

A novel pipeline of 2-(benzenesulfonamide)-N-(4-hydroxyphenyl) acetamide analgesics that lack hepatotoxicity and retain antipyresis

Hernan A. Bazan,^{a,1*} Surjyadipta Bhattacharjee,^{b,1} Carolina Burgos,^c Javier Recio,^c Valentina Abet,^c Amanda R. Pahng,^{d,e} Bokkyoo Jun,^b Jessica Heap,^b Alexander J. Ledet,^b William C. Gordon,^b Scott Edwards,^{b,d} Dennis Paul,^f Julio Alvarez-Buillac and Nicolas G. Bazan^b

^aSection of Vascular/Endovascular Surgery, Department of Surgery, Ochsner Clinic, New Orleans, LA 70118 USA

^bNeuroscience Center of Excellence, School of Medicine, Louisiana State University Health New Orleans, New Orleans, LA 70112 USA

^cDepartment of Organic Chemistry and IQAR, University of Alcalá, Alcalá de Henares, Madrid 28805 Spain

^dDepartment of Physiology, School of Medicine, Louisiana State University Health New Orleans, New Orleans, LA 70112 USA

^eSoutheast Louisiana Veterans Health Care System, New Orleans, LA 70119 USA

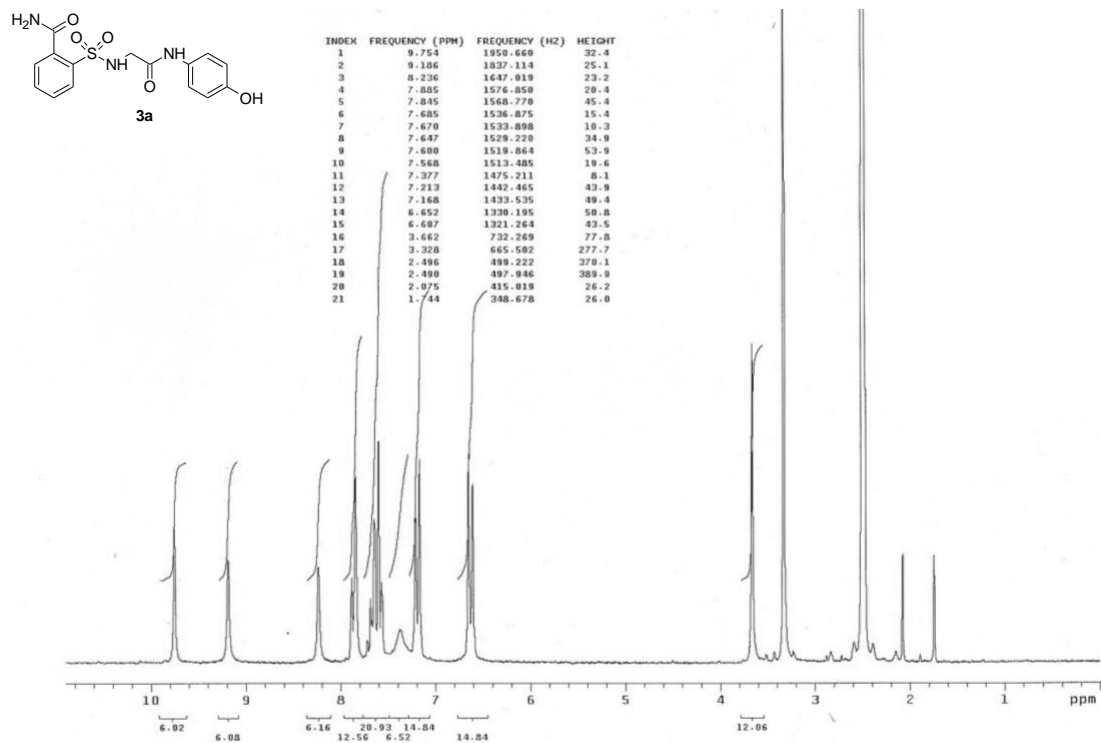
^fDepartment of Pharmacology and Experimental Therapeutics, School of Medicine, Louisiana State University Health New Orleans, New Orleans, LA 70112 USA

¹Share first authorship

*Corresponding author: Hernan Bazan, MD, FACS, 1514 Jefferson Hwy., New Orleans, LA 70121 USA. Phone: +1 (504) 842-9050; E-mail: hbazan@ochsner.org.

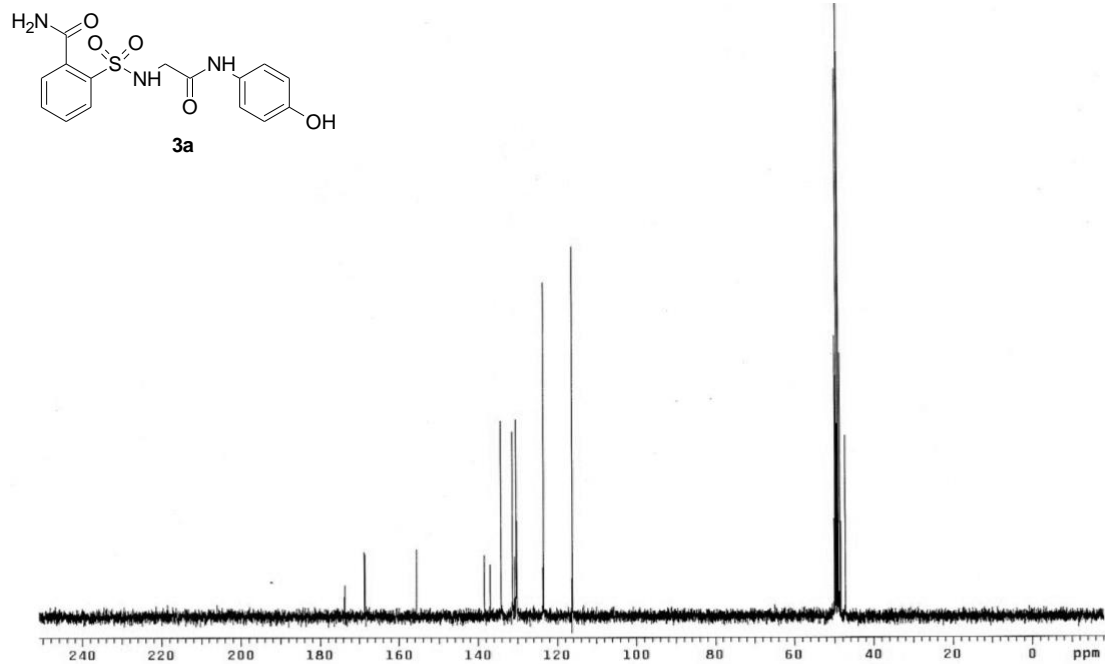
2-[[2-(4-Hydroxyanilino)-2-oxo-ethyl]sulfamoyl]benzamide 3a.

¹H-NMR 200 MHz, DMSO-d₆



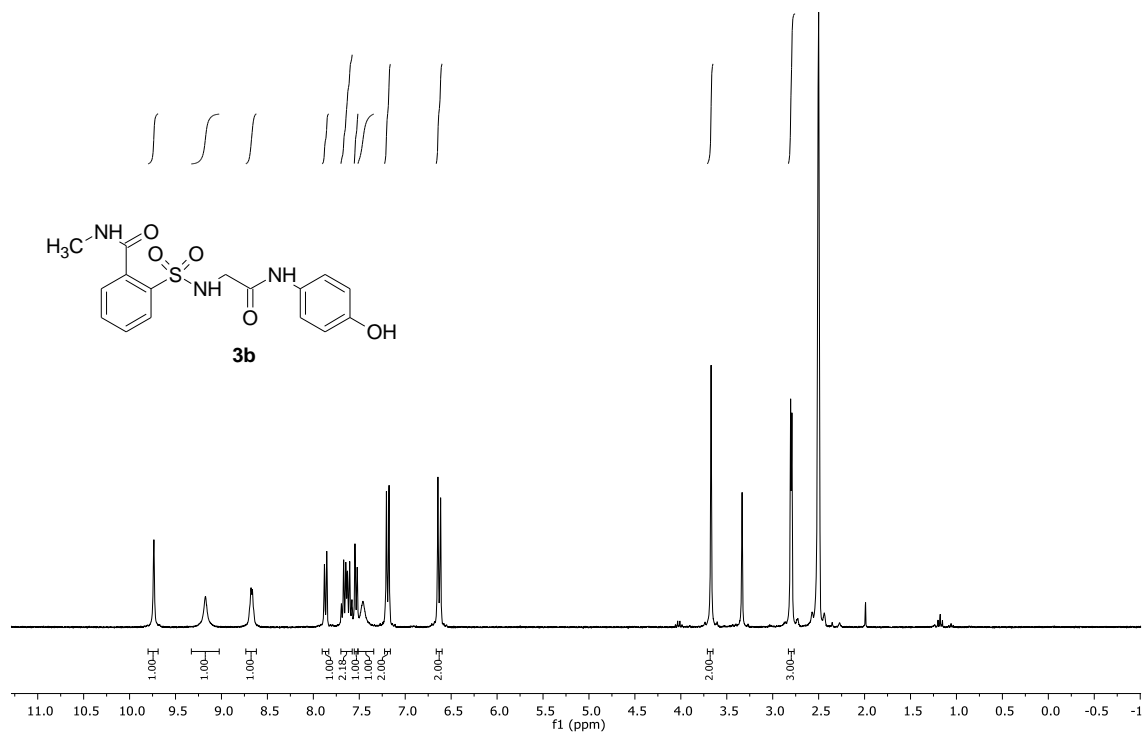
2-[[2-(4-Hydroxyanilino)-2-oxo-ethyl]sulfamoyl]benzamide 3a

¹³C-NMR 75 MHz, CD₃OD



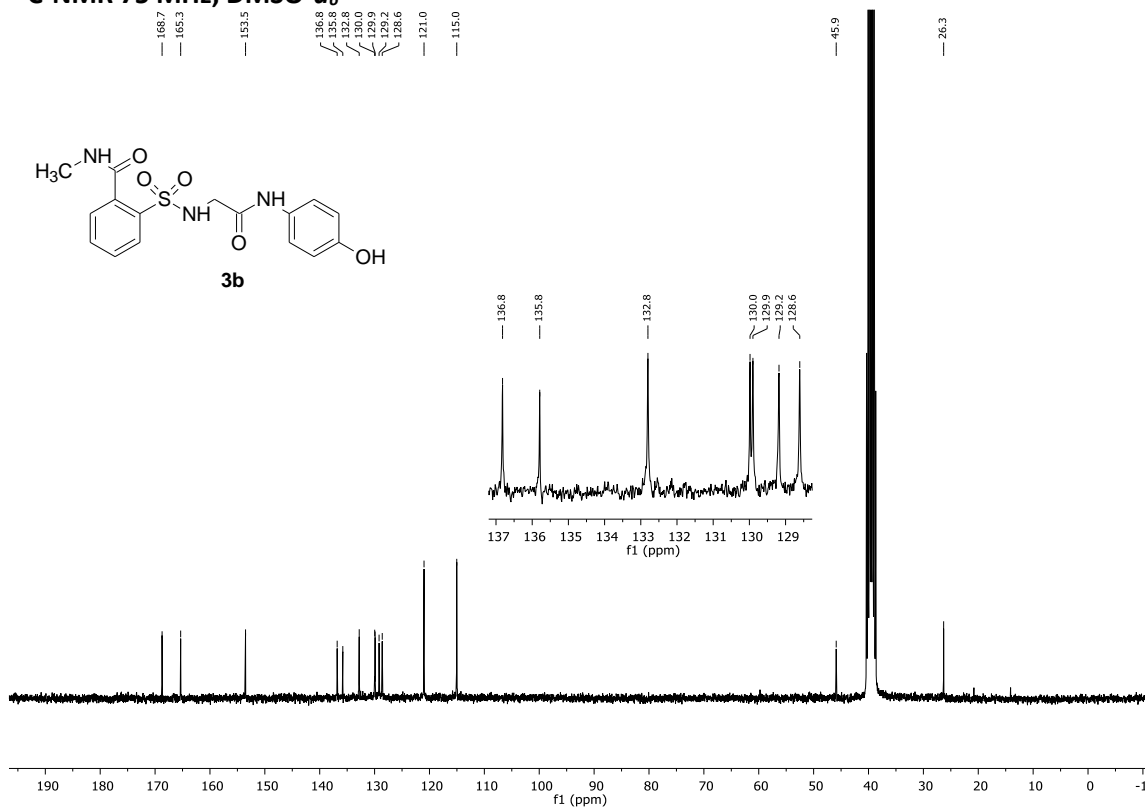
2-[[2-(4-Hydroxyanilino)-2-oxo-ethyl]sulfamoyl]-*N*-methylbenzamide **3b**

¹H-NMR 300 MHz, DMSO-*d*₆



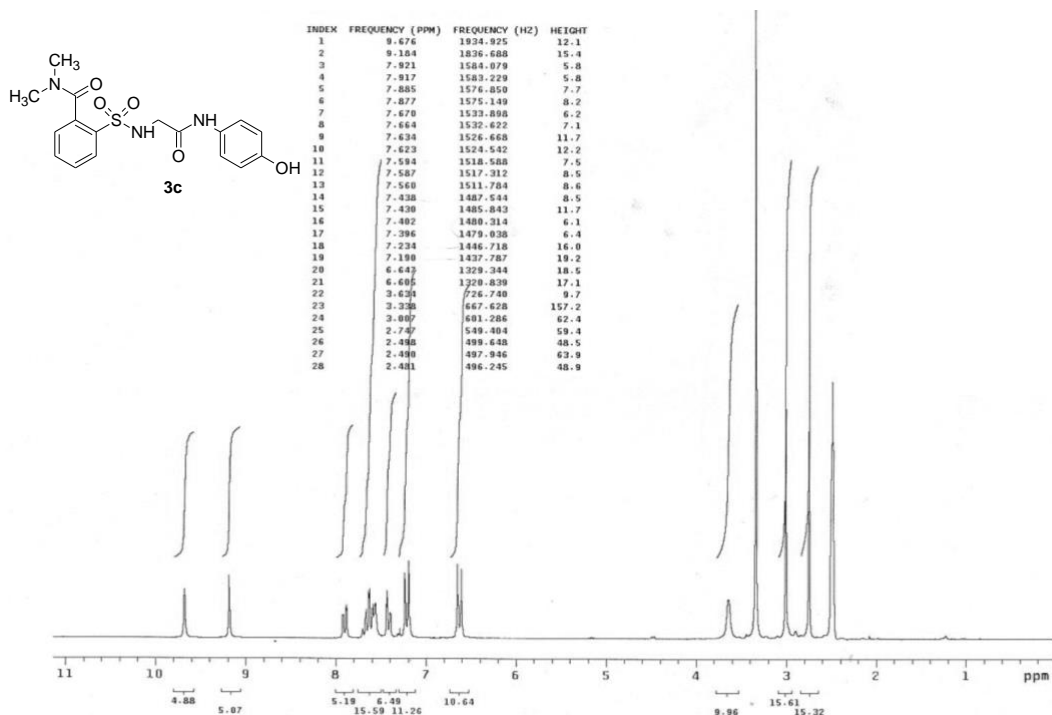
2-[[2-(4-Hydroxyanilino)-2-oxo-ethyl]sulfamoyl]-*N*-methylbenzamide **3b**

¹³C-NMR 75 MHz, DMSO-*d*₆



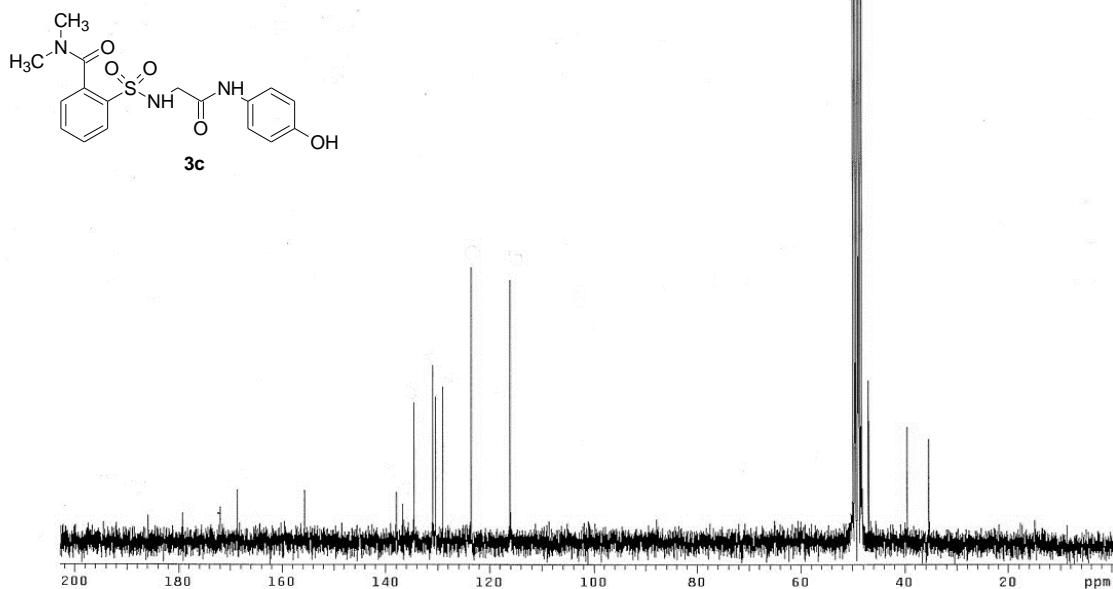
2-[[2-(4-Hydroxyanilino)-2-oxo-ethyl]sulfamoyl]-*N,N*-dimethylbenzamide 3c

¹H-NMR 200 MHz, DMSO-*d*₆



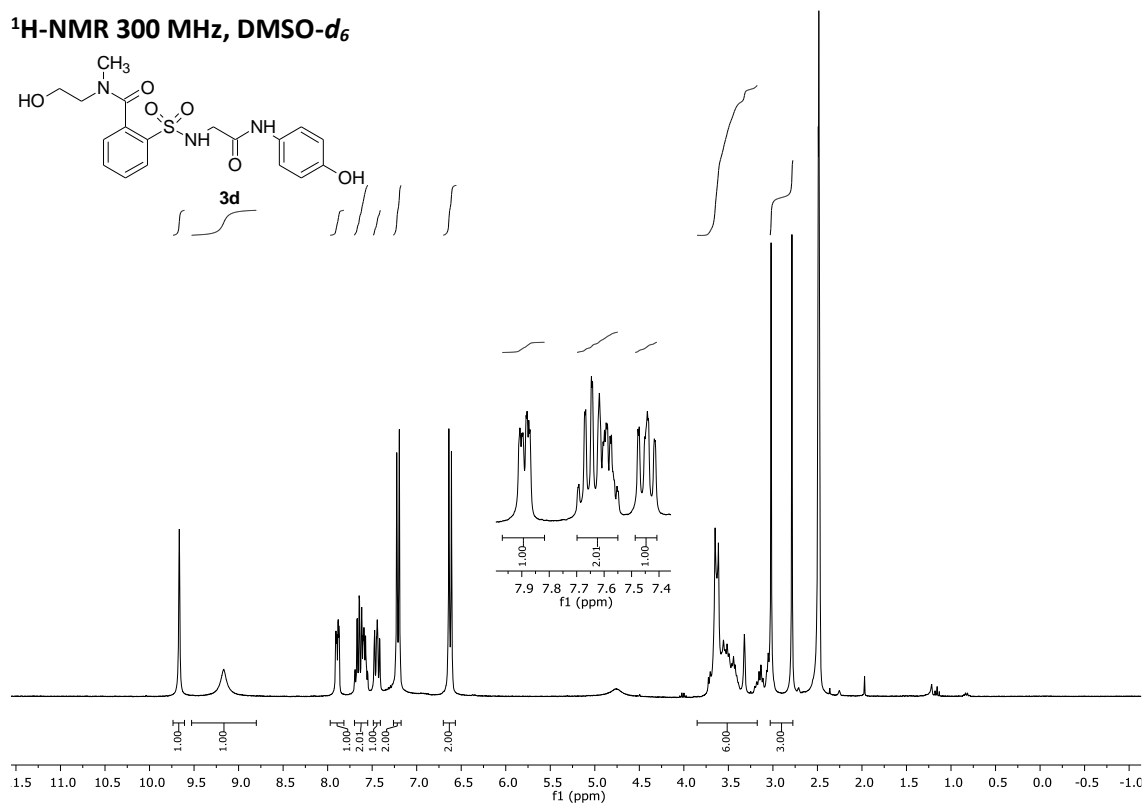
2-[[2-(4-Hydroxyanilino)-2-oxo-ethyl]sulfamoyl]-*N,N*-dimethylbenzamide 3c

¹³C-NMR 50 MHz, DMSO-*d*₆



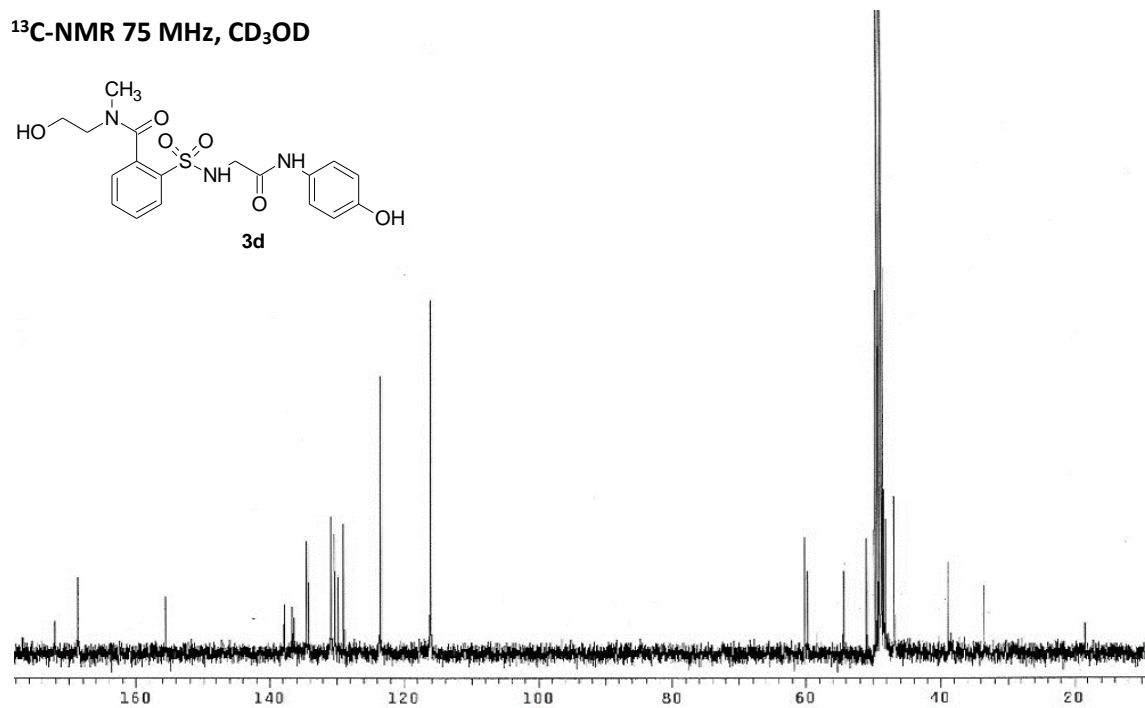
2-[[2-(4-Hydroxyanilino)-2-oxo-ethyl]sulfamoyl]-N-(2-hydroxyethyl)-N-methyl-benzamide 3d

¹H-NMR 300 MHz, DMSO-*d*₆



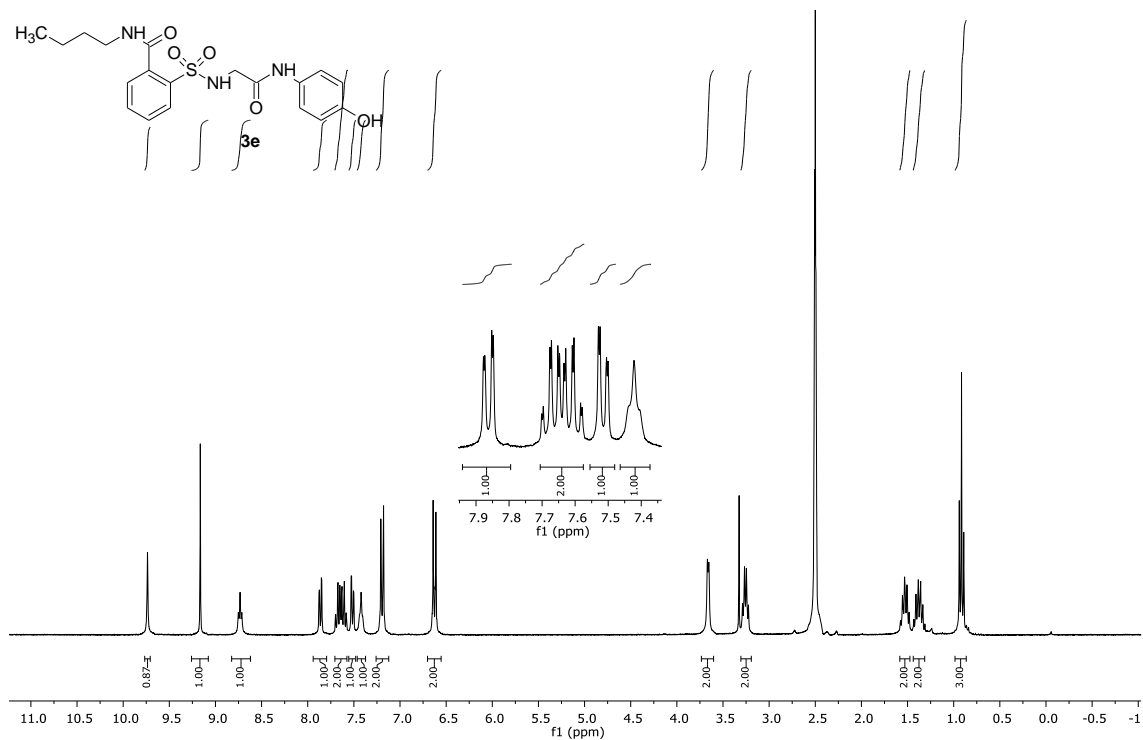
2-[[2-(4-Hydroxyanilino)-2-oxo-ethyl]sulfamoyl]-N-(2-hydroxyethyl)-N-methyl-benzamide 3d

¹³C-NMR 75 MHz, CD₃OD



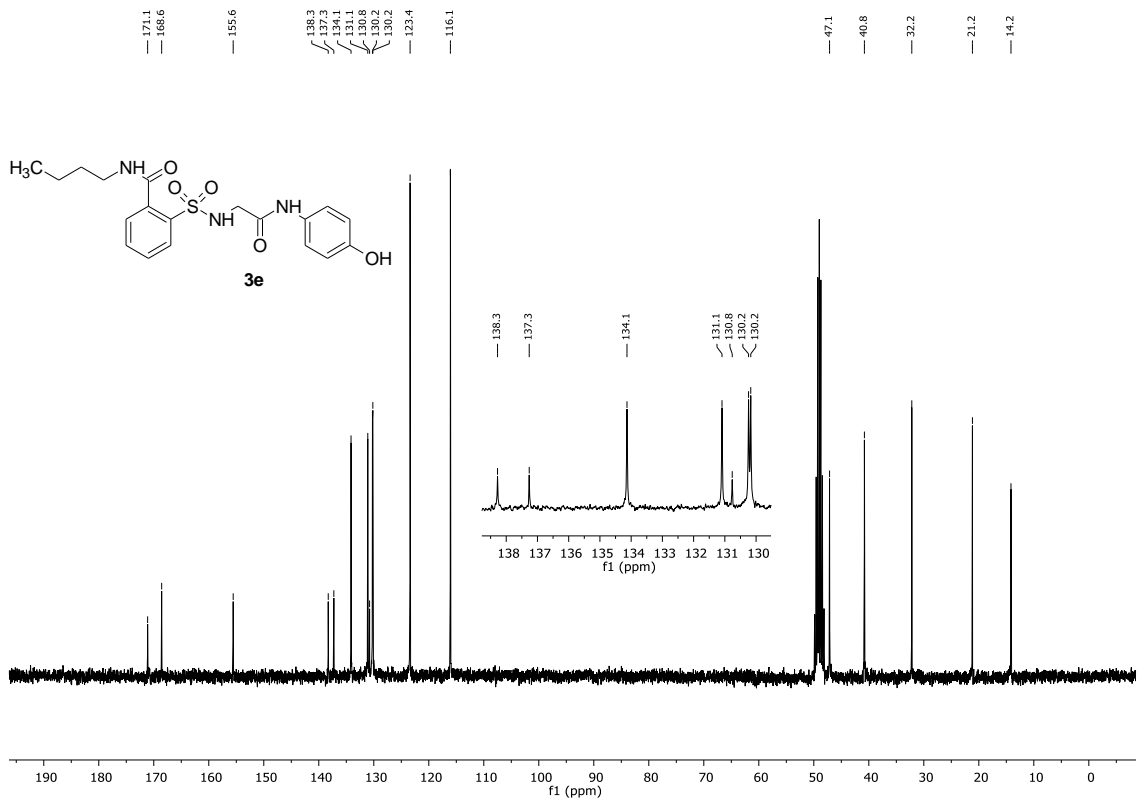
N-Butyl-2-[[2-(4-hydroxyanilino)-2-oxo-ethyl]sulfamoyl]benzamide **3e**

¹H-NMR 300 MHz, DMSO-*d*₆



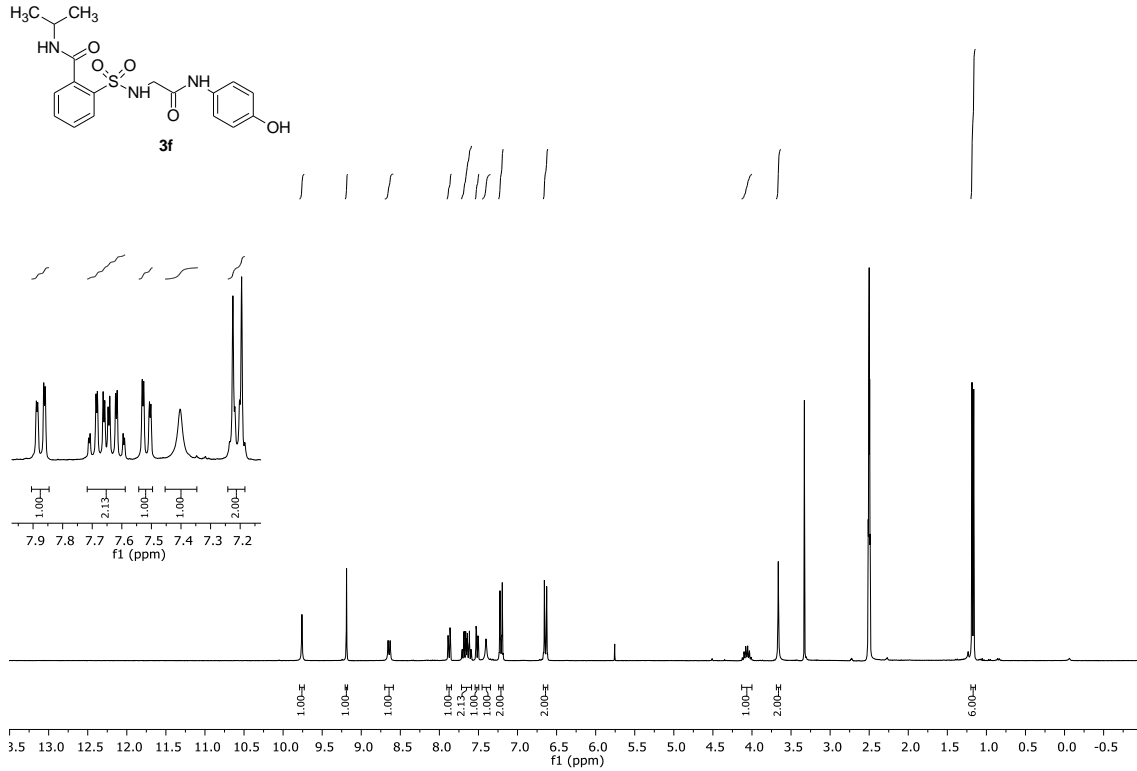
N-Butyl-2-[[2-(4-hydroxyanilino)-2-oxo-ethyl]sulfamoyl]benzamide **3e**

¹³C-NMR 75 MHz, CD₃OD.



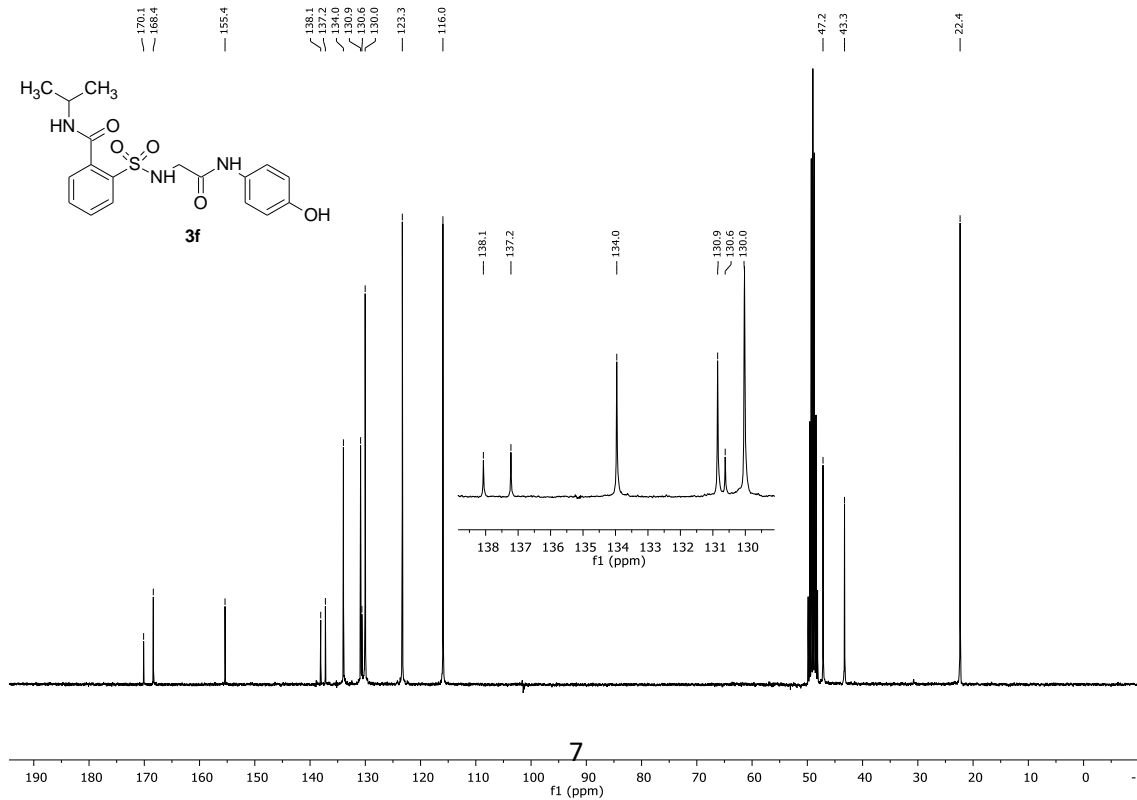
2-[[2-(4-Hydroxyanilino)-2-oxo-ethyl]sulfamoyl]-*N*-isopropylbenzamide 3f

¹H-NMR 300 MHz, DMSO-*d*₆



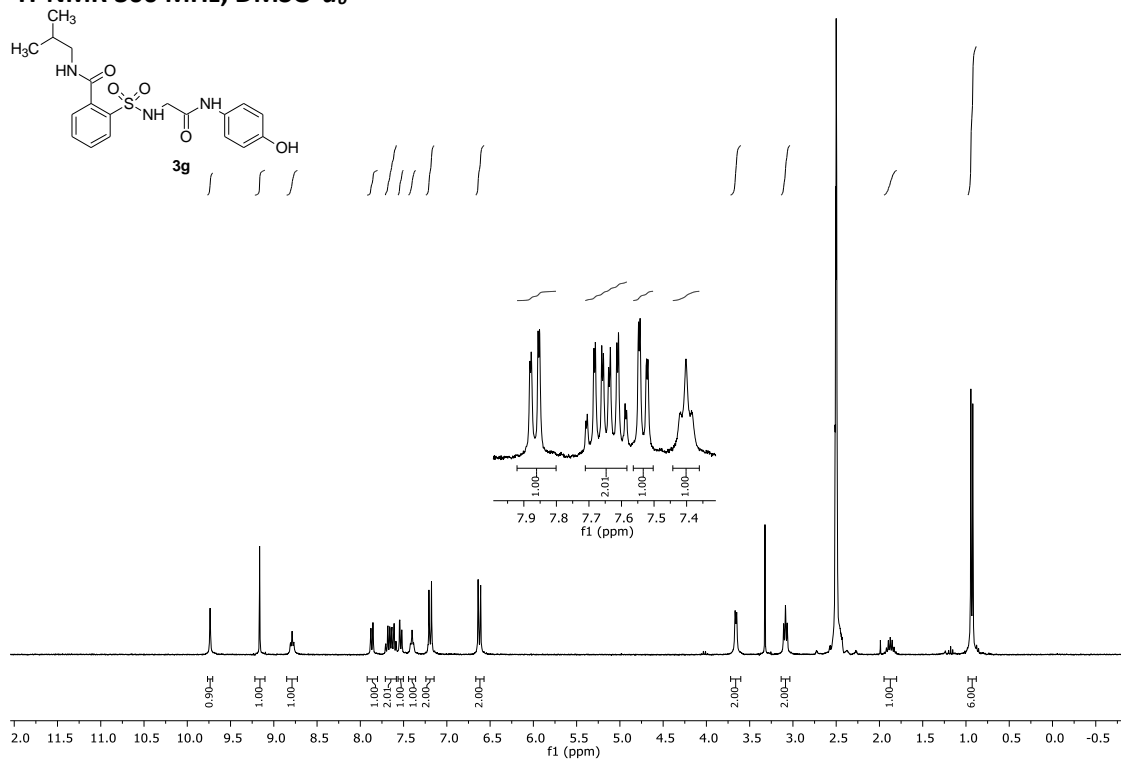
2-[[2-(4-Hydroxyanilino)-2-oxo-ethyl]sulfamoyl]-*N*-isopropylbenzamide 3f

¹³C-NMR 75 MHz, CD₃OD



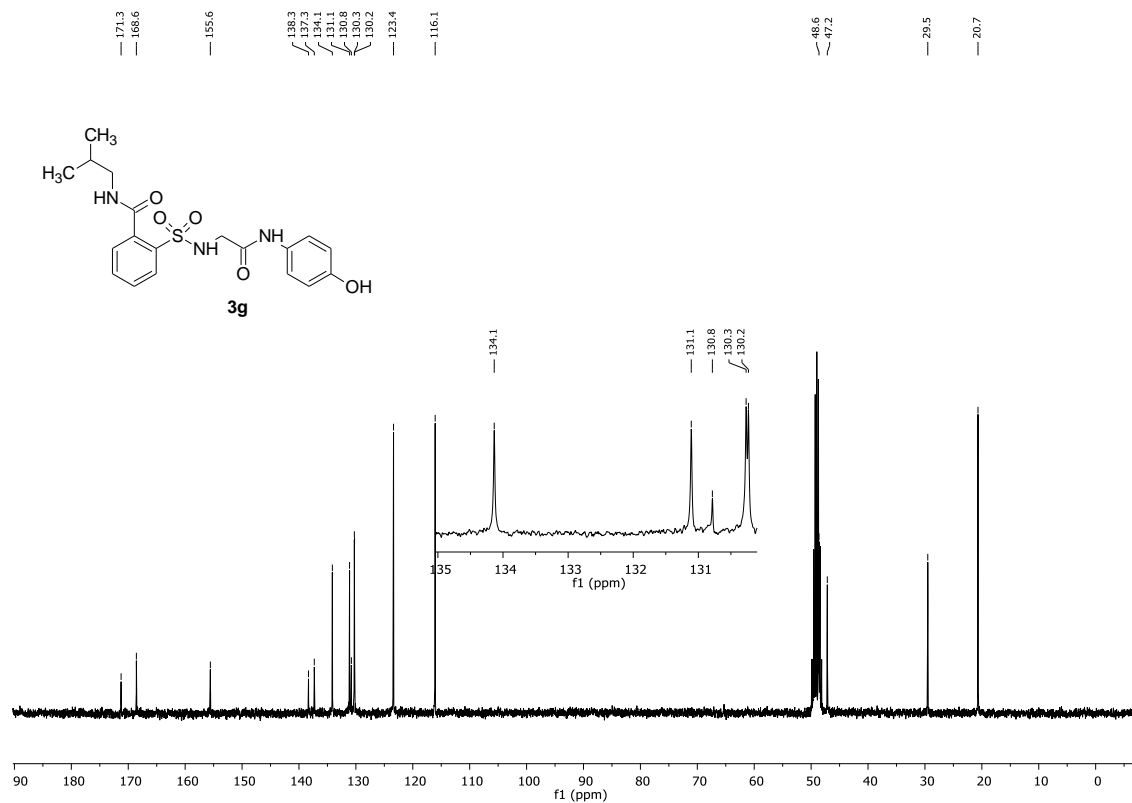
2-[[2-(4-Hydroxyanilino)-2-oxo-ethyl]sulfamoyl]-*N*-isobutylbenzamide 3g

¹H-NMR 300 MHz, DMSO-*d*₆



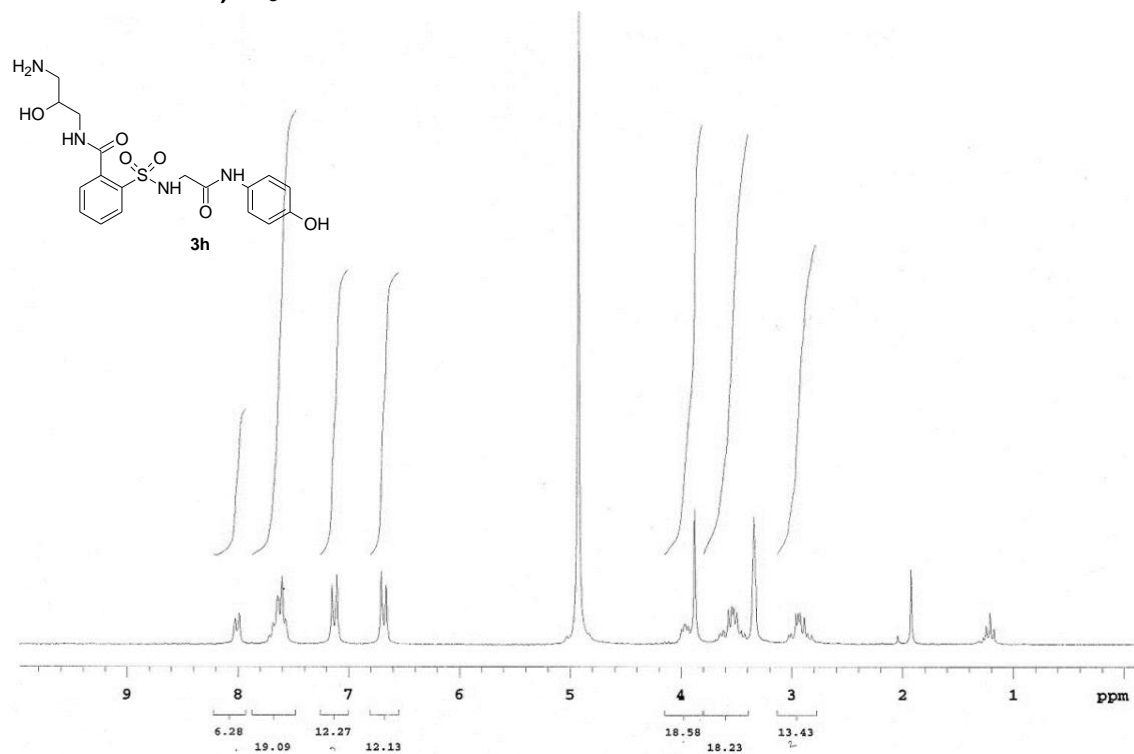
2-[[2-(4-Hydroxyanilino)-2-oxo-ethyl]sulfamoyl]-*N*-isobutylbenzamide 3g

¹³C-NMR 75 MHz, CD₃OD



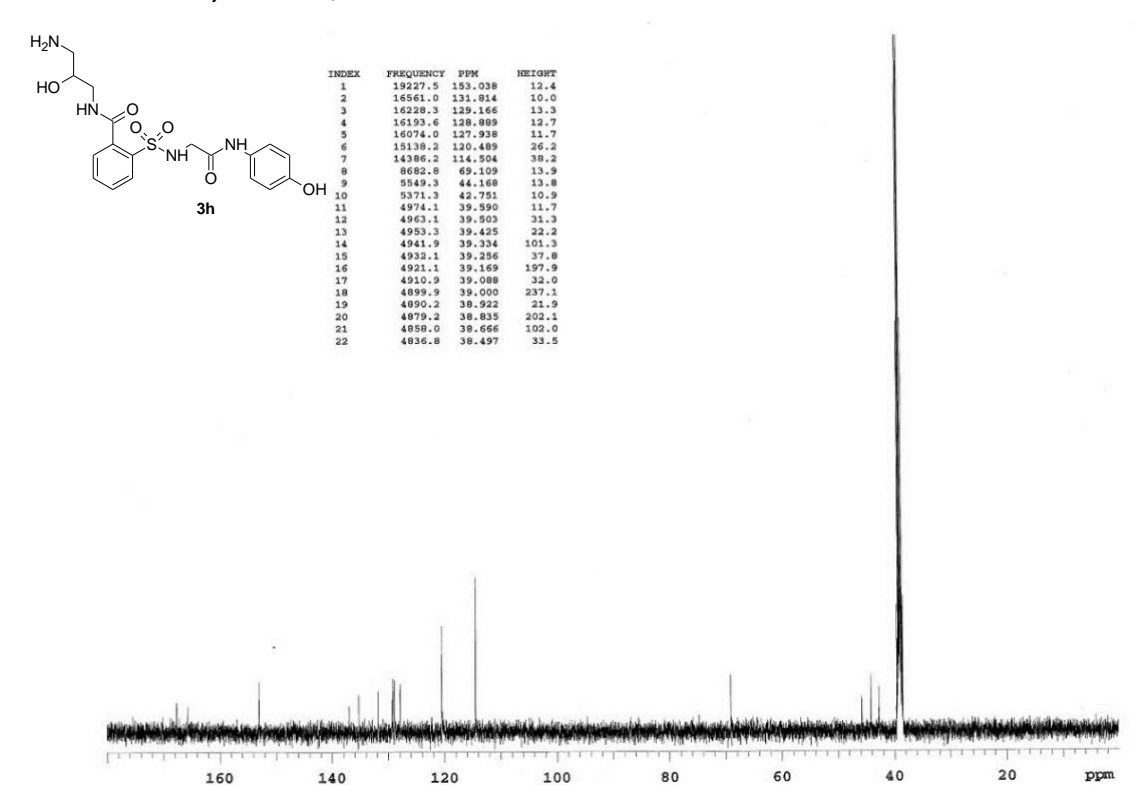
***N*-(3-Amino-2-hydroxypropyl)-2-[[2-(4-hydroxyanilino)-2-oxo-ethyl]sulfamoyl]benzamide 3h**

¹H-NMR 200 MHz, CD₃OD



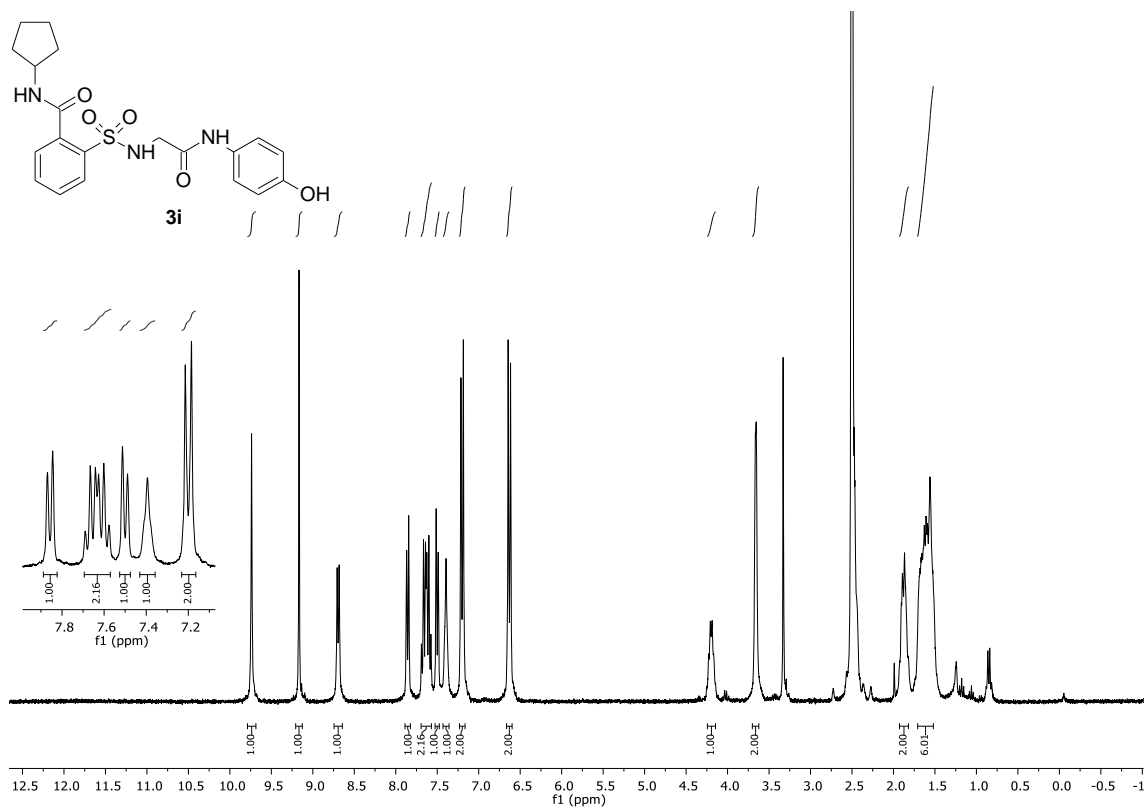
***N*-(3-Amino-2-hydroxypropyl)-2-[[2-(4-hydroxyanilino)-2-oxo-ethyl]sulfamoyl]benzamide 3h**

¹³C-NMR 75 MHz, DMSO-*d*₆



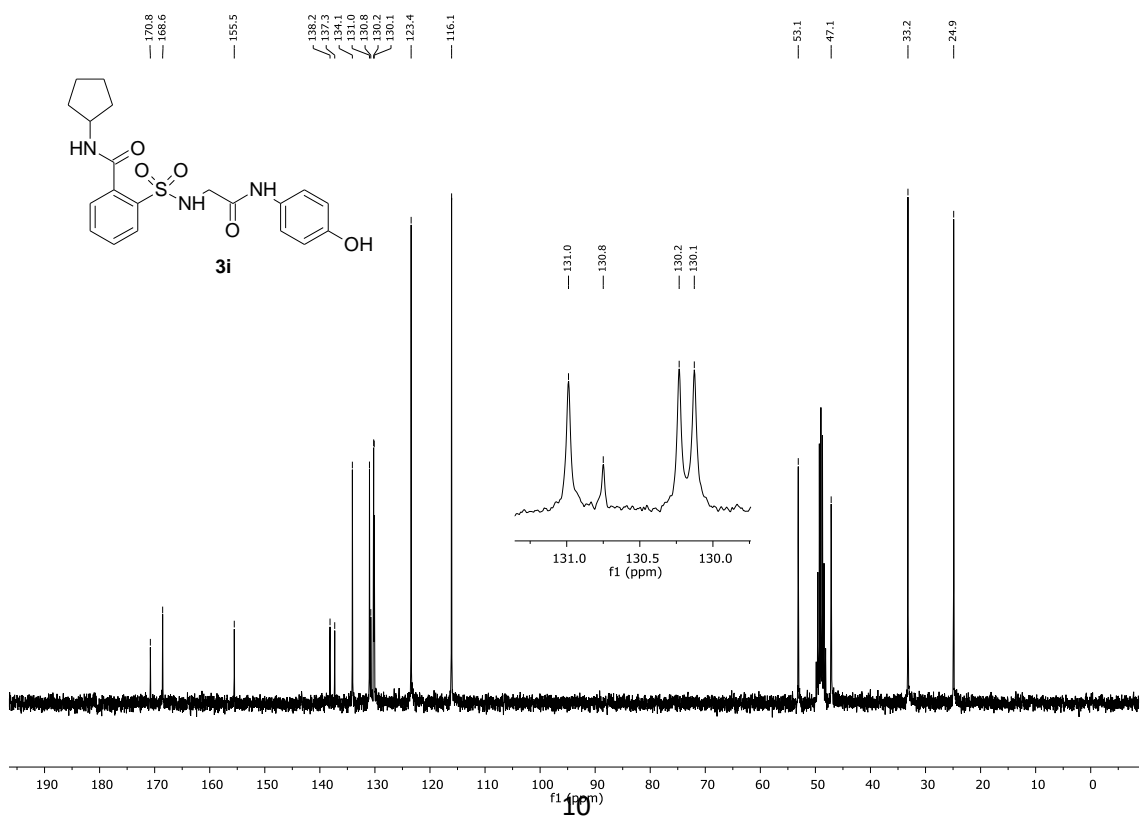
N-Cyclopentyl-2-[[2-(4-hydroxyanilino)-2-oxo-ethyl]sulfamoyl]benzamide 3i

¹H-NMR 300 MHz, CD₃OD



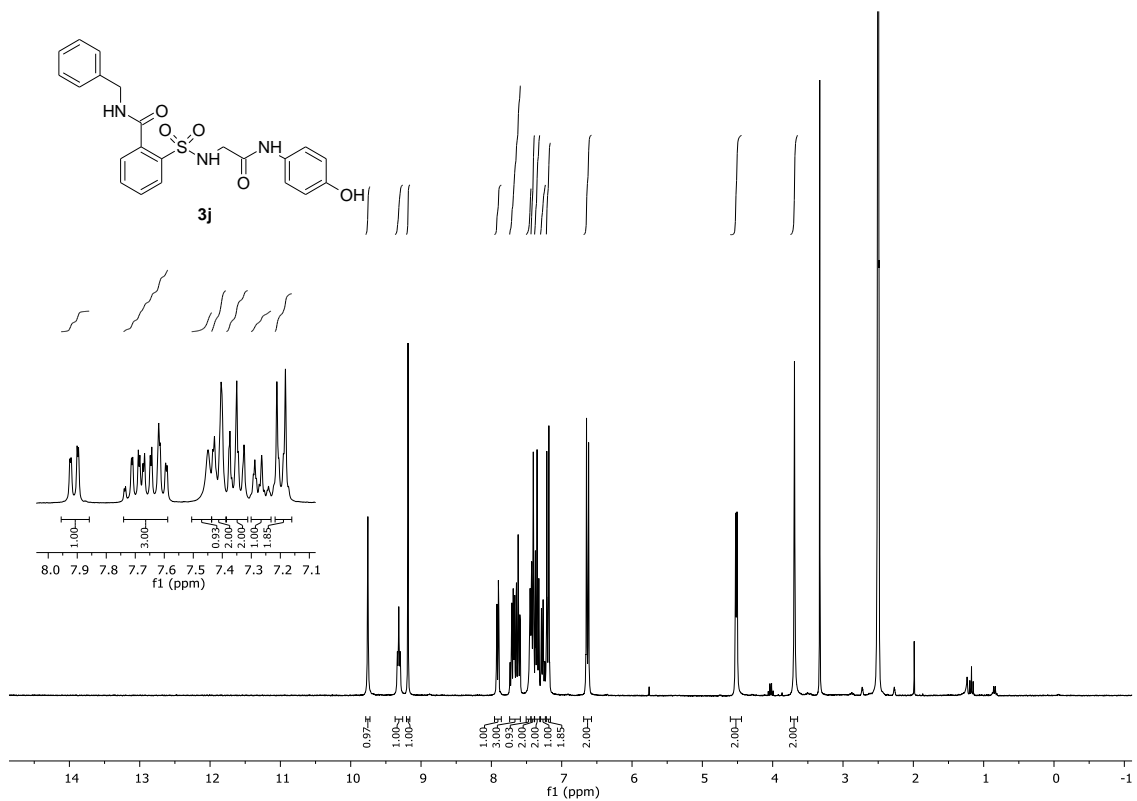
N-Cyclopentyl-2-[[2-(4-hydroxyanilino)-2-oxo-ethyl]sulfamoyl]benzamide 3i

¹³C-NMR 300 MHz, CD₃OD



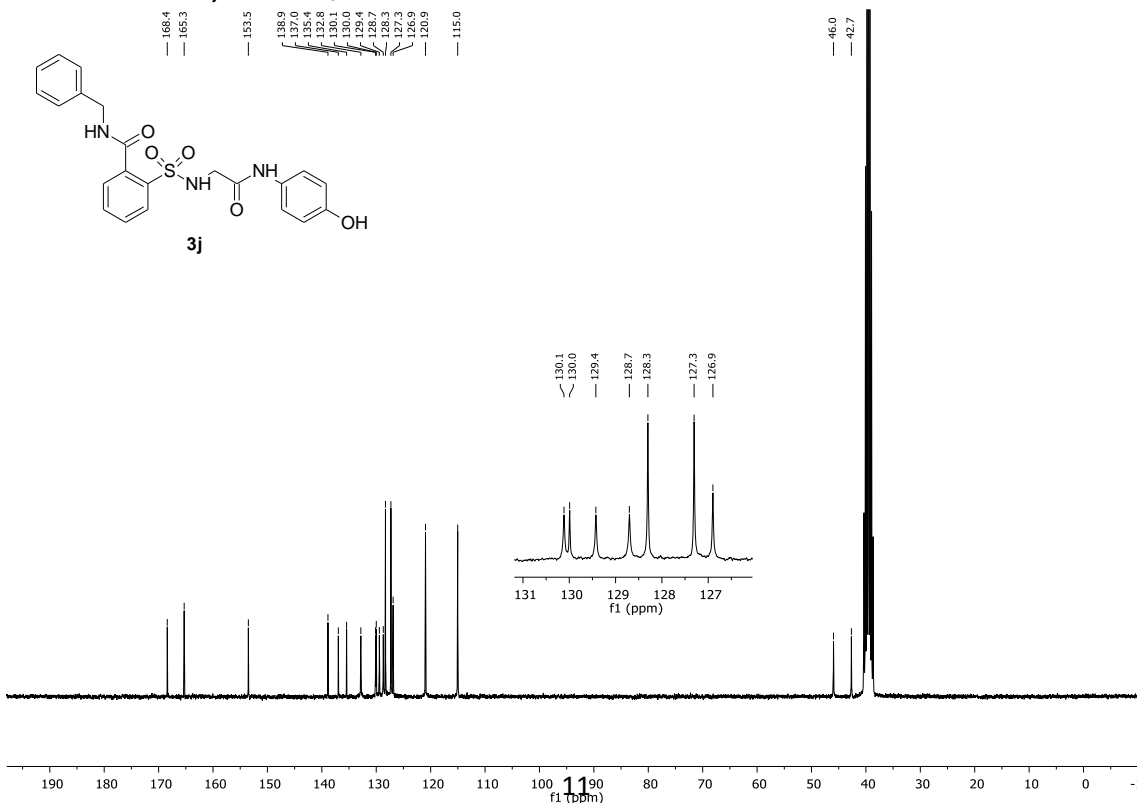
N-Benzyl-2-[[2-(4-hydroxyanilino)-2-oxo-ethyl]sulfamoyl]benzamide 3j

¹H-NMR 300 MHz, DMSO-d₆



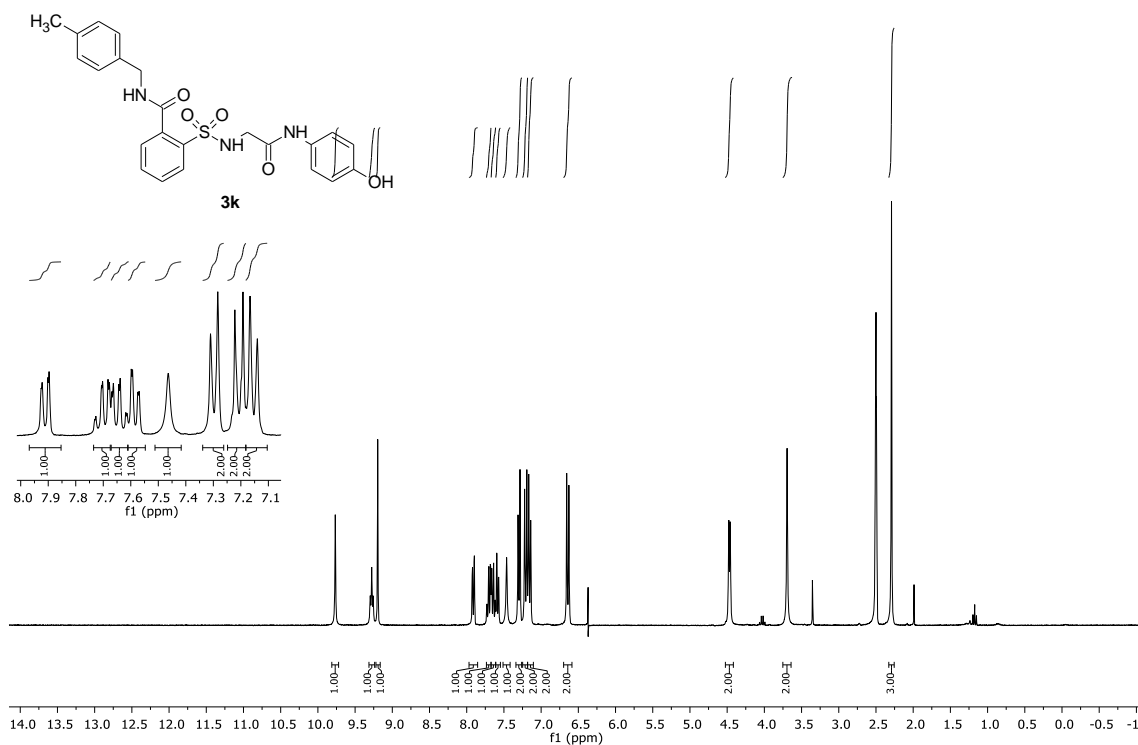
N-Benzyl-2-[[2-(4-hydroxyanilino)-2-oxo-ethyl]sulfamoyl]benzamide 3j

¹³C-NMR 75 MHz, DMSO-d₆



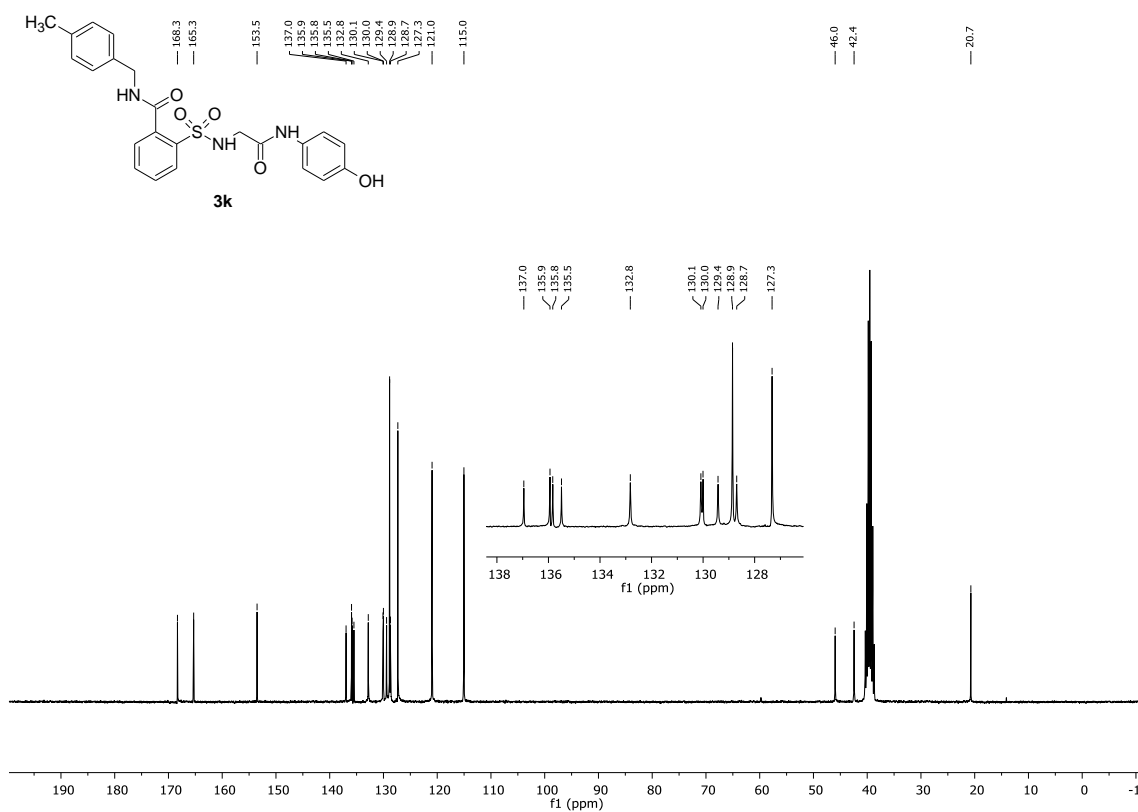
2-[[2-(4-Hydroxyanilino)-2-oxo-ethyl]sulfamoyl]-N-[(4-methylphenyl)methyl]benzamide 3k

¹H-NMR 300 MHz, DMSO-d₆



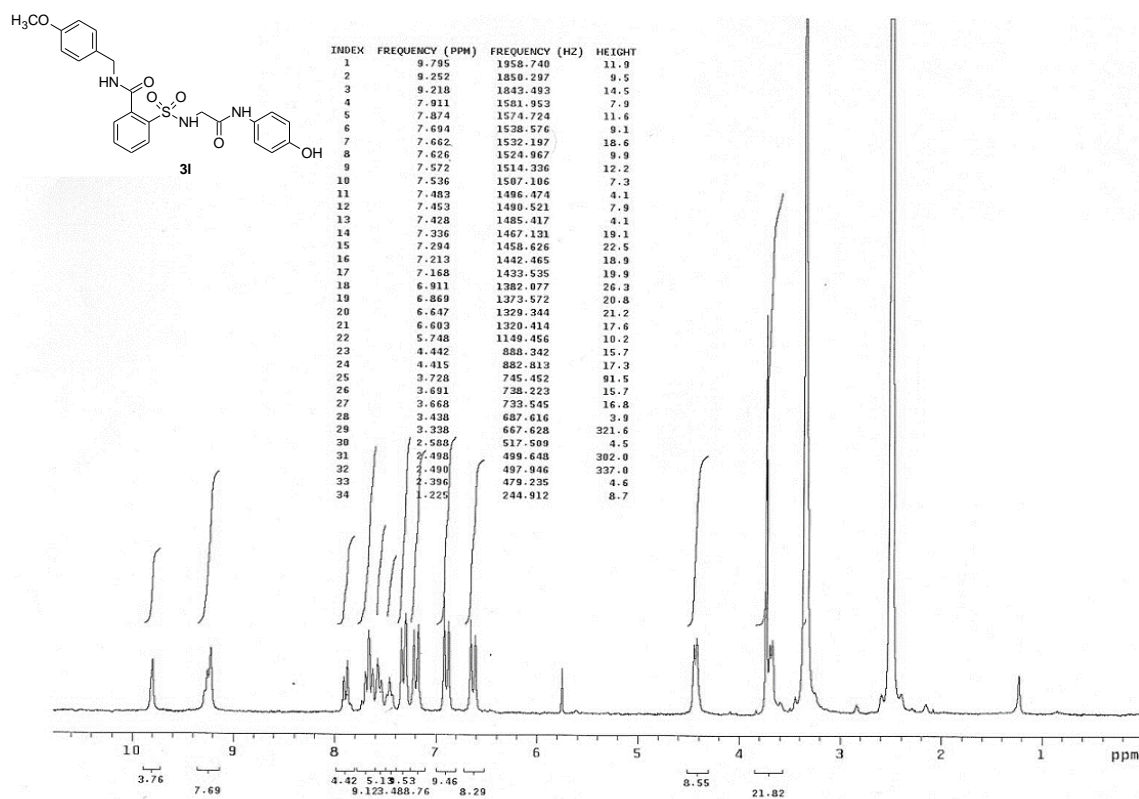
2-[[2-(4-Hydroxyanilino)-2-oxo-ethyl]sulfamoyl]-N-[(4-methylphenyl)methyl]benzamide 3k

¹³C-NMR 75 MHz, DMSO-d₆



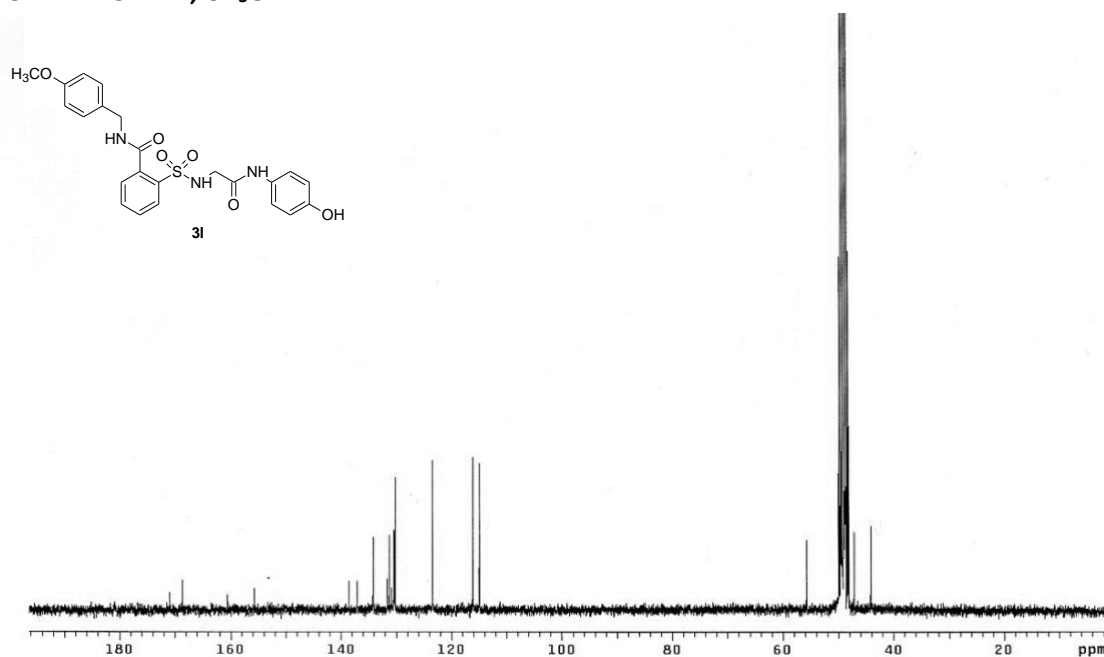
2-[[2-(4-Hydroxyanilino)-2-oxo-ethyl]sulfamoyl]-N-[(4-methoxyphenyl)methyl]benzamide 3I

¹H-NMR 300 MHz, DMSO-d₆



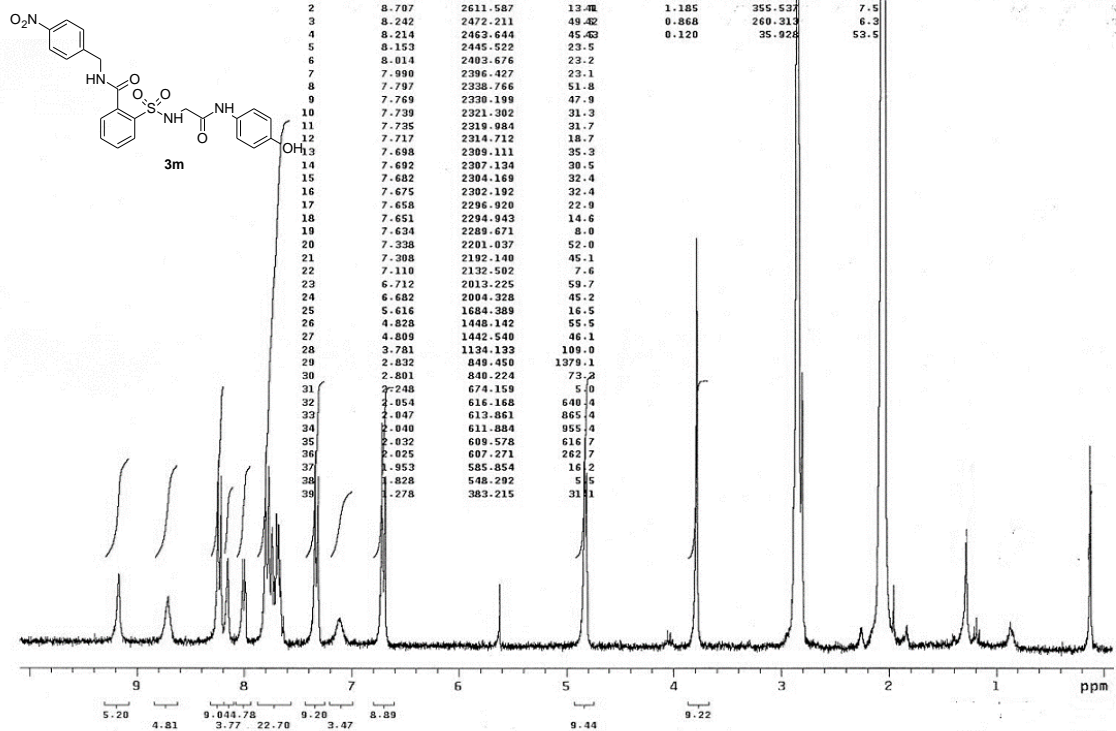
2-[[2-(4-Hydroxyanilino)-2-oxo-ethyl]sulfamoyl]-N-[(4-methoxyphenyl)methyl]benzamide 3I

¹³C-NMR 75 MHz, CD₃OD



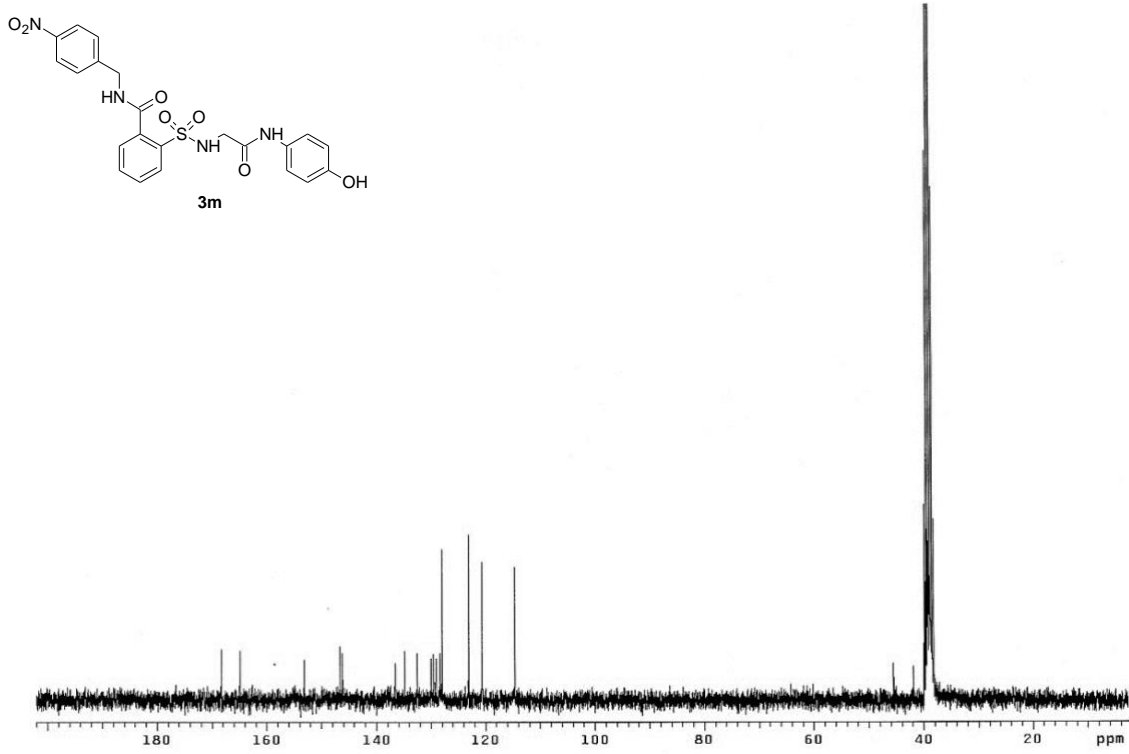
2-[[2-(4-Hydroxyanilino)-2-oxo-ethyl]sulfamoyl]-N-[(4-nitrophenyl)methyl]benzamide 3m

¹H-NMR 300 MHz, CD₃OD



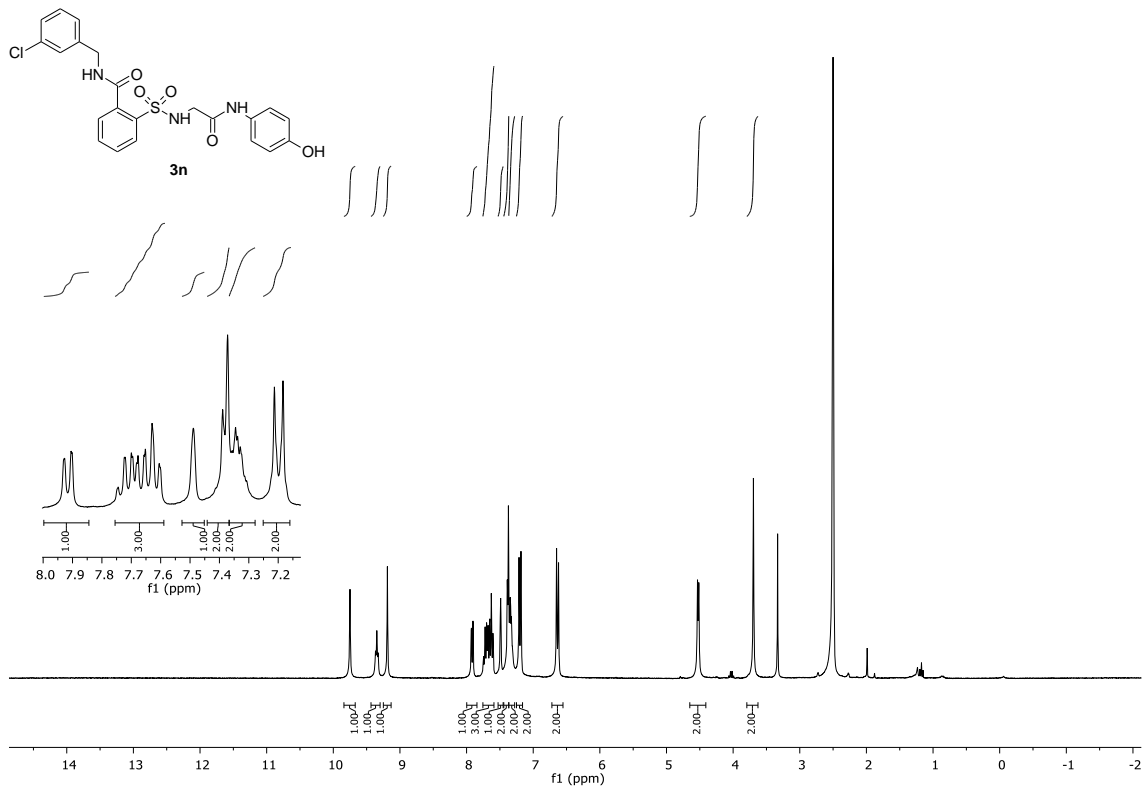
2-[[2-(4-Hydroxyanilino)-2-oxo-ethyl]sulfamoyl]-N-[(4-nitrophenyl)methyl]benzamide 3m

¹H-NMR 300 MHz, CD₃OD



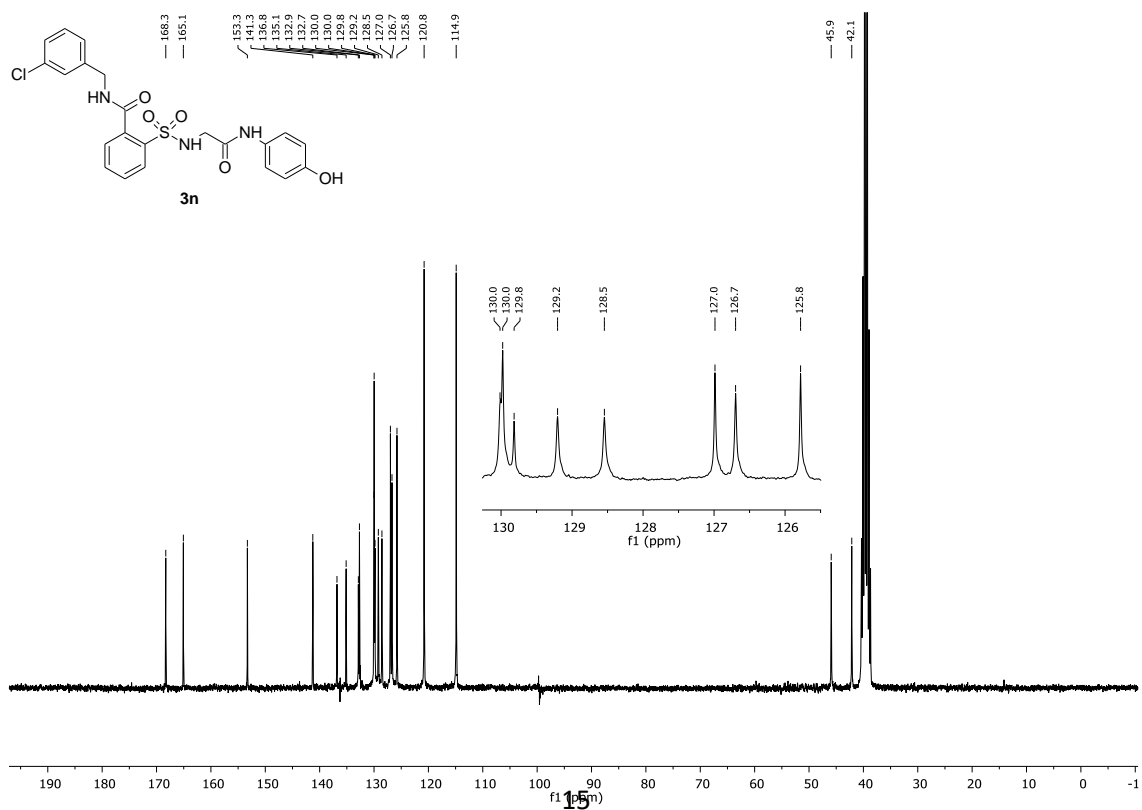
***N*-[(3-Chlorophenyl)methyl]-2-[[2-(4-hydroxyanilino)-2-oxo-ethyl]sulfamoyl]benzamide 3n**

¹H-NMR 300 MHz, DMSO-*d*₆



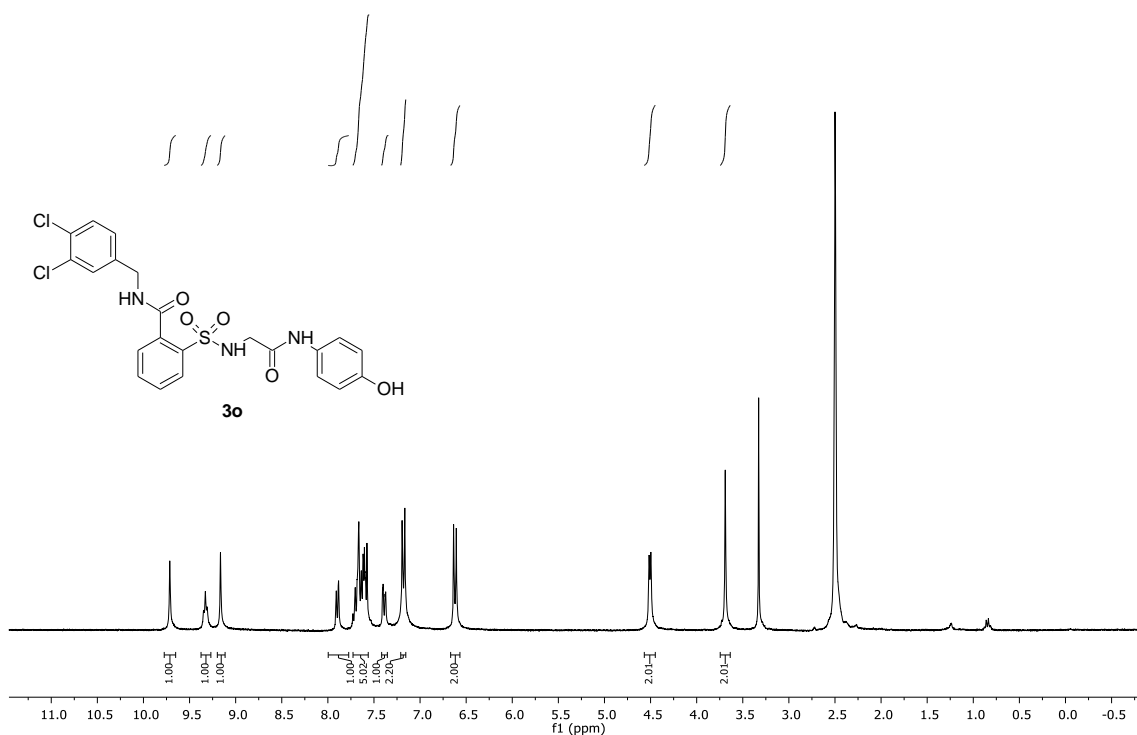
***N*-[(3-Chlorophenyl)methyl]-2-[[2-(4-hydroxyanilino)-2-oxo-ethyl]sulfamoyl]benzamide 3n**

¹³C-NMR 75 MHz, DMSO-*d*₆



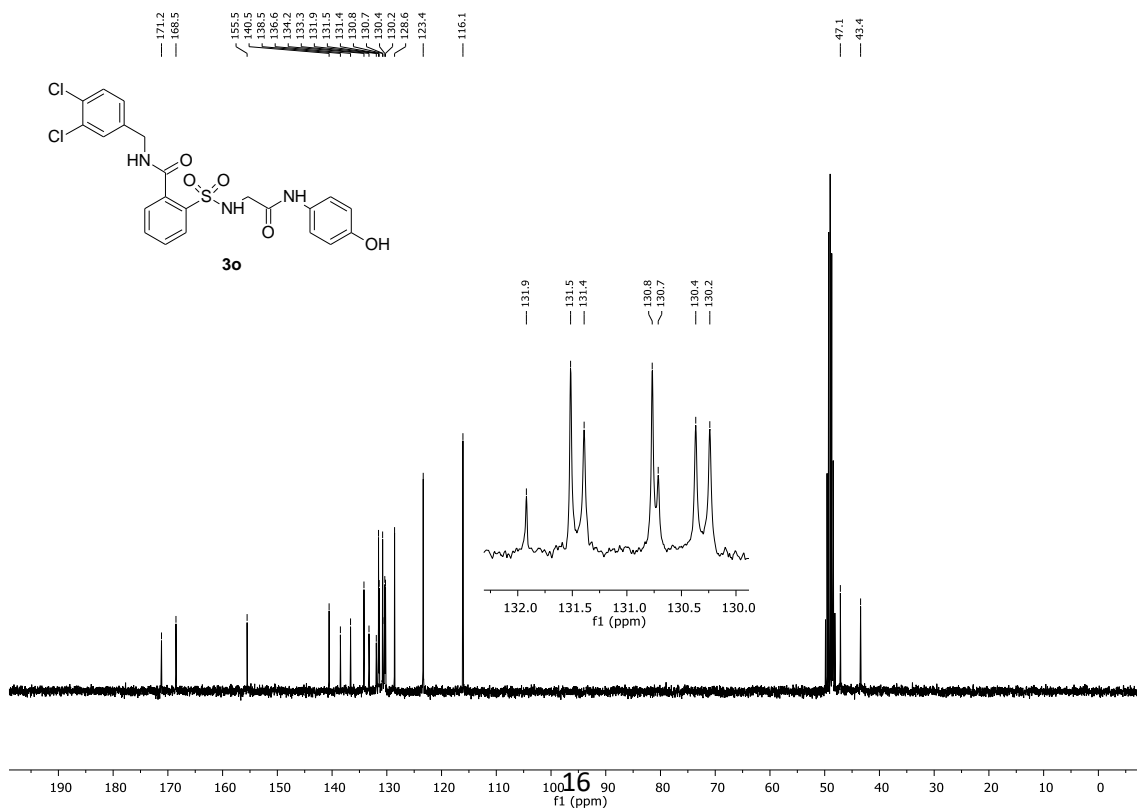
***N*-[(3,4-Dichlorophenyl)methyl]-2-[[2-(4-hydroxyanilino)-2-oxo-ethyl]sulfamoyl]benzamide
3o**

¹H-NMR 300 MHz, DMSO-*d*₆



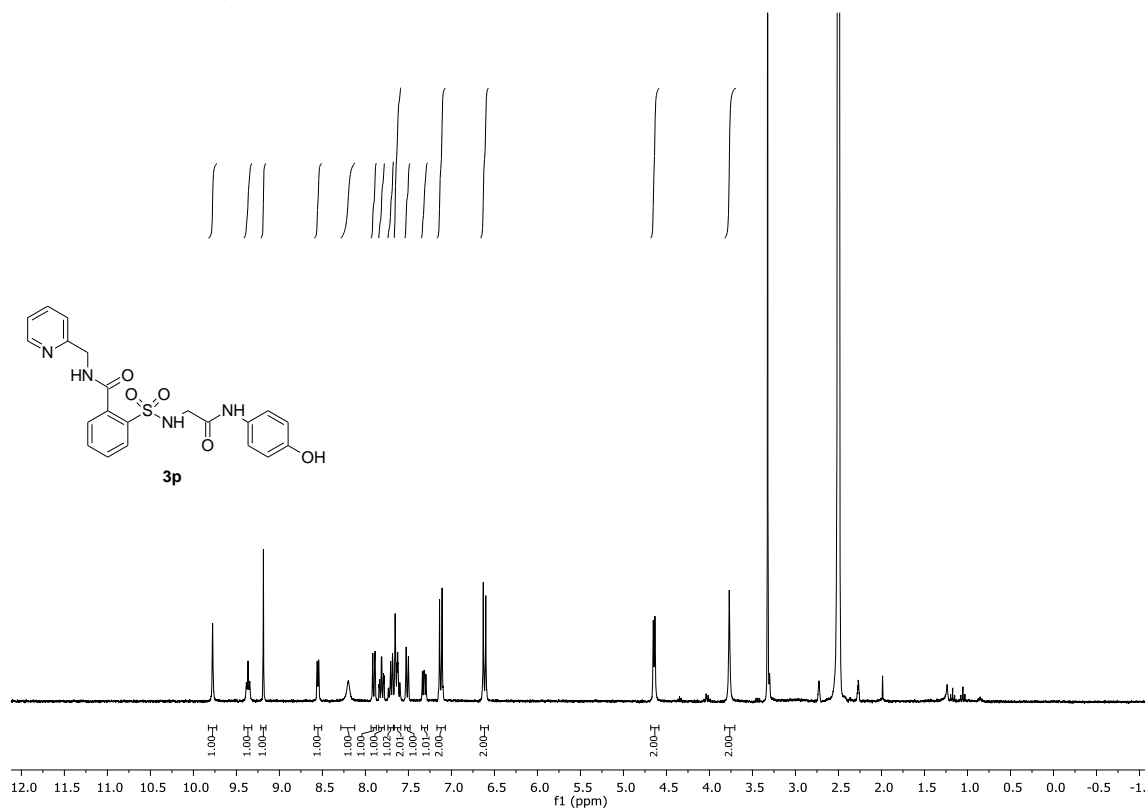
***N*-[(3,4-Dichlorophenyl)methyl]-2-[[2-(4-hydroxyanilino)-2-oxo-ethyl]sulfamoyl]benzamide
3o**

¹³C-NMR 75 MHz, CD₃OD



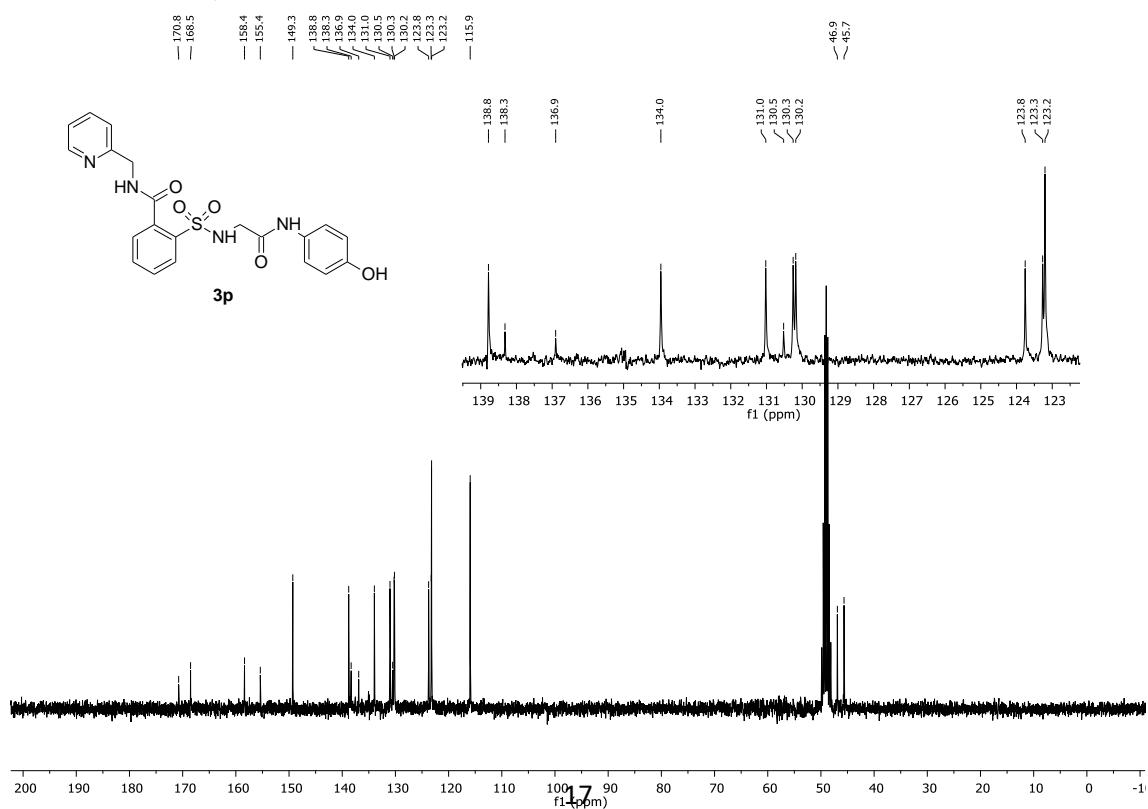
2-[[2-(4-Hydroxyanilino)-2-oxo-ethyl]sulfamoyl]-*N*-(2-pyridylmethyl)benzamide 3p

¹H-NMR 300 MHz, DMSO-*d*₆



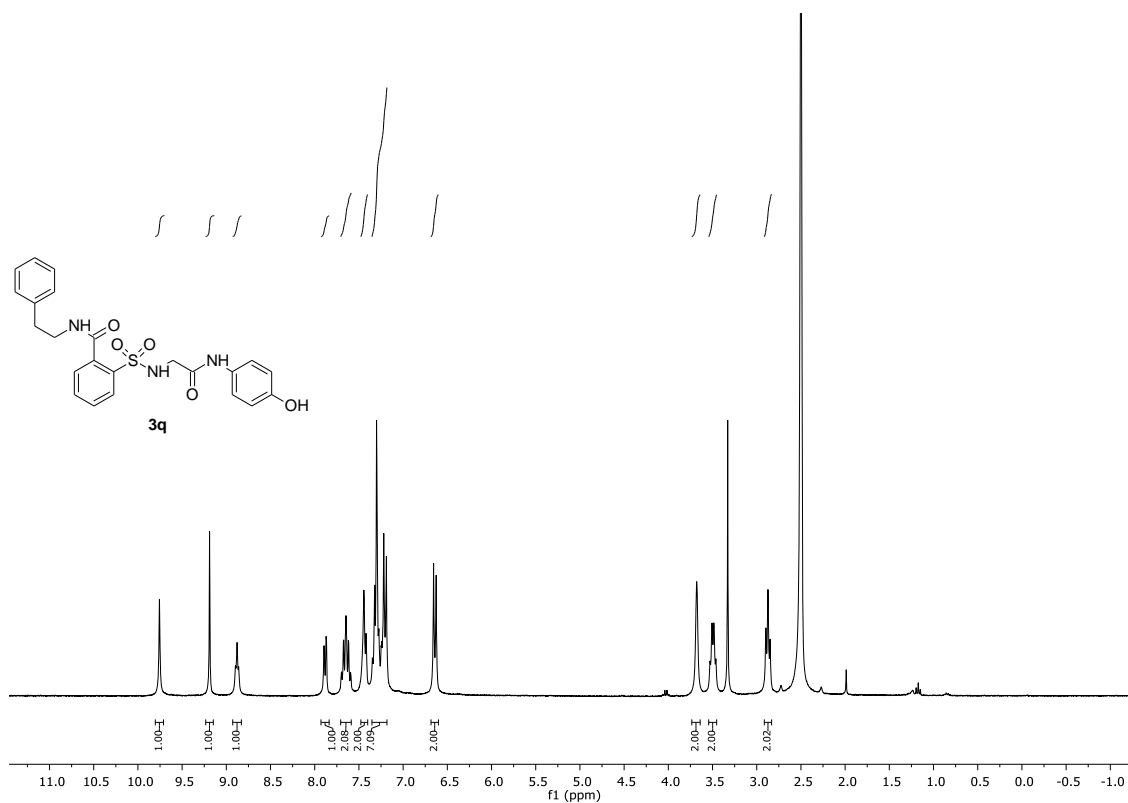
2-[[2-(4-Hydroxyanilino)-2-oxo-ethyl]sulfamoyl]-*N*-(2-pyridylmethyl)benzamide 3p

¹³C-NMR 75 MHz, CD₃OD



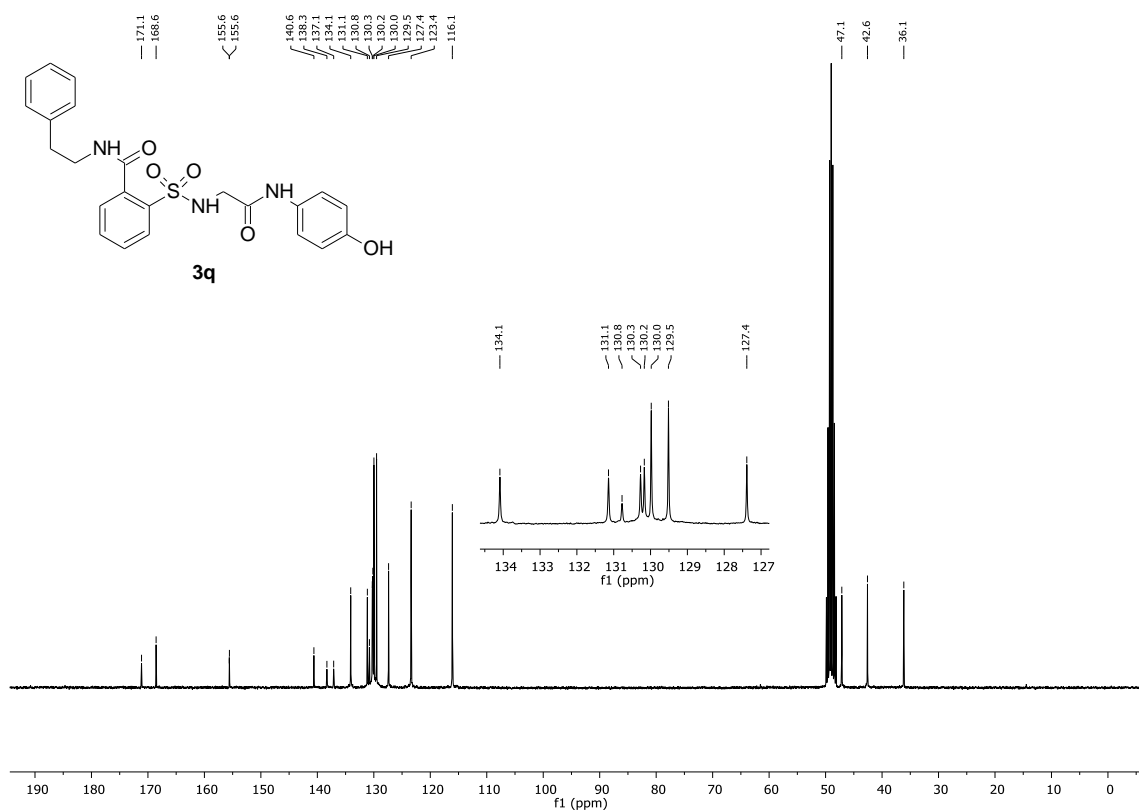
2-[[2-(4-Hydroxyanilino)-2-oxo-ethyl]sulfamoyl]-*N*-(2-phenylethyl)benzamide 3q

$^1\text{H-NMR}$ 300 MHz, $\text{DMSO-}d_6$



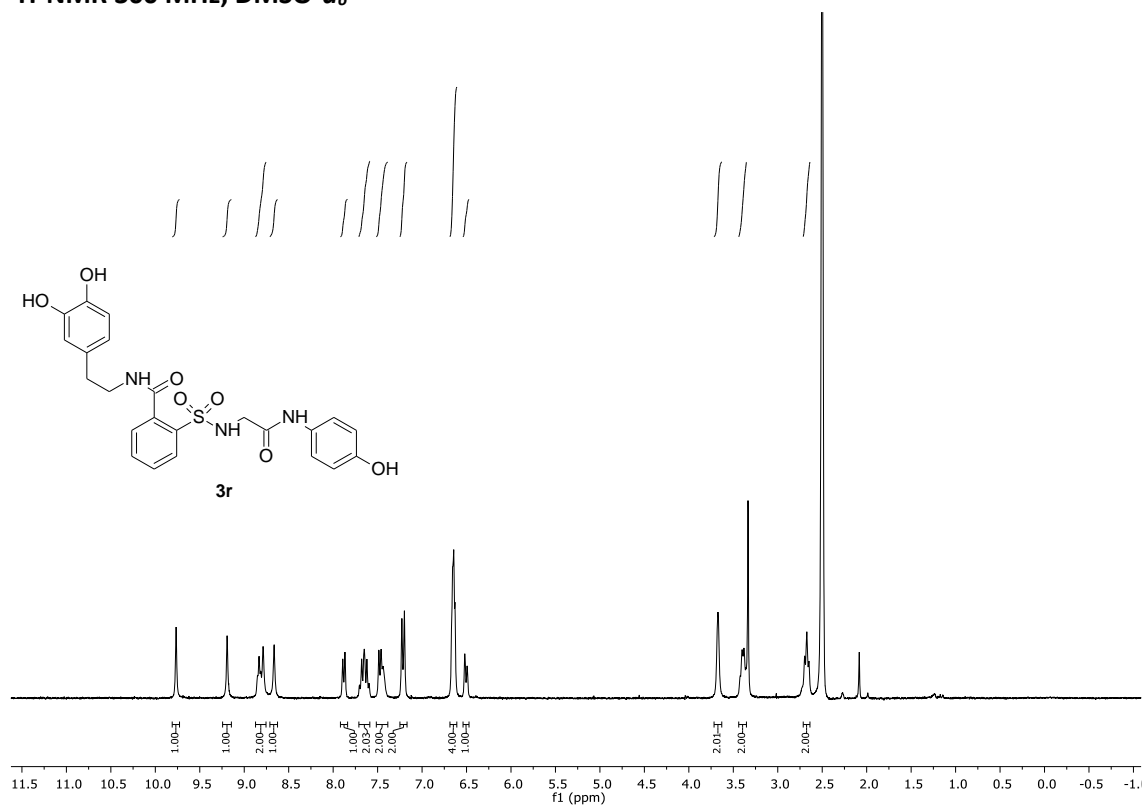
2-[[2-(4-Hydroxyanilino)-2-oxo-ethyl]sulfamoyl]-*N*-(2-phenylethyl)benzamide 3q

$^{13}\text{C-NMR}$ 75 MHz, CD_3OD



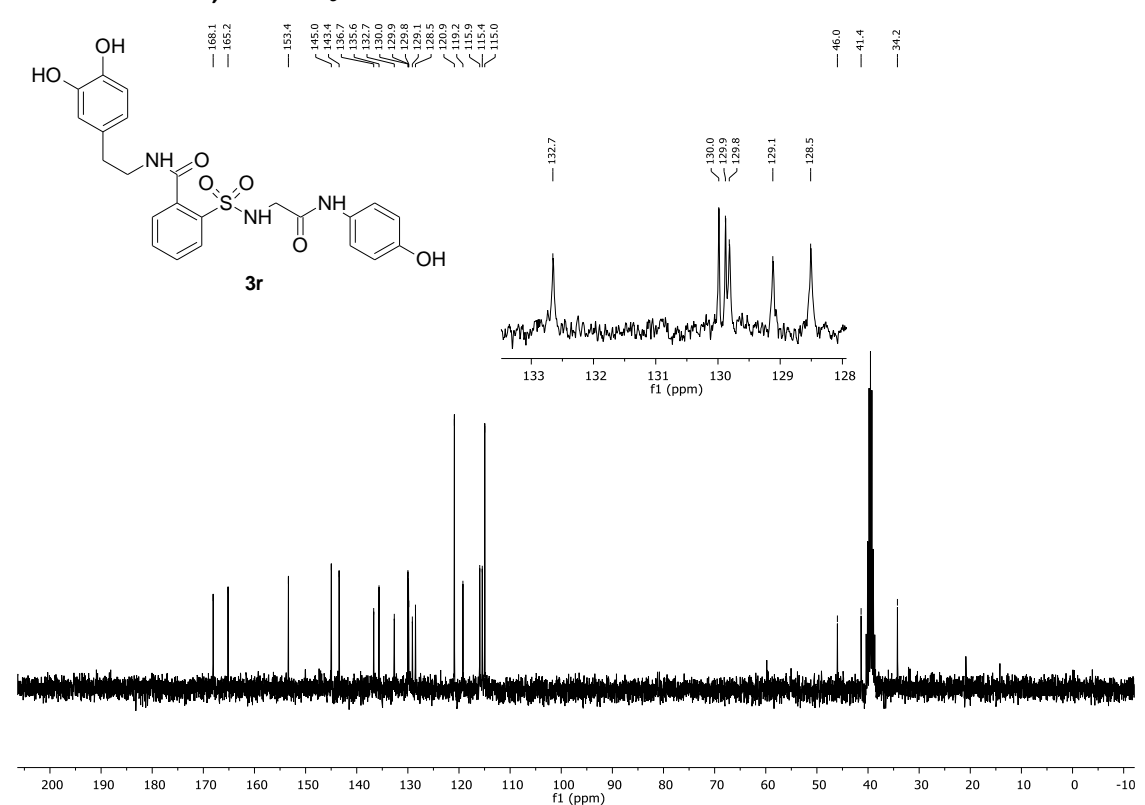
***N*-[2-(3,4-Dihydroxyphenyl)ethyl]-2-[[2-(4-hydroxyanilino)-2-oxo-ethyl]sulfamoyl]benzamide
3r**

¹H-NMR 300 MHz, DMSO-*d*₆



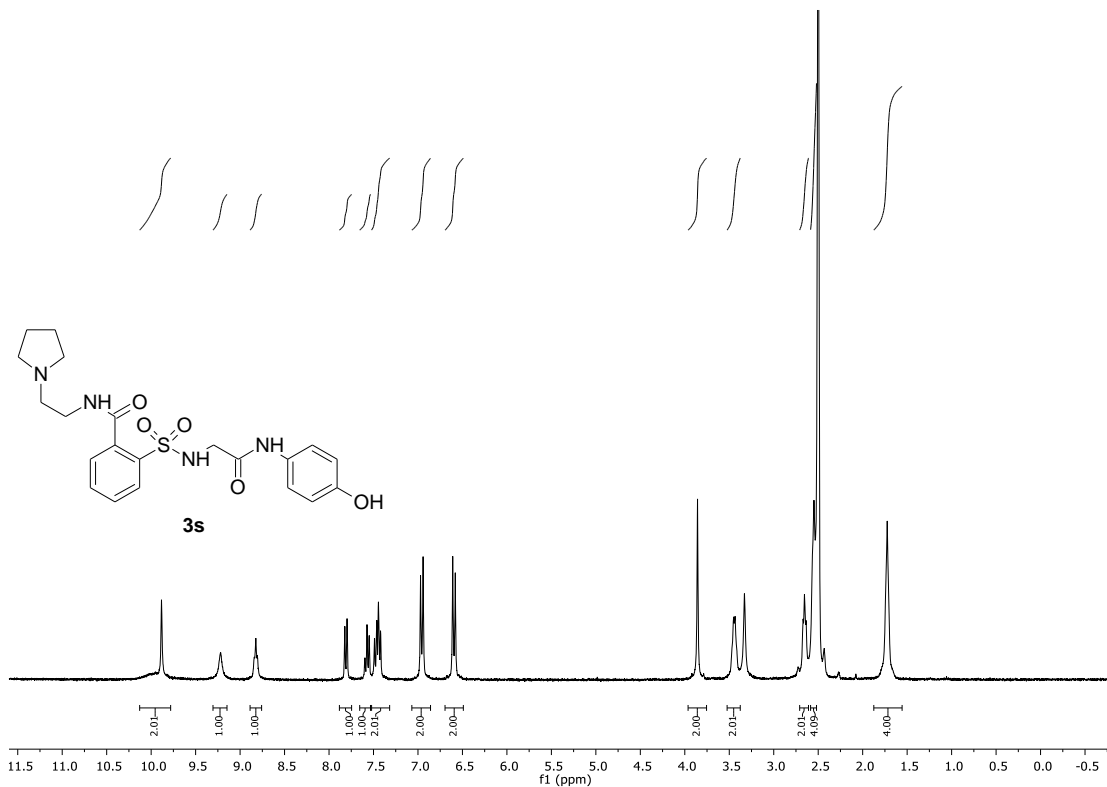
***N*-[2-(3,4-Dihydroxyphenyl)ethyl]-2-[[2-(4-hydroxyanilino)-2-oxo-ethyl]sulfamoyl]benzamide
3r**

¹³C-NMR 75 MHz, DMSO-*d*₆



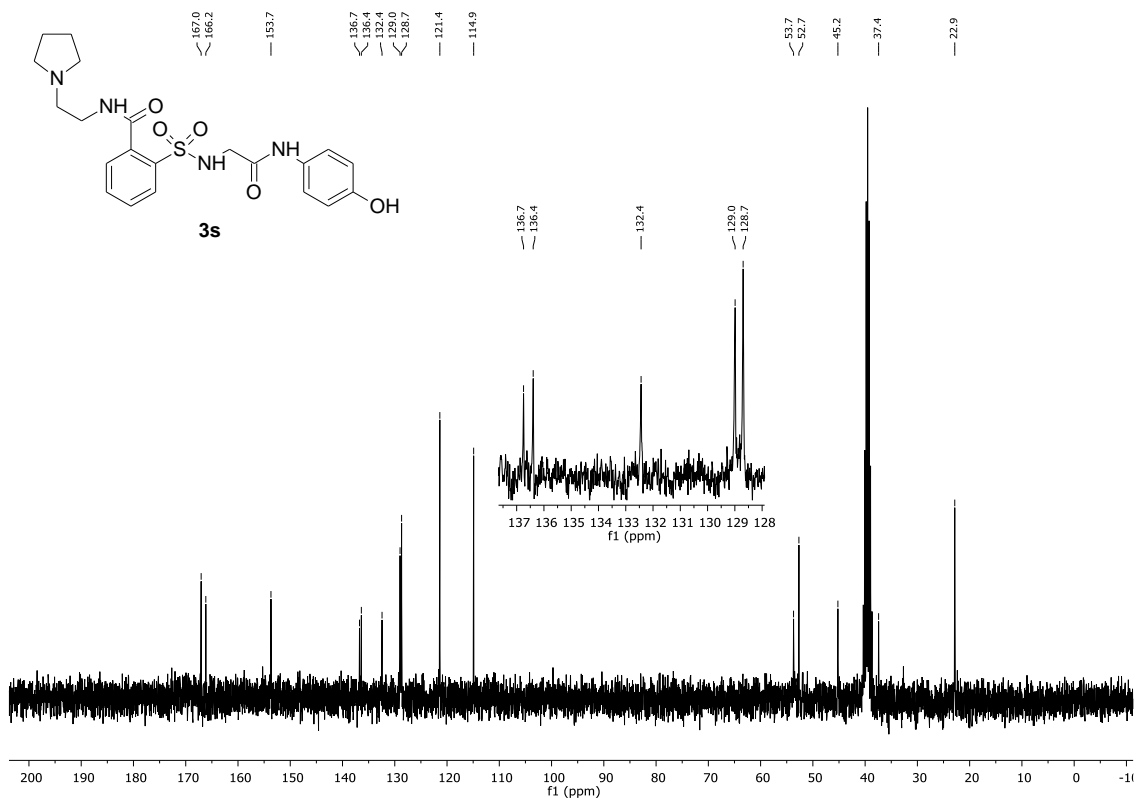
2-[[2-(4-Hydroxyanilino)-2-oxo-ethyl]sulfamoyl]-N-(2-pyrrolidin-1-ylethyl)benzamide 3s

¹H-NMR 300 MHz, DMSO-*d*₆

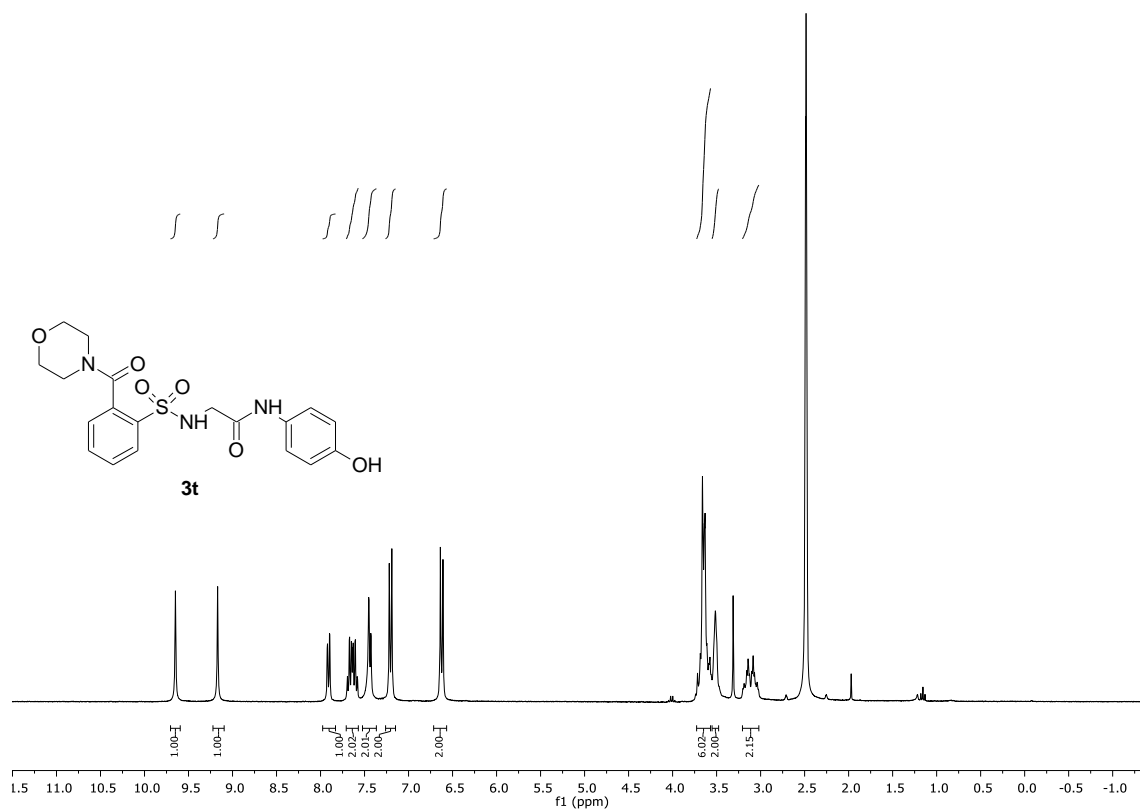


2-[[2-(4-Hydroxyanilino)-2-oxo-ethyl]sulfamoyl]-N-(2-pyrrolidin-1-ylethyl)benzamide 3s

¹³C-NMR 75 MHz, DMSO-*d*₆

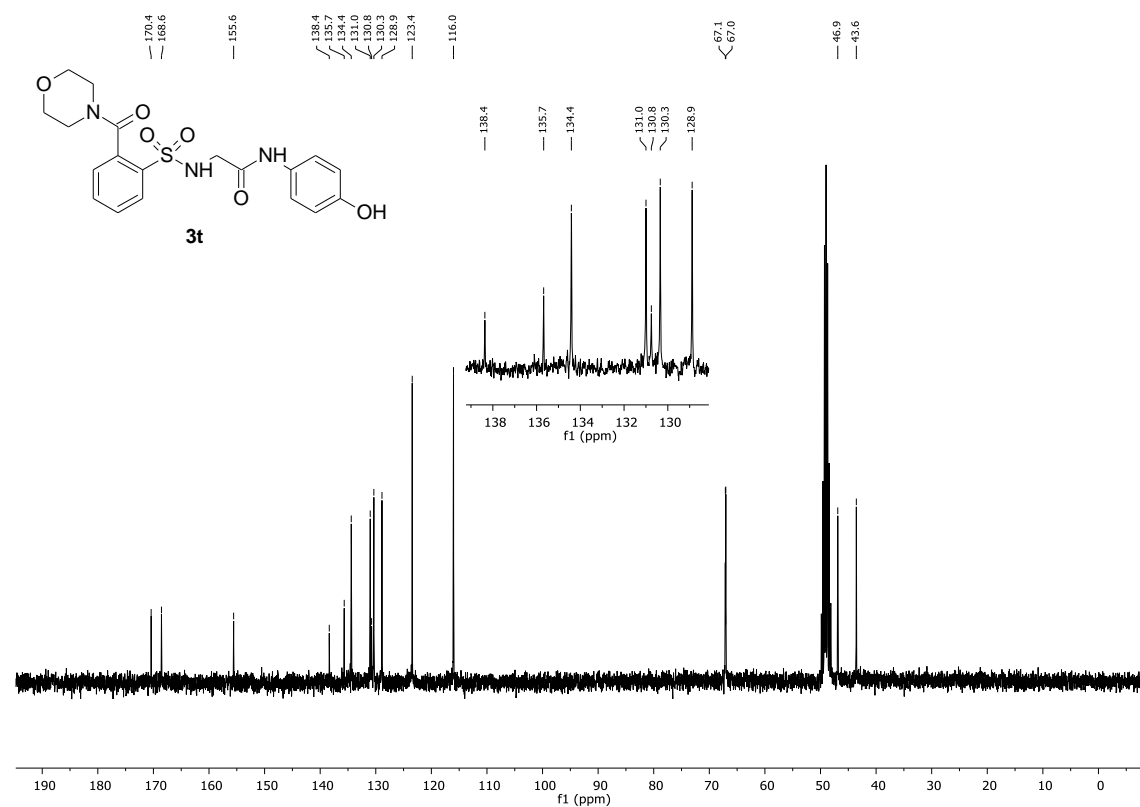


***N*-(4-Hydroxyphenyl)-2-[[2-(morpholine-4-carbonyl)phenyl]sulfonylamino]acetamide 3t**
¹H-NMR 300 MHz, DMSO-*d*₆



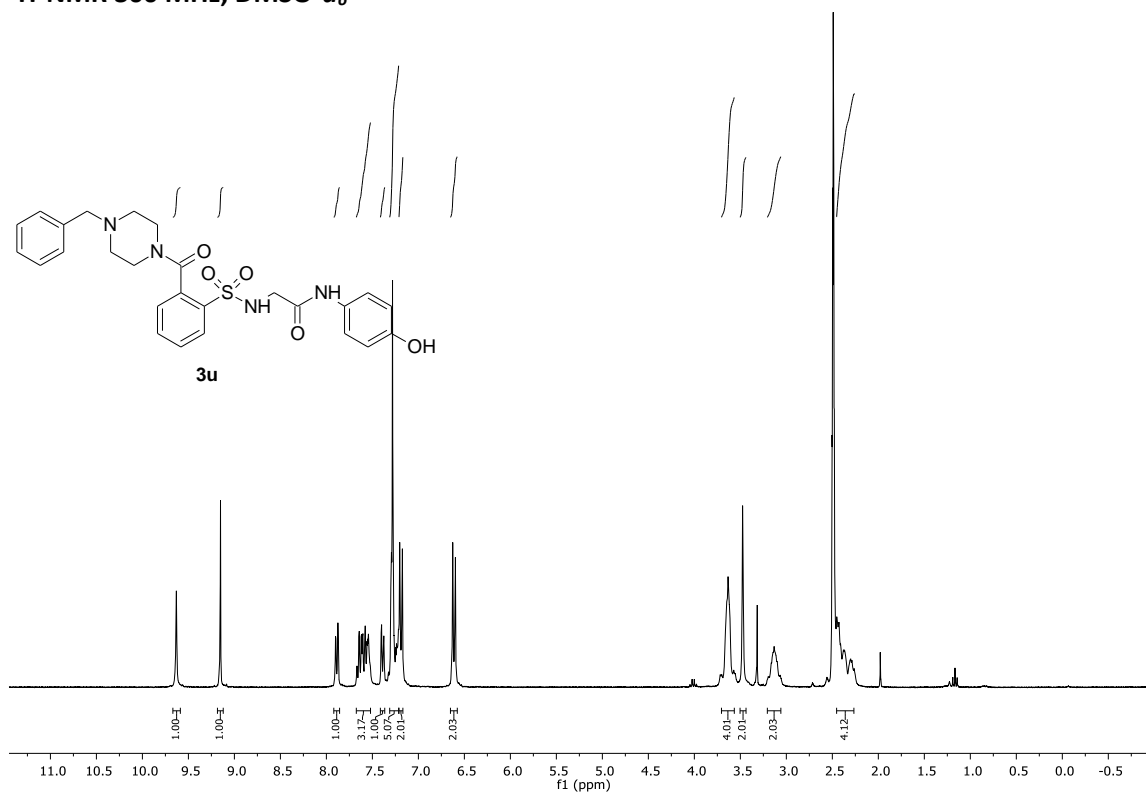
***N*-(4-Hydroxyphenyl)-2-[[2-(morpholine-4-carbonyl)phenyl]sulfonylamino]acetamide 3t**

¹³C-NMR 75 MHz, DMSO-*d*₆



2-[[2-(4-Benzylpiperazine-1-carbonyl)phenyl]sulfonylamino]-N-(4-hydroxyphenyl)acetamide
3u

¹H-NMR 300 MHz, DMSO-d₆



2-[[2-(4-Benzylpiperazine-1-carbonyl)phenyl]sulfonylamino]-N-(4-hydroxyphenyl)acetamide
3u

¹³C-NMR 75 MHz, DMSO-d₆

