



Supporting Information

for

On Reuben G. Jones synthesis of 2-hydroxypyrazines

Pierre Legrand and Yves L. Janin

Beilstein J. Org. Chem. **2022**, *18*, 935–943. [doi:10.3762/bjoc.18.93](https://doi.org/10.3762/bjoc.18.93)

Images of the experimental set up to run chromatography at 60 °C, a description of the crystallization, data collection, for the structural determination of compound 4{1,2} as well as copies of the ^1H and ^{13}C NMR spectra of all compounds described

Experimental set up to run chromatography at 60 °C

As depicted, double enveloped columns were used to maintain a 60 °C temperature with a heated water circulation on the outside. Moreover, the eluent bottles from which the solvent was pumped into the column, were placed in the heated water bath of the apparatus (a Bioblock polystat 12HT) insuring this water circulation. Note: Pumping the eluent up to one meter at 60 °C without encountering too much cavitation problems turns out to be possible with mixtures of ethyl acetate and cyclohexane.



Experimental setup to undertake a chromatography at 60 °C (at 52.5 °C on the right picture). Left: picture of a double enveloped column charged with silica gel and a hot water circulation on the outside. Right: picture of the entire setup, starting with the water heating apparatus set on the floor which pumps the hot water in the column via the two insulated tubes, the two solvent bottles warmed by the hot water bath and the PTFE tube placed in one of these bottles allows to pump it to the top of the column.

Crystallization, data collection, and structure determination

Suitable crystals of compound **4**{1,2} were obtained by recrystallization from acetic acid. Crystals were then flash-cooled in liquid nitrogen using Paratone-paraffin 50% (v/v) oil as the cryoprotectant. X-ray diffraction data were collected at a wavelength of 0.7293 Å on the beamline PROXIMA-2 at Synchrotron SOLEIL (St. Aubin, France). Diffraction data were integrated and reduced using the XDS program package.¹ Structures were solved using SHELXT² and refined with SHELXL.³

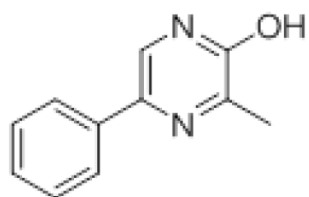
Parameters for compound **4**{1,2}: Datablock: YJ31780-038-4. Space group: *P21/c*. Unit cell parameters: $a = 12.424 \text{ \AA}$, $b = 11.184 \text{ \AA}$, $c = 9.634 \text{ \AA}$, $\alpha = 90.00(3)^\circ$, $\beta = 107.73(3)^\circ$, $\gamma = 90.00(3)$. CCDC Deposition Number: 2155463. CSD Refcode Entry: NAXMOS. DOI: 10.5517/ccdc.csd.cc2bby2q

References

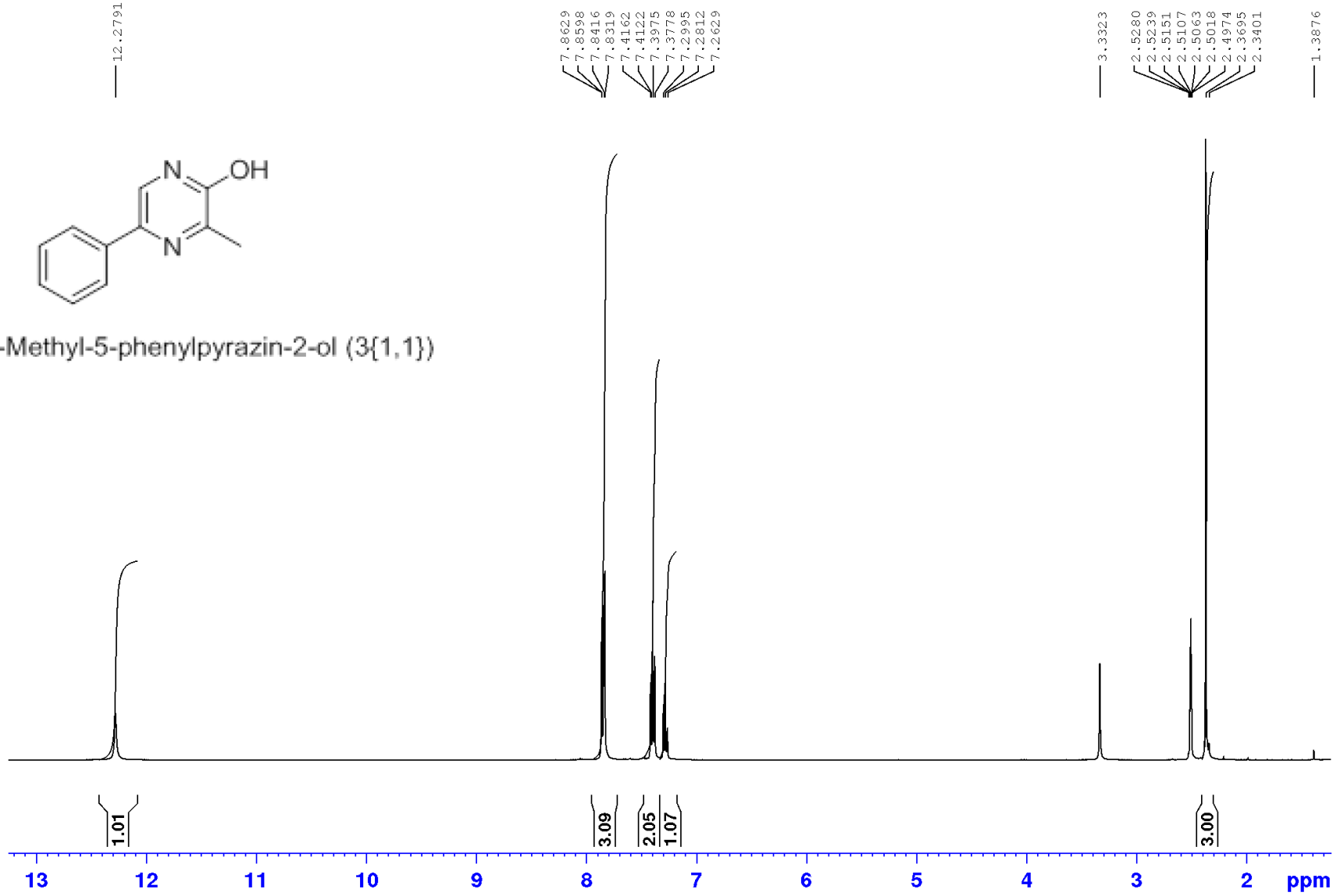
1. Kabsch, W. *Acta Cryst.* **2010**, *D66*, 125.
2. Sheldrick, G.M. *Acta Cryst.* **2015**, *A71*, 3.
3. Sheldrick, G.M. *Acta Cryst.* **2015**, *C71*, 3.

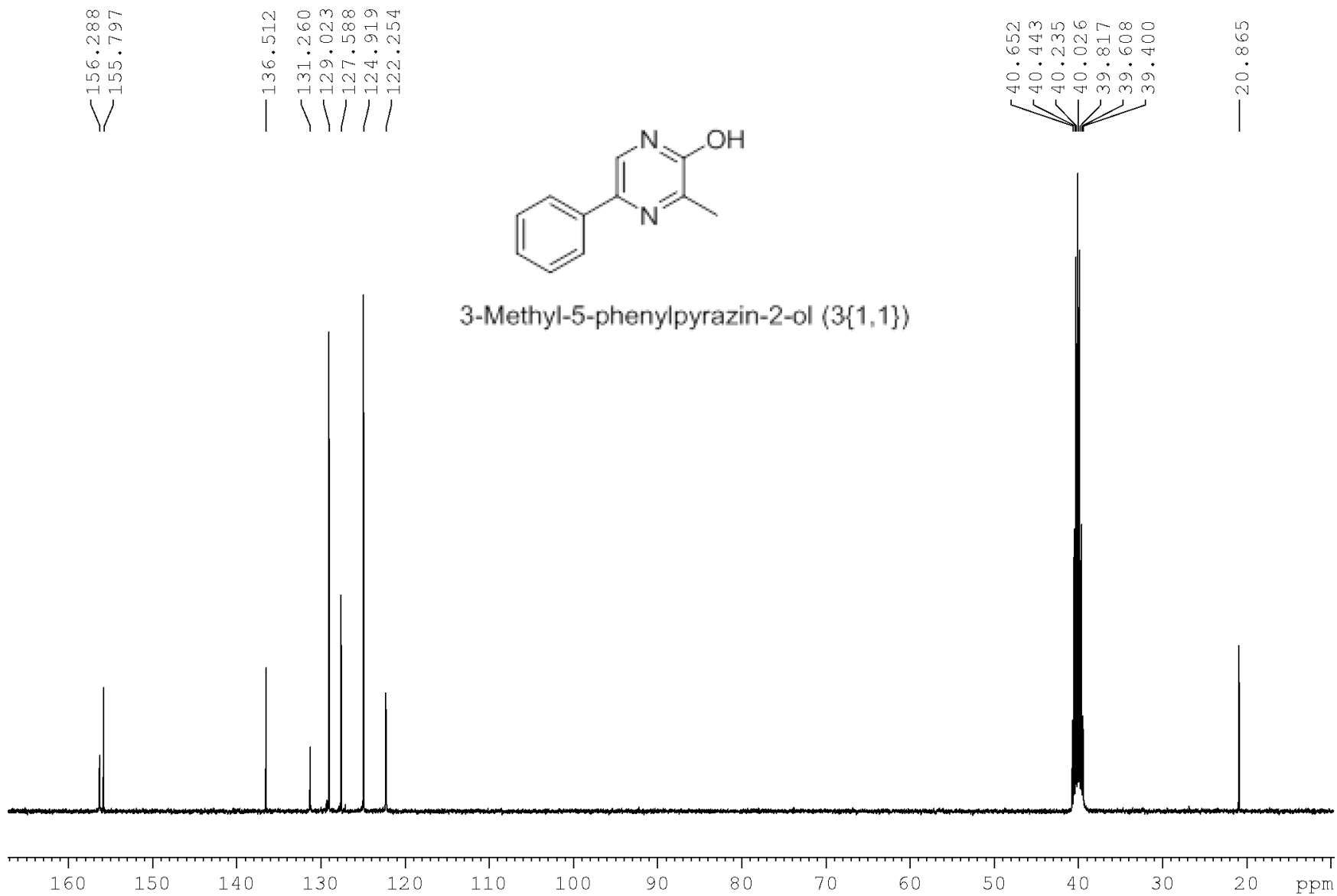
¹H and ¹³C NMR spectra

3-Methyl-5-phenylpyrazin-2-ol (3{1,1})



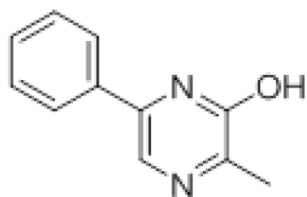
3-Methyl-5-phenylpyrazin-2-ol (3{1,1})





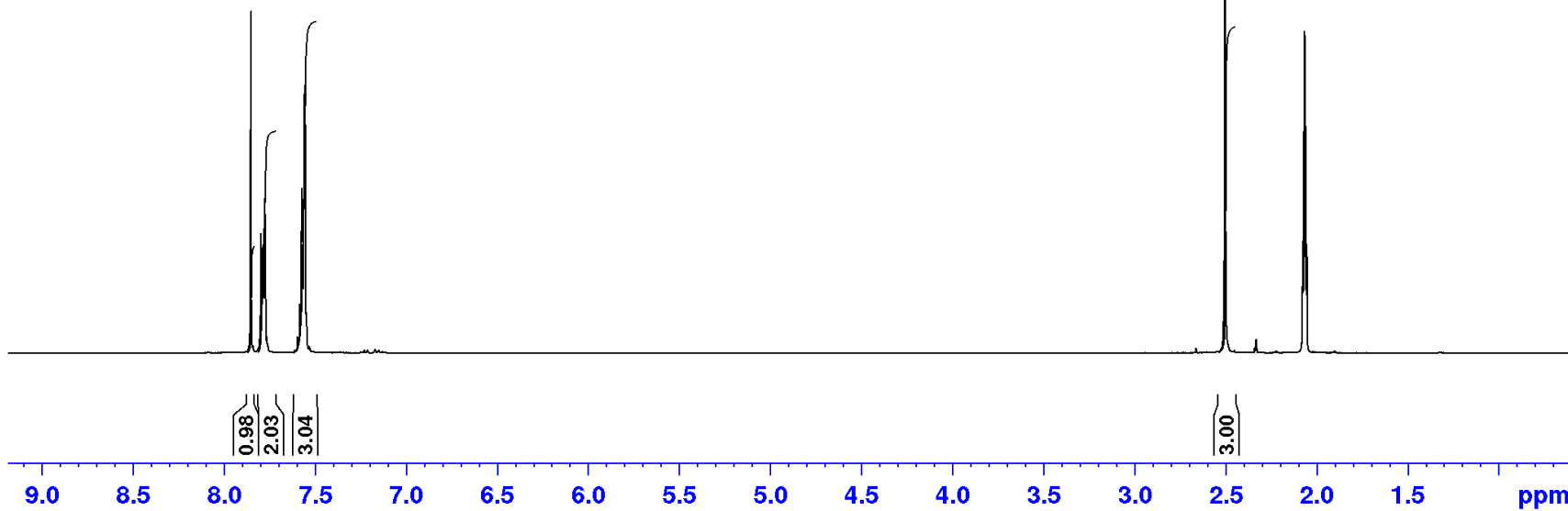
3-Methyl-6-phenylpyrazin-2-ol (4{1,1})

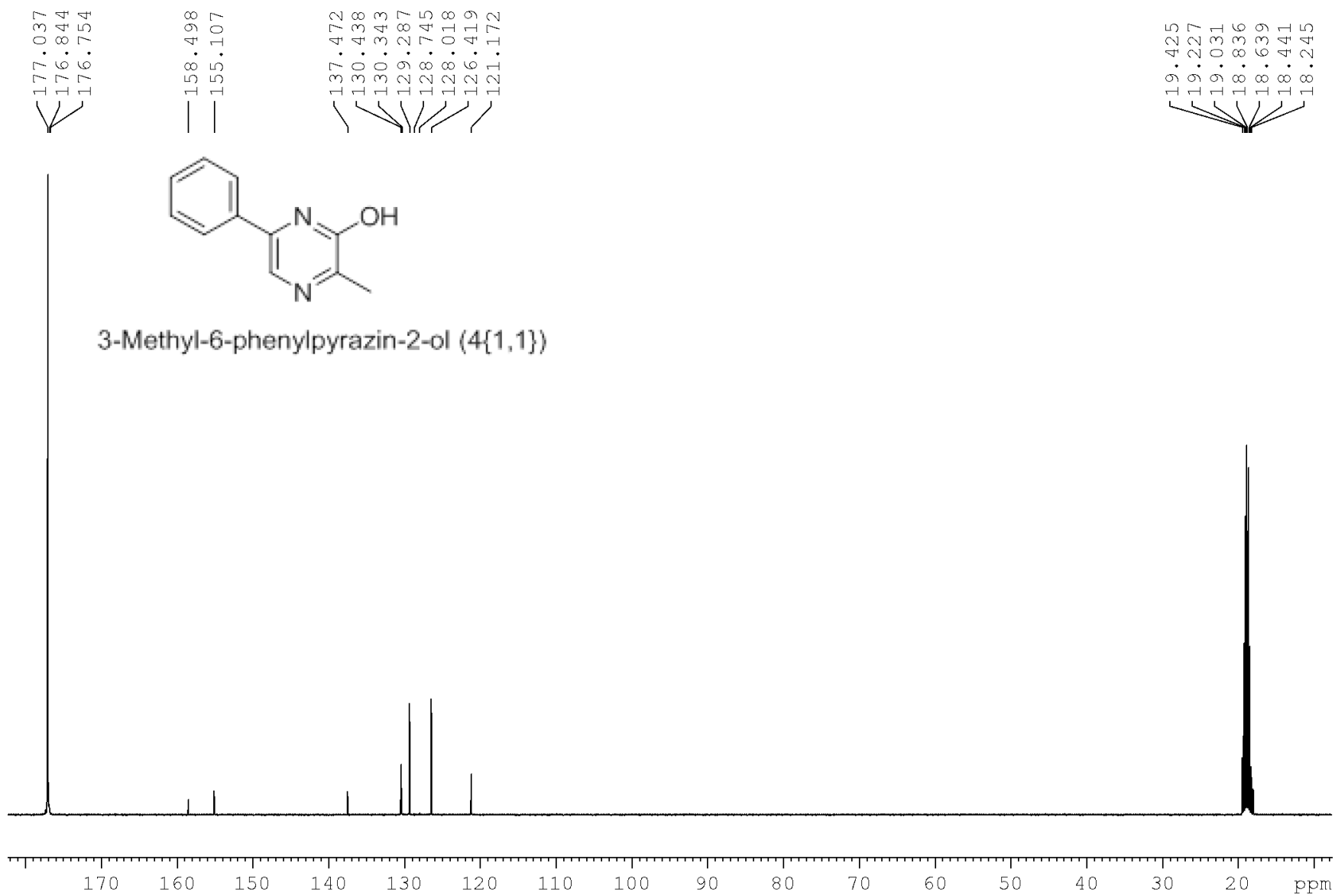
7.8524
7.7968
7.7897
7.7859
7.7771
7.7726
7.5832
7.5791
7.5725
7.5673
7.5592
7.5546
7.5485
7.5439



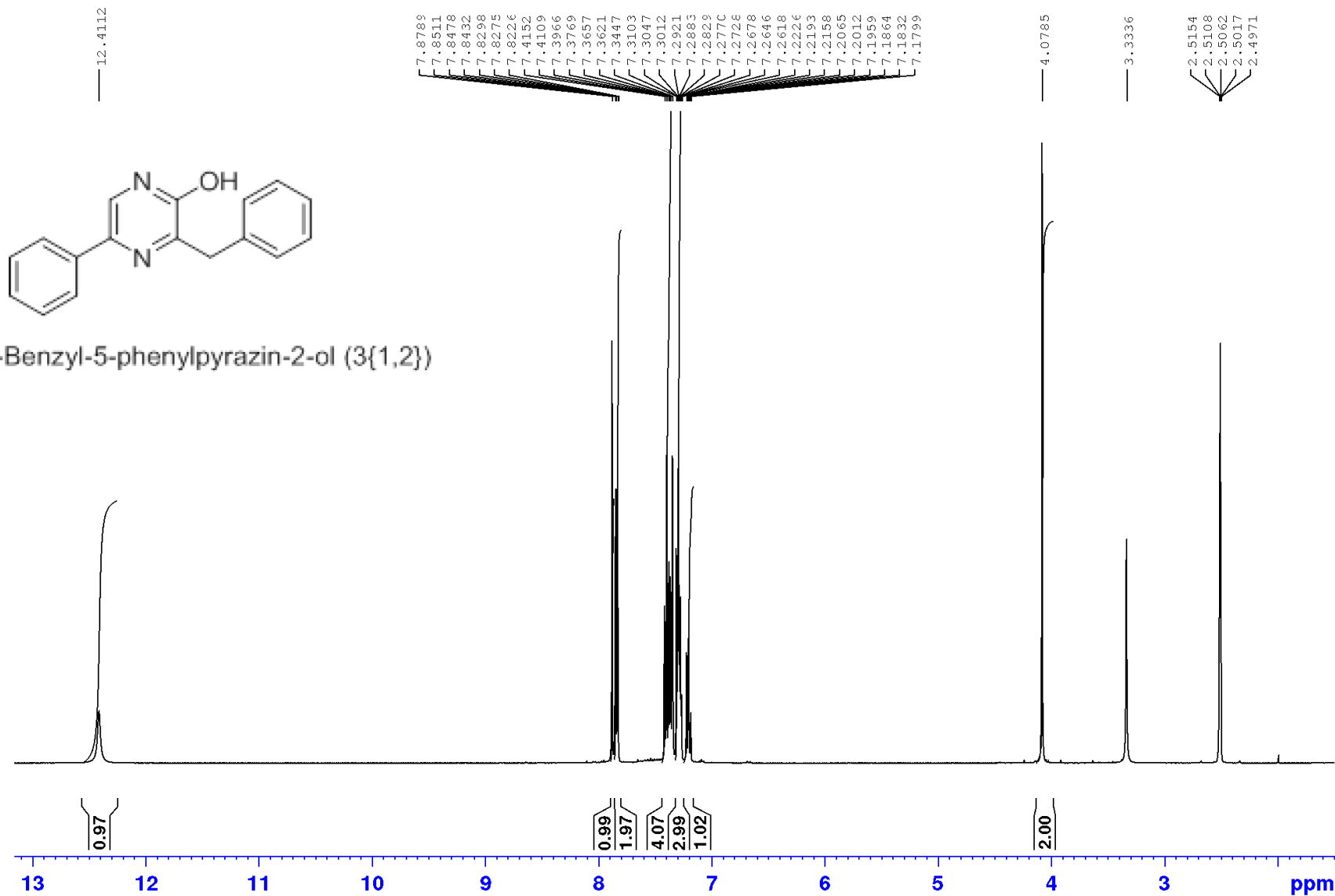
3-Methyl-6-phenylpyrazin-2-ol (4{1,1})

2.5016
2.0745
2.0690
2.0634
2.0579
2.0524





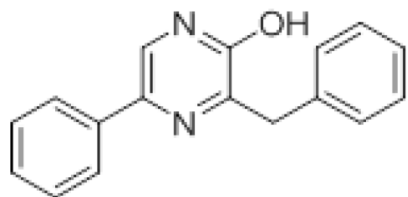
3-Benzyl-5-phenylpyrazin-2-ol (3{1,2})



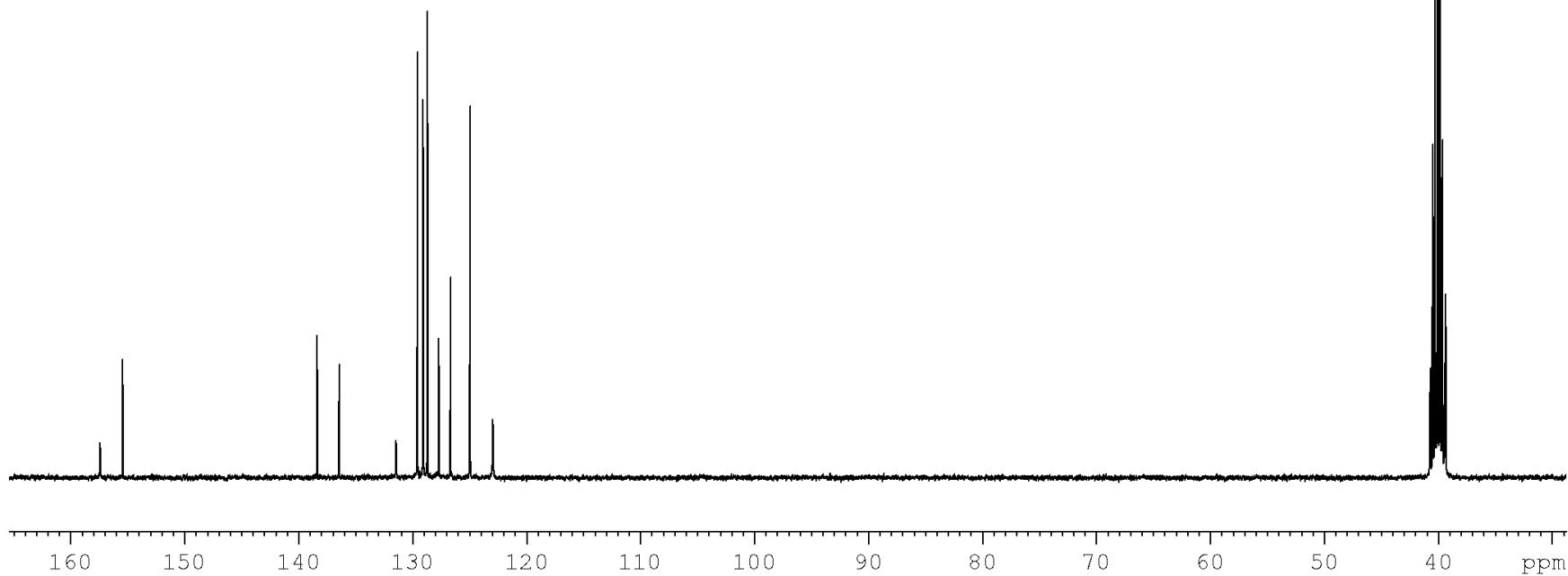
157.416
155.426

138.370
136.433
131.436
129.563
129.344
129.056
128.683
127.687
126.659
124.943
122.938

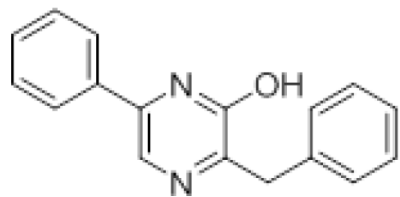
40.660
40.451
40.243
40.034
39.825
39.617
39.408
39.300



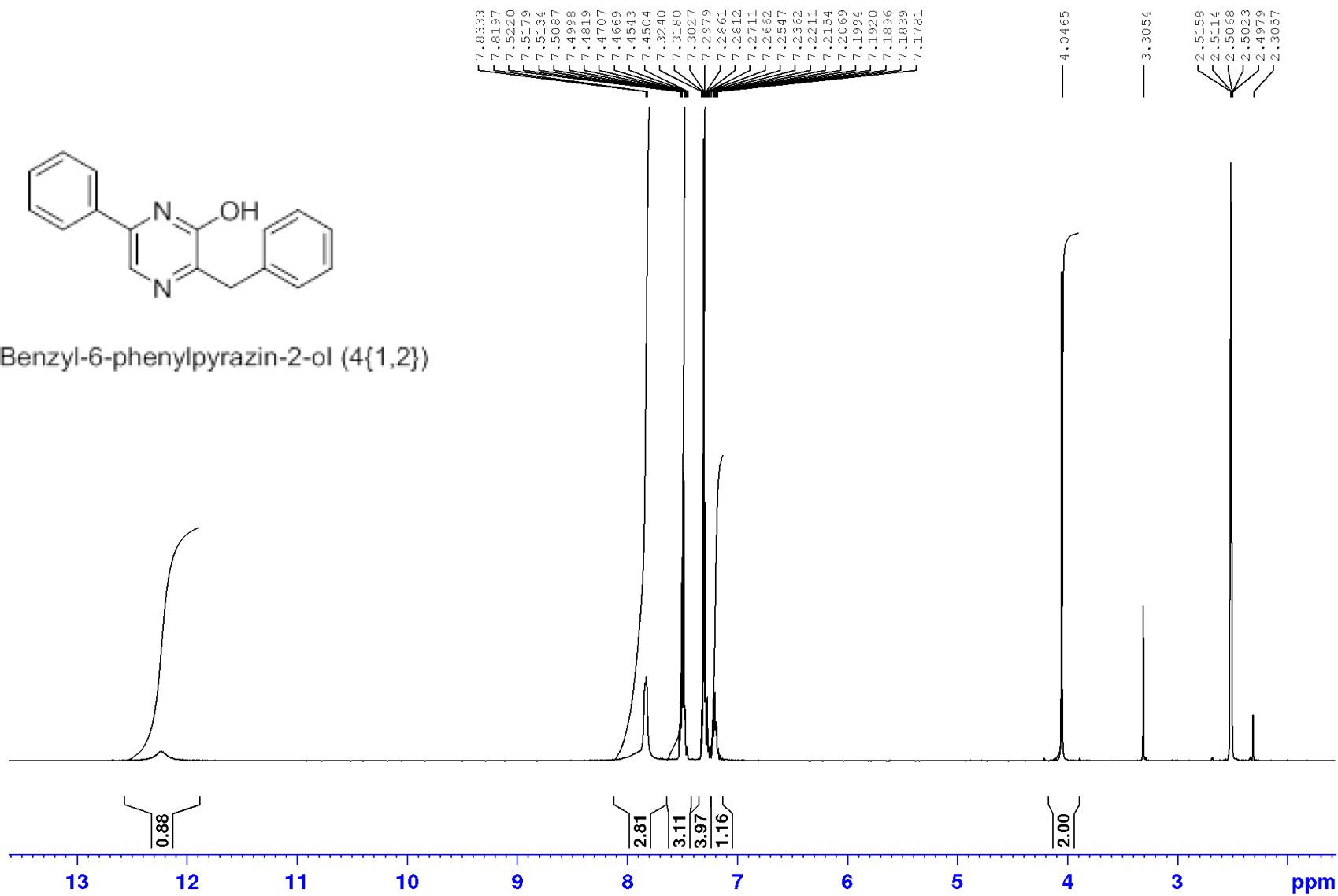
3-Benzyl-5-phenylpyrazin-2-ol (3{1,2})

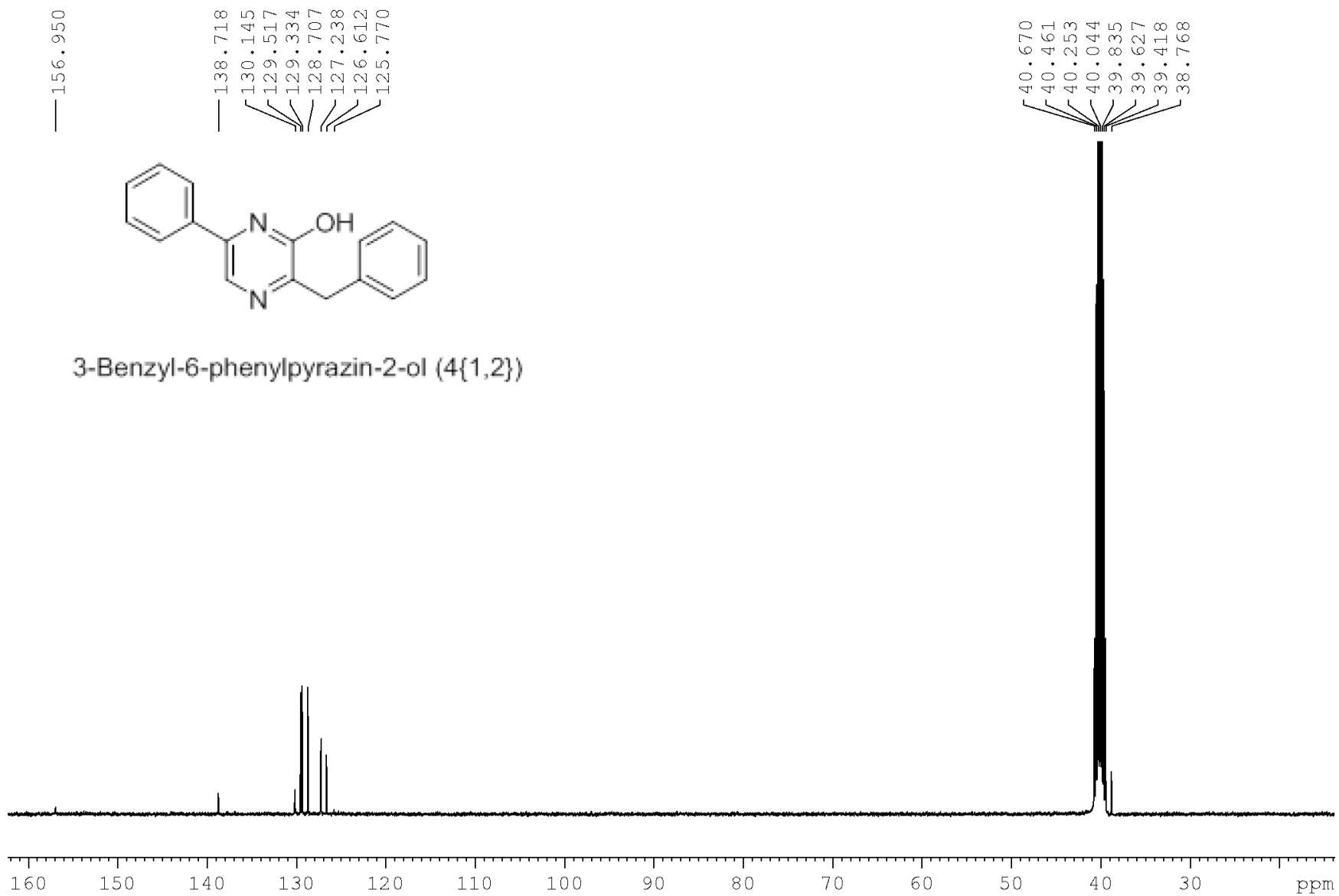


3-Benzyl-6-phenylpyrazin-2-ol (4{1,2})

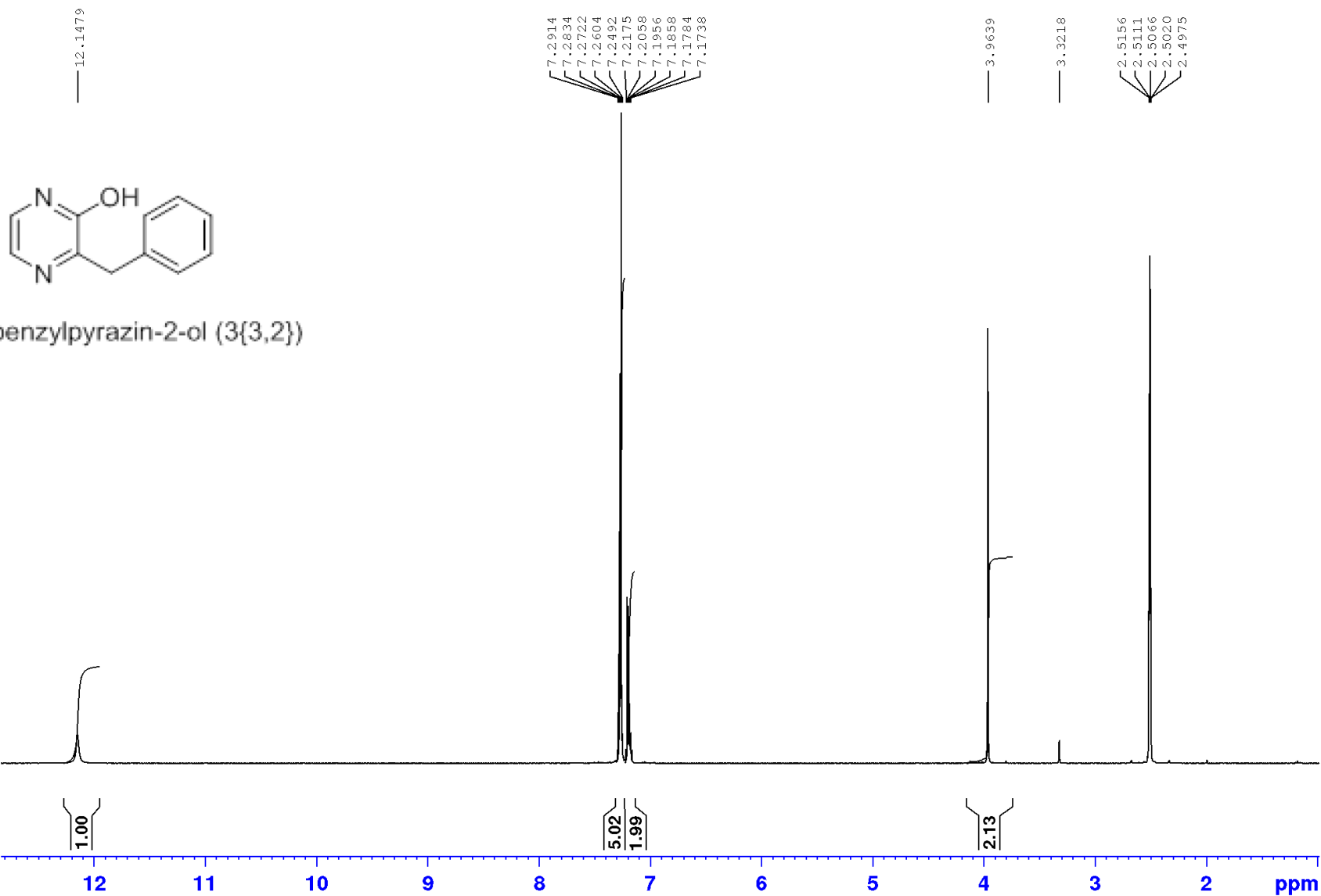


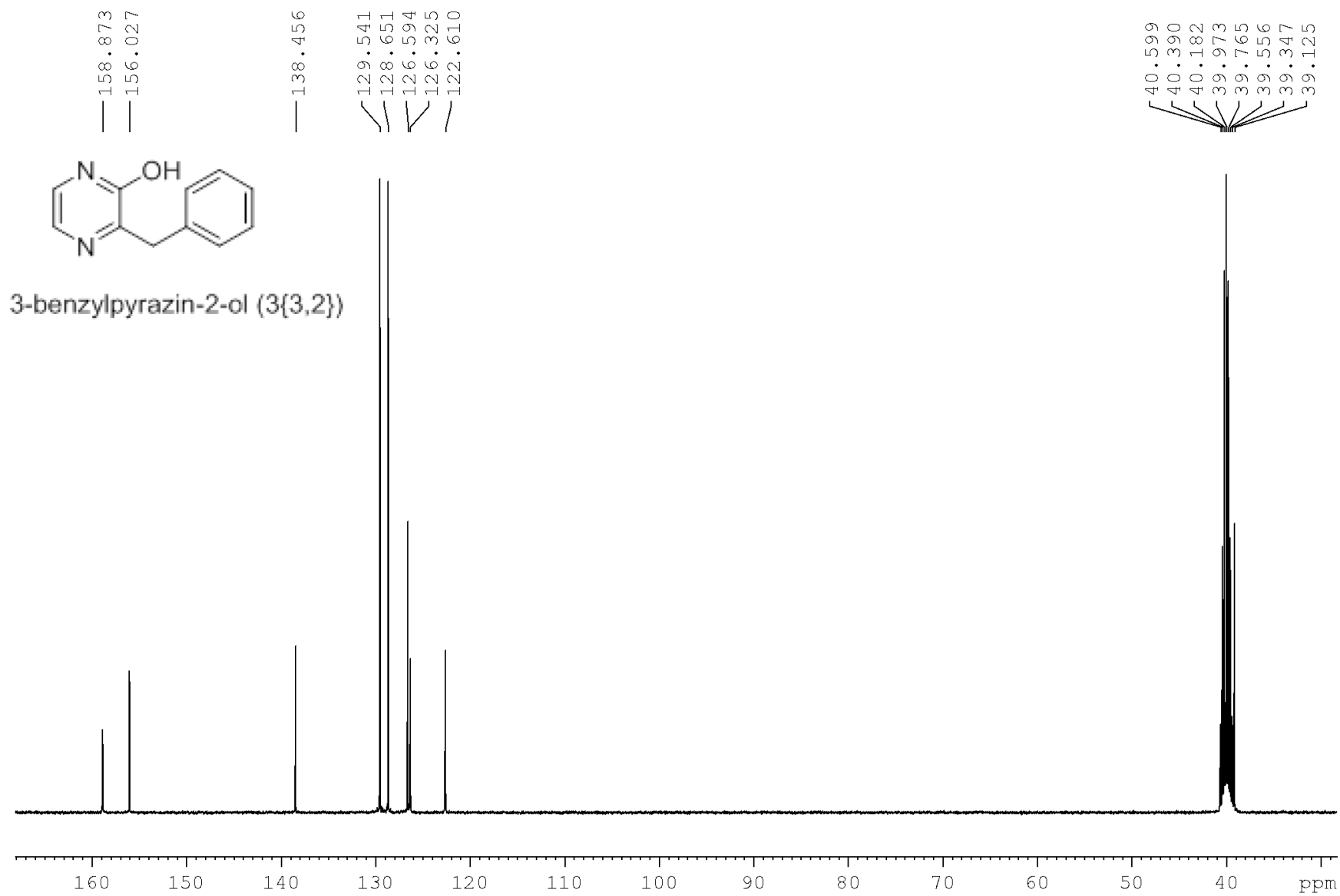
3-Benzyl-6-phenylpyrazin-2-ol (4{1,2})



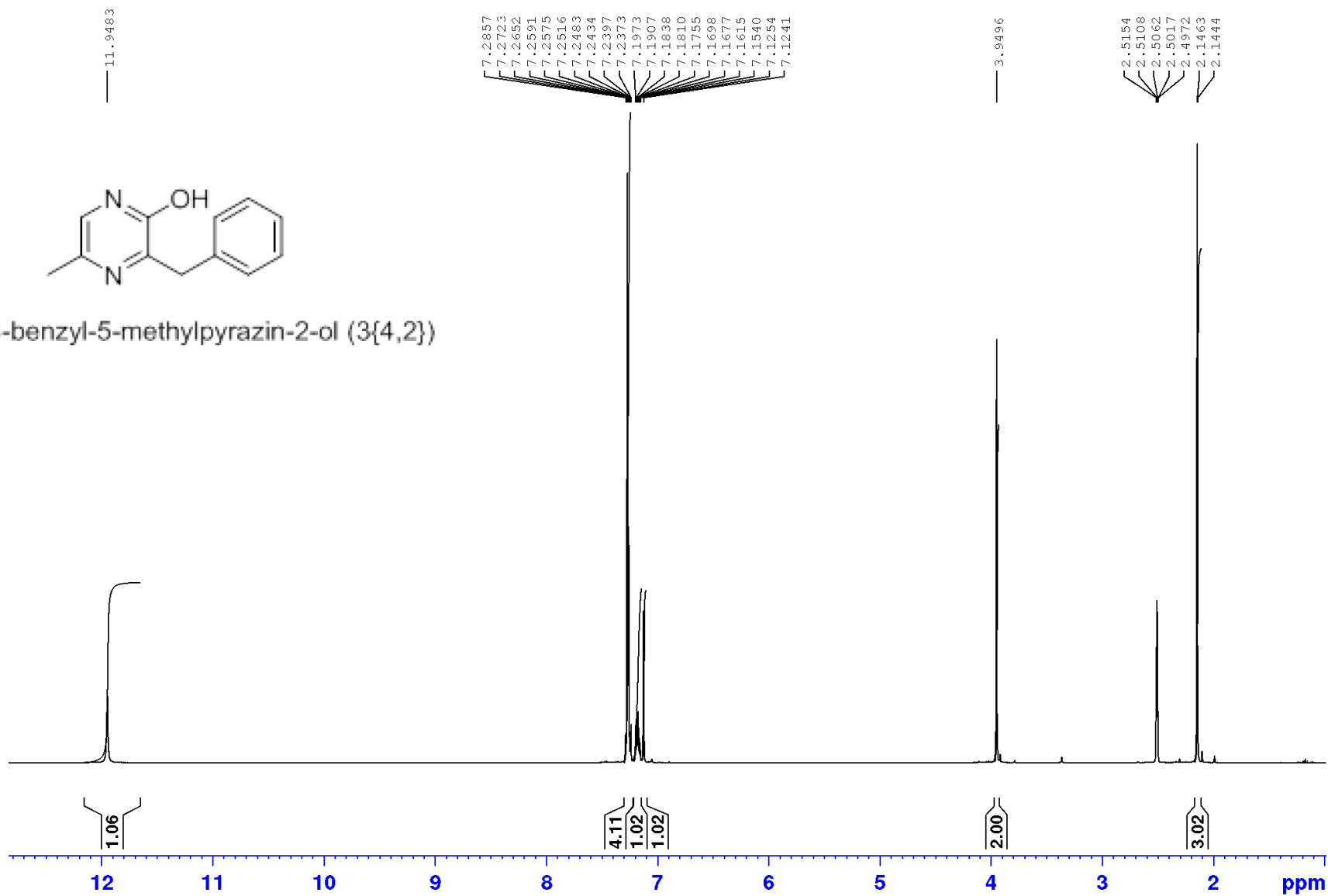


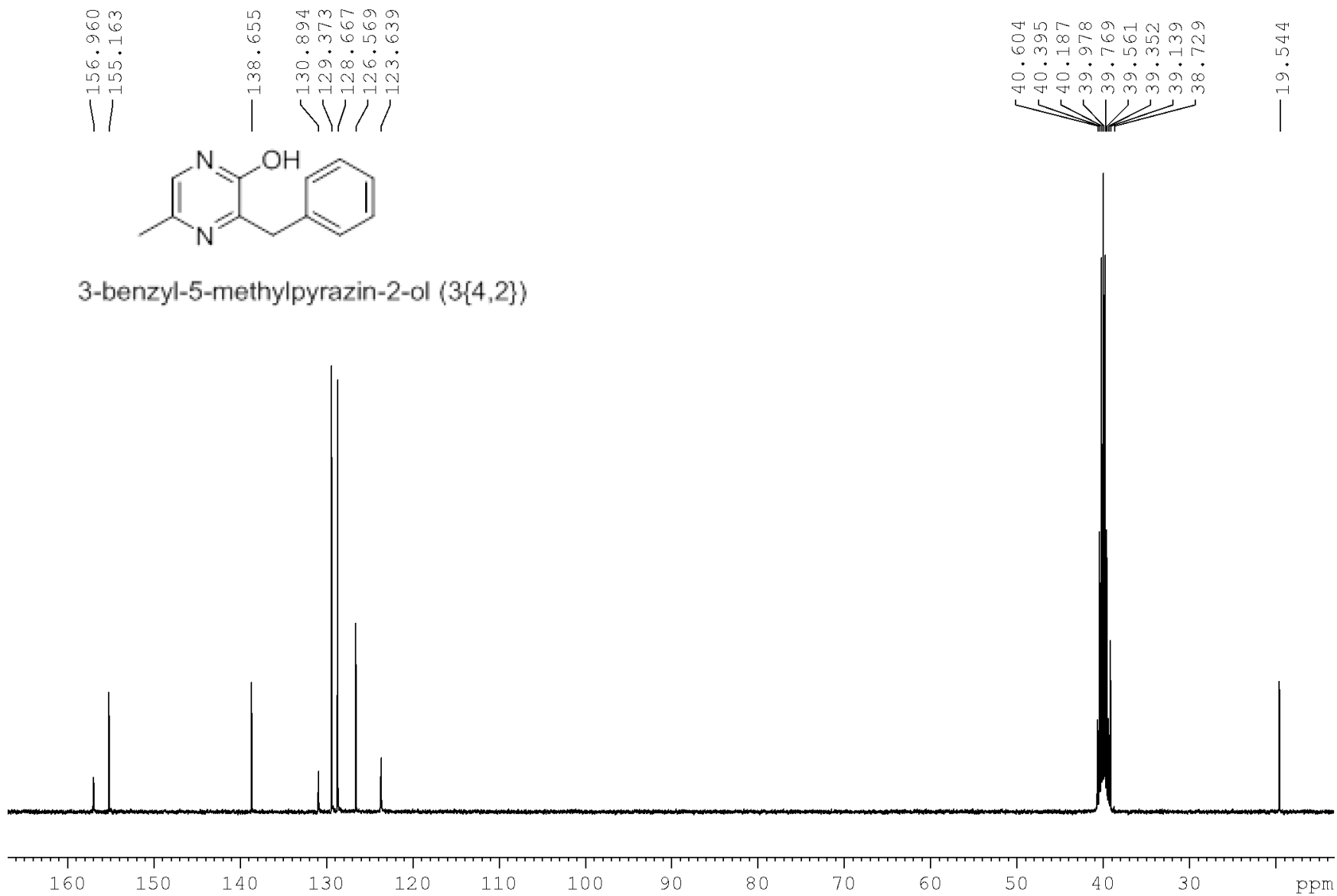
3-Benzylpyrazin-2-ol (3{3,2})



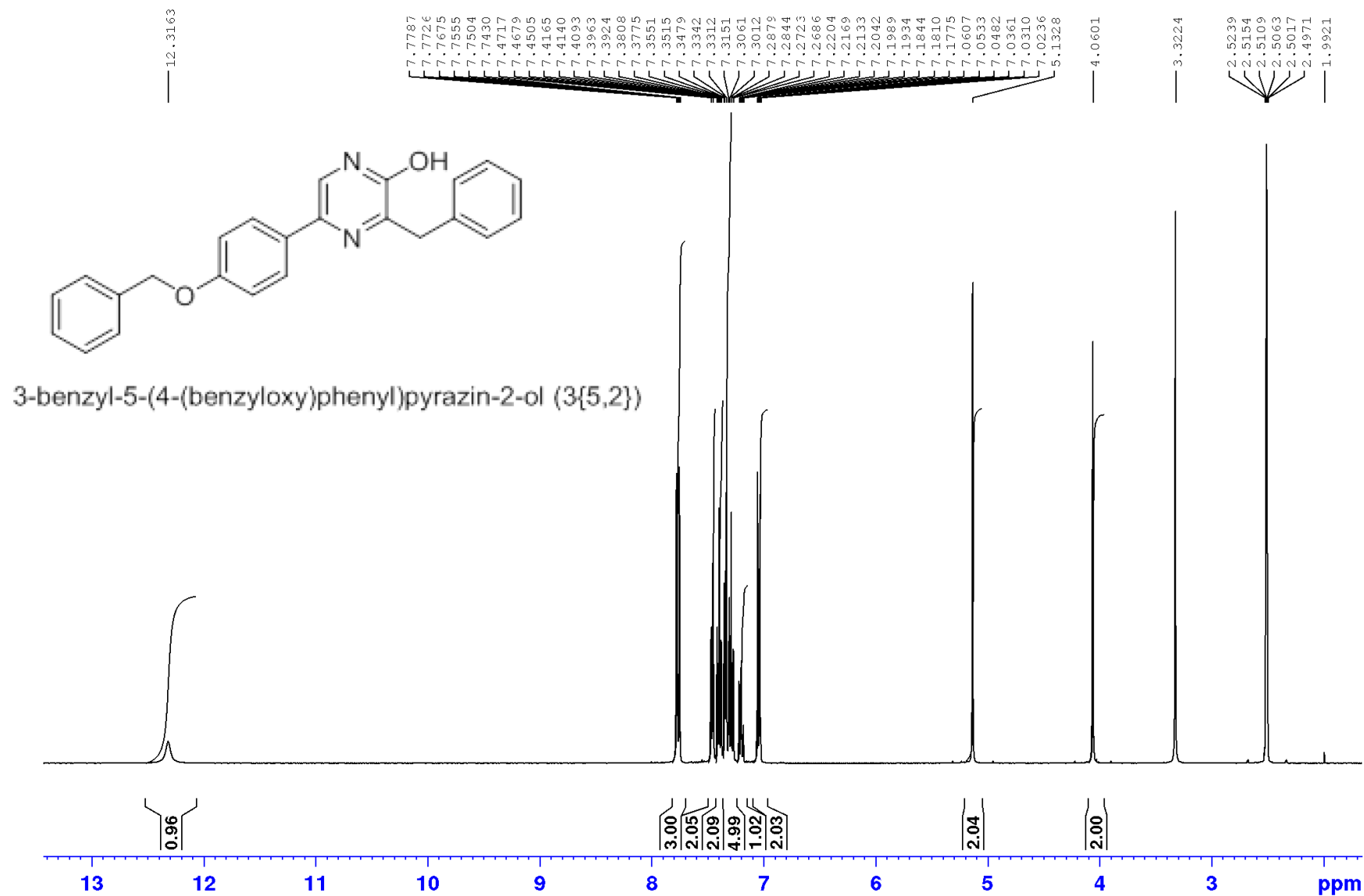


3-Benzyl-5-methylpyrazin-2-ol (3{4,2})





3-Benzyl-5-(4-(benzyloxy)phenyl)pyrazin-2-ol (3{5,2})

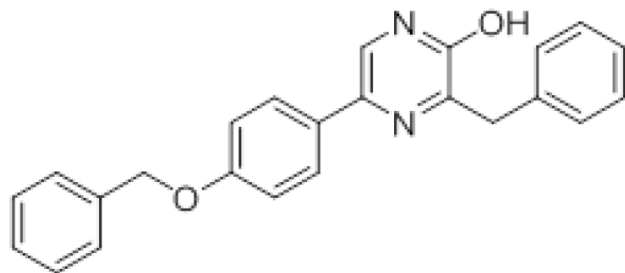


158.296
157.051
155.267

138.443
137.543
131.712
129.548
129.279
128.881
128.674
128.262
128.107
126.636
126.305
121.964
115.441

69.725

40.663
40.454
40.245
40.037
39.828
39.620
39.411
39.277



3-benzyl-5-(4-(benzyloxy)phenyl)pyrazin-2-ol (3{5,2})

