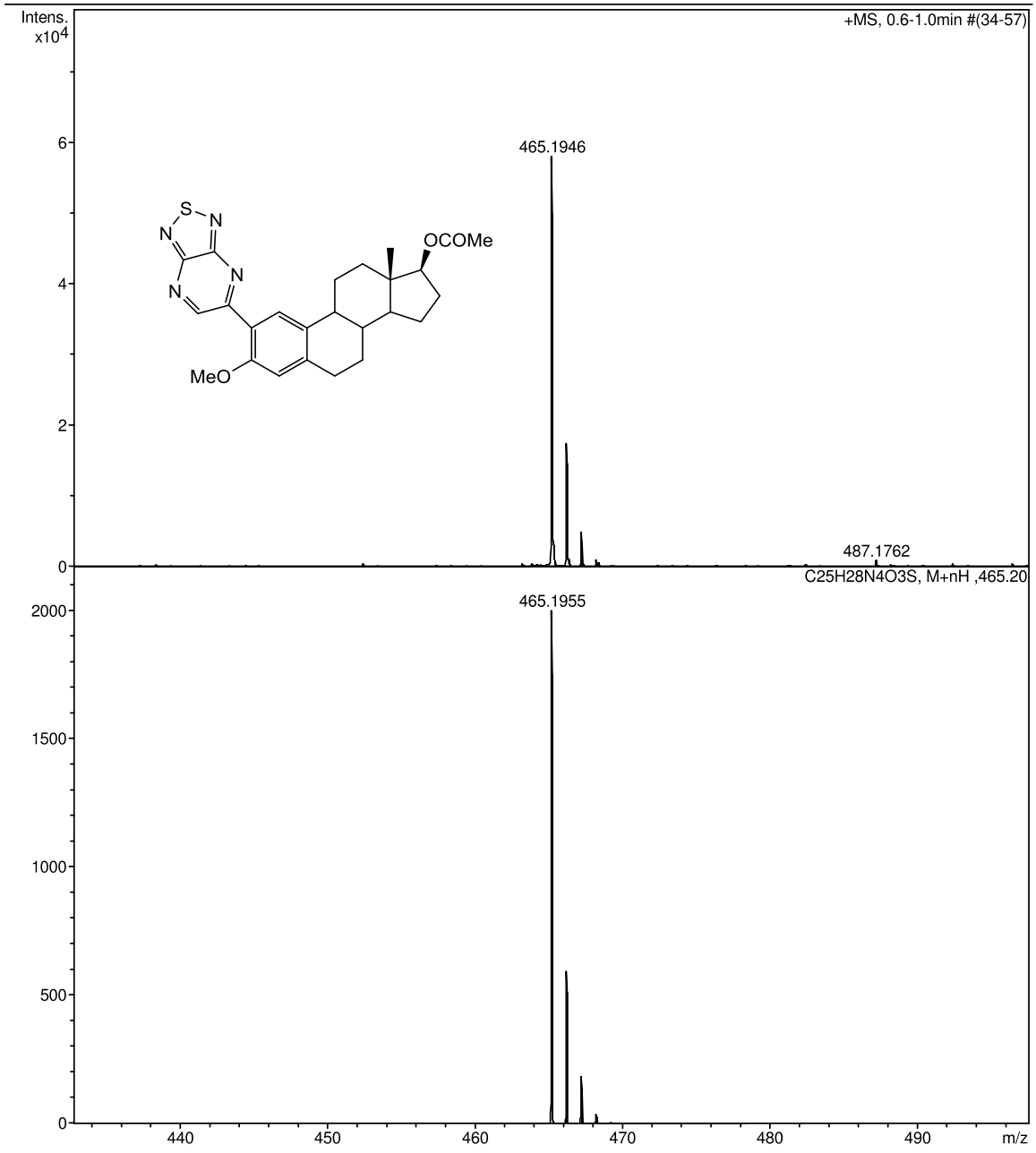
Scan End	1600 m/z	Set End Plate Offset	-500 V	Set Divert Valve	Waste



Mass-spectra of **2**.