

Glaser–Hay hetero-coupling in bimetallic regime: Ni(II)/Ag(I) assisted base, ligand and additive free route to selective unsymmetrical 1,3-diynes

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Experimental

Materials

Pre-coated silica gel 60F₂₅₄ was used for thin layer chromatography and silica gel 60-120 mesh was used for column chromatography. Nickel Acetate hydrate, Silver Triflate and other reagents were purchased from common commercial sources and were used without further purification. All chemicals were purchased from commercial sources and used as received. Solvents were dried by conventional methods and distilled prior to use. The functionalised starting material alkynes have been prepared following the reported procedures and have been characterised and confirmed by ¹H NMR spectroscopy.

Instrumentation

All inert reactions were carried out under aerobic condition. UV-Vis spectra were recorded by using a Perkin Elmer Lambda 35 spectrophotometer. ¹H NMR spectra were acquired on a Bruker Avance III 400 spectrometer using CDCl₃ solvent. ¹H chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance as the internal standard (deuteriochloroform: δ 7.26 ppm). Data are reported as follows: chemical shifts, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, br = broad, dd = double doublet, m = multiplet), coupling constant (Hz). ¹³C chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance as the internal standard (CDCl₃: δ 77.0 ppm).

Catalytic Studies

General procedure for C-C coupling of heteroalkynes:

A dry test tube with rubber septum and magnetic stirrer bar was charged with 1 mmol of aryl terminal alkyne **1** (1 mmol), propargyl alcohol **2** (2 mmol) along with Ni(OAc)₂·4H₂O, AgOTf catalysts (10 mol % each) and 1 ml of N,N-dimethyl formamide (DMF). The reaction mixture was stirred in a preheated oil bath maintained at 110 °C for the appropriate time mentioned. Reaction was quenched by adding excess methylene chloride. After removal of solvent the mixture was subjected to preparatory thin layered chromatography using petroleum ether/ethylacetate (4:1) as eluent.

¹H NMR studies on the interaction of Ni(II) and Ag(I) with alkynes:

¹H NMR spectra were recorded in CDCl₃ or DMSO-d₆. 1,3,5-trimethoxy benzene (hereafter TMB) was used as internal standard.

General Procedure for interaction of Ag(I) with alkynes:

Representative spectra of phenyl acetylene **1a** (0.05 mmol, 1 equivalent) and 2-methylbut-3-yn-2-ol **2c** (0.05 mmol, 1 equivalent) with TMB (0.05 mmol, 1 equivalent) are shown in Figure S-2a and S-3a.

(a) Silver(I) Acetylide Formation with Phenyl acetylene (1a):

In a NMR tube phenyl acetylene **1a** (0.05mmol, 1 equivalent) and AgOTf(0.05 mmol, 1 equivalent) were mixed in CDCl₃. An insoluble white precipitate of silver acetylide immediately formed and settled down. The CDCl₃ was decanted off and DMSO-d₆ solution containing TMB was added to the solid mass, shaken vigorously to dissolve and ¹H NMR was recorded immediately (Figure S-2b).

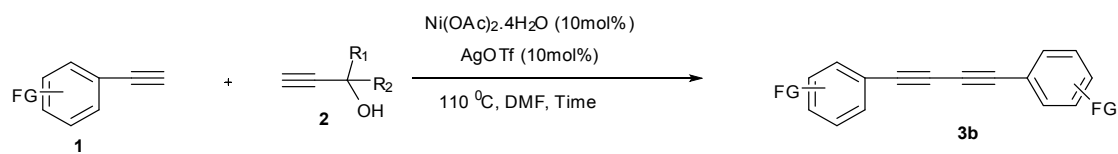
(b) ¹H NMR of a mixture of Ag(I) and 2-methylbut-3-yn-2-ol (2c):

In a NMR tube 2-methylbut-3-yn-2-ol **2c** (0.05 mmol, 1 equivalent), TMB and AgOTf (0.05 mmol, 1 equivalent) were mixed in CDCl₃ and shaken vigorously. The ¹H NMR spectrum was recorded after formation of a clear solution (Figure S-3b).

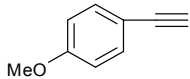
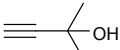
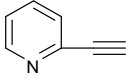
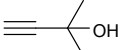
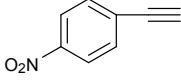
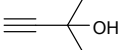
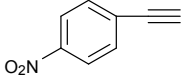
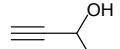
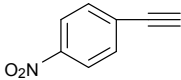
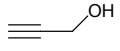
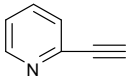
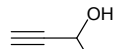
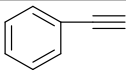
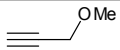
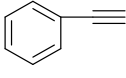
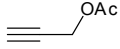
General procedure for the interaction of Ni(II) with 2-methylbut-3-yn-2-ol (2c):

¹H NMR spectrum of 2-methylbut-3-yn-2-ol **2c** (0.05 mmol, 1 equivalent) with TMB was recorded in DMSO-d₆. Ni(OAc)₂·4H₂O (0.1 mmol, 1 equivalent) was weighed and divided into 5 equal parts. To the solution of **2c** and TMB as above, Ni(OAc)₂·4H₂O was added incrementally; 0.02 mmol each time, and vigorously shaken to obtain a clear solution. ¹H NMR of the resulting solution was recorded each time. The five spectra thus obtained are shown in Figure S-4 and S-5a to S-5e.

Table TS1: Isolated yield of the corresponding homo-coupled symmetrical diynes.



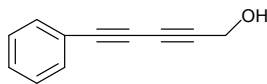
Entry	1	2	3(%)	Time (h)
1			11	3
2			14	4.5
3			19	5
4			12	12
5			17	3.5
6			17	5
7			21	6
8			11	12
9			14	3
10			10	4
11			11	12
12			11	16
13			10	6
14			10	12

15			11	12
16			3	16
17			10	12
18			20	12
19			19	8
20			10	16
21			9	8
22			12	8

^aReaction condition: Arylalkyne 1 (0.25 mmol), alcohol 2 (0.5 mmol), [Ag] (10 mol%), [Ni] (10 mol%), solvent (1 ml), 110° C, air

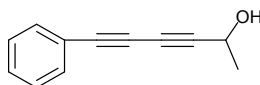
NMR Spectroscopic Data for Products:

3a: ¹



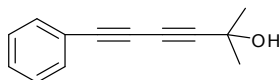
Yellow Solid (Isolated yield = 87 %). ¹H NMR (400MHz, CDCl₃, ppm): δ 7.50 (d, 2H, 4), 7.35 (m, 3H), 4.42 (s, 2H), 1.98 (s, 1H). ¹³C NMR (100MHz, CDCl₃, ppm): δ 51.78, 70.58, 73.29, 78.73, 80.58, 121.51, 128.56, 129.49, 132.73. Melting Point 41-42 °C

3b:



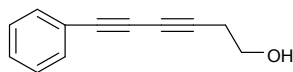
Yellow liquid (Isolated yield = 70 %). ¹H NMR (400MHz, CDCl₃, ppm): δ 7.49 (d, 2H, 8), 7.33 (m, 3H), 4.66 (q, 1H), 1.57 (s, 1H), 1.49 (d, 3H, 4). ¹³C NMR (100MHz, CDCl₃, ppm): δ 24.00, 58.07, 68.86, 73.10, 78.75, 83.98, 121.48, 128.43, 129.30, 132.56.

3c: ⁴



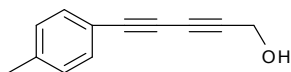
Brown Solid (Isolated yield = 76 %). ¹H NMR (400MHz, CDCl₃, ppm): δ 7.46 (d, 2H, 8), 7.33 (m, 3H), 2.01 (s, 1H), 1.55 (s, 6H). ¹³C NMR (100MHz, CDCl₃, ppm): δ 31.27, 65.91, 67.21, 73.27, 78.96, 86.82, 121.70, 128.57, 129.39, 132.67. Melting Point 59-61 °C

3d:



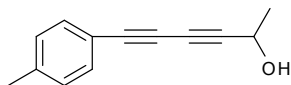
Yellow liquid (Isolated yield = 70 %). ¹H NMR (400MHz, CDCl₃, ppm): δ 7.47 (d, 2H, 8), 7.34 (m, 3H), 3.80 (t, 2H), 2.65 (t, 2H), 1.72 (s, br, 1H). ¹³C NMR (100MHz, CDCl₃, ppm): δ 24.17, 25.50, 60.94, 67.04, 74.08, 75.55, 81.10, 121.90, 128.53, 129.19, 132.70.

3e: ^{5,6}



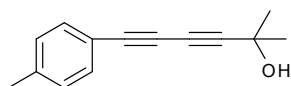
Yellow Solid (Isolated yield = 70 %). ^1H NMR (400MHz, CDCl_3 , ppm): δ 7.38 (d, 2H, 8), 7.13 (d, 2H, 8), 4.41 (s, 2H), 2.35 (s, 3H), 1.82 (s, br, 1H). ^{13}C NMR (100MHz, CDCl_3 , ppm): δ 21.75, 51.84, 70.76, 72.70, 79.06, 80.22, 118.38, 129.36, 132.67, 139.93. Melting Point 80.5-82 °C

3f: ³



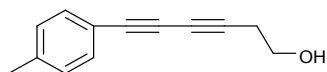
Brown Oil (Isolated yield = 74 %). ^1H NMR (400MHz, CDCl_3 , ppm): δ 7.31 (d, 2H, 8), 7.06 (d, 2H, 8), 4.59 (q, 1H), 2.29 (s, 3H), 1.64 (s, br, 1H), 1.45 (d, 3H, 8), ^{13}C NMR (100MHz, CDCl_3 , ppm): δ 21.73, 24.15, 59.03, 69.09, 72.65, 79.17, 83.82, 118.46, 129.34, 132.61, 139.85.

3g: ⁴



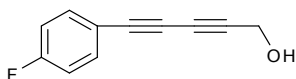
Yellow Solid (Isolated yield = 63 %). ^1H NMR (400MHz, CDCl_3 , ppm): δ 7.38 (d, 2H, 8), 7.12 (d, 2H, 8), 2.35 (s, 3H), 2.10 (s, br, 1H), 1.58 (s, 6H). ^{13}C NMR (100MHz, CDCl_3 , ppm): δ 21.73, 31.28, 65.89, 67.34, 72.66, 79.25, 86.49, 118.56, 129.34, 132.58, 139.79. Melting Point 75-76 °C

3h:



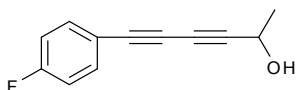
Yellow oil (Isolated yield = 65 %). ^1H NMR (400MHz, CDCl_3 , ppm): δ 7.31 (d, 2H, 8), 7.06 (d, 2H, 8), 3.72 (t, 2H), 2.57 (t, 2H, 12), 2.29 (s, 3H), 1.82 (s, br, 1H). ^{13}C NMR (100MHz, CDCl_3 , ppm): δ 21.72, 24.15, 60.95, 67.13, 73.44, 75.81, 80.70, 118.73, 129.31, 132.60, 139.56.

3i:⁵



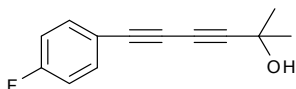
Yellow Solid (Isolated yield = 79 %). ¹H NMR (400MHz, CDCl₃, ppm): δ 7.42 (d, 2H, 8), 6.95 (t, 2H, 8), 4.35 (s, 2H), 1.81 (s, 1H). ¹³C NMR (100MHz, CDCl₃, ppm): δ 51.78, 70.45, 73.09, 80.58, 115.91, 116.14, 117.62, 134.75, 134.84, 162.00, 164.50. Melting Point 84.5-86.5 °C.

3j:



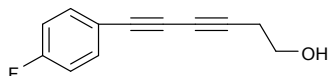
Yellow Solid (Isolated yield = 74 %). ¹H NMR (400MHz, CDCl₃, ppm): δ 7.44 (dd, 2H, 8), 6.99 (t, 2H, 16), 4.65 (q, 1H), 2.05 (s, br, 1H), 1.52 (d, 3H, 4). ¹³C NMR (100MHz, CDCl₃, ppm): δ 24.12, 59.02, 68.82, 73.04, 77.77, 84.14, 115.91, 116.13, 117.69, 117.72, 134.70, 134.78, 161.97, 164.47. Melting Point 92.5-94 °C

3k: ^{2,4}



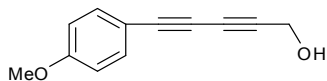
Yellow Solid (Isolated yield = 73 %). ¹H NMR (400MHz, CDCl₃, ppm): δ 7.47 (dd, 2H, 12), 7.02 (t, 2H, 12, 8), 1.99 (s, br, 1H), 1.58 (s, 6H). ¹³C NMR (100MHz, CDCl₃, ppm): δ 29.85, 31.26, 65.90, 115.91, 116.13, 134.66, 134.74, 159.8. Melting Point 110-111.5 °C

3l: ²



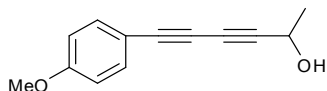
Yellow Solid (Isolated yield = 60 %). ¹H NMR (400MHz, CDCl₃, ppm): δ 7.44 (d, 2H, 12), 7.00 (t, 3H, 16), 3.77 (t, 2H, 12), 2.61 (t, 2H, 12), 1.90 (s, br, 1H). ¹³C NMR (100MHz, CDCl₃, ppm): δ 24.14, 60.90, 66.86, 73.89, 74.44, 81.17, 115.84, 116.07, 118.06, 134.65, 134.74, 161.84, 164.33. Melting Point 74.5-76 °C.

3m: ⁵



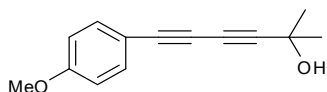
Yellow Solid (Isolated yield = 78 %). ¹H NMR (400MHz, CDCl₃, ppm): δ 7.43 (d, 2H, 8), 6.84 (d, 2H, 16), 4.41 (s, 1H), 3.81 (s, 3H), 1.82 (s, br, 1H). ¹³C NMR (100MHz, CDCl₃, ppm): δ 51.86, 55.49, 70.85, 72.13, 78.99, 80.01, 113.40, 114.28, 134.39, 160.59. Melting Point 92.1-93.6 °C

3n:



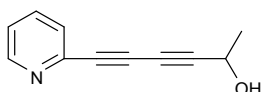
Yellow oil (Isolated yield = 72 %). ¹H NMR (400MHz, CDCl₃, ppm): δ 7.37 (d, 2H, 6), 6.77 (d, 2H, 8), 4.60 (q, 1H), 3.75 (s, 3H), 1.99 (s, 1H), 1.45 (d, 3H). ¹³C NMR (100MHz, CDCl₃, ppm): δ 24.24, 55.49, 59.09, 69.24, 72.09, 79.14, 83.59, 113.52, 114.30, 134.34, 160.59.

3o: ⁴



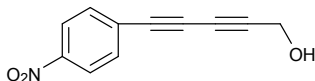
Reddish Brown Solid (Isolated yield = 75 %). ¹H NMR (400MHz, CDCl₃, ppm): δ 7.44 (m, 2H), 6.84 (d, 2H, 8), 3.82 (s, 3H), 1.58 (s, 3H), 2.04 (s, 1H) 1.85 (d, 6H). ¹³C NMR (100MHz, CDCl₃, ppm): δ 19.16, 29.70, 31.17, 55.34, 65.77, 114.15, 134.05, 134.05, 134.14, 160.25. Melting Point 67-68.5 °C

3p: ⁴



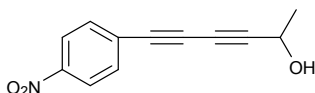
Brown oil (Isolated yield = 60 %). ^1H NMR (400MHz, CDCl_3 , ppm): δ 8.63 (d, 1H, 4), 7.69 (dt, 1H, 8), 7.55 (dt, 1H, 8), 7.29 (dd, 1H, 16), 4.67 (q, 1H), 1.65 (s, 3H). ^{13}C NMR (100MHz, CDCl_3 , ppm): δ 51.86, 55.49, 70.85, 72.13, 78.99, 80.01, 113.40, 114.28, 134.39, 160.59.

3q:



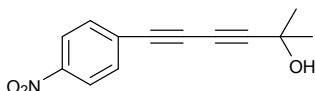
Yellow Solid (Isolated yield = 71 %) ^1H NMR (400MHz, CDCl_3 , ppm): δ 8.19 (d, 2H, 8), 7.62 (d, 2H, 8), 4.45 (s, 2H), 1.80 (s, 1H). ^{13}C NMR (100MHz, CDCl_3 , ppm): δ 51.64, 69.73, 76.05, 78.05, 81.49, 83.25, 123.58, 123.93, 128.35, 133.37, 133.43, 147.62. Melting Point 167.5-168.5 $^\circ\text{C}$

3r:



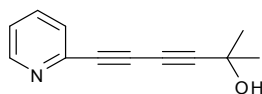
Yellow Solid (Isolated yield = 75 %) ^1H NMR (400MHz, CDCl_3 , ppm): δ 8.21 (d, 2H, 16), 7.62 (d, 2H, 12), 4.68 (q, 1H), 2.0 (s, 1H), 1.54 (d, 3H, 8). ^{13}C NMR (100MHz, CDCl_3 , ppm): δ 51.76, 69.86, 76.19, 78.18, 83.38, 123.81, 123.93, 128.48, 133.50, 133.56, 147.74. Melting Point 136.5-138 $^\circ\text{C}$

3s:⁴



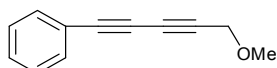
Yellow Solid (Isolated yield = 80 %) ^1H NMR (400MHz, CDCl_3 , ppm): δ 8.19 (d, 2H, 8), 7.56 (d, 2H, 12), 2.05 (s, br, 1H), 1.59 (s, 6H) ^{13}C NMR (100MHz, CDCl_3 , ppm): δ 23.9, 58.80, 68.92, 70.02, 84.14, 89.68, 126.92, 128.67, 134.48, 147.69. Melting Point 108-109 $^\circ\text{C}$

3t:⁴



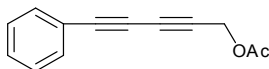
Yellow Solid (Isolated yield = 60 %). ^1H NMR (400MHz, CDCl_3 , ppm): δ 8.63 (d, 1H, 4), 7.70 (dt, 1H, 8,8), 7.55 (td, 1H, 8), 7.30 (m, 1H), 1.61 (s, 6H). ^{13}C NMR (100MHz, CDCl_3 , ppm): δ 29.15, 66.3, 73.36, 80.90, 81.04, 123.79, 128.43, 136.21, 141.93, 150.55. Melting Point 114.5-115.2 $^\circ\text{C}$

3u¹



Yellow Oil (Isolated yield = 65 %). ^1H NMR (400MHz, CDCl_3 , ppm): δ 7.50 (d, 2H, 8), 7.34 (m, 3H), 4.25 (s, 2H), 3.43 (s, 3H). ^{13}C NMR (100MHz, CDCl_3 , ppm): δ 58.12, 60.51, 71.21, 73.62, 78.25, 78.80, 121.61, 128.63, 129.52, 132.81.

3v¹



Yellow Oil (Isolated yield = 70 %). ^1H NMR (400MHz, CDCl_3 , ppm): δ 7.49 (d, 2H, 8), 7.36 (m, 3H), 4.82 (s, 2H), 2.12 (s, 3H). ^{13}C NMR (100MHz, CDCl_3 , ppm): δ 20.56, 52.56, 76.43, 78.92, 121.46, 128.59, 129.37, 132.87, 170.22.

UV-vis spectrometry on the interaction of Ni(II) and Ag(I) with Alkyne:

As shown in Figure S-1 below, the UV-vis spectrum of nickel acetate was markedly altered upon the addition of propargyl alcohol. Similarly, the spectrum of silver acetate was affected upon the addition of phenyl acetylene.

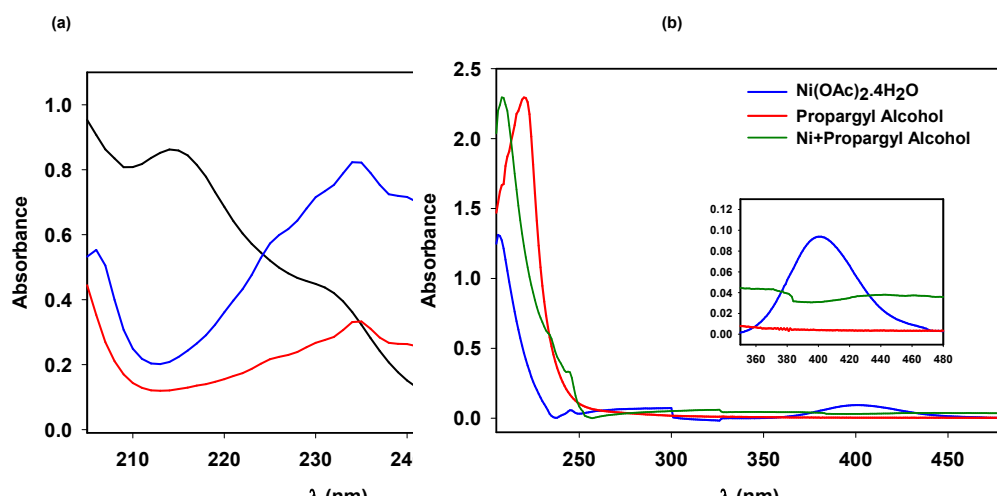


Figure S-1: (a) UV spectrum of AgOTf, AgOTf + phenyl acetylene and phenyl acetylene, (b) UV-Vis spectrum of nickel acetate, propargyl alcohol and Ni(II) + propargyl alcohol.

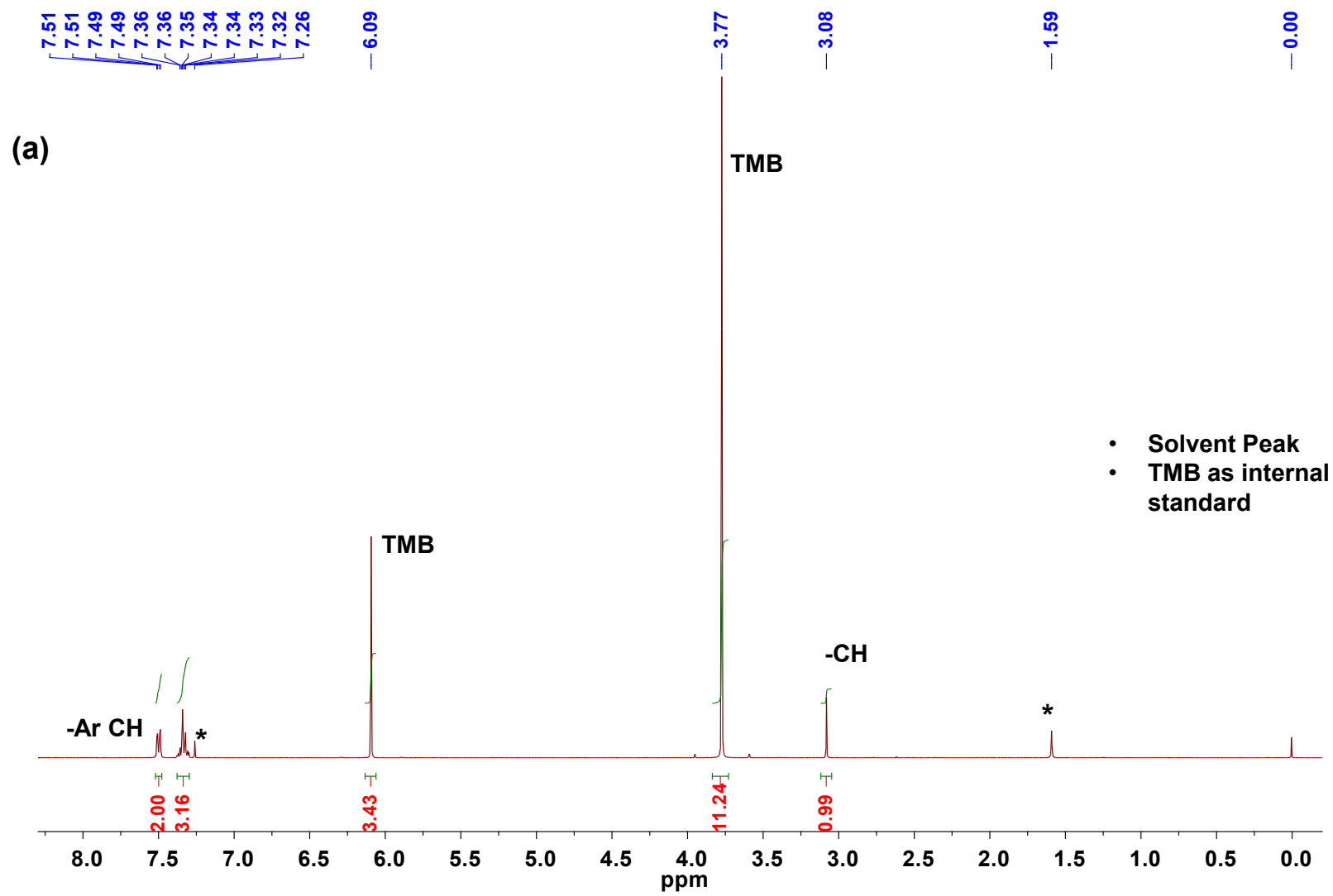


Figure S-2(a): ^1H NMR Spectra of phenyl acetylene with TMB in CDCl_3

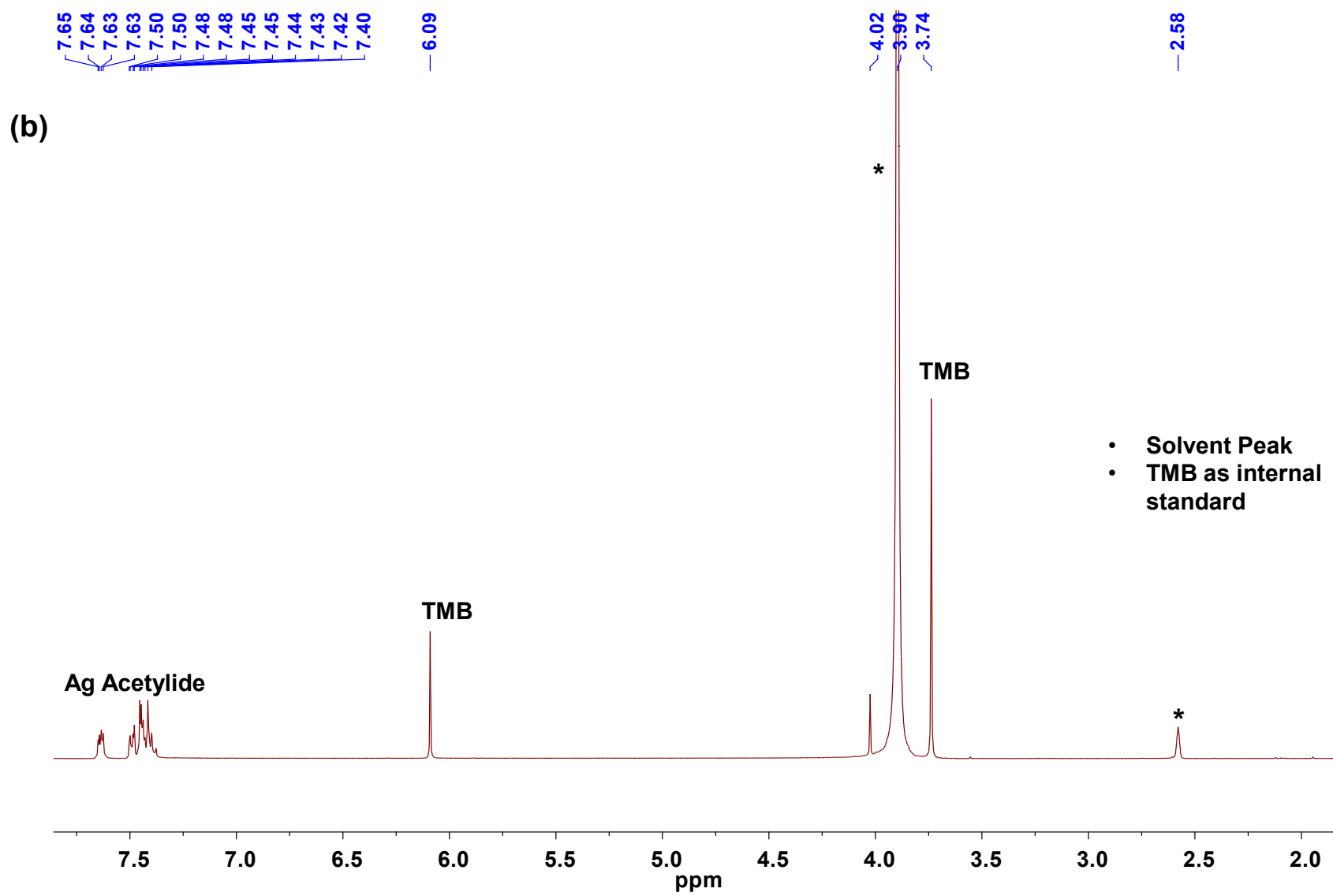


Figure S-2(b): ^1H NMR Spectra of white precipitate from the reaction of phenyl acetylene and AgOTf (see experimental section for details)

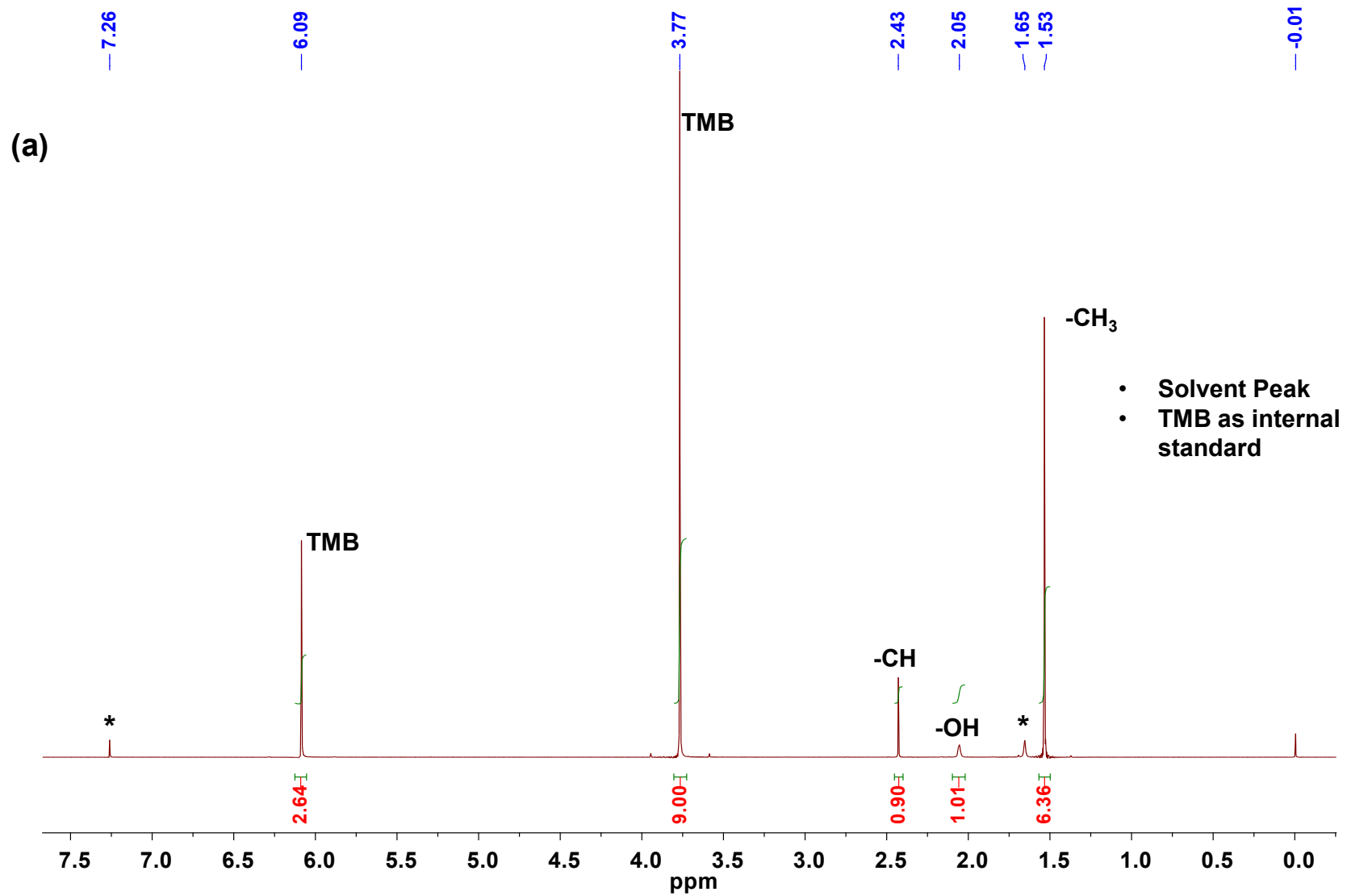


Figure S-3(a): ¹H NMR Spectra of 2-methylbut-3-yn-2-ol 2c with TMB in CDCl₃

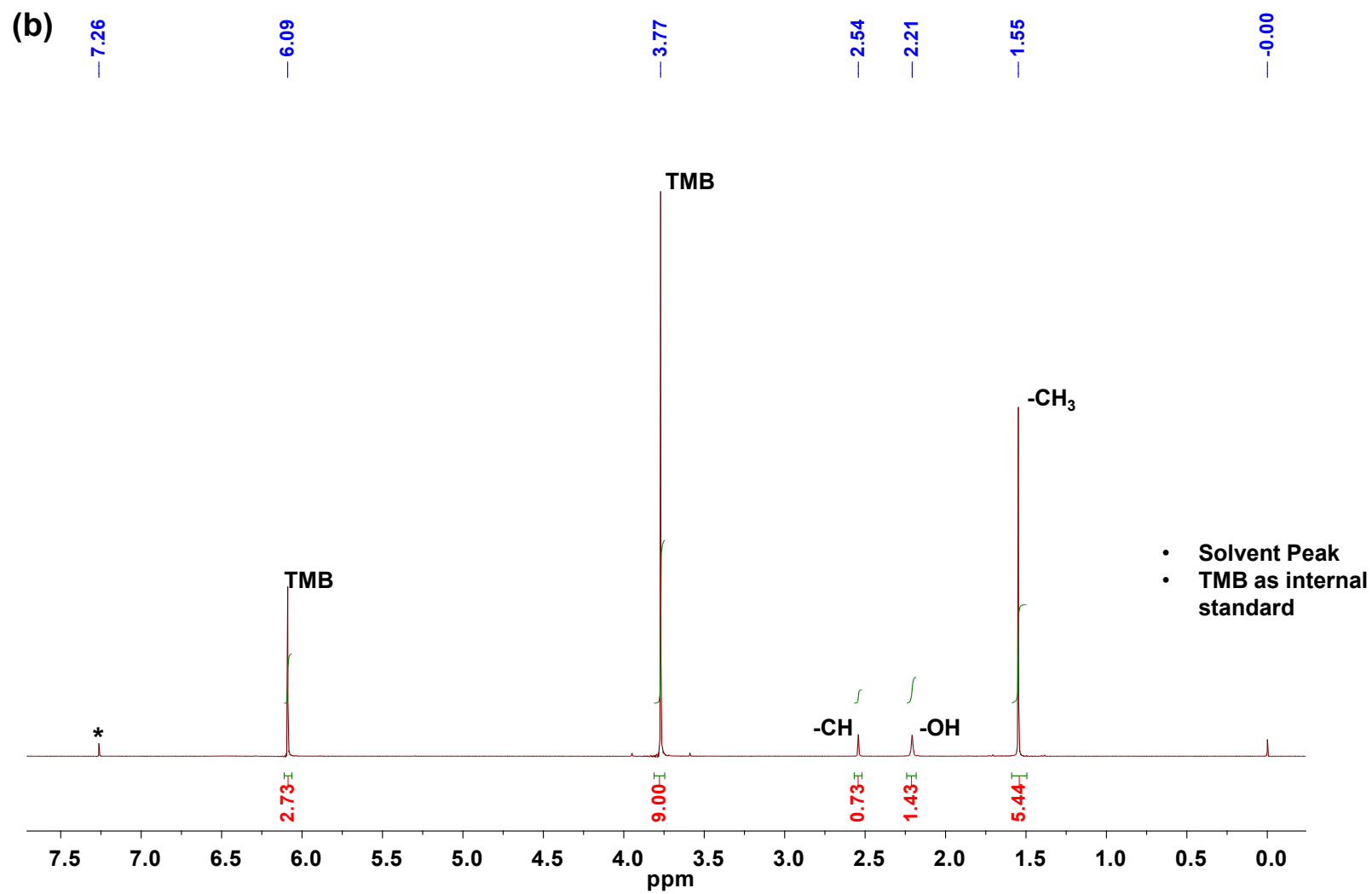


Figure S-3(b): ¹H NMR Spectra of 2-methylbut-3-yn-2-ol **2c** and AgOTf with TMB in CDCl₃

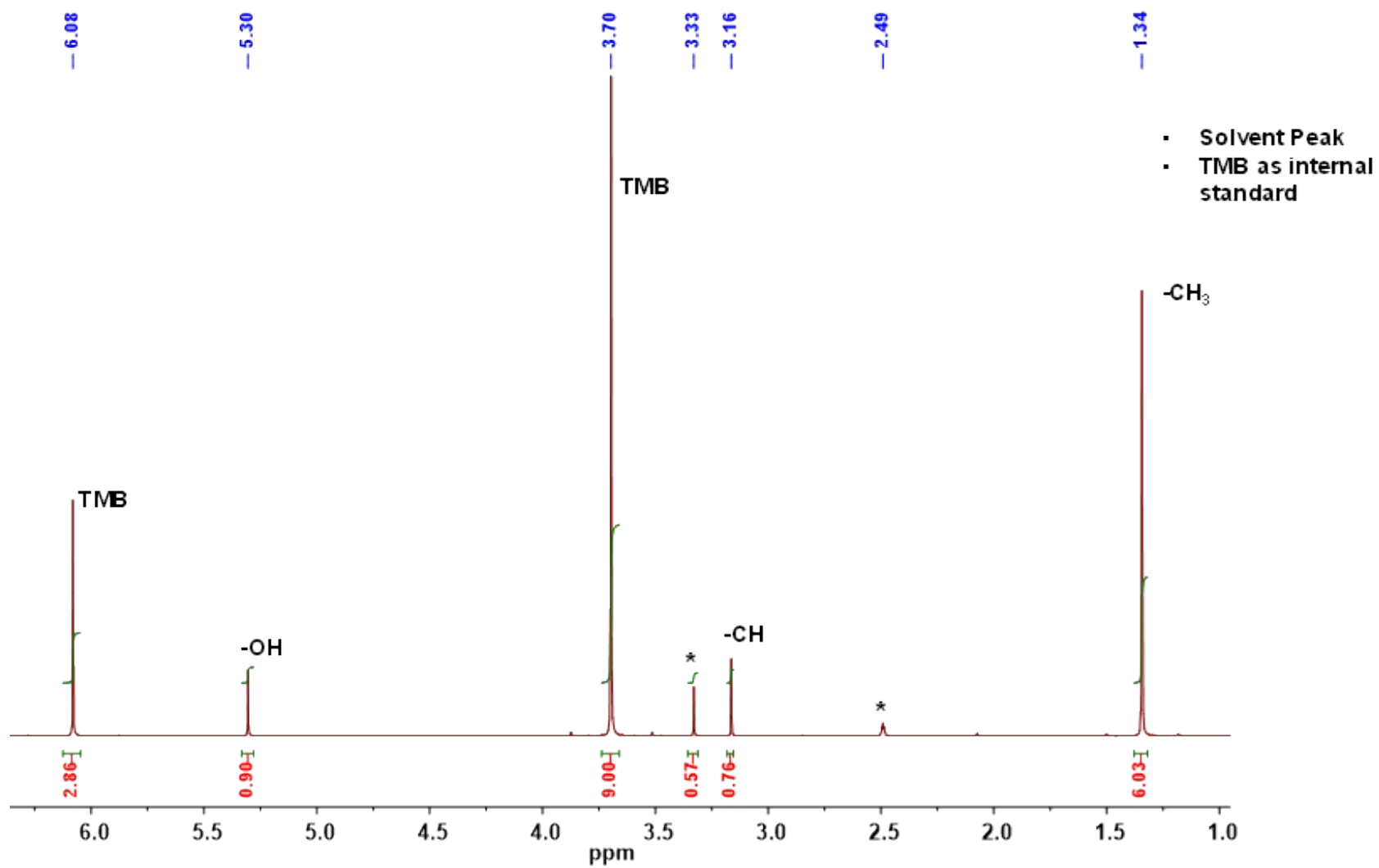


Figure S-4: ¹H NMR Spectra 2-methylbut-3-yn-2-ol **2c** with TMB in DMSO-d₆

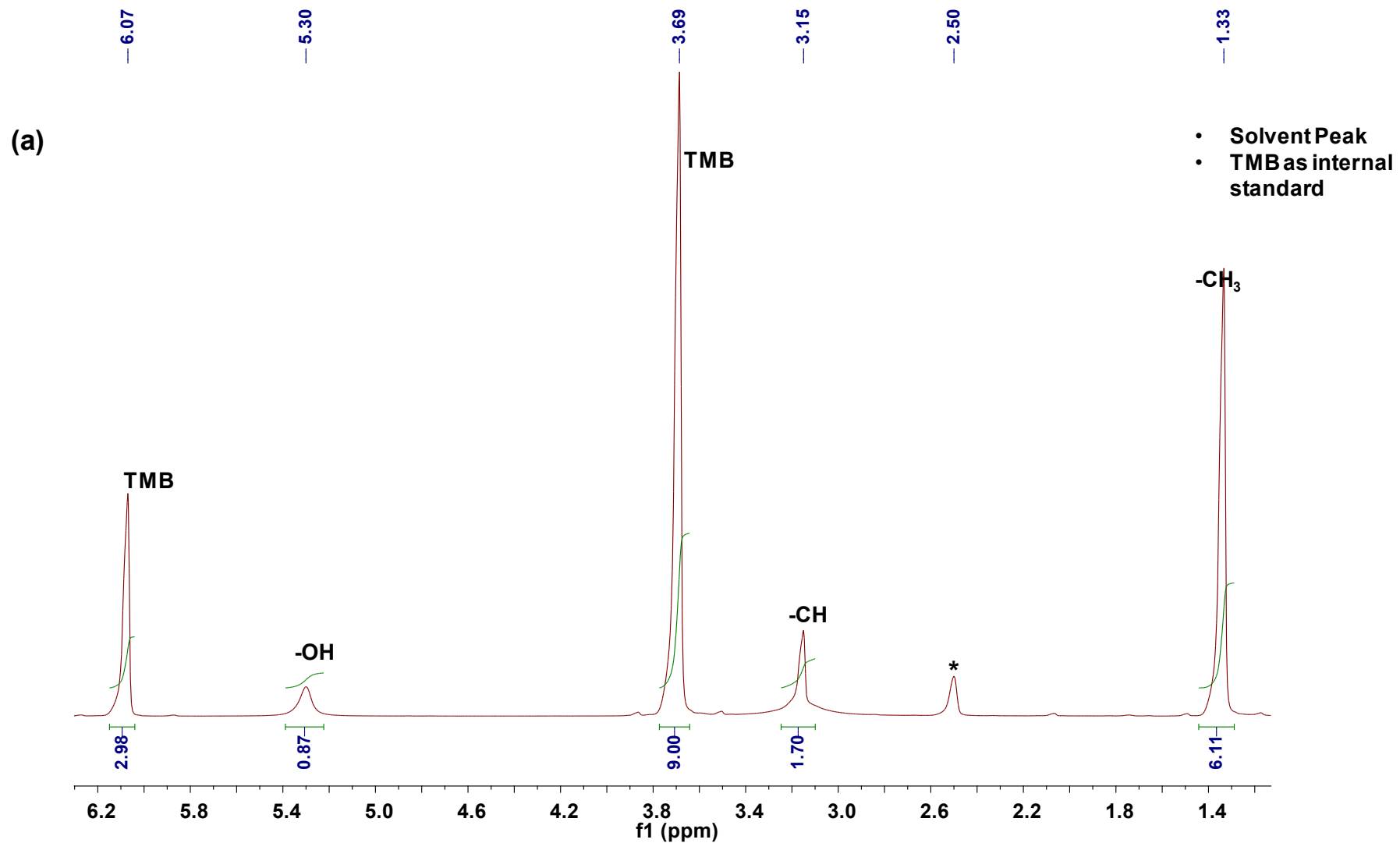


Figure S-5(a): ^1H NMR Spectra of Ni(II) with 2-methylbut-3-yn-2-ol and TMB in DMSO- d_6 (see experimental section for details)

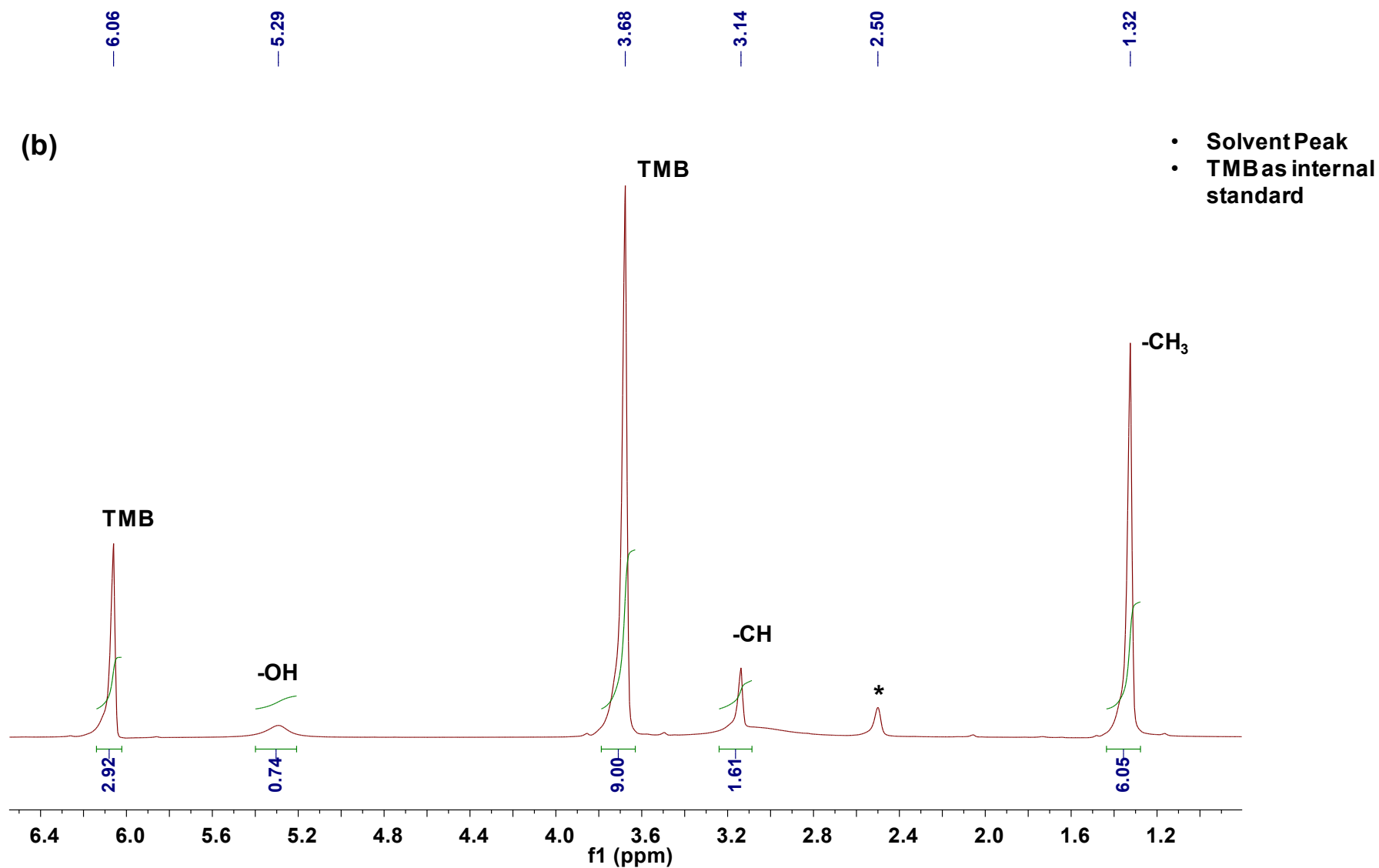


Figure S-5(b): ¹H NMR Spectra of Ni(II) with 2-methylbut-3-yn-2-ol and TMB in DMSO-d₆ (see experimental section for details)

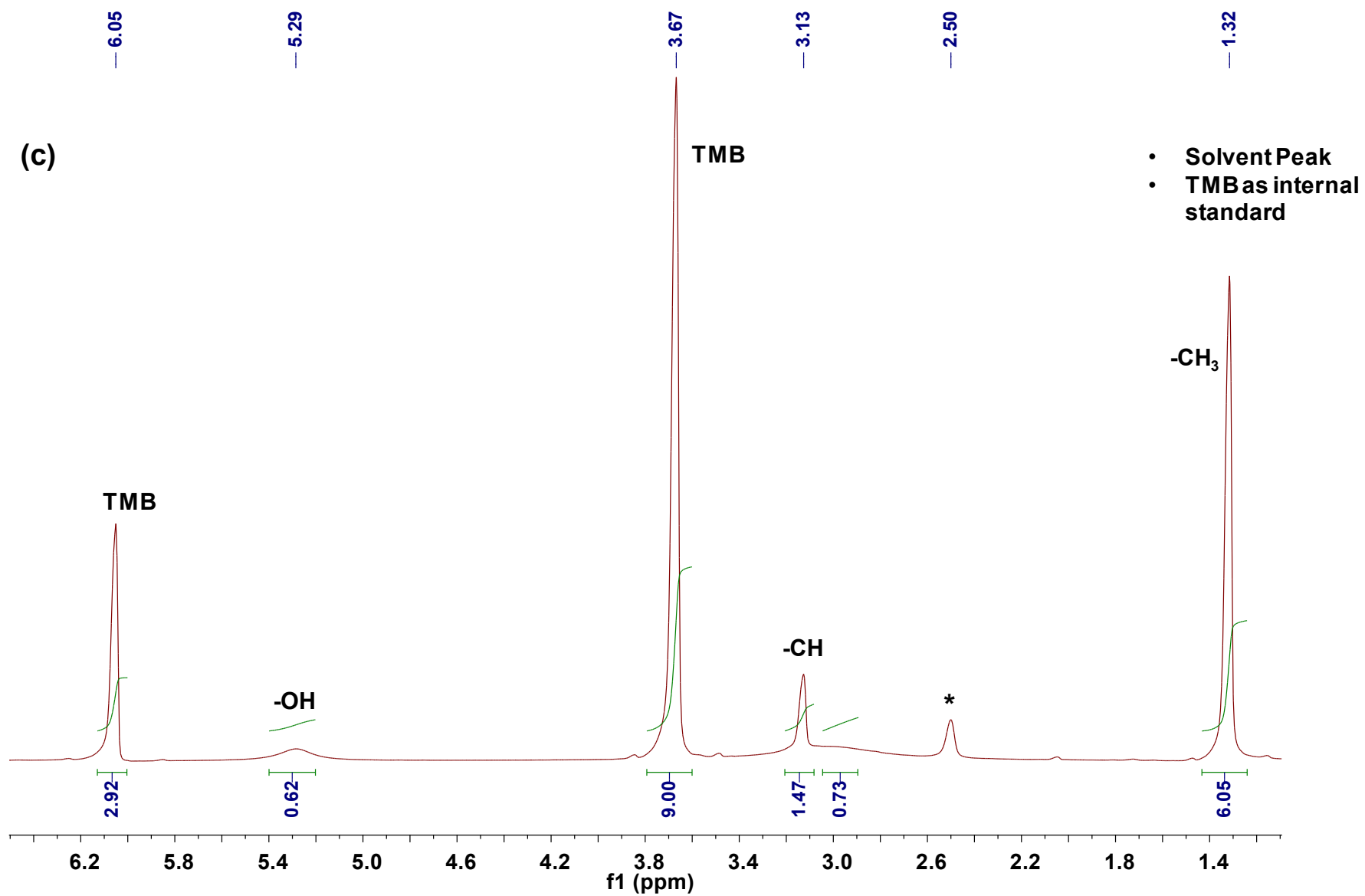


Figure S-5(c): ¹H NMR Spectra of Ni(II) with 2-methylbut-3-yn-2-ol and TMB in DMSO-d₆ (see experimental section for details)

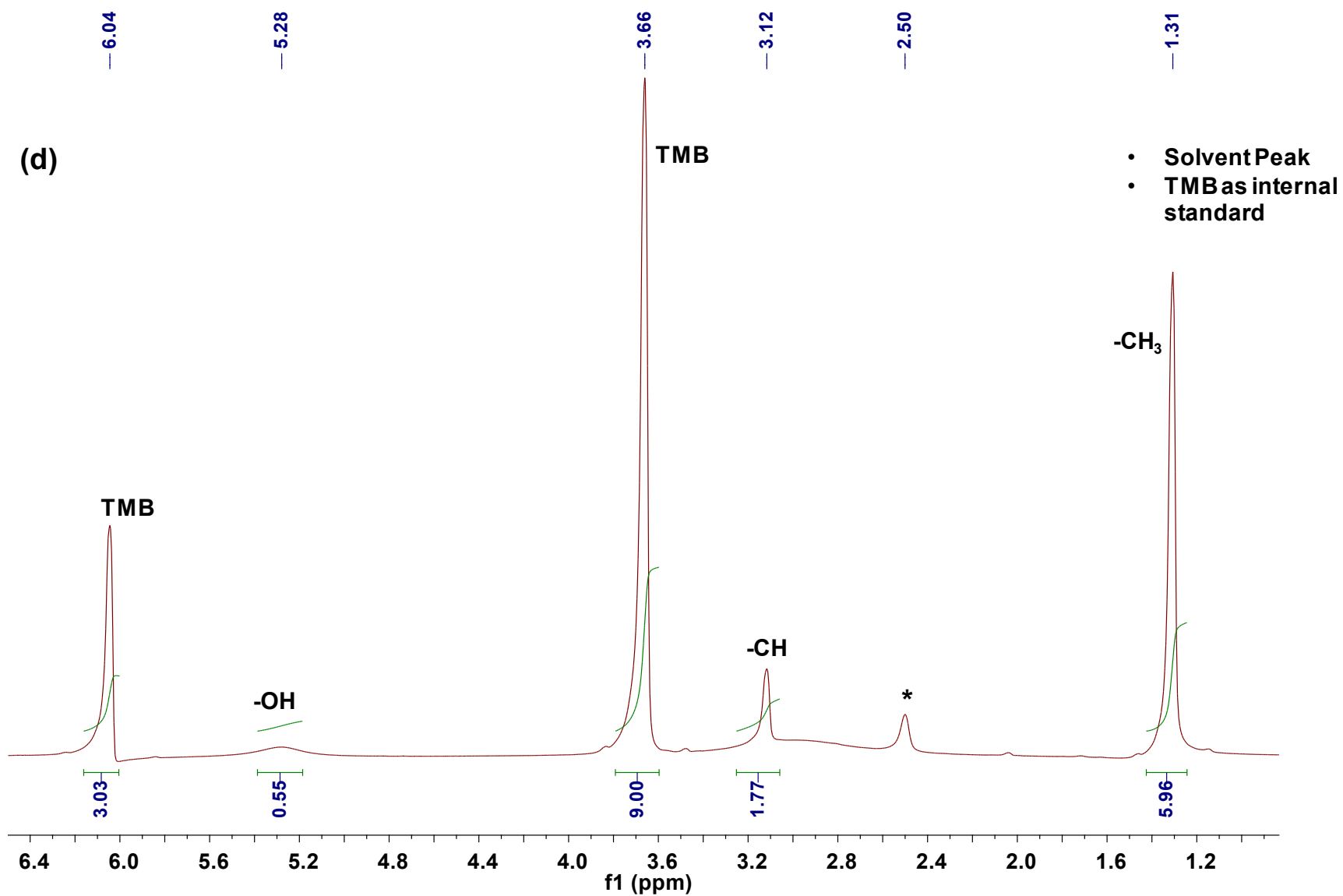


Figure S-5(d): ¹H NMR Spectra of Ni(II) with 2-methylbut-3-yn-2-ol and TMB in DMSO-d₆ (see experimental section for details)

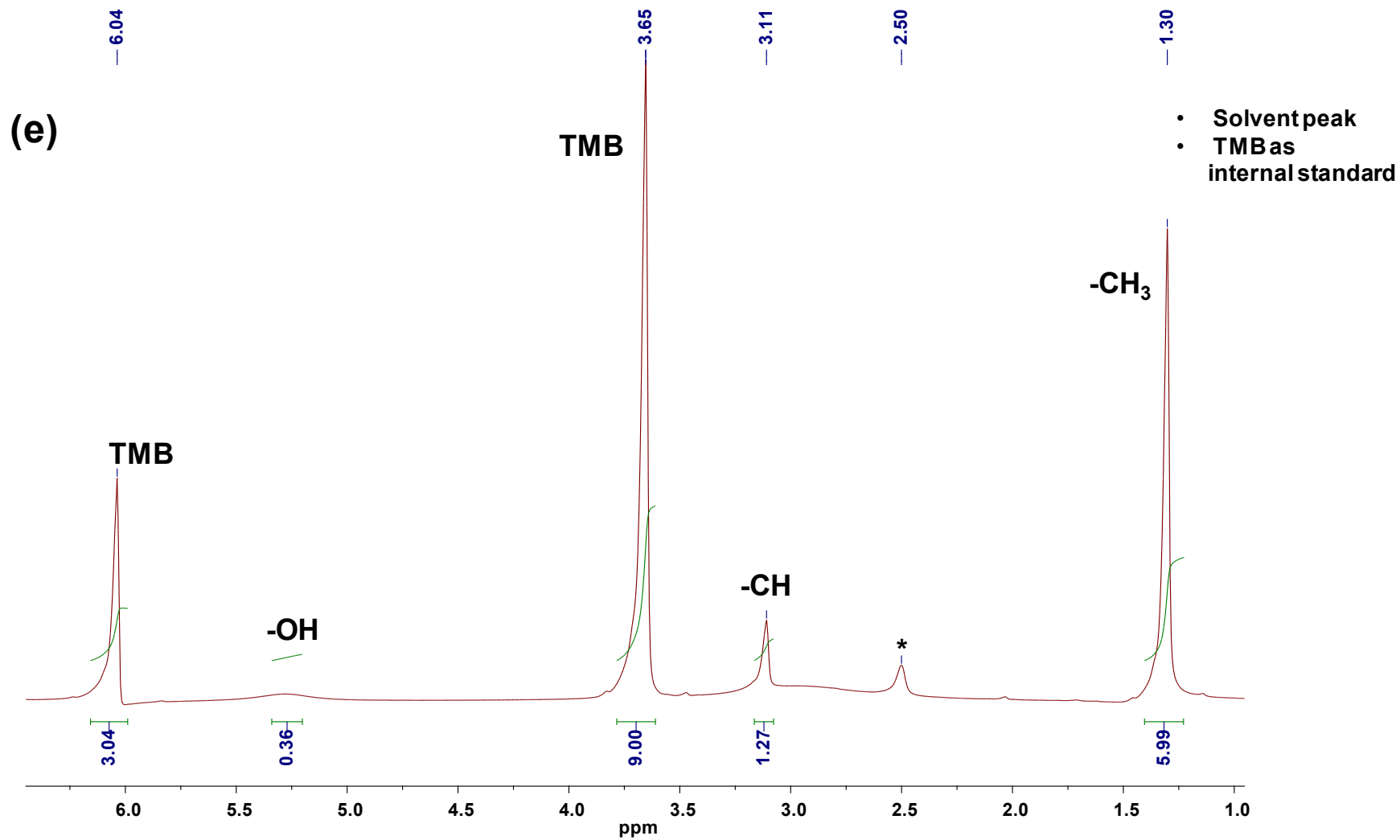


Figure S-5(e): ¹H NMR Spectra of Ni(II) with 2-methylbut-3-yn-2-ol and TMB in DMSO-d₆ (see experimental section for details)

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Representative Spectra

