

## **Antimicrobial toxicity studies of ionic liquids leading to a ‘hit’ *MRSA* selective antibacterial imidazolium salt**

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Electronic Supporting Information

## General Information

All chemicals used were purchased from Sigma Aldrich, with the exceptions of *N*-[(3-dimethylamino)propyl]-*N'*-ethyl carbodiimide hydrochloride (EDC) which were purchased from TCI Europe. Methanol, ethanol, hexane and triethylamine were dried over molecular sieves and distilled before use. 1-Butanol, 1-pentanol, and 1-decanol were dried over molecular sieves and used without further purification. THF and diethyl ether were dried over sodium wire, then sodium benzophenone, and distilled before use. DCM was dried over calcium hydride, and distilled before use. Riedel de Haën silica gel was used for flash and thin layer chromatography.

All NMR analysis was performed on a Bruker AC 400 MHz spectrometer in deuterated chloroform or dimethyl sulfoxide (DMSO- $d_6$ ), operating at 400 MHz for  $^1\text{H}$  NMR and 100 MHz for  $^{13}\text{C}$  NMR. A 600 MHz spectrometer, operating at 600 MHz for  $^1\text{H}$  NMR and 150 MHz for  $^{13}\text{C}$  NMR, was also used for analysis of some examples. Chemical shifts are reported in parts per million (ppm) are relative to the internal standard TMS and coupling constants ( $J$ ) in Hertz (Hz). When stating multiplicity of peaks in NMR the following abbreviations are used; s-singlet, d-doublet, t-triplet, q-quartet, qt-quintet, dd-doublet of doublets, dt doublet of triplets, dq-doublet of quartets, tt-triplet of triplets, tq-triplet of quartets, m-multiplet, br-broad.

Optical rotations were measured using a Perkin Elmer 343 Polarimeter in chloroform, water or ethanol at 20 °C. Melting points were determined using a Griffin melting point apparatus and the values are expressed in degrees celcius (°C). All IR analysis was carried out on a Perkin Elmer 100 FT-IR spectrometer with ATR. The strength of reported peaks are described as weak (w), medium (m), broad (b), strong (s) and very strong (vs). High resolution mass spectrometry was obtained for all bromide ILs. Mass spectrometry analysis was not obtained for the starting materials (namely  $\alpha$ -bromoester and amide intermediates) due to the reactivity and rapid hydrolysis of these compounds. High Resolution Mass Spectrometry (HRMS) was carried out on a Waters Corp. Liquid Chromatography Time of flight mass spectrometer at the Microanalytical Laboratory, University College Dublin or a Waters Micromass LCT Premier mass spectrometer at ABCRF laboratory, University College Cork.

### Antifungal activity

In vitro antifungal activities of the compounds were evaluated on a panel of four ATCC strains (*Candida albicans* ATCC 44859, *Candida albicans* ATCC 90028, *Candida parapsilosis* ATCC 22019, *Candida krusei* ATCC 6258) and eight clinical isolates of yeasts (*Candida krusei* E28, *Candida tropicalis* 156, *Candida glabrata* 20/I, *Candida lusitanae* 2446/I, *Trichosporon asahii* 1188) and filamentous fungi (*Aspergillus fumigatus* 231, *Absidia corymbifera* 272, *Trichophyton mentagrophytes* 445) from the collection of fungal strains deposited at the Department of Biological and Medical Sciences, Faculty of Pharmacy, Charles University, Hradec Králové, Czech Republic. Three ATCC strains were used as the quality control strains. All the isolates were maintained on Sabouraud dextrose agar prior to being tested.

Minimum inhibitory concentrations (MICs) were determined by modified CLSI standard of microdilution format of the M27-A3 and M38-A2 documents.<sup>1,2</sup> Dimethyl sulfoxide (100 %) served as a diluent for all compounds; the final concentration did not exceed 2 %. RPMI 1640 (Sevapharma, Prague) medium supplemented with *L*-glutamine and buffered with 0.165 M morpholinepropanesulfonic acid (Serva) to pH 7.0 by 10 M NaOH was used as the test medium. The wells of the microdilution tray contained 200 µl of the RPMI 1640 medium with 2-fold serial dilutions of the compounds (2000 to 0.488 µmol/l for the new compounds) and 10 µl of inoculum suspension. Fungal inoculum in RPMI 1640 was prepared to give a final concentration of  $5 \times 10^3 \pm 0.2$  cfu.ml<sup>-1</sup>. The trays were incubated at 35°C and MICs were read visually after 24 h and 48 h. The MIC values for the dermatophytic strain (*T. mentagrophytes*) were determined after 72 h and 120 h. The MICs were defined as 80 % inhibition (IC<sub>80</sub>) of the growth of control for yeasts and as 50 % inhibition (IC<sub>50</sub>) of the growth of control for filamentous fungi. MICs were determined twice and in duplicate. The deviations from the usually obtained values were no higher than the nearest concentration value up and down the dilution scale.

### Antibacterial activity

*In vitro* antibacterial activities<sup>3</sup> of the compounds were evaluated on a panel of three ATCC strains (*Staphylococcus aureus* ATCC 6538, *Escherichia coli* ATCC 8739, *Pseudomonas aeruginosa* ATCC 9027) and five clinical isolates (*Staphylococcus aureus*

MRSA HK5996/08, *Staphylococcus epidermidis* HK6966/08, *Enterococcus* sp. HK14365/08, *Klebsiella pneumoniae* HK11750/08, *Klebsiella pneumoniae* ESBL HK14368/08) from the collection of fungal strains deposited at the Department of Biological and Medical Sciences, Faculty of Pharmacy, Charles University, Hradec Králové, Czech Republic. The above-mentioned ATCC strains also served as the quality control strains. All the isolates were maintained on Mueller-Hinton agar prior to being tested.

Dimethyl sulfoxide (100 %) served as a diluent for all compounds; the final concentration did not exceed 2 %. Mueller-Hinton agar (MH, HiMedia, Čadersky-Envitek, Czech Republic) buffered to pH 7.4 ( $\pm 0.2$ ) was used as the test medium. The wells of the microdilution tray contained 200  $\mu\text{l}$  of the Mueller-Hinton medium with 2-fold serial dilutions of the compounds (2000 to 0.488  $\mu\text{mol/l}$ ) and 10  $\mu\text{l}$  of inoculum suspension. Inoculum in MH medium was prepared to give a final concentration of 0.5 McFarland scale ( $1.5 \times 10^8 \text{ cfu.ml}^{-1}$ ). The trays were incubated at 37°C and MICs were read visually after 24 h and 48 h. The MICs were defined as 95 % inhibition of the growth of control. MICs were determined twice and in duplicate. The deviations from the usually obtained values were no higher than the nearest concentration value up and down the dilution scale.

## **Biodegradation Studies**

### **CO<sub>2</sub> Headspace test**

To evaluate the biodegradability of the test ionic liquids, the “CO<sub>2</sub> Headspace” test (ISO 14593) was applied.<sup>4</sup> This method allows the evaluation of the ultimate aerobic biodegradability of an organic compound in aqueous medium at a given concentration of microorganisms by analysis of inorganic carbon. The test ionic liquid, as the only source of carbon and energy, was added to a buffer-mineral salts medium which had been inoculated with a mixed population of microorganisms derived from an activated sludge collected from a sewage treatment plant to give a final organic carbon concentration of 20 mg/L. These solutions were incubated in sealed vessels with a headspace of air, which provided a reservoir of oxygen for aerobic biodegradation. Biodegradation (mineralization to carbon dioxide) was determined by measuring the net increase in total inorganic carbon (TIC) levels over time compared to unamended blanks. Sodium n-dodecyl sulfate (SDS) was used as a reference substance. The test ran for 28 days. The extent of biodegradation was expressed as a percentage of the theoretical amount of inorganic carbon (ThID) based on the amount of IL

added initially. Assuming 100% mineralization of the test ionic liquid, the theoretical amount of inorganic carbon (ThIC) in excess of that produced in the blank controls equals the amount of total organic carbon (TOC) added as the test compound to each vessel at the start of the test, that is:

$$\text{ThIC} = \text{TOC}$$

Percentage biodegradation  $D_t$  in each case is given by:

$$D_t = \frac{(\text{TIC}_t - \text{TIC}_b)}{\text{TOC}_i} \times 100$$

where:

$\text{TIC}_t$  is the TIC, in milligrams, in test vessel at time  $t$ ;

$\text{TIC}_b$  is the mean TIC, in milligrams, in blank control vessels at time  $t$

$\text{TOC}_i$  is the TOC, in milligrams, initially added to the test vessel

## References

- 1) Reference Method for Broth Dilution Antifungal Susceptibility Testing of Yeasts. Approved standard. Document M27-A3. Clinical Laboratory Standard Institute, Wayne, PA, **2008**.
- 2) Reference Method for Broth Dilution Antifungal Susceptibility Testing of Filamentous Fungi. Approved standard. Document M38-A2. Clinical Laboratory Standard Institute, Wayne, PA, **2008**.
- 3) Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria that Grow Aerobically. Approved Standard – Seventh Edition. Document M07-A7. Clinical Laboratory Standard Institute, Wayne, PA, **2006**.
- 4) ISO 14593: Water quality, Evaluation of ultimate aerobic biodegradability of organic compounds in aqueous medium. Method by analysis of inorganic carbon in sealed vessels  $\text{CO}_2$ , headspace test,

## Biodegradation Data

**Table 1:** Biodegradation data obtained for **2c** vs SDS (Sodium Dodecyl Sulphate) reference

Compound	% Biodegradation				
	7 d	14 d	21 d	28 d	95% CI*
SDS	78	89	91	94	89-99
<b>2c</b>	16	59	61	61	55-66

IL initial concentration= 20 mg C/L, \*confidence limits were calculated from 4 replicates

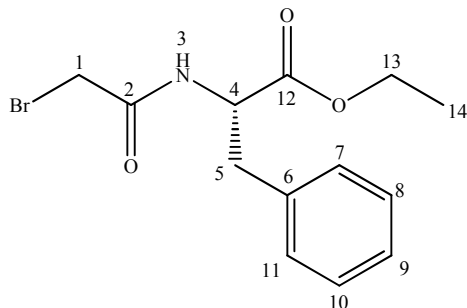
**Table 2:** Biodegradation data obtained for **18c** vs SDS (Sodium Dodecyl Sulphate) reference

Compound	% Biodegradation				
	6 d	13 d	20 d	28 d	95% CI*
SDS	67	91	91	81	76-88
<b>18c</b>	42	65	68	64	59-68

IL initial concentration= 20 mg C/L, \*confidence limits were calculated from 4 replicates

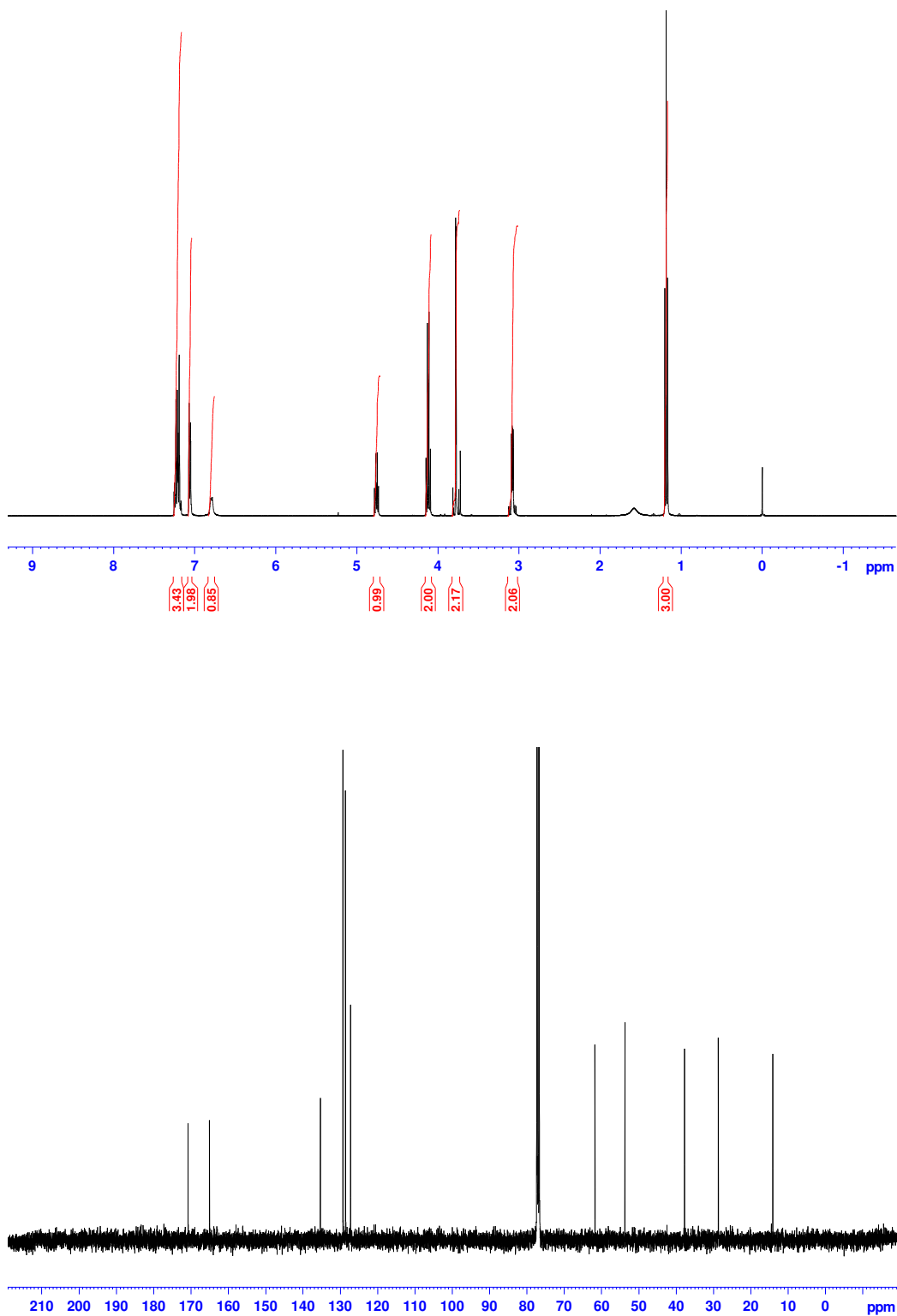
## Preparation of Chiral dipeptidyl $\alpha$ -bromoamides

### *Representative procedure for the preparation of chiral $\alpha$ -bromoamides: L-Phenylalanine-ethyl ester bromoacetate -1b*



To a stirred solution of DCM, L-phenylalanine ethyl ester hydrochloride (**1a**) (2.220 g, 10.30 mmol), and triethylamine (1.355 g, 13.39 mmol), under a nitrogen atmosphere at -78 °C was added dropwise bromoacetyl bromide (2.503 g, 12.40 mmol). After stirring at -78 °C for 5 h, the reaction mixture was allowed warm up to -20 °C and quenched by addition of water (10 mL). The organic phase was washed with distilled water (3 x 10 mL), saturated ammonium chloride (3 x 10 mL), saturated sodium bicarbonate (3 x 10 mL) and brine (3 x 10 mL). The organic phase was then dried over anhydrous magnesium sulfate, filtered and volatiles removed *via* rotary evaporation to give a crude product. The crude product was purified by column chromatography (eluant, ethyl acetate:hexane, 50:50) to give the title compound (**1b**) as a white solid in 64 % yield (2.078 g, 6.62 mmol).

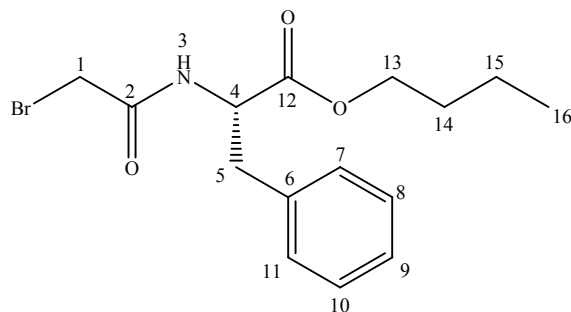
m.p. 65-67 °C,  $[\alpha]_D^{20} = +40.7^\circ$  (0.9 c, CHCl<sub>3</sub>). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 7.25-7.03 (m, 5H, *H*7-11), 6.82 (d, *J* = 7.2 Hz, 1H, *H*3), 4.78 (ddd, *J* = 8.0, 5.6, 5.6 Hz, 1H, *H*4), 4.14 (q, *J* = 7.0 Hz, 2H, *H*13), 3.78 (d, *J* = 2.8 Hz, 2H, *H*1), 3.09 (dd, *J* = 14.0, 6.0 Hz, 1H, *H*5), 3.04 (dd, *J* = 14.0, 6.0 Hz, 1H, *H*5), 1.20 (t, *J* = 7.0 Hz, 3H, *H*14). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 170.85 (CO, C2), 165.15 (CO, C12), 135.39 (ArC, C6), 129.36 (ArCH), 128.64 (ArCH), 127.31 (ArCH, C9), 61.78 (OCH<sub>2</sub>, C13), 53.76 (CH, C4), 37.77 (CH<sub>2</sub>, C5), 28.69 (CH<sub>2</sub>, C1), 14.11 (CH<sub>3</sub>, C14)



$^1\text{H}$  and  $^{13}\text{C}$  NMR Spectra (**1b**)

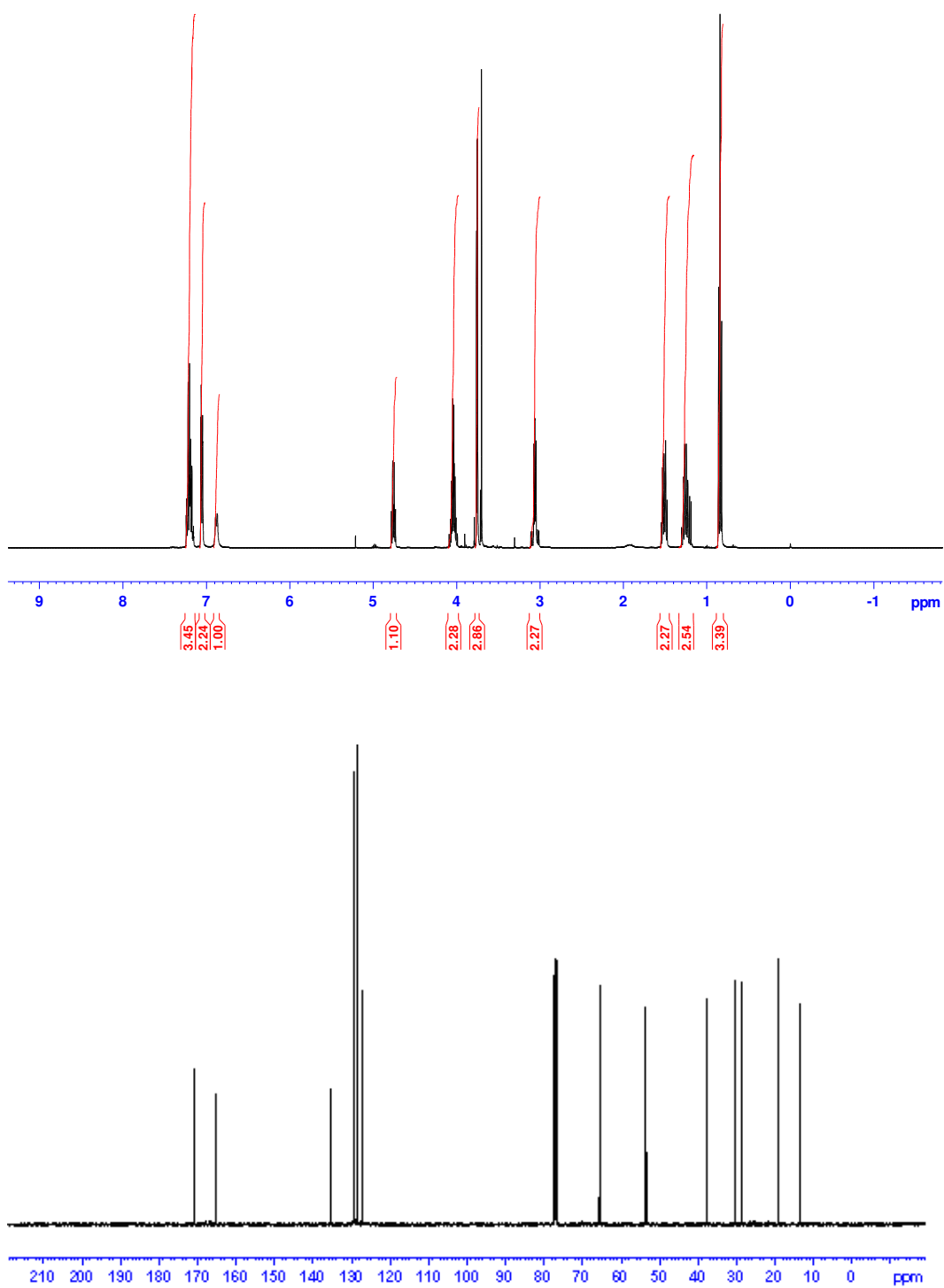


### L-Phenylalanine butyl ester bromoacetate-2b



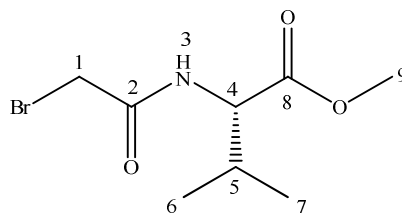
The title compound (**2b**) was prepared from L-phenylalanine butyl ester hydrochloride (**2a**) (2.001 g, 7.80 mmol) and bromoacetyl bromide (1.881 g, 9.30 mmol) according to the general procedure as a white solid in 79 % yield (2.112 g, 6.17 mmol).

m.p. 66-68 °C,  $[\alpha]_D^{20} = +28.9^\circ$  (0.9 c, CHCl<sub>3</sub>). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 7.23-7.03 (m, 5H, *H*7,11), 6.98 (d, *J* = 7.6 Hz, 1H, *H*3), 4.77 (ddd, *J* = 8.0, 6.0, 6.0 Hz, 1H, *H*4), 4.06 (q, *J* = 6.0 Hz, 2H, *H*13), 3.87 (d, *J* = 2.0 Hz, 2H, *H*1), 3.09 (dd, *J* = 14.0, 6.0 Hz, 1H, *H*5), 3.05 (dd, *J* = 14.0, 6.0 Hz, 1H, *H*5), 1.52 (tt, *J* = 7.0, 6.8 Hz, 2H, *H*14), 1.26 (tq, *J* = 7.6, 7.0 Hz, 2H, *H*15), 0.94 (t, *J* = 7.4 Hz, 3H, *H*16). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 170.90 (CO,C2), 165.04 (CO,C12), 135.40 (ArC,C6), 129.33 (ArCH), 128.65 (ArCH), 127.30 (ArCH,C9), 65.61 (OCH<sub>2</sub>,C13), 53.78 (CH,C4), 37.84 (CH<sub>2</sub>,C5), 30.45 (CH<sub>2</sub>,C14), 28.70 (CH<sub>2</sub>,C1), 19.05 (CH<sub>2</sub>,C15), 13.65 (CH<sub>3</sub>,C16)



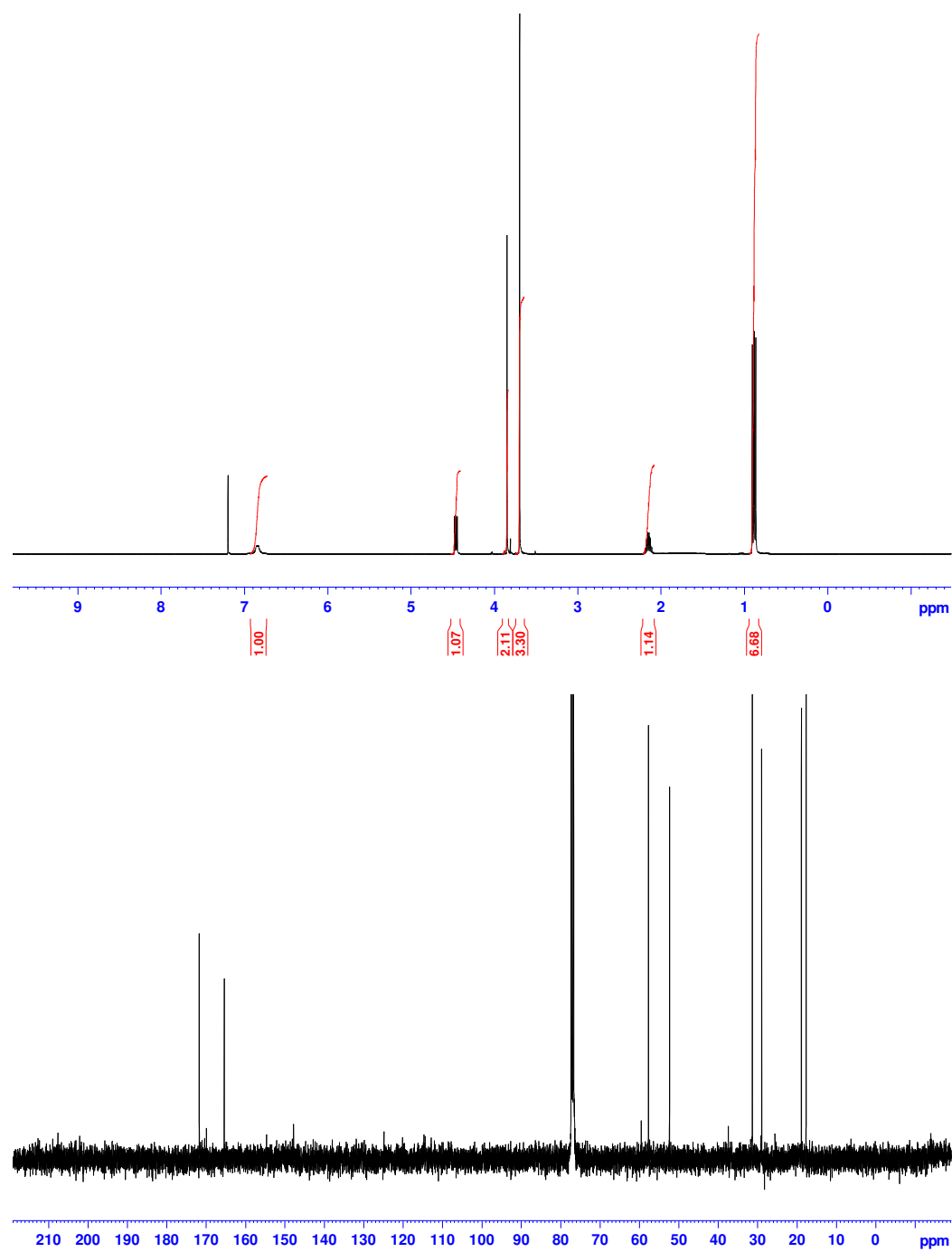
$^1\text{H}$  and  $^{13}\text{C}$  NMR Spectra (**2b**)

### L-Valine methyl ester bromoacetate-3b



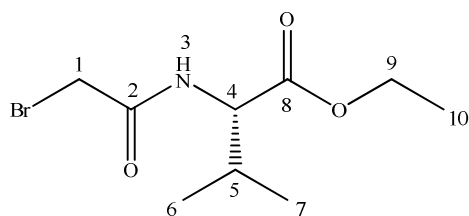
The title compound (**3b**) was prepared from L-valine methyl ester hydrochloride (**3a**) (1.042 g, 6.00 mmol) and bromoacetyl bromide (1.464 g, 7.20 mmol) according to the general procedure as a pale yellow liquid in 60 % yield (0.904 g, 3.60 mmol).

$[\alpha]_D^{20} = +21.0^\circ$  (0.9 c,  $\text{CHCl}_3$ ).  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 6.90 (d,  $J = 7.2$  Hz, 1H,  $H3$ ), 4.48 (dd,  $J = 8.8, 4.8$  Hz, 1H,  $H4$ ), 3.86 (s, 2H,  $H1$ ), 3.70 (s, 3H,  $H9$ ), 2.13 (qqd,  $J = 6.8, 6.4, 4.8$  Hz, 1H,  $H5$ ), 0.88 (dd,  $J = 9.6, 6.8$  Hz, 6H,  $H6,7$ ).  $^{13}\text{C NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 171.51 (CO,  $C2$ ), 169.46 (CO,  $C8$ ), 59.02 (CH,  $C4$ ), 50.23 ( $\text{OCH}_3$ ,  $C9$ ), 35.78 (CH,  $C5$ ), 30.11 ( $\text{CH}_2$ ,  $C1$ ), 18.85 ( $\text{CH}_3$ ,  $C6/C7$ ), 18.06 ( $\text{CH}_3$ ,  $C6/C7$ )



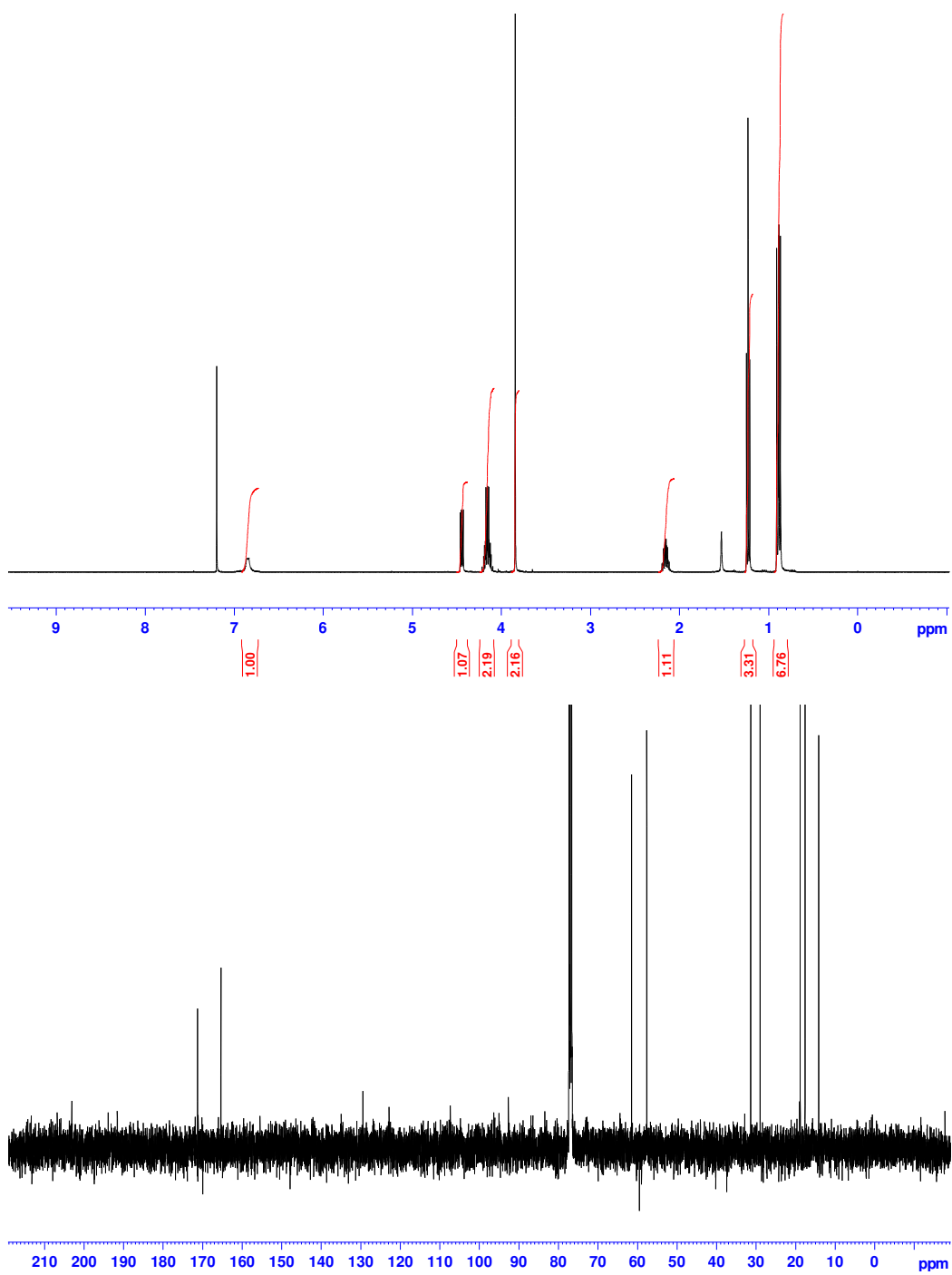
$^1\text{H}$  and  $^{13}\text{C}$  NMR Spectra (**3b**)

### L-Valine ethyl ester bromoacetate-4b



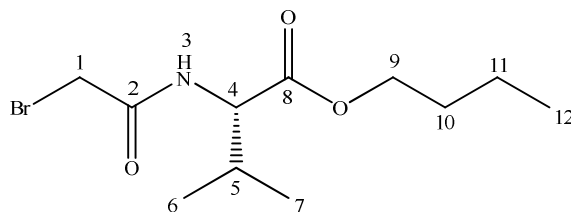
The title compound (**4b**) was prepared from L-valine ethyl ester hydrochloride (**4a**) (2.001 g, 11.0 mmol) and bromoacetyl bromide (2.649 g, 13.20 mmol) according to the general procedure as a pale yellow liquid in 40 % yield (1.166 g, 4.38 mmol).

$[\alpha]_D^{20} = +18.0^\circ$  (1.0 c,  $\text{CHCl}_3$ ).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 6.84 (d,  $J = 6.8$  Hz, 1H,  $H_3$ ), 4.44 (dd,  $J = 8.8, 4.8$  Hz, 1H,  $H_4$ ), 4.17 (dq,  $J = 7.2, 7.2$  Hz, 1H,  $H_9$ ), 4.14 (dq,  $J = 7.2, 7.0$  Hz, 1H,  $H_9$ ), 3.85 (s, 2H,  $H_1$ ), 2.15 (qqd,  $J = 6.8, 6.8, 4.8$  Hz, 1H,  $H_5$ ), 1.23 (t,  $J = 7.2$  Hz, 3H,  $H_{10}$ ), 0.88 (dd,  $J = 9.2, 6.8$  Hz, 6H,  $H_{6,7}$ ).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 171.29 (CO,  $C_2$ ), 165.36 (CO,  $C_8$ ), 61.51 ( $\text{OCH}_2$ ,  $C_9$ ), 57.68 (CH,  $C_4$ ), 31.37 (CH,  $C_5$ ), 29.01 ( $\text{CH}_2$ ,  $C_1$ ), 18.87 ( $\text{CH}_3$ ,  $C_6/C_7$ ), 17.66 ( $\text{CH}_3$ ,  $C_6/C_7$ ), 14.22 ( $\text{CH}_3$ ,  $C_{10}$ )



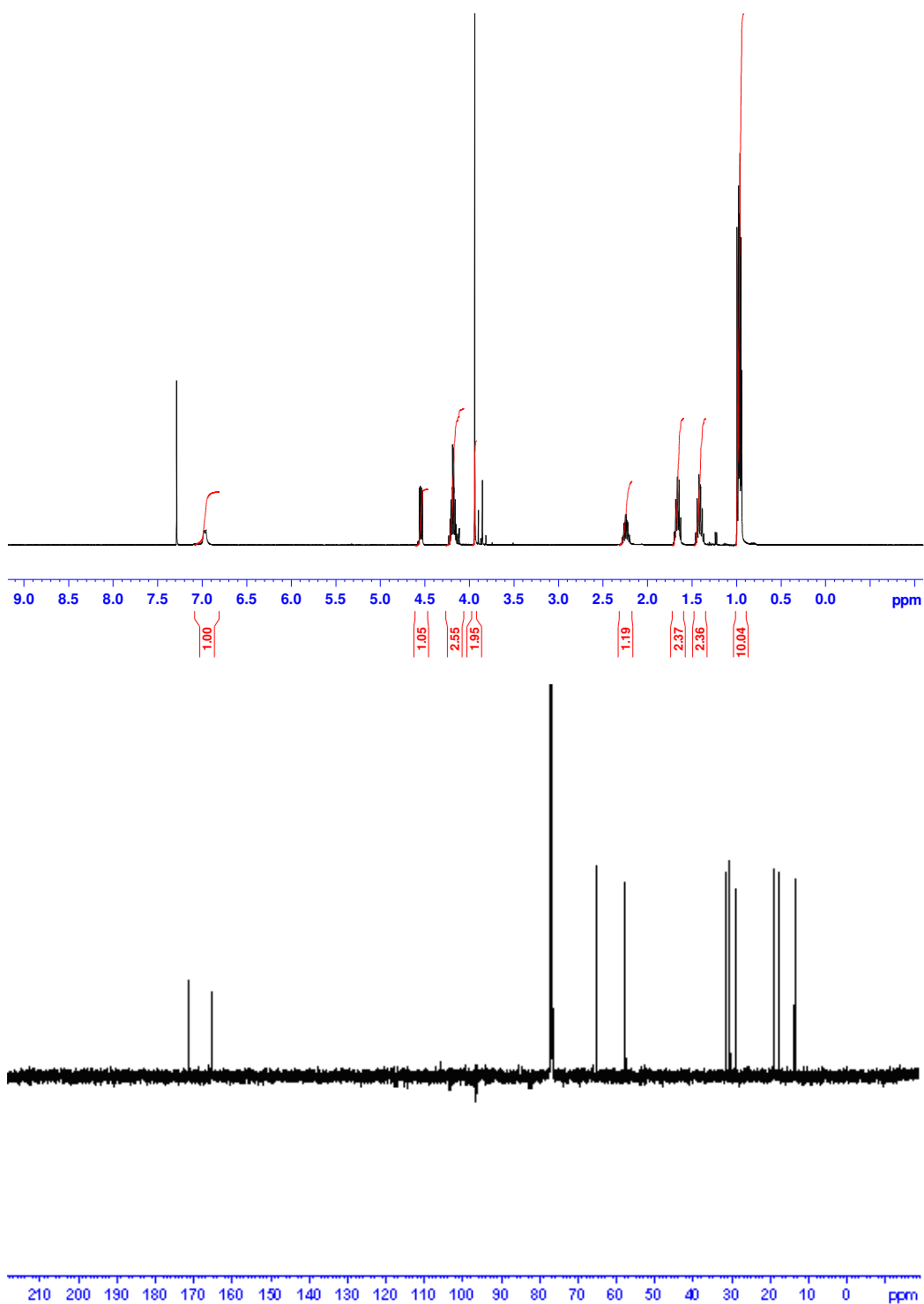
$^1\text{H}$  and  $^{13}\text{C}$  NMR Spectra (**4b**)

### L-Valine butyl ester bromoacetate-5b



The title compound (**5b**) was prepared from L-valine butyl ester hydrochloride (**5a**) (2.010 g, 9.60 mmol) and bromoacetyl bromide (2.321 g, 11.50 mmol) according to the general procedure as a colourless liquid in 58 % yield (1.640 g, 5.58 mmol).

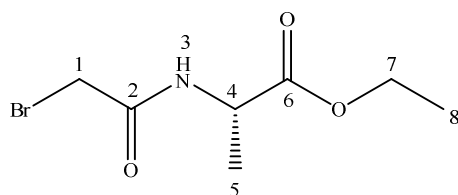
$[\alpha]_D^{20} = +15.1^\circ$  (1.0 c,  $\text{CHCl}_3$ ).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 6.97 (d,  $J = 8.0$  Hz, 1H,  $H_3$ ), 4.57 (dd,  $J = 8.0, 4.8$  Hz, 1H,  $H_4$ ), 4.28 (q,  $J = 7.2$  Hz, 2H,  $H_9$ ), 3.94 (s, 2H,  $H_1$ ), 2.15 (qqd,  $J = 6.8, 6.8, 4.4$  Hz, 1H,  $H_5$ ), 1.63 (m, 2H,  $H_{10}$ ), 1.46-1.36 (m, 2H,  $H_{11}$ ), 0.99-0.94 (m, 9H,  $H_{6,7,12}$ ).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 171.40 (CO,  $C_2$ ), 165.45 (CO,  $C_8$ ), 65.41 ( $\text{OCH}_2$ ,  $C_9$ ), 57.73 (CH,  $C_4$ ), 31.41 ( $\text{CH}_2$ ,  $C_{10}$ ), 30.43 (CH,  $C_5$ ), 29.02 ( $\text{CH}_2$ ,  $C_1$ ), 19.11 ( $\text{CH}_3$ ,  $C_6/C_7$ ), 19.00 ( $\text{CH}_3$ ,  $C_6/C_7$ ), 17.65 ( $\text{CH}_2$ ,  $C_{11}$ ), 13.66 ( $\text{CH}_3$ ,  $C_{12}$ )



$^1\text{H}$  and  $^{13}\text{C}$  NMR Spectra (**5b**)

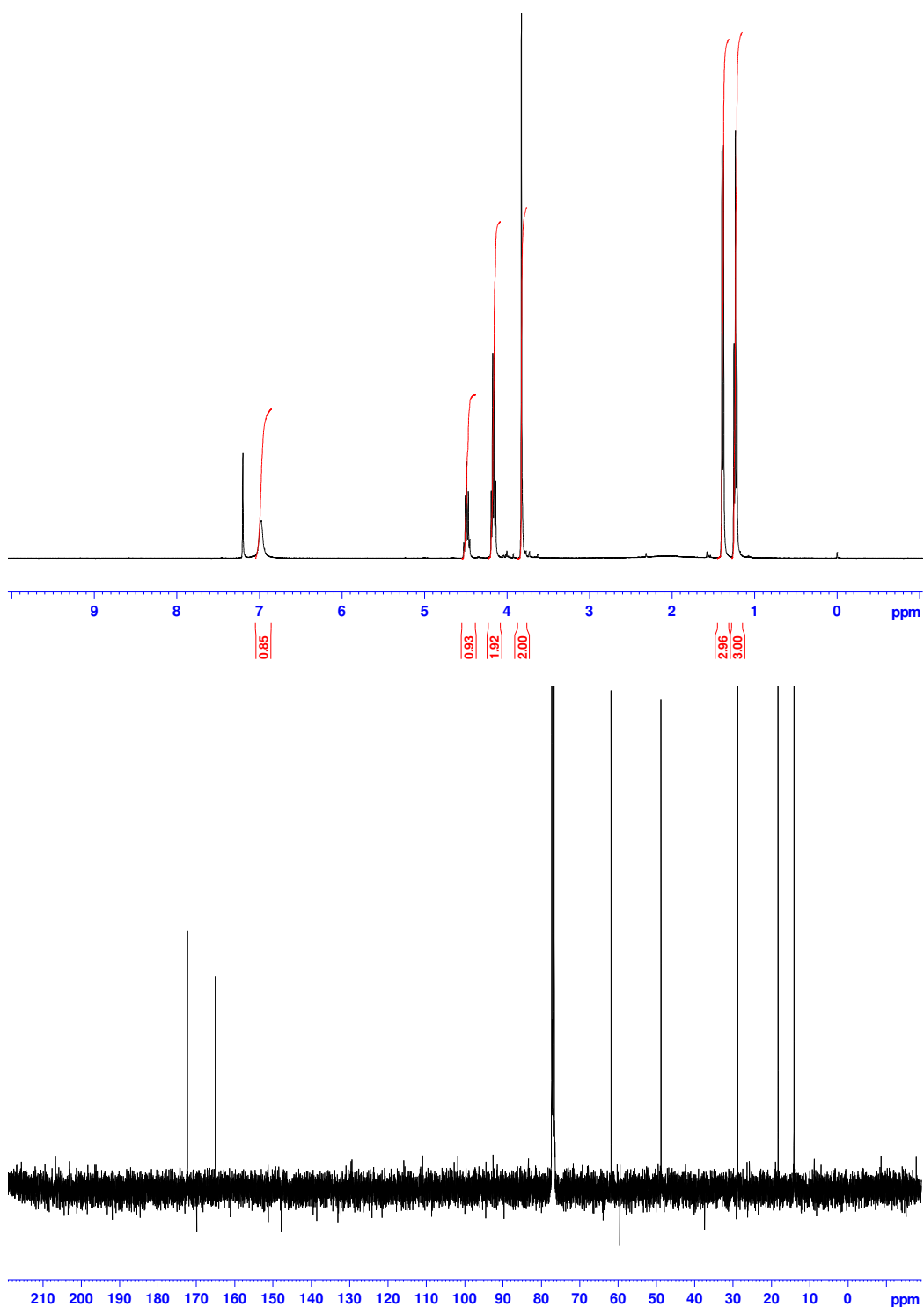


**L-Alanine ethyl ester bromoacetate-6b**



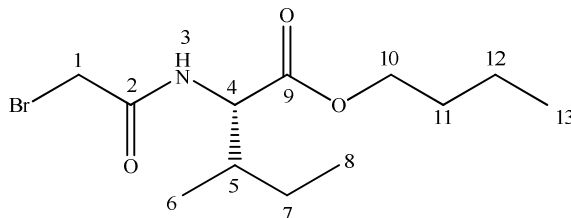
The title compound (**6b**) was prepared from L-alanine ethyl ester hydrochloride (**6a**) (1.012 g, 6.80 mmol) and bromoacetyl bromide (1.642 g, 8.10 mmol) according to the general procedure as a pale yellow liquid in 40 % yield (0.647 g, 2.72 mmol).

$[\alpha]_D^{20} = +14.4^\circ$  (0.8 c,  $\text{CHCl}_3$ ).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 6.96 (d,  $J = 7.8$  Hz, 1H,  $H3$ ), 4.52 (dq,  $J = 7.2, 7.2$  Hz, 1H,  $H4$ ), 4.19 (q,  $J = 7.0$  Hz, 2H,  $H7$ ), 3.82 (s, 2H,  $H1$ ), 1.39 (d,  $J = 7.2$  Hz, 3H,  $H5$ ), 1.25 (t,  $J = 7.0$  Hz, 3H,  $H8$ ).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 169.83 (CO,  $C2$ ), 162.64 (CO,  $C6$ ), 59.51 ( $\text{OCH}_2$ ,  $C7$ ), 46.27 (CH,  $C4$ ), 26.17 ( $\text{CH}_2$ ,  $C1$ ), 19.03 ( $\text{CH}_3$ ,  $C5$ ), 15.69 ( $\text{CH}_3$ ,  $C8$ )



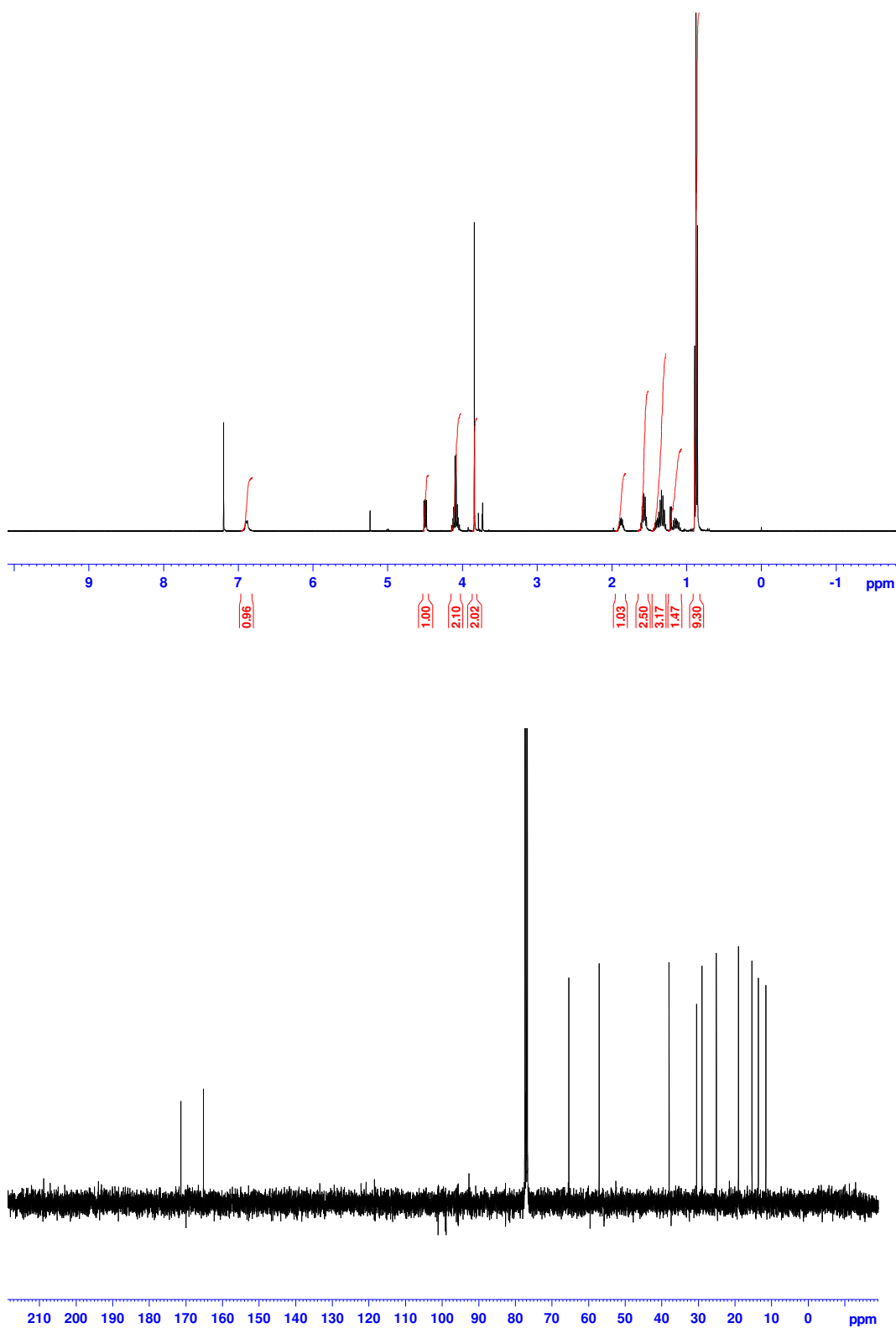
$^1\text{H}$  and  $^{13}\text{C}$  NMR Spectra (**6b**)

### L-Isoleucine butyl ester bromoacetate -7b



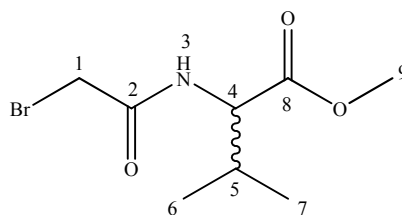
The title compound (**7b**) was prepared from L-isoleucine butyl ester hydrochloride (**7a**) (1.528 g, 6.85 mmol) and bromoacetyl bromide (1.65 g, 8.20 mmol) according to the general procedure as a pale yellow liquid in 68 % yield (1.443 g, 4.68 mmol)

$[\alpha]_D^{20} = +22.0^\circ$  (0.7 c in  $\text{CHCl}_3$ ).  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 6.86 (d,  $J = 7.6$  Hz, 1H,  $H3$ ), 4.50 (dd,  $J = 8.4, 4.8$  Hz, 1H,  $H4$ ), 4.12 (dq,  $J = 7.0, 7.0$  Hz, 1H,  $H10$ ), 4.11 (dq,  $J = 7.2, 7.0$  Hz, 1H,  $H10$ ), 3.84 (s, 2H,  $H1$ ), 1.92 (dddq,  $J = 8.0, 8.0, 6.6, 4.8$  Hz, 1H,  $H5$ ), 1.49 (ddq,  $J = 8.0, 8.0, 7.2$  Hz, 1H,  $H7$ ), 1.25-1.11 (m, 5H,  $H7, H11, H12$ ), 0.97 (t,  $J = 7.2$  Hz, 3H,  $H13$ ), 0.89 (t,  $J = 7.2$  Hz, 6H,  $H6,8$ ).  $^{13}\text{C NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 171.56 (CO,  $C2$ ), 164.98 (CO,  $C9$ ), 61.37 ( $\text{OCH}_2$ ,  $C10$ ), 56.66 (CH,  $C4$ ), 37.92 (CH,  $C5$ ), 31.42 ( $\text{CH}_2$ ,  $C11$ ), 28.33 ( $\text{CH}_2$ ,  $C1$ ), 25.17 ( $\text{CH}_2$ ,  $C7$ ), 22.34 ( $\text{CH}_2$ ,  $C12$ ), 15.35 ( $\text{CH}_3$ ,  $C6/C8$ ), 14.18 ( $\text{CH}_3$ ,  $C6/C8$ ), 11.60 ( $\text{CH}_3$ ,  $C13$ )



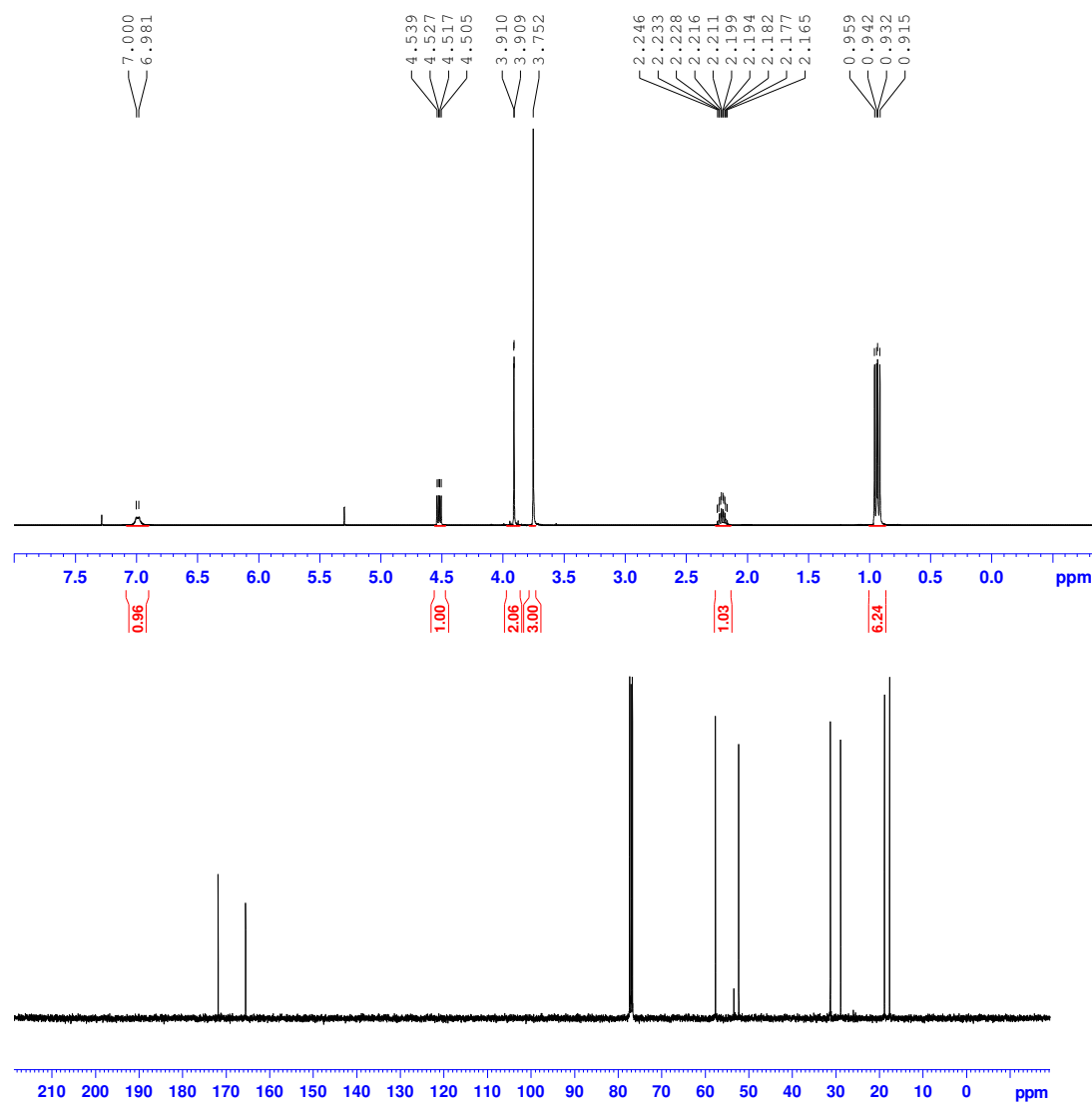
$^1\text{H}$  and  $^{13}\text{C}$  NMR Spectra (7b)

### DL-Valine methyl ester bromoacetate-8b



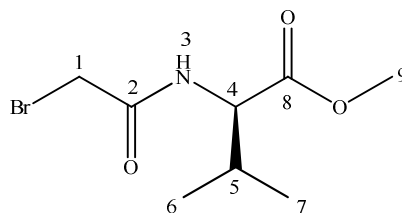
The title compound (**8b**) was prepared from DL-valine methyl ester hydrochloride (**8a**) (2.011 g, 12.00 mmol) and bromoacetyl bromide (2.901 g, 14.40 mmol) according to the general procedure as a yellow liquid in 82 % yield (2.471 g, 9.84 mmol).

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 6.99 (d,  $J = 8.8$  Hz, 1H,  $H_3$ ), 4.52 (dd,  $J = 8.8, 4.8$  Hz, 1H,  $H_4$ ), 3.91 (s, 2H,  $H_1$ ), 3.75 (s, 3H,  $H_9$ ), 2.20 (qqd,  $J = 6.8, 6.8, 4.8$  Hz, 1H,  $H_5$ ), 0.95 (d,  $J = 6.8$  Hz, 3H,  $H_6/7$ ), 0.92 (d,  $J = 6.8$  Hz, 3H,  $H_6/7$ ).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 171.85 (CO,  $C_2$ ), 166.88 (CO,  $C_8$ ), 57.53 (CH,  $C_4$ ), 52.40 ( $\text{OCH}_3$ ,  $C_9$ ), 31.11 (CH,  $C_5$ ), 28.89 ( $\text{CH}_2$ ,  $C_1$ ), 18.88 ( $\text{CH}_3$ ,  $C_6/C_7$ ), 17.69 ( $\text{CH}_3$ ,  $C_6/C_7$ )



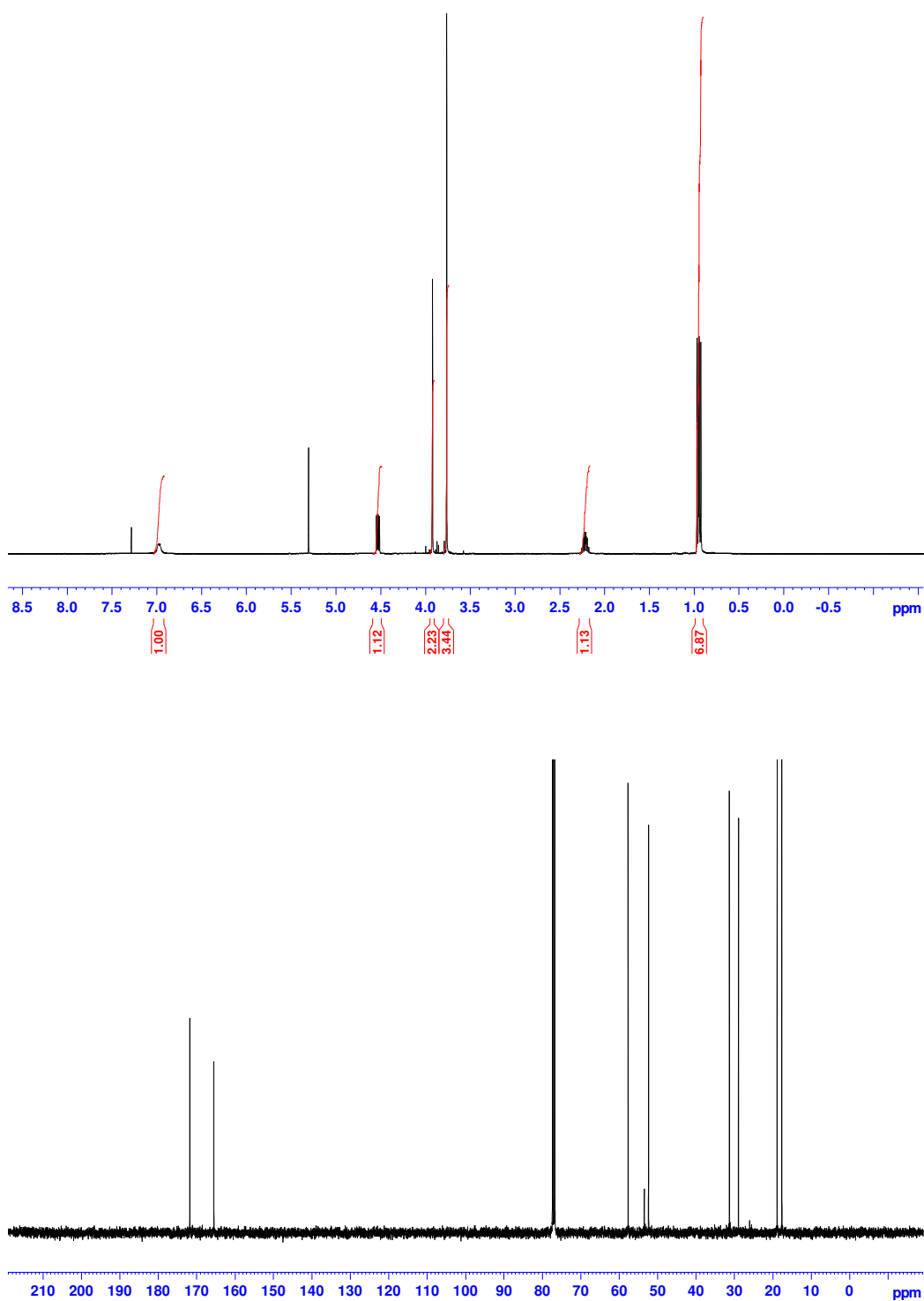
$^1\text{H}$  and  $^{13}\text{C}$  NMR Spectra (**8b**)

### D-Valine methyl ester bromoacetate-9b



The title compound (**9b**) was prepared from D-valine methyl ester hydrochloride (**9a**) (2.031 g, 15.30 mmol) and bromoacetyl bromide (3.673 g, 18.20 mmol) according to the general procedure as a slightly viscous yellow liquid in 45 % yield (1.750 g, 6.94 mmol).

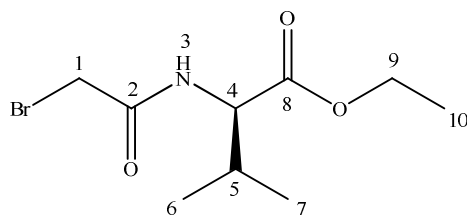
$[\alpha]_D^{20} = -22.7^\circ$  (0.9 c,  $\text{CHCl}_3$ ).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 7.16 (d,  $J = 8.4$  Hz, 1H,  $H3$ ), 4.44 (dd,  $J = 8.0, 4.8$  Hz, 1H,  $H4$ ), 3.88 (s, 2H,  $H1$ ), 3.68 (s, 3H,  $H9$ ), 2.17 (qqd,  $J = 6.8, 6.8, 4.8$  Hz, 1H,  $H5$ ), 0.90 (d,  $J = 6.8$ , Hz, 3H,  $H6/7$ ), 0.84 (d,  $J = 6.8$ , Hz, 3H,  $H6/7$ ).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 171.84 (CO,  $C2$ ), 166.32 (CO,  $C8$ ), 57.59 (CH,  $C4$ ), 52.35 ( $\text{OCH}_3$ ,  $C9$ ), 31.09 (CH,  $C5$ ), 28.93 ( $\text{CH}_2$ ,  $C1$ ), 18.84 ( $\text{CH}_3$ ,  $C6/C7$ ), 17.55 ( $\text{CH}_3$ ,  $C6/C7$ )



$^1\text{H}$  and  $^{13}\text{C}$  NMR Spectra (**9b**)

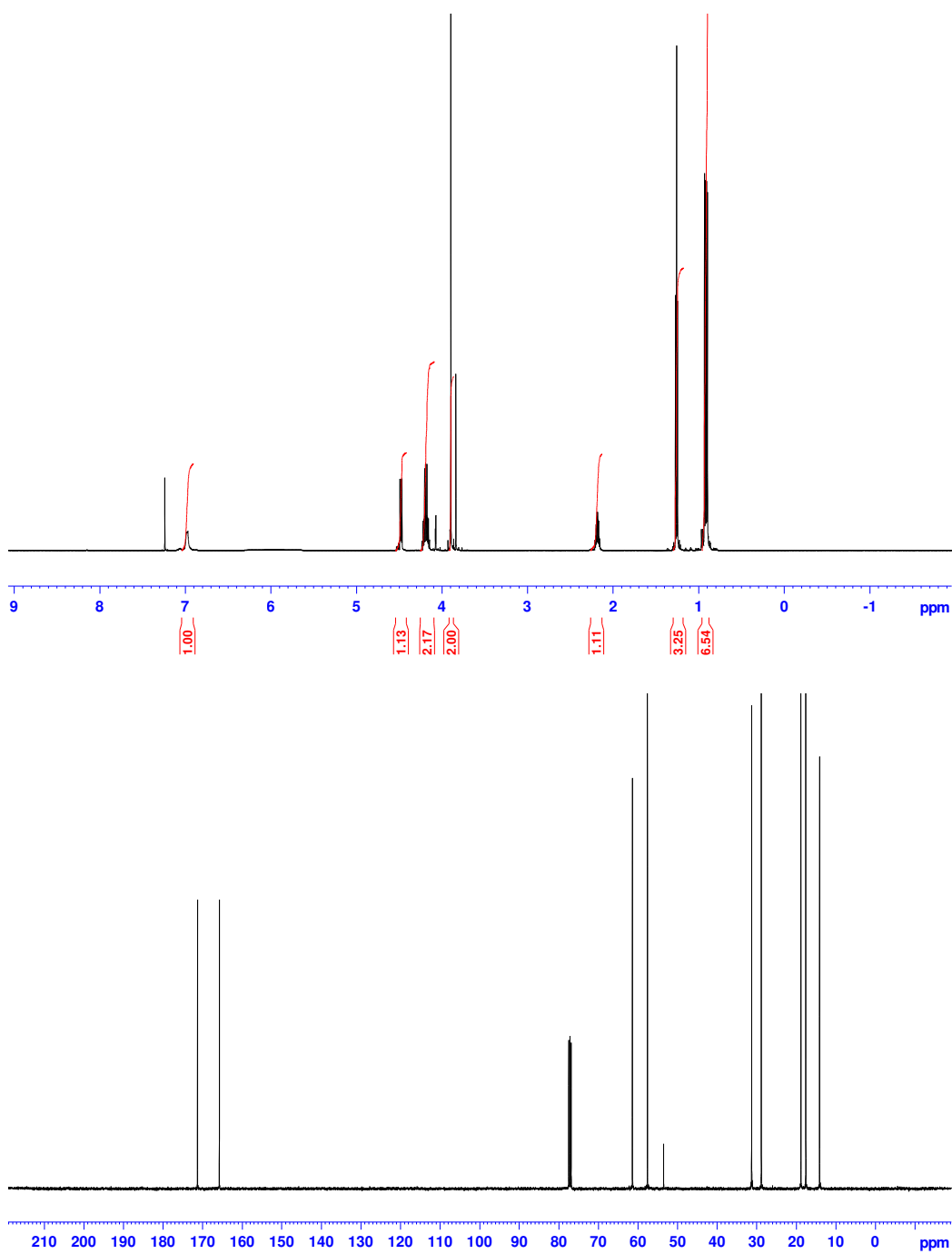


### D-Valine ethyl ester bromoacetate-10b



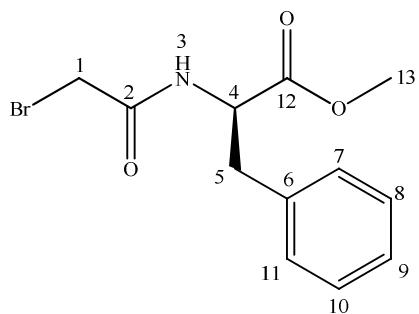
The title compound (**10b**) was prepared from D-valine ethyl ester hydrochloride (**10a**) (2.001 g, 11.00 mmol) and bromoacetyl bromide (2.664 g, 13.20 mmol) according to the general procedure as a colourless liquid in 59 % yield (1.731 g, 6.50 mmol).

$[\alpha]_D^{20} = -18.4^\circ$  (0.9 c,  $\text{CHCl}_3$ ).  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 6.69 (d,  $J = 8.0$  Hz, 1H,  $H3$ ), 4.48 (dd,  $J = 8.8, 4.4$  Hz, 1H,  $H4$ ), 4.18 (dq,  $J = 7.2, 7.0$  Hz, 1H,  $H9$ ), 4.16 (dq,  $J = 7.0, 7.0$  Hz, 1H,  $H9$ ), 3.85 (s, 2H,  $H1$ ), 2.17 (qqd,  $J = 6.4, 6.4, 4.4$  Hz, 1H,  $H5$ ), 1.23 (t,  $J = 7.0$  Hz, 3H,  $H10$ ), 0.91 (d,  $J = 6.8$  Hz, 3H,  $H6/7$ ), 0.87 (d,  $J = 6.8$  Hz, 3H,  $H6/7$ ).  $^{13}\text{C NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 171.34 (CO,  $C2$ ), 165.82 (CO,  $C8$ ), 61.28 ( $\text{OCH}_2$ ,  $C9$ ), 57.60 (CH,  $C4$ ), 31.27 (CH,  $C5$ ), 28.82 ( $\text{CH}_2$ ,  $C1$ ), 18.81 ( $\text{CH}_3$ ,  $C6/C7$ ), 17.61 ( $\text{CH}_3$ ,  $C6/C7$ ), 14.15 ( $\text{CH}_3$ ,  $C10$ )



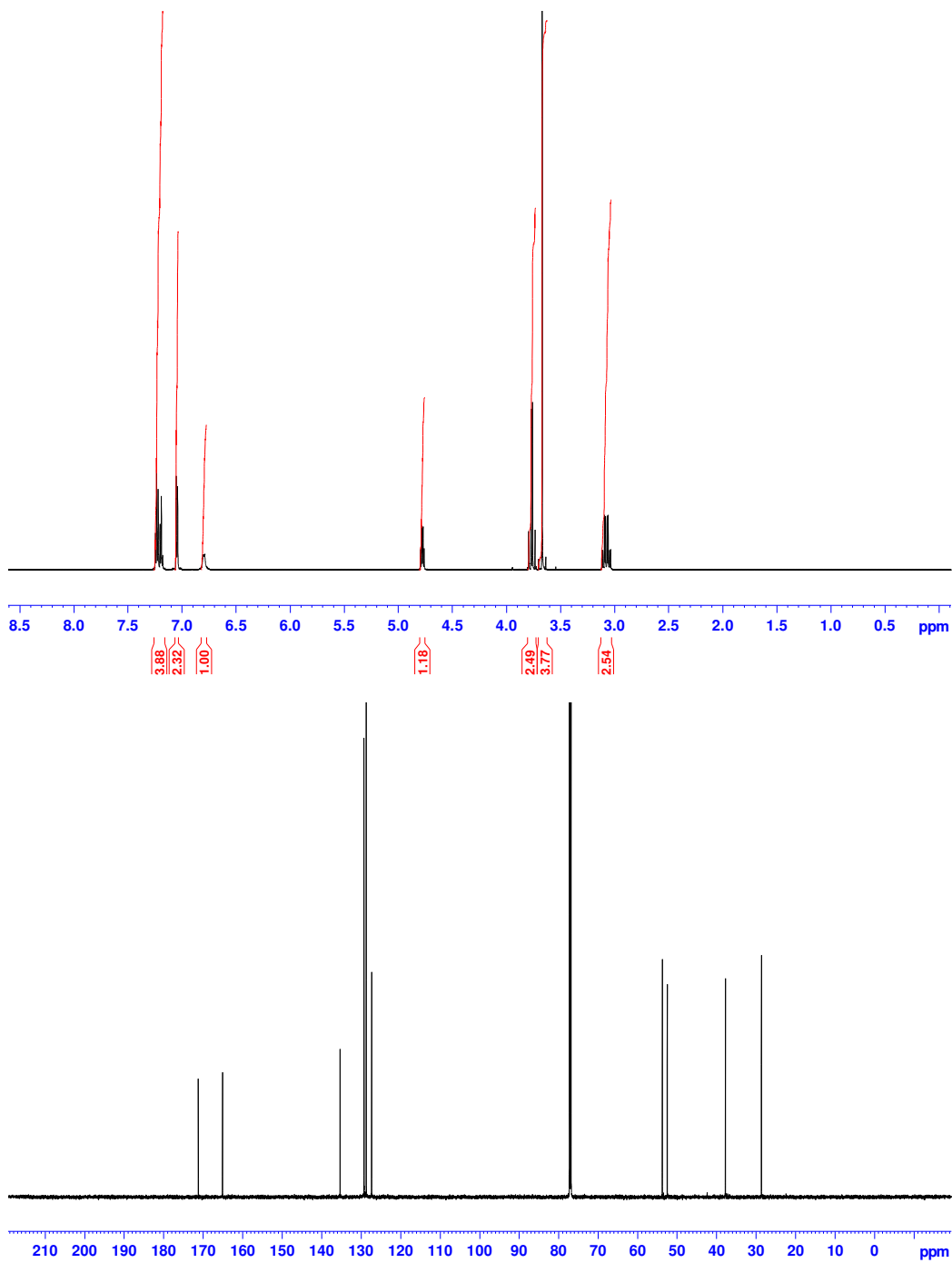
$^1\text{H}$  and  $^{13}\text{C}$  NMR Spectra (**10b**)

### D-Phenylalanine methyl ester bromoacetate-11b



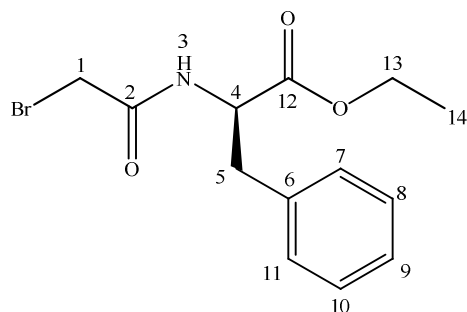
The title compound (**11b**) was prepared from D-phenylalanine methyl ester hydrochloride (**11a**) (2.096 g, 9.75 mmol) and bromoacetyl bromide (2.509 g, 11.70 mmol) according to the general procedure as a white solid in 65 % yield (1.901 g, 6.34 mmol).

m.p. 92-94 °C  $[\alpha]_D^{20} = -47.3^\circ$  (0.9 c, CHCl<sub>3</sub>). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  ppm 7.26-7.04 (m, 5H, *H*7-11), 6.77 (d, *J* = 6.8 Hz, 1H, *H*3), 4.78 (ddd, *J* = 7.0, 5.6, 5.6 Hz, 1H, *H*4), 3.78 (d, *J* = 3.6 Hz, 2H, *H*1), 3.68 (s, 3H, *H*13), 3.12 (dd, *J* = 13.6, 5.6 Hz, 1H, *H*5), 3.09 (dd, *J* = 13.6, 5.6 Hz, 1H, *H*5). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 171.30 (CO,*C*2), 165.28 (CO,*C*12), 135.28 (ArC,*C*6), 129.31 (ArCH), 128.72 (ArCH), 127.70 (ArCH,*C*9), 53.68 (CH,*C*4), 52.52 (OCH<sub>3</sub>,*C*13), 37.71 (CH<sub>2</sub>,*C*5), 25.50 (CH<sub>2</sub>,*C*1)



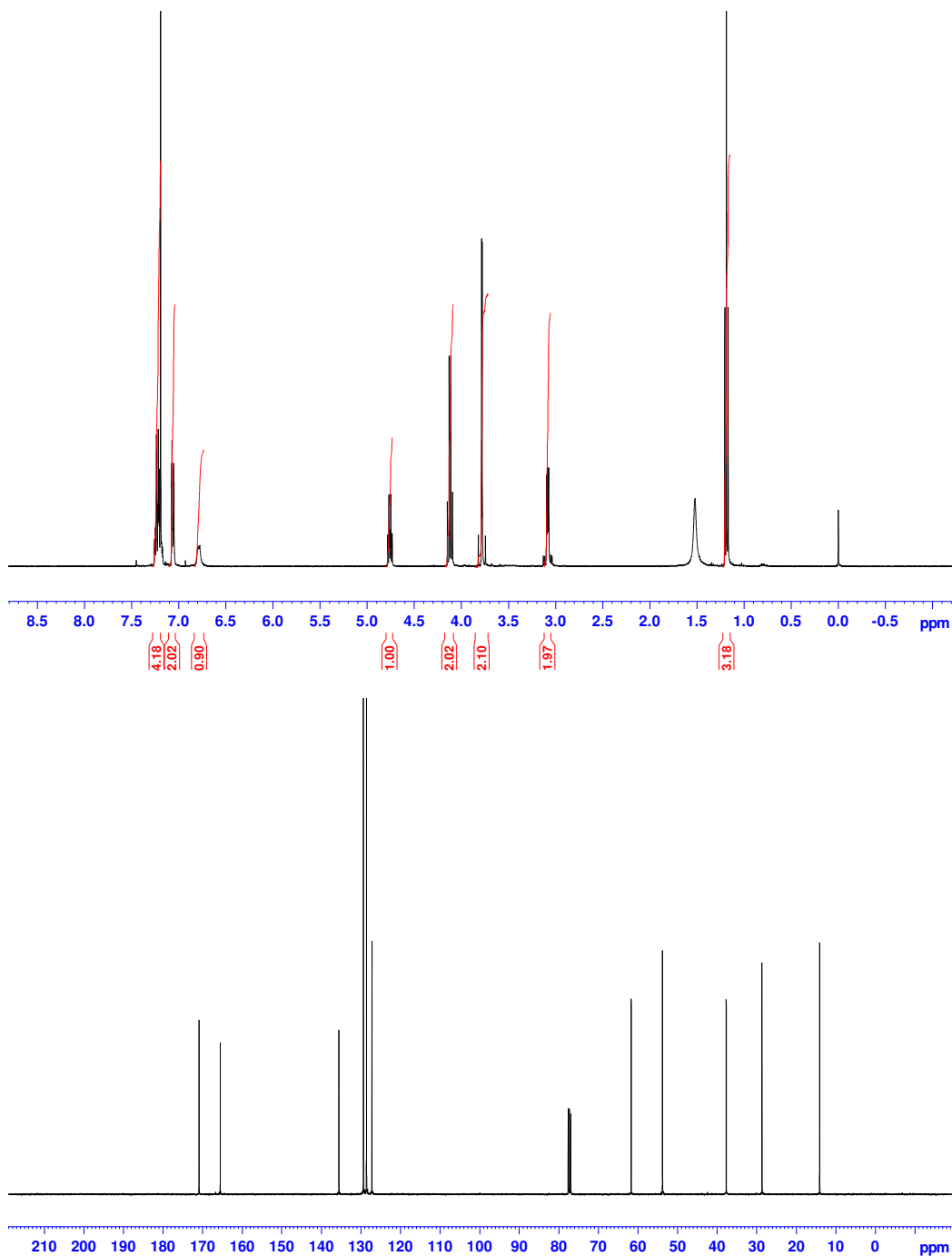
$^1\text{H}$  and  $^{13}\text{C}$  NMR Spectra (**11b**)

### D-Phenylalanine ethyl ester bromoacetate-12b



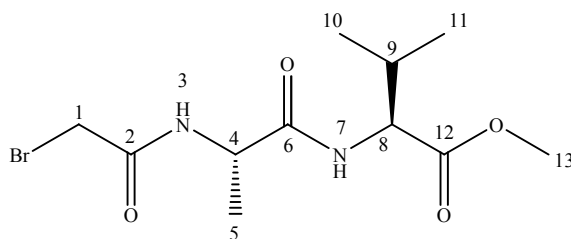
The title compound (**12b**) was prepared from D-phenylalanine ethyl ester hydrochloride (**12a**) (1.721 g, 8.00 mmol) and bromoacetyl bromide (1.942 g, 9.60 mmol) according to the general procedure as a white solid in 70 % yield (1.750 g, 5.57 mmol).

m.p. 94-96 °C,  $[\alpha]_D^{20} = -40.3^\circ$  (0.9 c, CHCl<sub>3</sub>). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 7.19-7.03 (m, 5H, *H*7-11), 6.86 (d, *J* = 6.8 Hz, 1H, *H*3), 4.73 (ddd, *J* = 8.0, 6.4, 6.4 Hz, 1H, *H*4), 4.08 (q, *J* = 7.2 Hz, 2H, *H*13), 3.71 (d, *J* = 2.0 Hz, 2H, *H*1), 3.14 (dd, *J* = 13.6, 5.6 Hz, 1H, *H*5), 3.02 (dd, *J* = 13.6, 5.6 Hz, 1H, *H*5), 1.14 (t, *J* = 7.2 Hz, 3H, *H*14). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  ppm 170.95 (CO, *C*2), 165.82 (CO, *C*12), 135.58 (ArC, *C*6), 129.17 (ArCH), 128.33 (ArCH), 127.22 (ArCH, *C*9), 61.70 (OCH<sub>2</sub>, *C*13), 53.81 (CH, *C*4), 37.70 (CH<sub>2</sub>, *C*5), 28.37 (CH<sub>2</sub>, *C*1), 14.13 (CH<sub>3</sub>, *C*14)



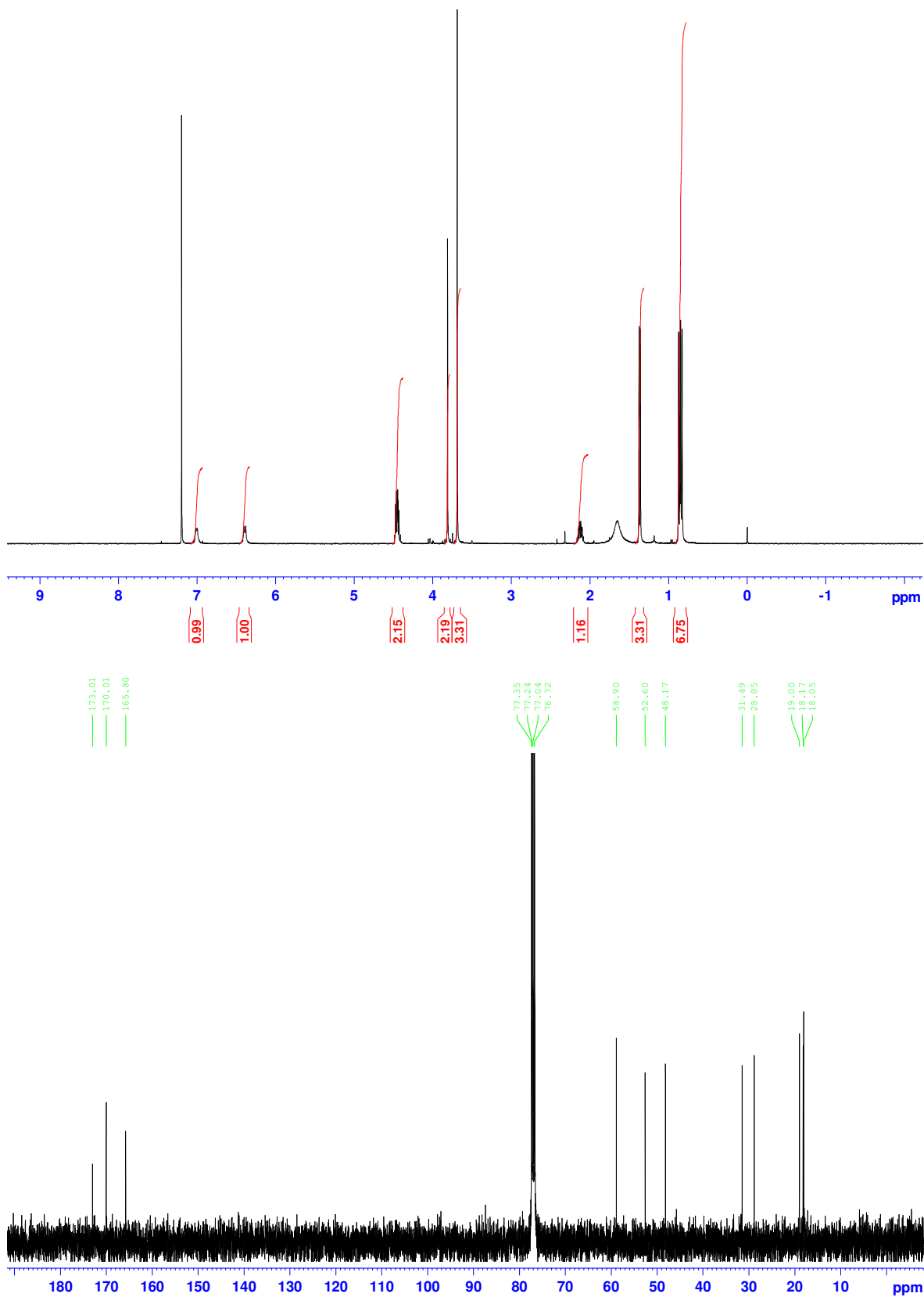
$^1\text{H}$  and  $^{13}\text{C}$  NMR Spectra (12b)

### L-Alanine-L-valine methyl ester bromoacetate-13b



The title compound (**13b**) was prepared from L-alanine-L-valine methyl ester hydrochloride (**13a**) (1.411 g, 5.95 mmol) and bromoacetyl bromide (1.433 g, 7.10 mmol) according to the general procedure as a beige solid in 67 % yield (1.295 g, 4.01 mmol).

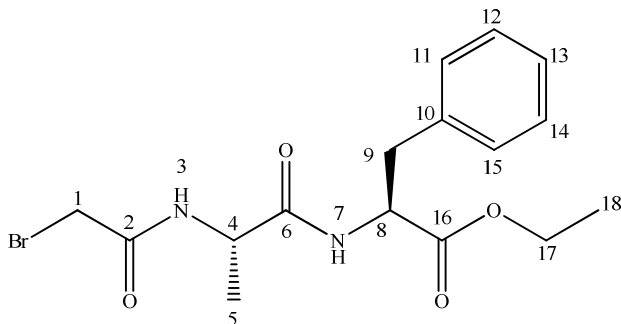
m.p. 94-96 °C [ $\alpha$ ]<sub>D</sub><sup>20</sup> = -22.0 ° (0.8 c, CHCl<sub>3</sub>). <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 6.96 (d, *J* = 7.6 Hz, 1H, *H*3), 6.31 (d, *J* = 8.4 Hz, 1H, *H*7), 4.48 (dd, *J* = 8.8, 4.8 Hz, 1H, *H*8), 4.40 (dq, *J* = 7.2, 7.2 Hz, 1H, *H*4), 3.81 (s, 2H, *H*1), 3.69 (s, 3H, *H*13), 2.17 (qqd, *J* = 6.6, 6.8, 4.8 Hz, 1H, *H*9), 1.38 (d, *J* = 7.0 Hz, 3H, *H*5), 0.90 (d, *J* = 6.8 Hz, 3H, *H*10/*H*11), 0.87 (d, *J* = 6.8 Hz, 3H, *H*10/*H*11). <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 172.05 (CO, *C*2), 171.38 (CO, *C*12), 165.55 (CO, *C*6), 57.35 (CH, *C*8), 52.21 (CH, *C*4), 49.48 (OCH<sub>3</sub>, *C*13), 31.12 (CH, *C*9), 28.55 (CH<sub>2</sub>, *C*1), 18.93 (CH<sub>3</sub>, *C*10/*C*11), 17.92 (CH<sub>3</sub>, *C*10/*C*11), 17.71 (CH<sub>3</sub>, *C*5)



$^1\text{H}$  and  $^{13}\text{C}$  NMR Spectra (**13b**)

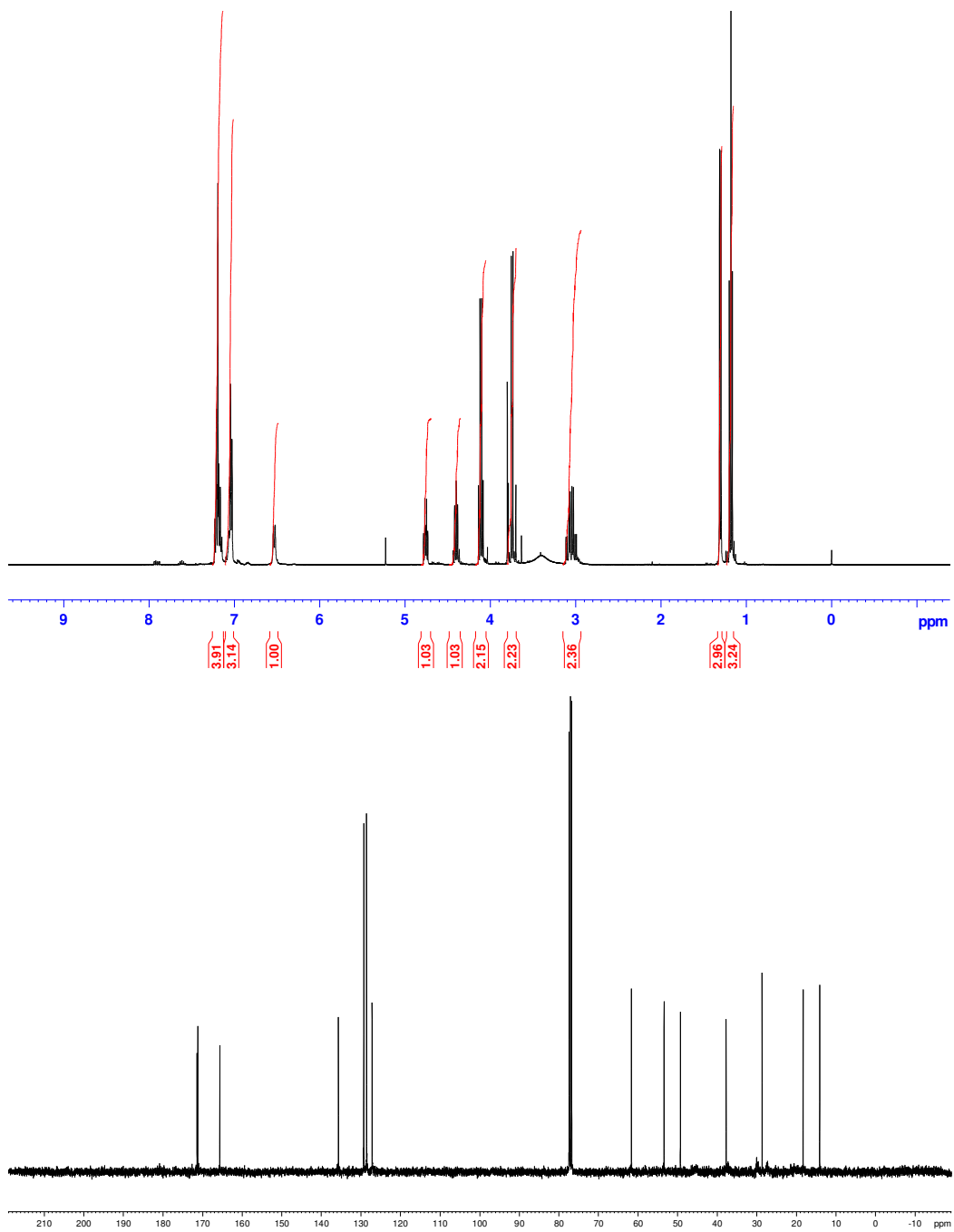


**L-Alanine-L-phenylalanine ethyl ester bromoacetate-14b**



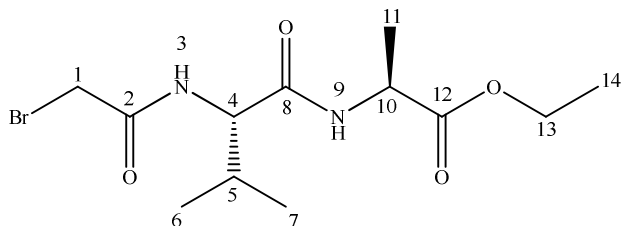
The title compound (**14b**) was prepared from L-alanine–L-phenylalanine ethyl ester hydrochloride (**14a**) (1.862 g, 6.20 mmol) and bromoacetyl bromide (1.503 g, 7.45 mmol) according to the general procedure) as an off-white solid in 76 % yield (1.828 g, 4.75 mmol).

m.p. 90-92 °C,  $[\alpha]_D^{20} = +22.4^\circ$  (1.4 c, CHCl<sub>3</sub>). <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 7.23-7.03 (m, 6H, *H*7,*11-15*), 6.54 (d, *J* = 8.0 Hz, 1H, *H*7), 4.78 (ddd, *J* = 8.0, 6.4, 6.0 Hz, 1H, *H*8), 4.40 (dq, *J* = 7.2, 7.2 Hz, 1H, *H*4), 4.12 (q, *J* = 7.2 Hz, 2H, *H*17), 3.76 (d, *J* = 8.4 Hz, 2H, *H*1), 3.09 (dd, *J* = 14.0, 6.0 Hz, 1H, *H*9), 3.01 (dd, *J* = 13.6, 6.4 Hz, 1H, *H*9), 1.31 (d, *J* = 7.2 Hz, 3H, *H*5), 1.18 (t, *J* = 7.2 Hz, 3H, *H*18). <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 171.16 (CO,*C*2), 168.13 (CO,*C*16), 165.64 (CO,*C*6), 135.60 (ArC,*C*10), 129.29 (ArCH), 128.60 (ArCH), 127.22 (ArCH,*C*13), 61.73 (OCH<sub>2</sub>,*C*17), 53.34 (CH,*C*8), 49.34 (CH,*C*4), 37.73 (CH<sub>2</sub>,*C*9), 28.60 (CH<sub>2</sub>,*C*1), 18.09 (CH<sub>3</sub>,*C*5), 14.11 (CH<sub>3</sub>,*C*18)



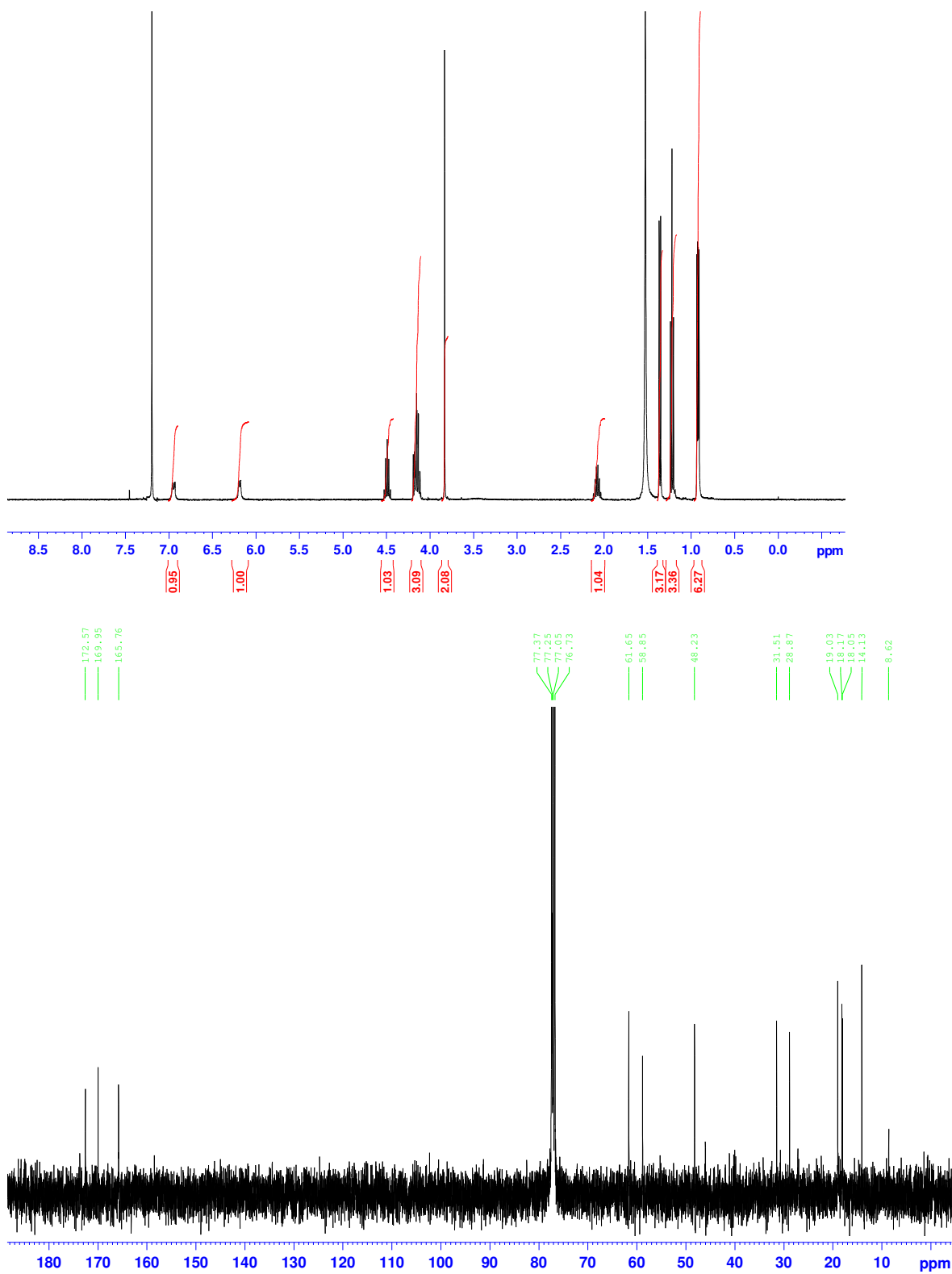
$^1\text{H}$  and  $^{13}\text{C}$  NMR Spectra (**14b**)

### L-Valine-L-alanine ethyl ester bromoacetate-15b



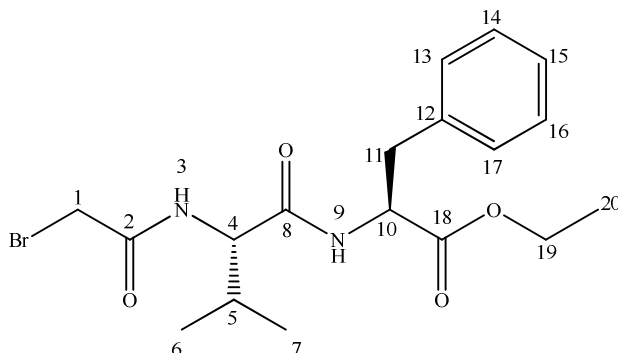
The title compound (**15b**) was prepared from L-valine–L-alanine ethyl ester hydrochloride (**15a**) (1.901 g, 7.55 mmol) and bromoacetyl bromide (1.830 g, 9.06 mmol) according to the general procedure as a white solid in 84 % yield (2.151 g, 6.38 mmol).

m.p. 75-77 °C,  $[\alpha]_D^{20} = -10.6^\circ$  (0.6 c, CHCl<sub>3</sub>). <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 6.96 (d,  $J = 8.4$  Hz, 1H, *H*3), 6.20 (d,  $J = 6.8$  Hz, 1H, *H*9), 4.49 (dq,  $J = 7.2, 7.2$  Hz, 1H, *H*10), 4.32 (dd,  $J = 8.0, 4.8$  Hz, 1H, *H*4), 4.17 (q,  $J = 7.2$  Hz, 2H, *H*13), 3.83 (s, 2H, *H*1), 2.16 (qqd,  $J = 7.0, 6.8, 4.8$  Hz, 1H, *H*5), 1.37 (d,  $J = 7.2$  Hz, 3H, *H*11), 1.22 (t,  $J = 7.2$  Hz, 3H, *H*14), 0.92 (dd,  $J = 7.2, 3.6$  Hz, 6H, *H*6,7). <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 172.35 (CO, *C*2), 170.37 (CO, *C*12), 165.93 (CO, *C*8), 60.38 (CH, *C*4), 57.30 (CH<sub>2</sub>, *C*13), 47.62 (CH, *C*10), 31.06 (CH, *C*5), 29.35 (CH<sub>2</sub>, *C*1), 18.95 (CH<sub>3</sub>, *C*6/*C*7), 17.98 (CH<sub>3</sub>, *C*6/*C*7), 16.67 (CH<sub>3</sub>, *C*11), 13.95 (CH<sub>3</sub>, *C*14)



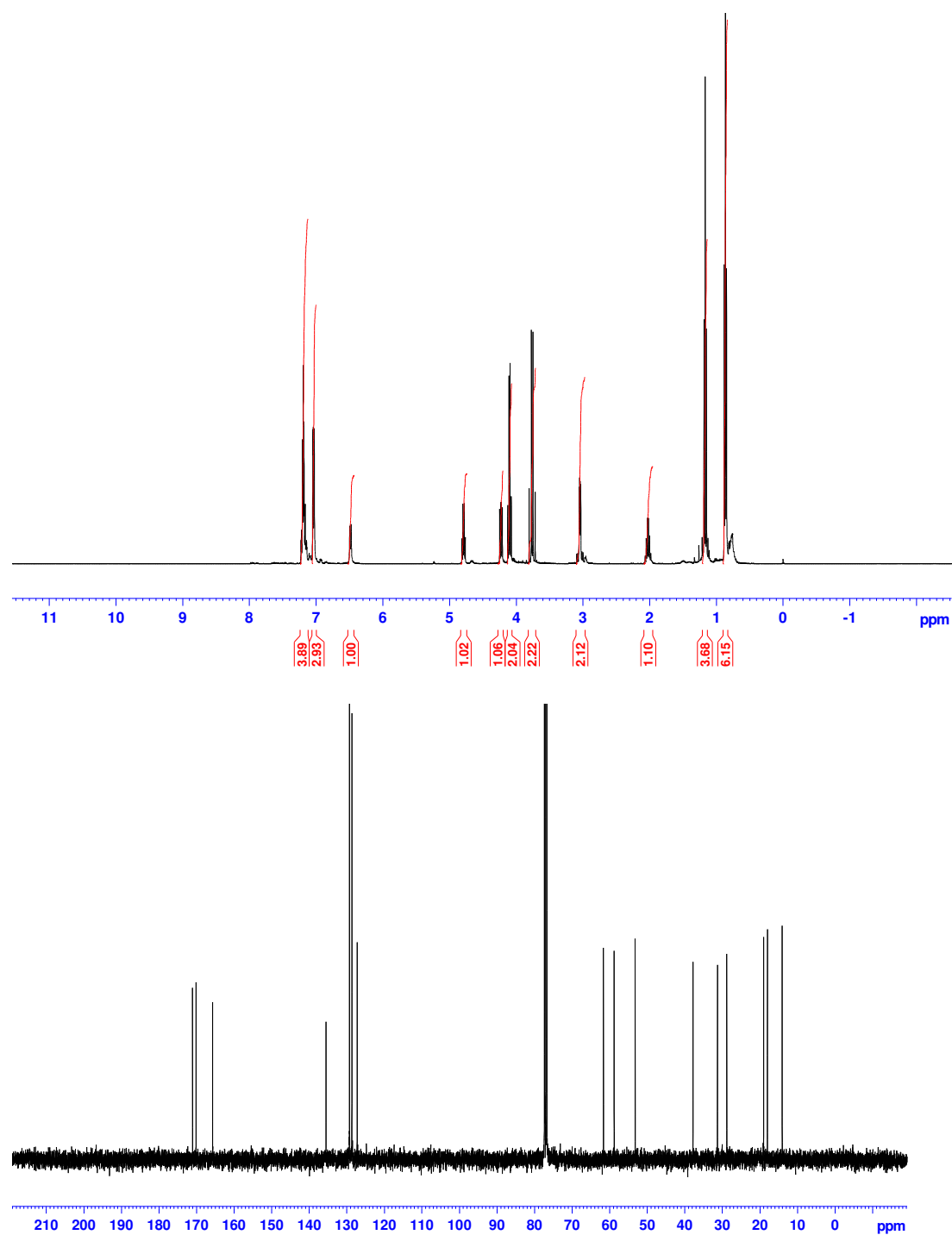
$^1\text{H}$  and  $^{13}\text{C}$  NMR Spectra (**15b**)

### L-Valine-L-phenylalanine ethyl ester bromoacetate-16b



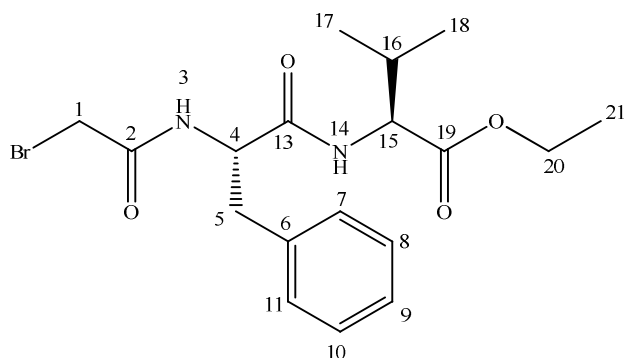
The title compound (**16b**) was prepared from L-valine–L-phenylalanine ethyl ester hydrochloride (**16a**) (1.720 g, 5.24 mmol) and bromoacetyl bromide (1.24 g, 7.44 mmol) according to the general procedure as a white solid in 77 % yield (1.66 g, 4.02 mmol).

m.p. 166-168 °C,  $[\alpha]_D^{20} = -20.0^\circ$  (0.7 c, CHCl<sub>3</sub>). <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 7.23-7.03 (m, 5H, *H*13-17), 7.12 (d, *J* = 6.8 Hz, 1H, *H*9), 6.89 (d, *J* = 8.8 Hz, 1H, *H*3), 4.79 (ddd, *J* = 8.0, 6.0, 6.0 Hz, 1H, *H*10), 4.22 (dd, *J* = 8.8, 6.8 Hz, 2H, *H*4), 4.12 (q, *J* = 7.2 Hz, 2H, *H*19), 3.80 (d, *J* = 9.6 Hz, 2H, *H*1), 3.09-2.94 (m, 2H, *H*11), 2.12 (qqd, *J* = 6.8, 6.8, 6.4 Hz, 1H, *H*5), 1.16 (t, *J* = 7.2 Hz, 3H, *H*20), 0.86 (dd, *J* = 9.8, 6.8 Hz, 6H, *H*6,7). <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 171.12 (CO, *C*2), 170.19 (CO, *C*18), 165.78 (CO, *C*8), 135.55 (ArC, *C*12), 129.31 (ArCH), 128.3 (ArCH), 127.25 (ArCH, *C*15), 61.63 (CH, *C*4), 58.81 (OCH<sub>2</sub>, *C*19), 53.22 (CH, *C*10), 37.85 (CH<sub>2</sub>, *C*11), 31.32 (CH, *C*5), 28.83 (CH<sub>2</sub>, *C*1), 19.03 (CH<sub>3</sub>, *C*6/*C*7), 18.02 (CH<sub>3</sub>, *C*6/*C*7), 14.11 (CH<sub>3</sub>, *C*20)



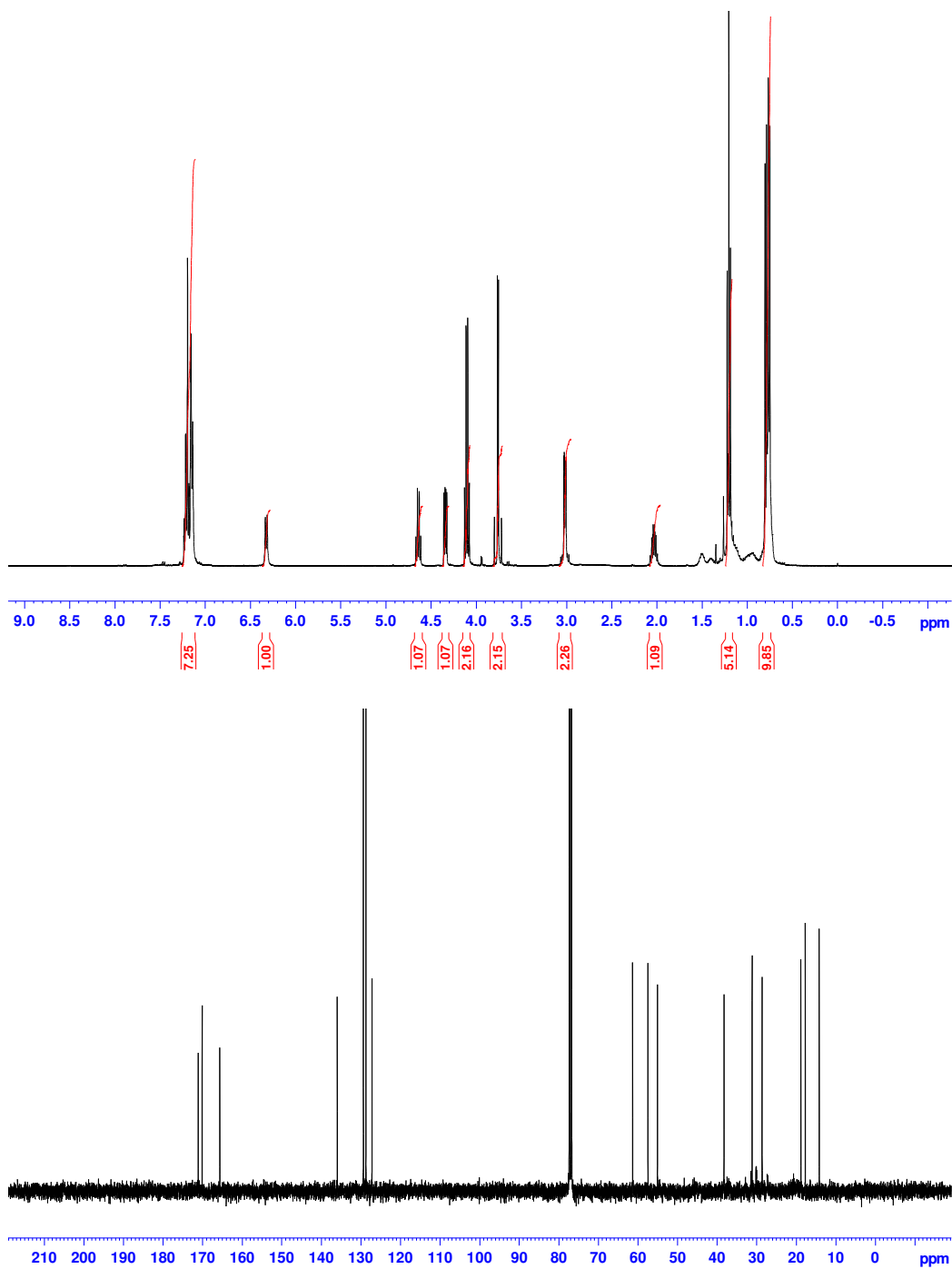
$^1\text{H}$  and  $^{13}\text{C}$  NMR Spectra (**16b**)

**L-Phenylalanine-L-valine ethyl ester bromoacetate -17b**



The title compound (**17b**) was prepared from L-phenylalanine–L-valine ethyl ester hydrochloride (**17a**) (1.688 g, 5.79 mmol) and bromoacetyl bromide (1.382 g, 6.84 mmol) according to the general procedure as pale yellow liquid in 72 % yield (1.733 g, 4.20 mmol).

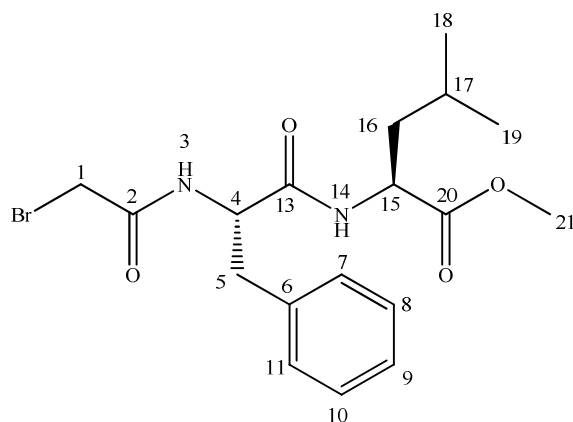
$[\alpha]_D^{20} = +13.9^\circ$  (1.0 c,  $\text{CHCl}_3$ ).  $^1\text{H NMR}$  (600 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 7.24-7.14 (m, 6H, *H*3,7-11), 6.31 (d,  $J = 8.4$  Hz, 1H, *H*14), 4.63 (ddd,  $J = 8.0, 6.4, 6.0$  Hz, 1H, *H*4), 4.33 (dd,  $J = 8.8, 5.2$  Hz, 1H, *H*15), 4.09 (q,  $J = 7.2$  Hz, 2H, *H*20), 3.75 (d,  $J = 4.4$  Hz, 2H, *H*1), 3.09 (dd,  $J = 14.0, 6.4$  Hz, 1H, *H*5), 2.98 (dd,  $J = 14.0, 6.4$  Hz, 1H, *H*5), 2.02 (qqd,  $J = 6.8, 6.8, 4.8$  Hz, 1H, *H*16), 1.20 (t,  $J = 7.2$  Hz, 2H, *H*21), 0.78 (dd,  $J = 6.8, 6.8$  Hz, 6H, *H*17,18).  $^{13}\text{C NMR}$  (150 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 171.15 (CO,*C*2), 170.17 (CO,*C*19), 165.69 (CO,*C*13), 135.96 (ArC,*C*6), 129.39 (ArCH), 128.73 (ArCH), 127.20 (ArCH,*C*9), 61.33 (OCH<sub>2</sub>,*C*20), 57.47 (CH,*C*15), 55.08 (CH,*C*4), 38.25 (CH<sub>2</sub>,*C*5), 31.45 (CH<sub>2</sub>,*C*16), 28.61 (CH<sub>2</sub>,*C*1), 18.82 (CH<sub>3</sub>,*C*17/*C*18), 17.74 (CH<sub>3</sub>,*C*17/*C*18), 14.24 (CH<sub>3</sub>,*C*21)



$^1\text{H}$  and  $^{13}\text{C}$  NMR Spectra (**17b**)

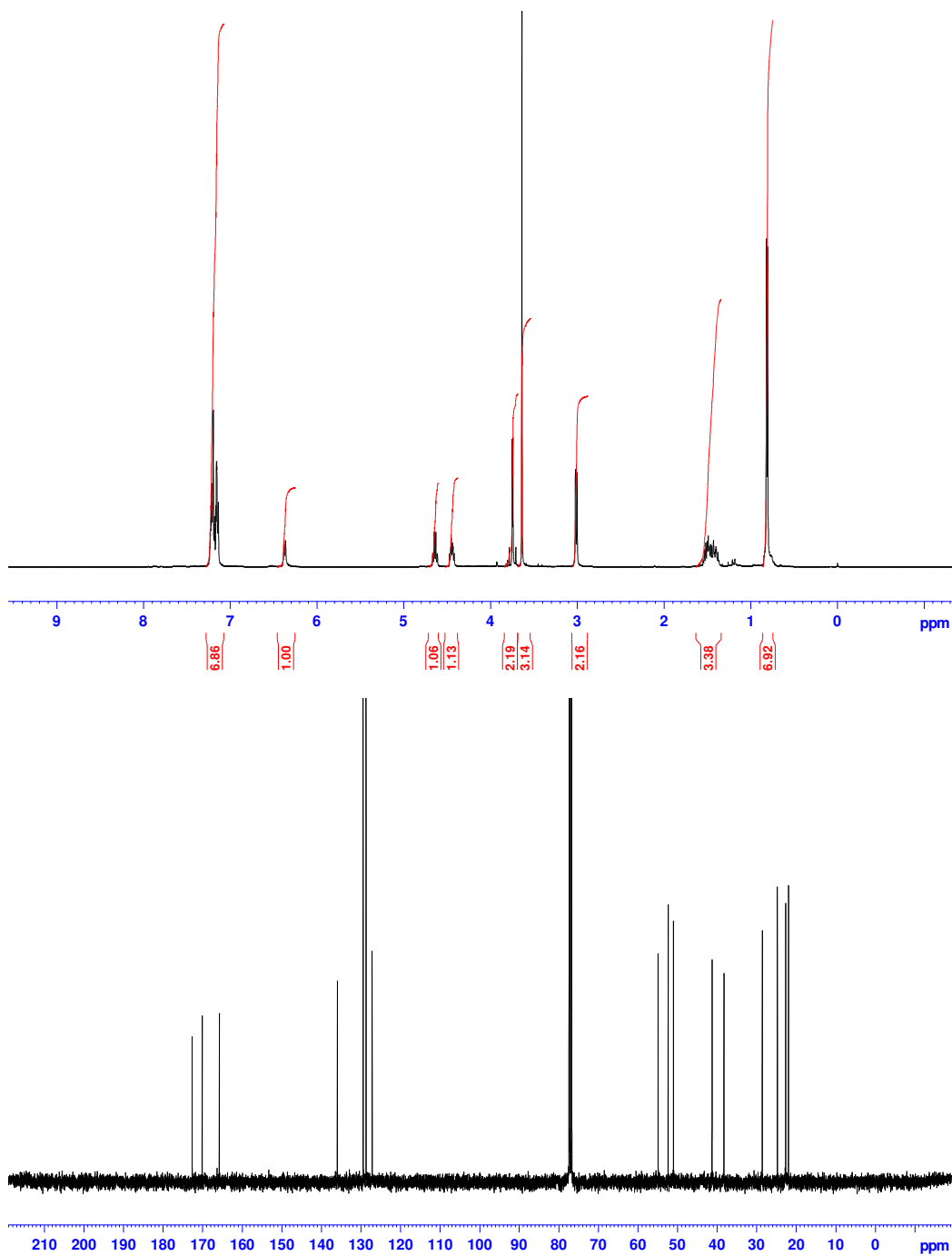


**L-Phenylalanine-L-leucine methyl ester bromoacetate-18b**



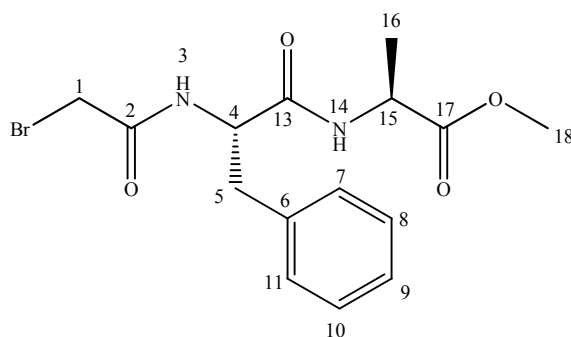
The title compound (**18b**) was prepared from L-phenylalanine–L-leucine methyl ester hydrochloride (**18a**) (1.681 g, 5.12 mmol) and bromoacetyl bromide (1.238 g, 6.14 mmol) according to the general procedure as a pale orange liquid in 74 % yield (1.558 g, 3.77 mmol).

$[\alpha]_D^{20} = +14.3^\circ$  (0.9 c,  $\text{CHCl}_3$ ).  $^1\text{H NMR}$  (600 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 7.24-7.14 (m, 6H, *H*7-11,14), 6.37 (d,  $J = 7.6$  Hz, 1H, *H*3), 4.63 (dt,  $J = 7.2, 7.0$  Hz, 1H, *H*4), 4.44 (ddd,  $J = 8.0, 8.0, 5.6$  Hz, 1H, *H*15), 3.74 (d,  $J = 3.6$  Hz, 2H, *H*1), 3.64 (s, 3H, *H*16), 3.01 (d,  $J = 7.2$  Hz, 2H, *H*5), 1.59-1.37 (m, 3H, *H*16,17), 0.80 (d,  $J = 6.4$  Hz, 6H, *H*18,19).  $^{13}\text{C NMR}$  (150 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 172.72 (CO,C2), 170.16 (CO,C20), 165.85 (CO,C13), 135.96 (ArC,C6), 129.46 (ArCH), 128.69 (ArCH), 127.19 (ArCH,C9), 54.90 (CH,C4), 52.39 (CH,C15), 51.03 (OCH<sub>3</sub>,C21), 41.26 (CH<sub>2</sub>,C16), 38.27 (CH<sub>2</sub>,C5), 28.59 (CH<sub>2</sub>,C1), 24.77 (CH,C17), 22.68 (CH<sub>3</sub>,C18/C19), 21.95 (CH<sub>3</sub>,C18/C19)



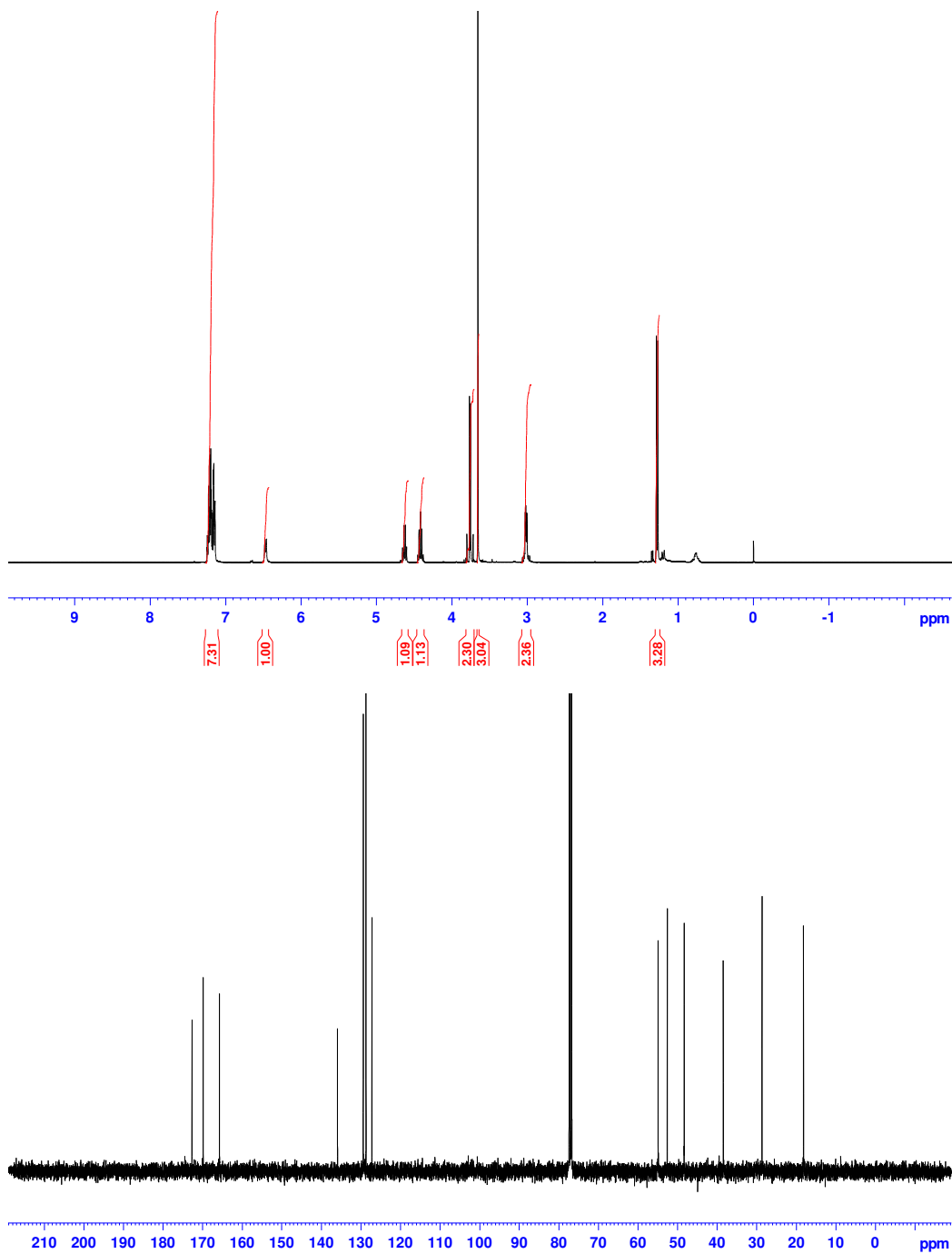
$^1\text{H}$  and  $^{13}\text{C}$  NMR Spectra (**18b**)

**L-Phenylalanine-L-alanine methyl ester bromoacetate-19b**



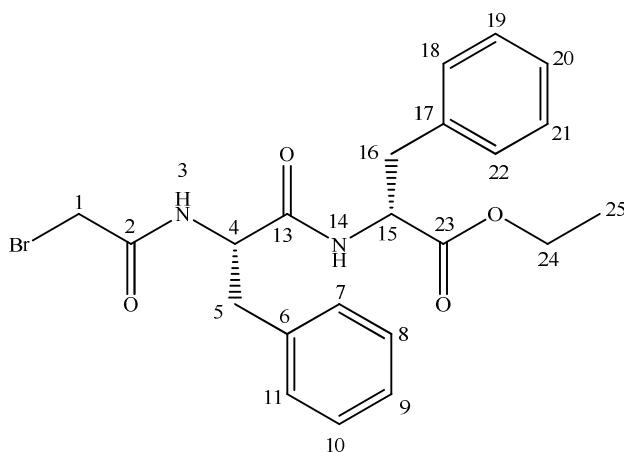
The title compound (**19b**) was prepared from L-phenylalanine-L-alanine methyl ester hydrochloride (**19a**) (1.768 g, 6.32 mmol) and bromoacetyl bromide (1.532 g, 7.58 mmol) according to the general procedure as a white solid in 73 % yield (1.710 g, 4.61 mmol).

m.p. 128-130 °C,  $[\alpha]_D^{20} = +24.4^\circ$  (0.8 c,  $\text{CHCl}_3$ ).  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 7.27-7.16 (m, 5H, *H7-11*), 7.05 (d,  $J = 7.6$  Hz, 1H, *H3*), 6.14 (d,  $J = 6.8$  Hz, 1H, *H14*), 4.52 (ddd,  $J = 8.0, 6.4, 6.0$  Hz, 1H, *H4*), 4.53 (dq,  $J = 7.4, 7.2$  Hz, 1H, *H15*), 3.79 (d,  $J = 4.8$  Hz, 2H, *H1*), 3.66 (s, 3H, *H18*), 3.08 (dd,  $J = 14.0, 6.4$  Hz, 1H, *H5*), 2.98 (dd,  $J = 14.0, 7.6$  Hz, 1H, *H5*), 1.29 (d,  $J = 7.2$  Hz, 3H, *H16*).  $^{13}\text{C}$  NMR (150 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 172.72 (CO, *C2*), 169.90 (CO, *C17*), 165.78 (CO, *C13*), 135.91 (ArC, *C6*), 129.42 (ArCH), 128.71 (ArCH), 127.23 (ArCH, *C9*), 54.91 (CH, *C4*), 52.58 (OCH<sub>3</sub>, *C18*), 48.30 (CH, *C15*), 38.44 (CH<sub>2</sub>, *C5*), 28.63 (CH<sub>2</sub>, *C1*), 18.16 (CH<sub>3</sub>, *C16*)



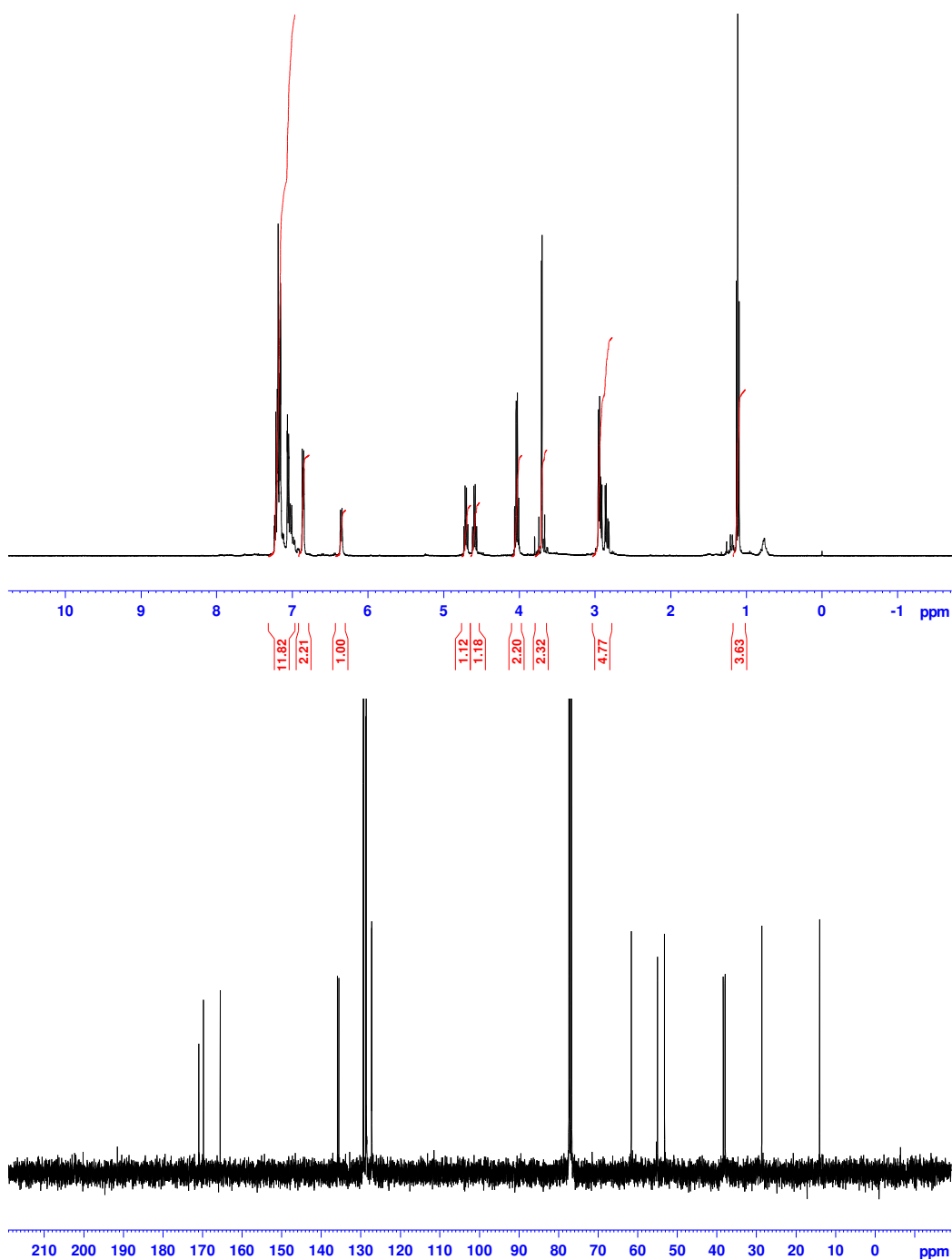
$^1\text{H}$  and  $^{13}\text{C}$  NMR Spectra (**19b**)

**L-Phenylalanine-D-phenylalanine ethyl ester bromoacetate-20b**



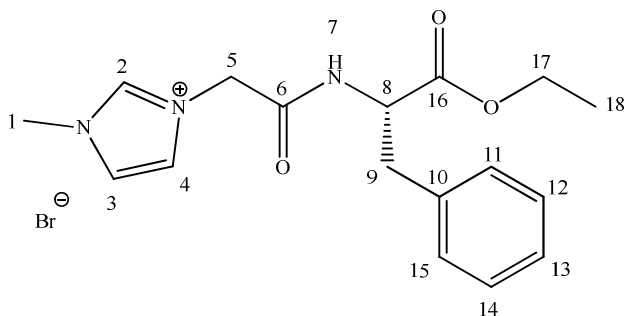
The title compound (**20b**) was prepared from L-phenylalanine–D-phenylalanine ethyl ester hydrochloride (**20a**) (2.050 g, 5.40 mmol) and bromoacetyl bromide (1.322 g, 6.50 mmol) according to the general procedure as a white solid in 69 % yield (1.731 g, 3.75 mmol).

m.p. 110-112 °C,  $[\alpha]_D^{20} = -30.0^\circ$  (0.9 c, CHCl<sub>3</sub>). <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 7.35-7.18 (m, 10H, *H*7-11,18-22), 6.99 (d, *J* = 8.0 Hz, 1H, *H*3), 6.13 (d, *J* = 8.4 Hz, 1H, *H*14), 4.83 (ddd, *J* = 8.0, 6.4, 6.0 Hz, 1H, *H*4), 4.64 (ddd, *J* = 8.4, 6.0, 6.0 Hz, 1H, *H*15), 4.18 (dq, *J* = 7.2, 7.2 Hz, 1H, *H*24), 4.16 (dq, *J* = 7.2, 7.2 Hz, 1H, *H*24), 3.83 (s, 2H, *H*1), 3.11-2.89 (m, 4H, *H*5,16), 1.22 (t, *J* = 7.2 Hz, 3H, *H*25). <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 170.01 (CO,C2), 169.81 (CO,C23), 165.59 (CO,C13), 135.94 (ArC,C6/C17), 135.56 (ArC,C6/C17), 129.42 (ArCH), 129.34 (ArCH), 128.76 (ArCH), 128.60 (ArCH), 127.27 (ArCH,C9/C20), 127.22 (ArCH,C9/C20), 61.63 (OCH<sub>2</sub>,C24), 55.28 (CH,C4), 53.23 (CH,C15), 38.37 (CH<sub>2</sub>,C5/C16), 37.91 (CH<sub>2</sub>,C5/C16), 28.28 (CH<sub>2</sub>,C1), 14.07 (CH<sub>3</sub>,C25)



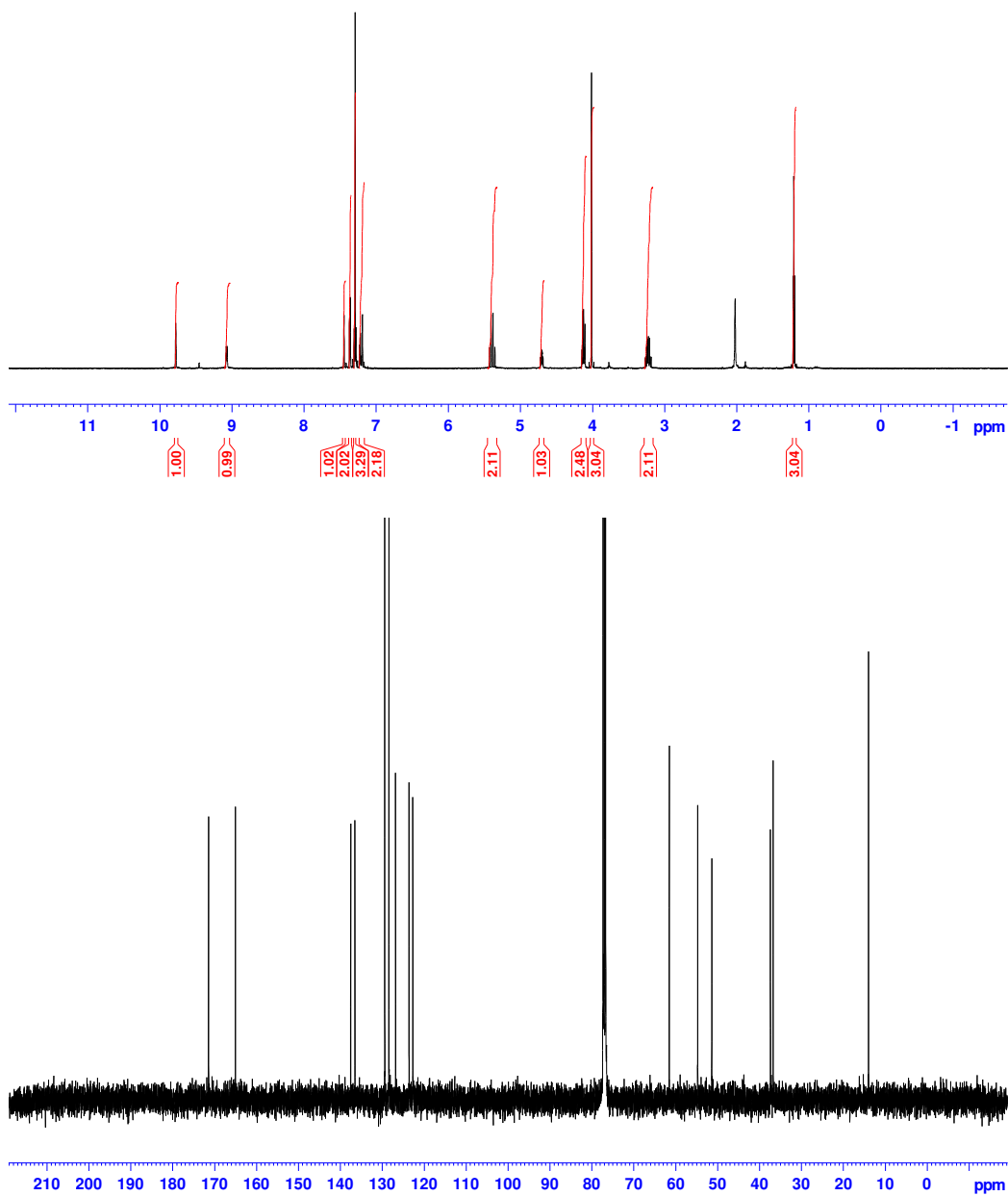
$^1\text{H}$  and  $^{13}\text{C}$  NMR Spectra (**20b**)

### 3-Methyl-1-L-phenylalanine ethyl ester imidazolium bromide-1c



To a stirred solution of 1-methylimidazole (0.454 g, 5.55 mmol) in tetrahydrofuran at -78 °C under a nitrogen atmosphere L-phenylalanine ethyl ester bromoacetate (**1b**) (2.081 g, 6.60 mmol) was added dropwise. The reaction mixture was stirred vigorously at -15 °C for 2h, then at RT overnight. The THF top phase was decanted and the IL washed with diethyl ether (3 x 10 mL). The residual solvent was removed on the rotary evaporator and the product was dried under high vacuum for 24 h to yield the title product (**1c**) as a colourless viscous liquid in 98 % yield (2.152 g, 5.43 mmol).

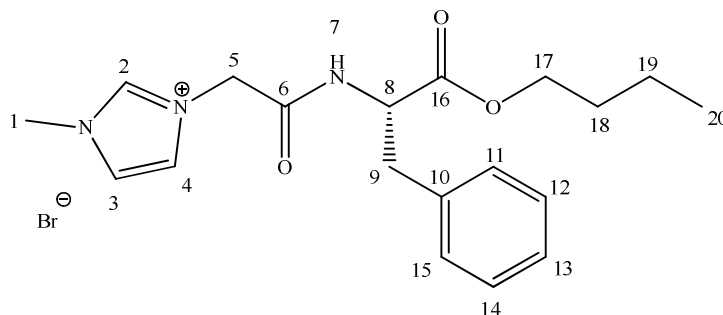
$[\alpha]_D^{20} = +17.0^\circ$  (0.7 c,  $\text{CHCl}_3$ ).  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 9.74 (s, 1H,  $H_2$ ), 9.01 (d,  $J = 7.6$  Hz, 1H,  $H_7$ ), 7.68 (t,  $J = 1.6$  Hz, 1H,  $H_4$ ), 7.60 (t,  $J = 1.8$  Hz, 1H,  $H_3$ ), 7.33-7.22 (m, 5H,  $H_{11-15}$ ), 5.42 (d,  $J = 5.6$  Hz, 2H,  $H_5$ ), 4.46 (ddd,  $J = 7.8, 5.6, 5.6$  Hz, 1H,  $H_8$ ), 4.04 (q,  $J = 7.2$  Hz, 2H,  $H_{17}$ ), 3.92 (s, 3H,  $H_1$ ), 3.07 (dd,  $J = 13.0, 6.0$  Hz, 1H,  $H_9$ ), 2.96 (dd,  $J = 10.0, 8.8$  Hz, 1H,  $H_9$ ), 1.14 (t,  $J = 7.2$  Hz, 3H,  $H_{18}$ ).  $^{13}\text{C NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 171.22 (CO,  $C_{16}$ ), 164.80 (CO,  $C_6$ ), 137.78 (NCHN,  $C_2$ ) 136.66 (ArC,  $C_{10}$ ), 129.52 (ArCH), 128.48 (ArCH), 126.79 (ArCH,  $C_{13}$ ), 123.69 (NCH,  $C_4$ ), 122.39 (NCH,  $C_3$ ), 61.50 ( $\text{OCH}_2$ ,  $C_{17}$ ), 54.81 (CH,  $C_8$ ), 51.54 ( $\text{NCH}_2$ ,  $C_5$ ), 37.40 ( $\text{CH}_2$ ,  $C_9$ ), 36.76 ( $\text{NCH}_3$ ,  $C_1$ ), 14.06 ( $\text{CH}_3$ ,  $C_{18}$ ). IR (neat) ( $\text{cm}^{-1}$ ) 3160 (b), 3034 (w), 1735 (m), 1682 (s), 1548 (s), 1172 (vs), 747 (m), 701 (m). MS ( $m/z$ ) Found  $[\text{M}-\text{Br}]^+$  316.1653,  $\text{C}_{17}\text{H}_{22}\text{N}_3\text{O}_3^+$  requires 316.1655



$^1\text{H}$  and  $^{13}\text{C}$  NMR Spectra (**1c**)

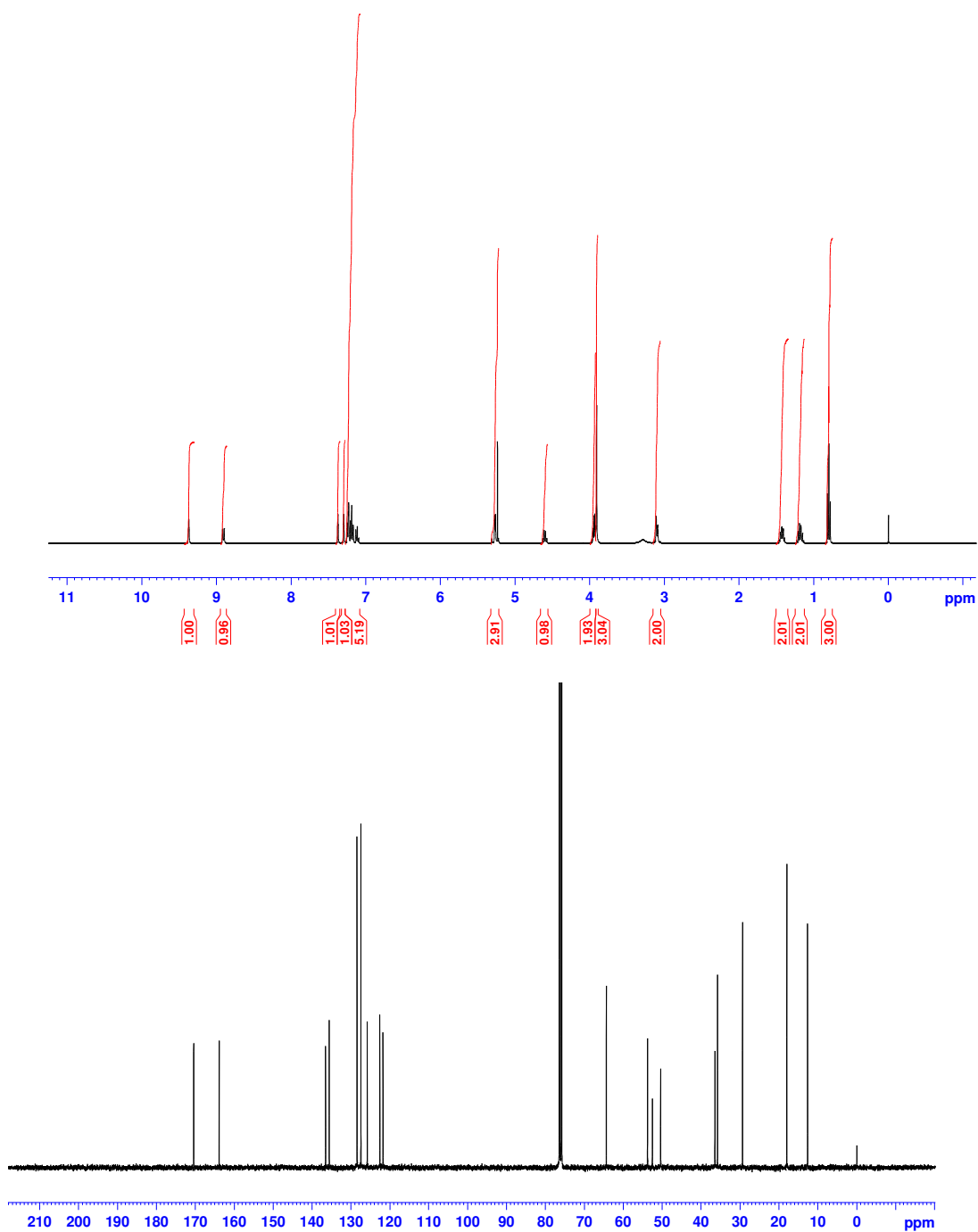


### 3-Methyl-1-L-phenylalanine butyl ester imidazolium bromide-2c



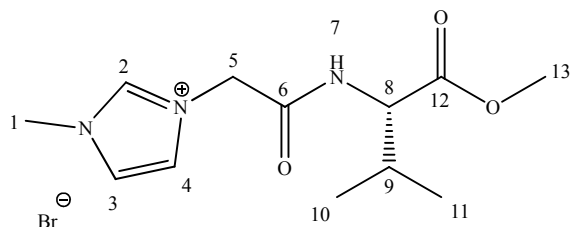
The title compound (**2c**) was prepared from 1-methylimidazole (0.401 g, 4.90 mmol) and L-phenylalanine butyl ester bromoacetate (**2b**) (1.991 g, 5.85 mmol) according to the general procedure as a colourless viscous liquid in 99 % yield (2.072 g, 4.89 mmol).

$[\alpha]_D^{20} = +20.0^\circ$  (0.9 c,  $\text{CHCl}_3$ ).  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 9.48 (s, 1H, *H*2), 8.95 (d,  $J = 7.6$  Hz, 1H, *H*7), 7.36 (t,  $J = 1.6$  Hz, 1H, *H*4), 7.30-7.12 (m, 6H, *H*3, *H*11-15), 5.33 (d,  $J = 8.4$  Hz, 2H, *H*5), 4.63 (ddd,  $J = 7.8, 5.2, 5.2$  Hz, 1H, *H*8), 4.10 (dq,  $J = 7.2, 7.2$  Hz, 1H, *H*17), 4.09 (dq,  $J = 7.2, 7.2$  Hz, 1H, *H*17), 3.92 (s, 3H, *H*1), 3.11 (dd,  $J = 13.6, 6.0$  Hz, 1H, *H*9), 3.07 (dd,  $J = 13.6, 5.6$  Hz, 1H, *H*9), 1.45 (tt,  $J = 7.0, 6.8$  Hz, 2H, *H*18), 1.24 (tq,  $J = 7.2, 7.0$  Hz, 2H, *H*19), 0.83 (t,  $J = 7.4$  Hz, 3H, *H*20).  $^{13}\text{C NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 171.33 (CO, *C*16), 164.76 (CO, *C*6), 137.77 (NCHN, *C*2), 136.64 (ArC, *C*10), 129.49 (ArCH), 128.44 (ArCH), 126.79 (ArCH, *C*13), 123.69 (NCH, *C*4), 122.38 (NCH, *C*3), 65.39 (OCH<sub>2</sub>, *C*17), 54.80 (CH, *C*8), 51.55 (NCH<sub>2</sub>, *C*5), 37.43 (CH<sub>2</sub>, *C*9), 36.77 (NCH<sub>3</sub>, *C*1), 35.48 (CH<sub>2</sub>, *C*18), 19.00 (CH<sub>2</sub>, *C*19), 13.70 (CH<sub>3</sub>, *C*20). IR (neat) ( $\text{cm}^{-1}$ ) 3423 (b), 3214 (w), 2959 (w), 1735 (m), 1683 (s), 1561 (m), 1174 (vs), 744 (m), 700 (m). MS ( $m/z$ ) Found  $[\text{M}-\text{Br}]^+$  344.1964,  $\text{C}_{19}\text{H}_{26}\text{N}_3\text{O}_3^+$  requires 344.1968



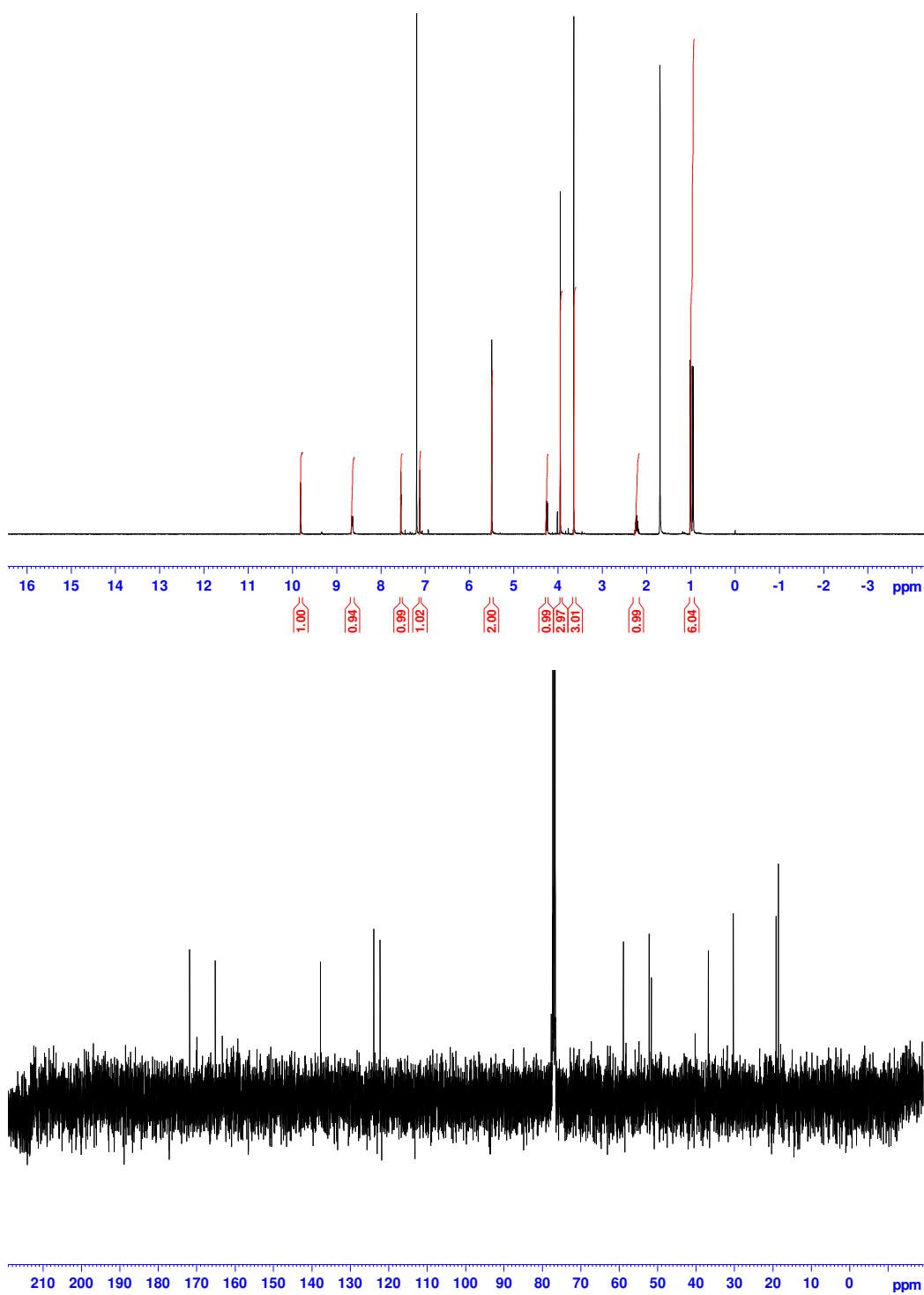
$^1\text{H}$  and  $^{13}\text{C}$  NMR Spectra (**2c**)

### 3-Methyl-1-L-valine methyl ester imidazolium bromide-3c



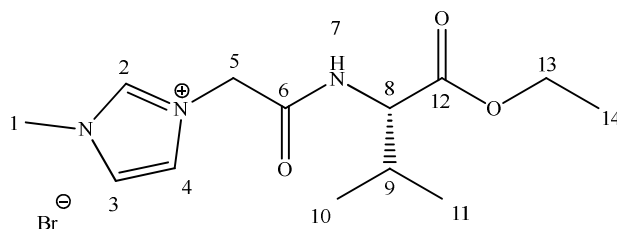
The title compound (**3c**) was prepared from 1-methylimidazole (0.123 g, 1.45 mmol) and L-valine methyl ester bromoacetate (**3b**) (0.552 g, 2.20 mmol) according to the general procedure as a pale yellow liquid in 85 % yield (0.412 g, 1.23 mmol).

$[\alpha]_D^{20} = -9.6^\circ$  (0.7 c,  $\text{CHCl}_3$ ).  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 9.55 (s, 1H, *H*2), 8.53 (d,  $J = 7.6$  Hz, 1H, *H*7), 7.45 (t,  $J = 1.6$  Hz, 1H, *H*4), 7.27 (t,  $J = 1.6$  Hz, 1H, *H*3), 5.36 (s, 2H, *H*5), 4.30 (dd,  $J = 8.8, 4.8$  Hz, 1H, *H*8), 3.86 (s, 3H, *H*1), 3.52 (s, 3H, *H*13), 2.15 (qqd,  $J = 6.8, 6.4, 4.8$  Hz, 1H, *H*9), 0.90 (d,  $J = 6.8$  Hz, 3H, *H*10/*H*11), 0.85 (d,  $J = 7.2$  Hz, 3H, *H*10/*H*11).  $^{13}\text{C NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 171.96 (CO, *C*12), 165.28 (CO, *C*6), 137.79 (NCHN, *C*2), 123.95 (NCH, *C*4), 122.31 (NCH, *C*3), 58.90 (CH, *C*8), 52.26 (NCH<sub>2</sub>, *C*5), 51.68 (OCH<sub>3</sub>, *C*13), 36.80 (NCH<sub>3</sub>, *C*1), 30.32 (CH, *C*9), 19.18 (CH<sub>3</sub>, *C*10/*C*11), 18.55 (CH<sub>3</sub>, *C*10/*C*11). IR (neat) ( $\text{cm}^{-1}$ ) 3386 (b), 3232 (b), 2965 (w), 1733 (m), 1678 (s), 1545 (m), 1209 (s), 1174 (vs). MS ( $m/z$ ) Found  $[\text{M}-\text{Br}]^+$  254.1493,  $\text{C}_{12}\text{H}_{20}\text{N}_3\text{O}_3^+$  requires 254.1499



$^1\text{H}$  and  $^{13}\text{C}$  NMR Spectra (**3c**)

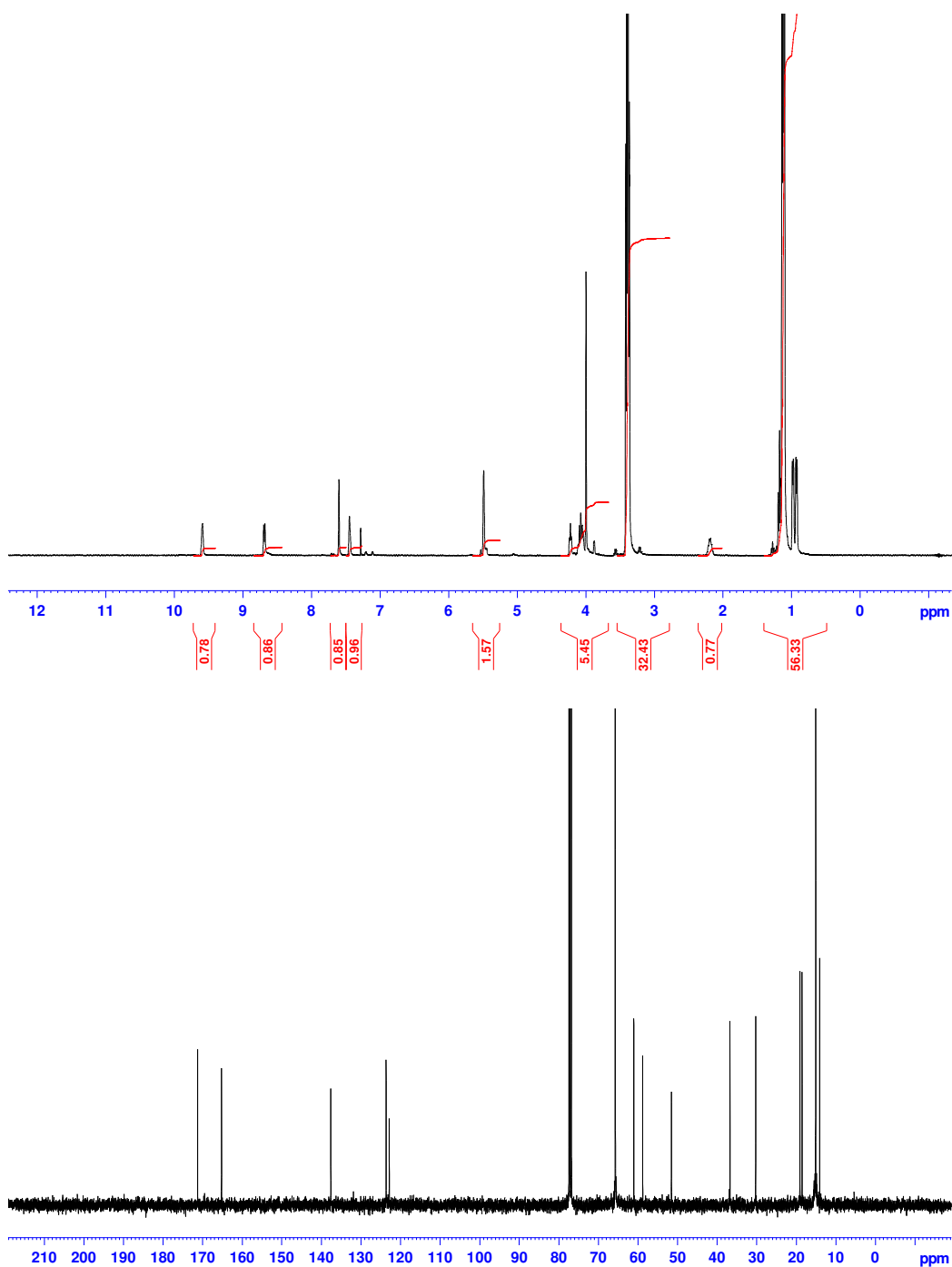
### 3-Methyl-1-L-valine ethyl ester imidazolium bromide-4c



The title compound (**4c**) was prepared from 1-methylimidazole (0.418 g, 5.10 mmol) and L-valine ethyl ester bromoacetate (**4b**) (1.532 g, 6.15 mmol) according to the general procedure (Section 7.3.3, page 295) as a pale yellow liquid in 98 % yield (1.744 g, 5.01 mmol).

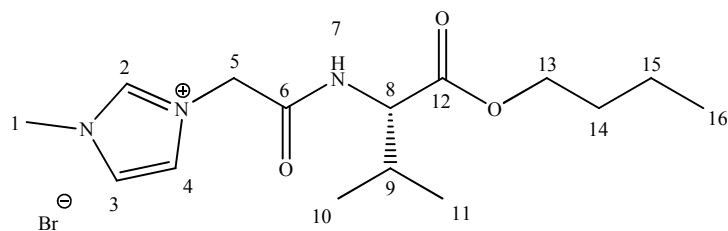
$[\alpha]_D^{20} = -11.2^\circ$  (0.8 c,  $\text{CHCl}_3$ ).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 9.60 (s, 1H,  $H_2$ ), 8.82 (d,  $J = 8.0$  Hz, 1H,  $H_7$ ), 7.64 (t,  $J = 1.8$  Hz, 1H,  $H_4$ ), 7.38 (t,  $J = 1.8$  Hz, 1H,  $H_3$ ), 5.53 (d,  $J = 4.0$  Hz, 2H,  $H_5$ ), 4.44 (dd,  $J = 8.0, 4.8$  Hz, 1H,  $H_8$ ), 4.18 (dq,  $J = 7.2, 7.2$  Hz, 1H,  $H_{13}$ ), 4.17 (dq,  $J = 7.2, 7.0$  Hz, 1H,  $H_{13}$ ), 4.04 (s, 3H,  $H_1$ ), 2.16 (qqd,  $J = 6.8, 6.8, 4.8$  Hz, 1H,  $H_9$ ), 1.21 (t,  $J = 7.2$  Hz, 3H,  $H_{14}$ ), 1.06 (d,  $J = 6.8$  Hz, 3H,  $H_{10/11}$ ), 0.96 (d,  $J = 6.8$  Hz, 3H,  $H_{10/11}$ )

$^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 170.96 (CO,  $C_{12}$ ), 165.33 (CO,  $C_6$ ), 137.74 (NCHN,  $C_2$ ), 123.75 (NCH,  $C_4$ ), 122.95 (NCH,  $C_3$ ), 60.56 ( $\text{OCH}_3$ ,  $C_{13}$ ), 57.72 (CH,  $C_8$ ), 50.26 (NCH<sub>2</sub>,  $C_5$ ), 35.78 (NCH<sub>3</sub>,  $C_1$ ), 30.11 (CH,  $C_9$ ), 18.84 ( $\text{CH}_3$ ,  $C_{10}$ ), 18.03 ( $\text{CH}_3$ ,  $C_{11}$ ), 14.07 ( $\text{CH}_3$ ,  $C_{14}$ ). IR (neat) ( $\text{cm}^{-1}$ ) 3401 (b), 3219 (b), 2967 (w), 1733 (s), 1681 (vs), 1545 (s), 1373 (m), 1173 (vs), 1022 (s). MS ( $m/z$ ) Found  $[\text{M}-\text{Br}]^+$  268.1661,  $\text{C}_{13}\text{H}_{22}\text{N}_3\text{O}_3^+$  requires 268.1655



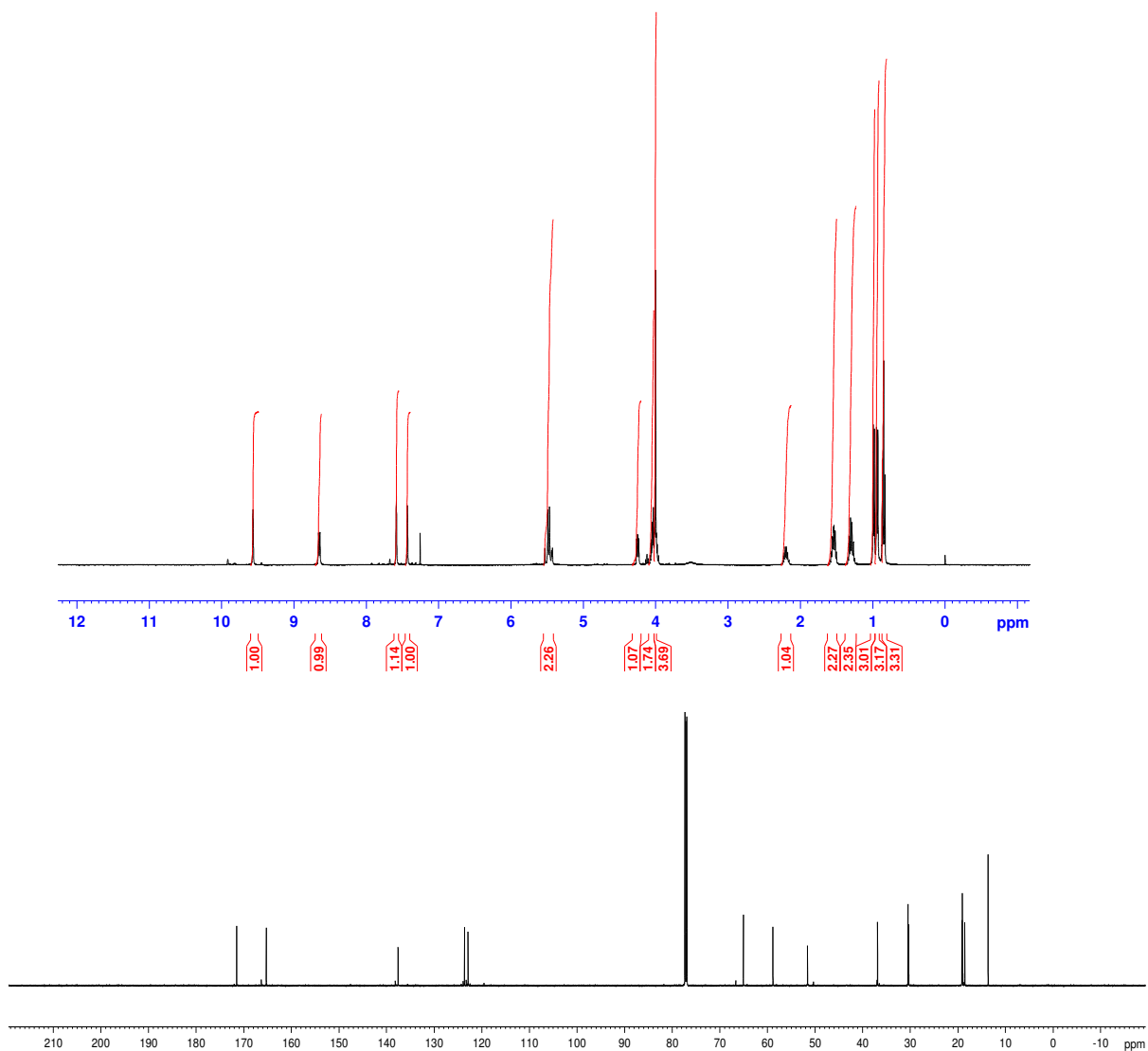
$^1\text{H}$  and  $^{13}\text{C}$  NMR Spectra (4c)

### 3-Methyl-1-L-valine butyl ester imidazolium bromide-5c



The title compound (**5c**) was prepared from 1-methylimidazole (0.399 g, 4.86 mmol) and L-valine butyl ester bromoacetate (**5b**) (1.641 g, 5.85 mmol) according to the general procedure as a viscous pale yellow liquid in 96 % yield (1.755 g, 4.67 mmol).

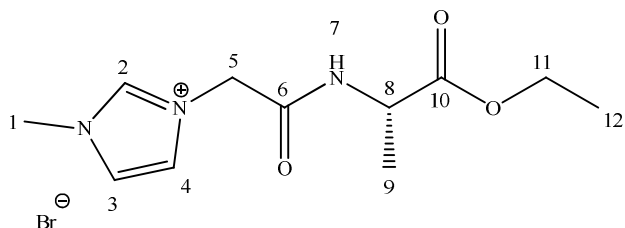
$[\alpha]_D^{20} = -5.0^\circ$  (0.8 c,  $\text{CHCl}_3$ ).  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 9.59 (s, 1H, *H*2), 8.81 (d,  $J = 8.0$  Hz, 1H, *H*7), 7.70 (t,  $J = 1.8$  Hz, 1H, *H*4), 7.64 (t,  $J = 1.6$  Hz, 1H, *H*3), 5.10 (d,  $J = 4.0$  Hz, 2H, *H*5), 4.23 (dd,  $J = 8.8, 4.4$  Hz, 1H, *H*8), 4.09 (dq,  $J = 7.2, 7.2$  Hz, 1H, *H*13), 4.08 (dq,  $J = 7.2, 7.2$  Hz, 1H, *H*13), 3.92 (s, 3H, *H*1), 2.12 (qqd,  $J = 6.8, 6.0, 4.8$  Hz, 1H, *H*9), 1.58 (tt,  $J = 7.0, 6.8$  Hz, 2H, *H*14), 1.33 (tq,  $J = 7.2, 7.0$  Hz, 2H, *H*15), 0.93-0.87 (m, 9H, *H*10,11,16).  $^{13}\text{C NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 171.51 (CO,*C*12), 165.22 (CO,*C*6), 137.77 (NCHN,*C*2), 123.85 (NCH,*C*4), 122.44 (NCH,*C*3), 65.15 (OCH<sub>2</sub>,*C*13), 58.91 (CH,*C*8), 51.65 (NCH<sub>2</sub>,*C*5), 36.84 (NCH<sub>3</sub>,*C*1), 30.54 (CH<sub>2</sub>,*C*14), 30.35 (CH,*C*9), 19.23 (CH<sub>2</sub>,*C*15), 19.13 (CH<sub>3</sub>,*C*10/*C*11), 18.51 (CH<sub>3</sub>,*C*10/*C*11), 13.71 (CH<sub>3</sub>,*C*16). IR (neat) ( $\text{cm}^{-1}$ ) 3386 (b), 3197 (w), 2961 (m), 1733 (s), 1678 (vs), 1545 (s), 1209 (m), 1174 (vs). MS ( $m/z$ ) Found  $[\text{M}-\text{Br}]^+$  296.1967,  $\text{C}_{15}\text{H}_{26}\text{N}_3\text{O}_3^+$  requires 296.1968



$^1\text{H}$  and  $^{13}\text{C}$  NMR Spectra (**5c**)

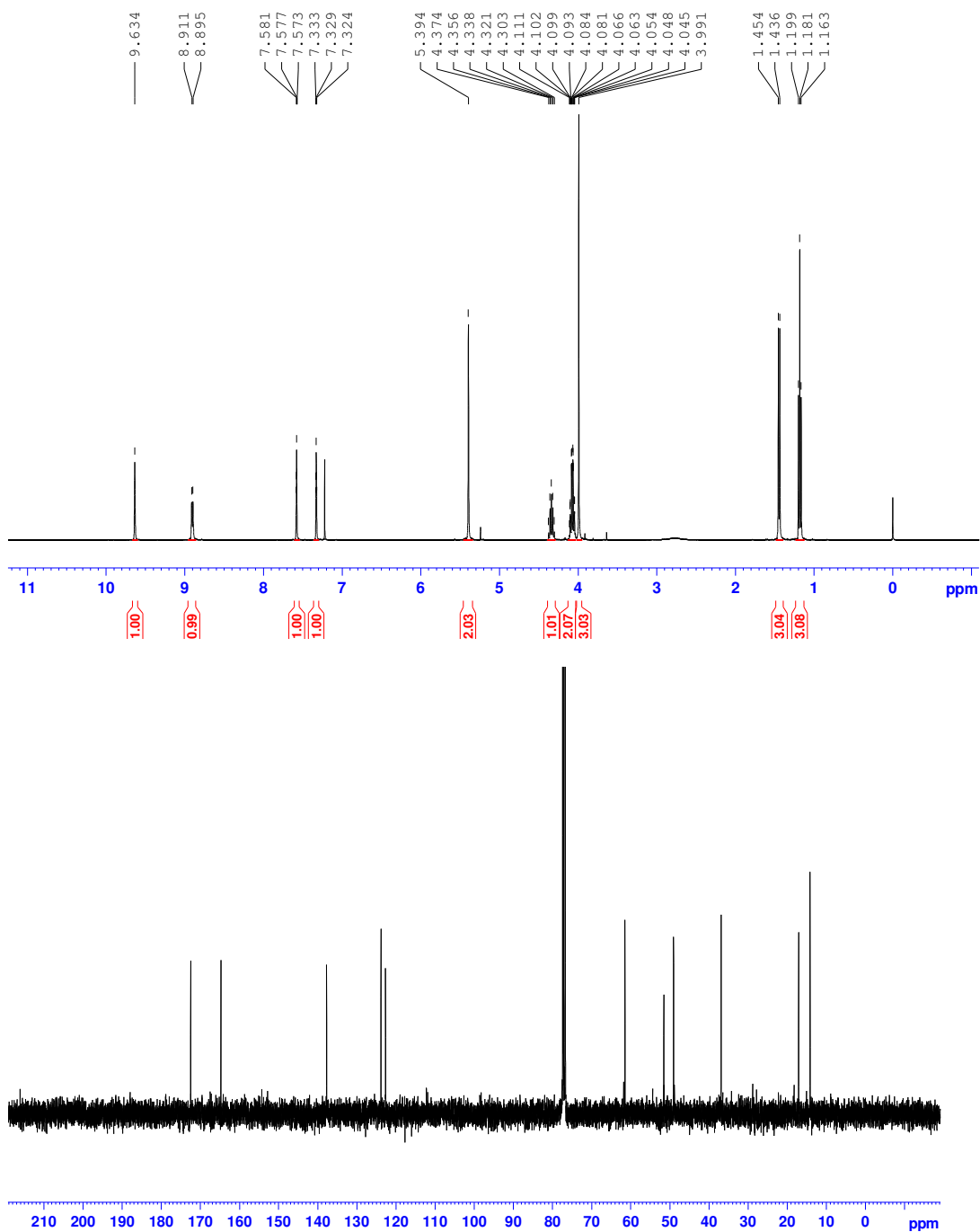


### 3-Methyl-1-L-alanine ethyl ester imidazolium bromide-6c



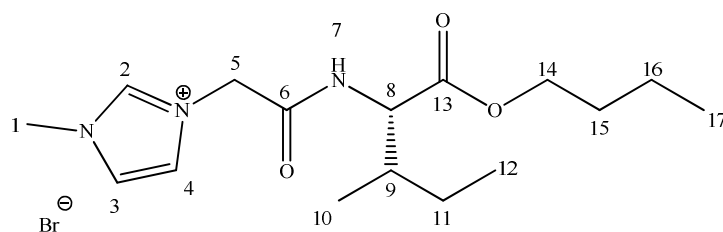
The title compound was prepared from 1-methylimidazole (0.190 g, 2.70 mmol) and L-alanine ethyl ester bromoacetate (**6b**) (0.653 g, 2.70 mmol) according to the general procedure as a pale yellow liquid in 90 % yield (0.781 g, 2.44 mmol).

$[\alpha]_D^{20} = -16.0^\circ$  (1.0 c,  $\text{CHCl}_3$ ).  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 9.63 (s, 1H, *H*2), 8.90 (d,  $J = 6.4$  Hz, 1H, *H*7), 7.58 (t,  $J = 1.8$  Hz, 1H, *H*4), 7.33 (t,  $J = 1.6$  Hz, 1H, *H*3), 5.39 (s, 2H, *H*5), 4.33 (dq,  $J = 7.2, 7.2$  Hz, 1H, *H*8), 4.09 (dq,  $J = 7.2, 7.2$  Hz, 1H, *H*11), 4.08 (dq,  $J = 7.2, 7.2$  Hz, 1H, *H*11), 3.99 (s, 3H, *H*1), 1.44 (d,  $J = 7.2$  Hz, 3H, *H*9), 1.18 (t,  $J = 7.2$  Hz, 3H, *H*12).  $^{13}\text{C NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 172.49 (CO, *C*10), 164.76 (CO, *C*6), 137.75 (NCHN, *C*2), 123.85 (NCH, *C*4), 122.67 (NCH, *C*3), 61.48 ( $\text{OCH}_2$ , *C*11), 51.52 ( $\text{NCH}_2$ , *C*5), 49.03 (CH, *C*8), 36.88 ( $\text{NCH}_3$ , *C*1), 17.05 ( $\text{CH}_3$ , *C*9), 14.15 ( $\text{CH}_3$ , *C*12). IR (neat) ( $\text{cm}^{-1}$ ) 3406 (b), 2985 (w), 1731 (m), 1681 (s), 1564 (m), 1210 (s), 1183 (s), 1173(vs). MS ( $m/z$ ) Found  $[\text{M}-\text{Br}]^+$  240.1342,  $\text{C}_{11}\text{H}_{18}\text{N}_3\text{O}_3^+$  requires 240.1342



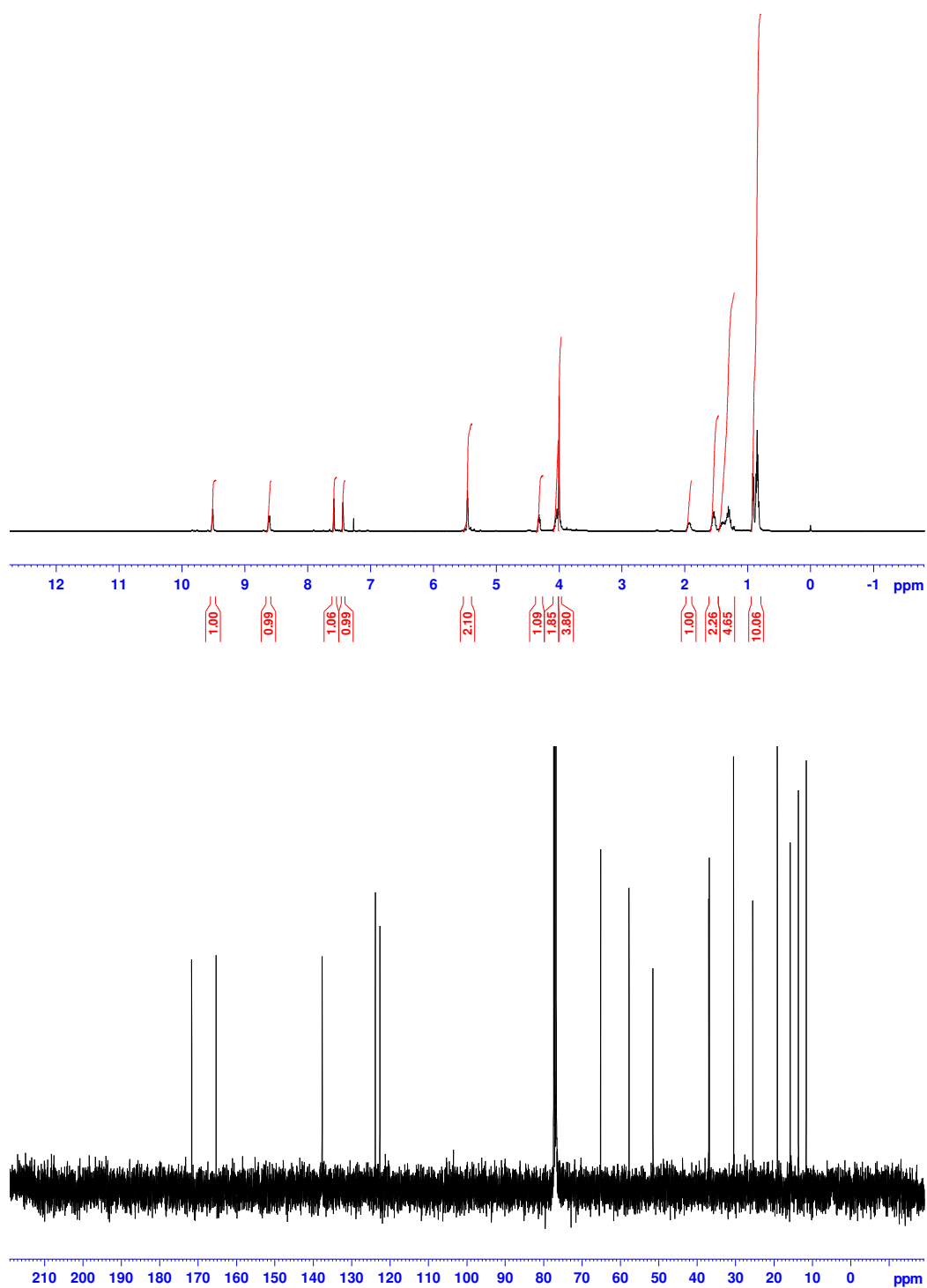
$^1\text{H}$  and  $^{13}\text{C}$  NMR Spectra (6c)

### 3-Methyl-1-L-isoleucine butyl ester imidazolium bromide-7c



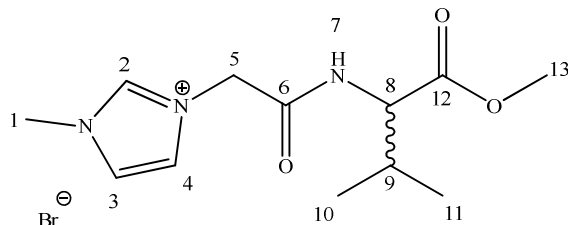
The title compound (**7c**) was prepared from 1-methylimidazole (0.276 g, 3.37 mmol) and L-isoleucine butyl ester bromoacetate (**7b**) (1.451 g, 4.72 mmol) according to the general procedure as a colourless viscous liquid in 98 % yield (1.284 g, 3.29 mmol).

$[\alpha]_D^{20} = -3.2^\circ$  (0.9 c,  $\text{CHCl}_3$ ).  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 9.42 (s, 1H, *H2*), 8.55 (d,  $J = 7.6$  Hz, 1H, *H7*), 7.54 (t,  $J = 1.8$  Hz, 1H, *H4*), 7.29 (t,  $J = 1.8$  Hz, 1H, *H3*), 5.38 (s, 2H, *H5*), 4.34 (dd,  $J = 8.8, 6.8$  Hz, 1H, *H8*), 4.09-3.98 (m, 2H, *H14*), 3.95 (s, 3H, *H1*), 1.97 (dddq,  $J = 8.0, 8.0, 7.2, 6.8$  Hz, 1H, *H9*), 1.46 (ddq,  $J = 8.0, 8.0, 7.2$  Hz, 1H, *H11*), 1.38 (ddq,  $J = 8.0, 8.0, 7.0$  Hz, 1H, *H11*), 1.45-1.23 (m, 4H, *H15,16*), 0.92 (d,  $J = 6.8$  Hz, 3H, *H10*), 0.87-0.82 (m, 6H, *H12,17*).  $^{13}\text{C NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 171.70 (CO, *C13*), 165.33 (CO, *C6*), 137.69 (NCHN, *C2*), 123.84 (NCH, *C4*), 122.64 (NCH, *C3*), 65.16 (OCH<sub>2</sub>, *C14*), 57.75 (CH, *C8*), 51.52 (NCH<sub>2</sub>, *C5*), 36.96 (CH, *C9*), 36.84 (NCH<sub>3</sub>, *C1*), 30.51 (CH<sub>2</sub>), 25.51 (CH<sub>2</sub>, *C11*), 19.11 (CH<sub>2</sub>), 15.78 (CH<sub>3</sub>, *C10*), 13.66 (CH<sub>3</sub>, *C17*), 11.63 (CH<sub>3</sub>, *C12*). IR (neat) ( $\text{cm}^{-1}$ ) 3405 (b), 2961 (m), 1735 (s), 1682 (vs), 1545 (s), 1382 (w), 1174 (vs). MS ( $m/z$ ) Found  $[\text{M}-\text{Br}]^+$  310.2119,  $\text{C}_{16}\text{H}_{28}\text{N}_3\text{O}_3^+$  requires 310.2125



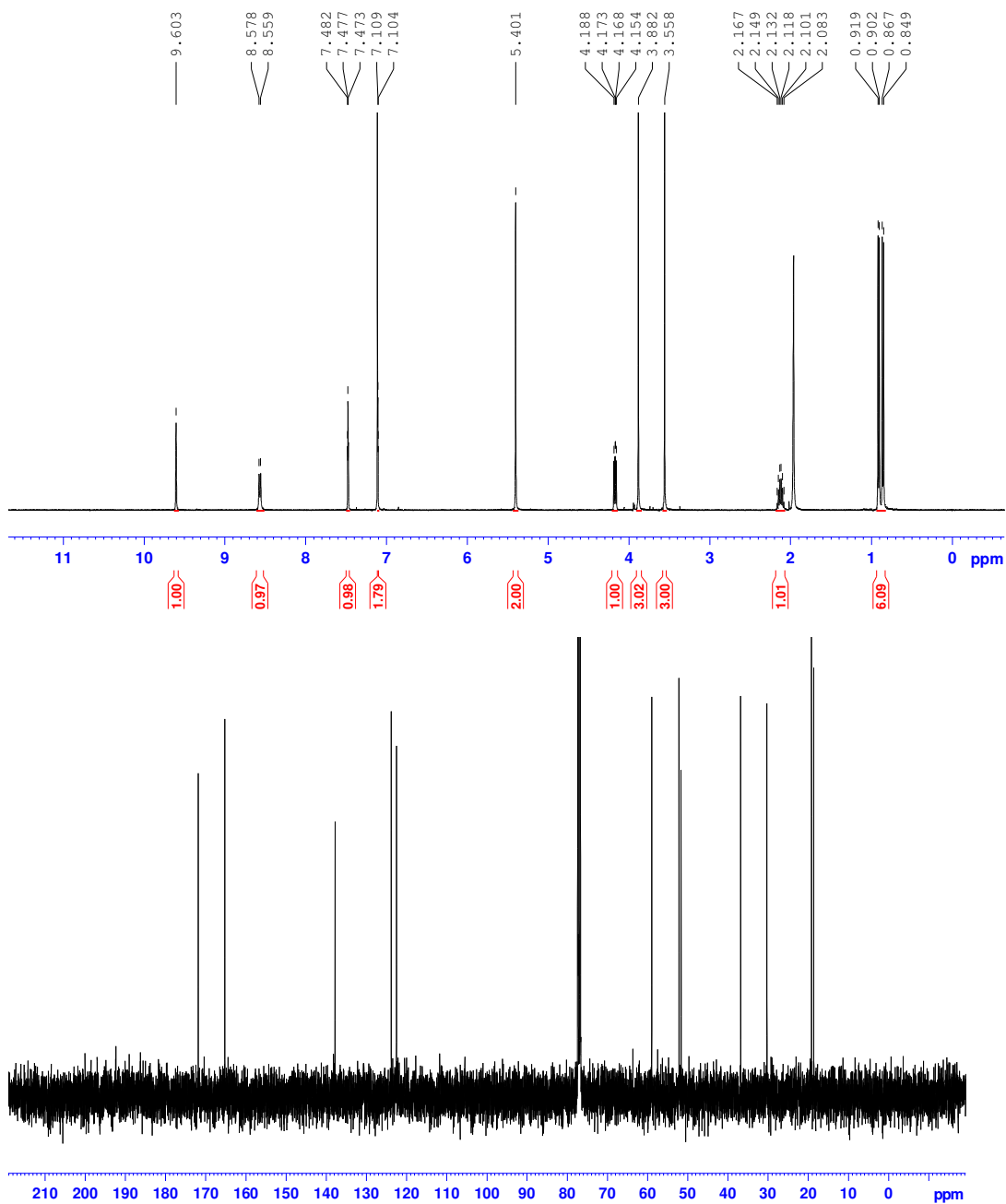
$^1\text{H}$  and  $^{13}\text{C}$  NMR Spectra (7c)

### 3-Methyl-1-DL-valine methyl ester imidazolium bromide-8c



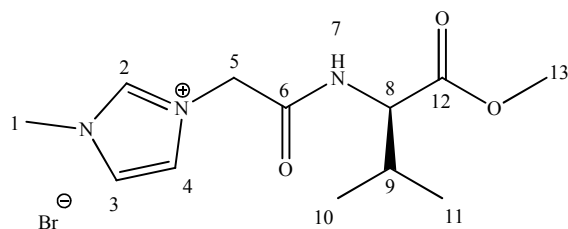
The title compound (**8c**) was prepared from 1-methylimidazole (0.283 g, 3.45 mmol) and DL-valine methyl ester bromoacetate (**8b**) (1.035 g, 4.12 mmol) according to the general procedure as a colourless viscous liquid in 87 % yield (1.003 g, 3.00 mmol).

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ (ppm) 9.60 (s, 1H, *H*2), 8.56 (d, *J* = 7.6 Hz, 1H, *H*7), 7.48 (t, *J* = 1.8 Hz, 1H, *H*4), 7.10 (t, *J* = 1.8 Hz, 1H, *H*3), 5.40 (s, 2H, *H*5), 4.17 (dd, *J* = 8.0, 5.6 Hz, 1H, *H*8), 3.88 (s, 3H, *H*1), 3.56 (s, 3H, *H*13), 2.13 (qqd, *J* = 6.8, 6.8, 5.2 Hz, 1H, *H*9), 0.90 (d, *J* = 6.8 Hz, 3H, *H*10/*H*11), 0.85 (d, *J* = 6.8 Hz, 3H, *H*10/*H*11). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ (ppm) 170.91 (CO, *C*12), 164.88 (CO, *C*6), 137.66 (NCHN, *C*2), 123.91 (NCH, *C*4), 122.43 (NCH, *C*3), 59.04 (CH, *C*8), 52.02 (NCH<sub>2</sub>, *C*5), 51.68 (OCH<sub>3</sub>, *C*13), 36.81 (NCH<sub>3</sub>, *C*1), 30.28 (CH, *C*9), 19.17 (CH<sub>3</sub>, *C*10/*C*11), 18.54 (CH<sub>3</sub>, *C*10/*C*11). IR (neat) (cm<sup>-1</sup>) 3149 (w), 2966 (m), 1736 (s), 1672 (vs), 1552 (m), 1203 (s), 1175 (s), 1147 (s). MS (*m/z*) Found [M-Br<sup>-</sup>]<sup>+</sup> 254.1501, C<sub>12</sub>H<sub>20</sub>N<sub>3</sub>O<sub>3</sub><sup>+</sup> requires 254.1499



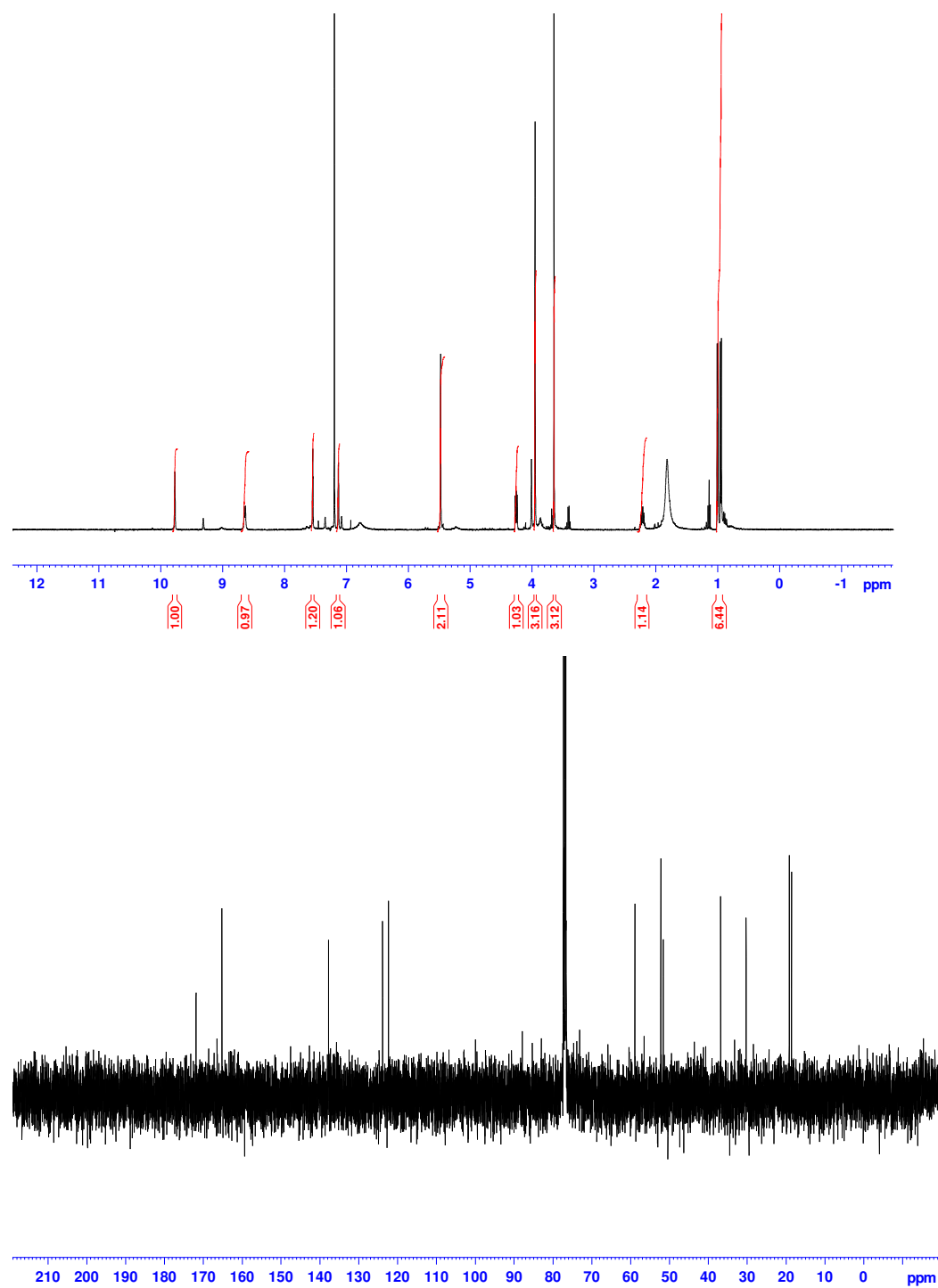
$^1\text{H}$  and  $^{13}\text{C}$  NMR Spectra (8c)

### 3-Methyl-1-D-valine methyl ester imidazolium bromide-9c



The title compound (**9c**) was prepared from 1-methylimidazole (0.283 g, 3.45 mmol) and D-valine methyl ester bromoacetate (**9b**) (1.035 g, 4.12 mmol) according to the general procedure as a colourless viscous liquid in 89 % yield (1.028 g, 3.08 mmol).

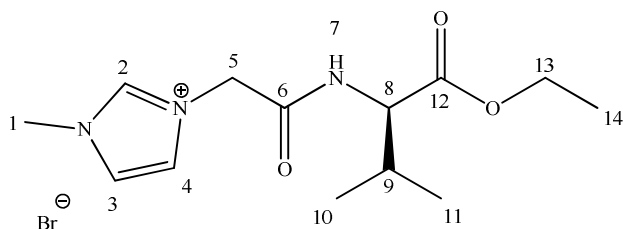
$[\alpha]_D^{20} = +9.3^\circ$  (0.7 c,  $\text{CHCl}_3$ ).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 9.77 (s, 1H, *H*2), 8.60 (d,  $J = 7.6$  Hz, 1H, *H*7), 7.57 (t,  $J = 1.8$  Hz, 1H, *H*4), 7.17 (t,  $J = 1.6$  Hz, 1H, *H*3), 5.42 (s, 2H, *H*5), 4.18 (dd,  $J = 8.0, 4.4$  Hz, 1H, *H*8), 3.88 (s, 3H, *H*1), 3.55 (s, 3H, *H*13), 2.18 (qqd,  $J = 6.8, 6.8, 4.4$  Hz, 1H, *H*9), 0.91 (d,  $J = 6.8$  Hz, 3H, *H*10/*H*11), 0.85 (d,  $J = 6.8$  Hz, 3H, *H*10/*H*11).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 171.87 (CO, *C*12), 165.27 (CO, *C*6), 137.78 (NCHN, *C*2), 123.83 (NCH, *C*4), 122.51 (NCH, *C*3), 58.98 (CH, *C*8), 52.15 (NCH<sub>2</sub>, *C*5), 51.66 (OCH<sub>3</sub>, *C*13), 36.82 (NCH<sub>3</sub>, *C*1), 30.29 (CH, *C*9), 19.19 (CH<sub>3</sub>, *C*10/*C*11), 18.66 (CH<sub>3</sub>, *C*10/*C*11). IR (neat) ( $\text{cm}^{-1}$ ) 3456 (b), 3148 (w), 2966 (w), 1736 (s), 1672 (vs), 1551 (m), 1203 (s), 1174 (s), 1147 (s). MS ( $m/z$ ) Found  $[\text{M}-\text{Br}]^+$  254.1499,  $\text{C}_{12}\text{H}_{20}\text{N}_3\text{O}_3^+$  requires 254.1499



$^1\text{H}$  and  $^{13}\text{C}$  NMR Spectra (**9c**)

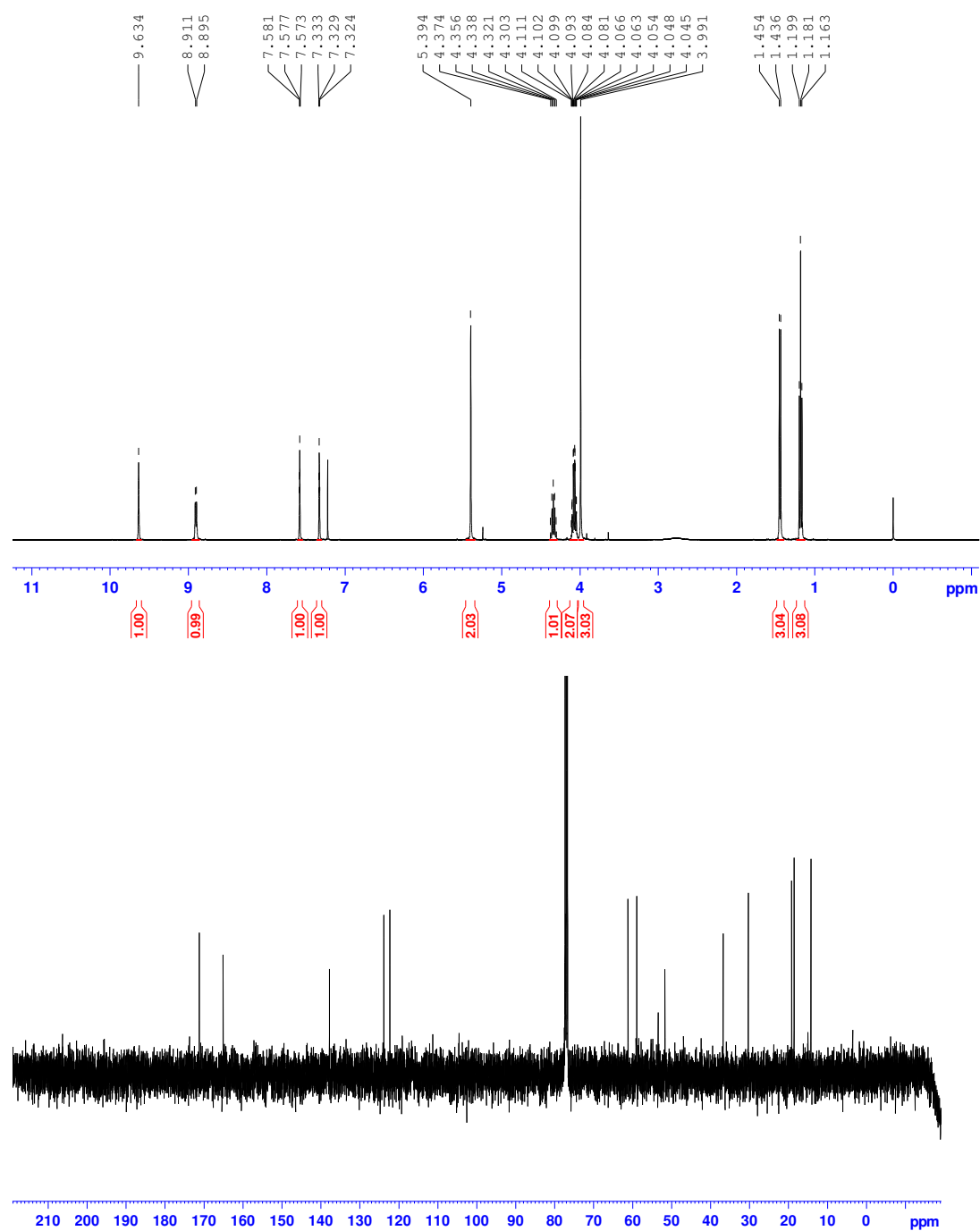


### 3-Methyl-1-D-valine ethyl ester imidazolium bromide-10c



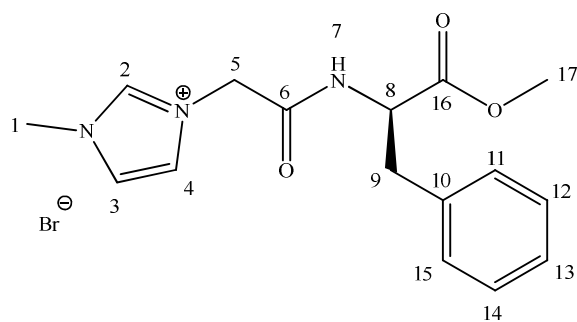
The title compound (**10c**) was prepared from 1-methylimidazole (0.382 g, 4.65 mmol) and D-valine ethyl ester bromoacetate (**10b**) (1.609 g, 6.04 mmol) according to the general procedure as a colourless liquid in 79 % yield (1.282 g, 3.68 mmol).

$[\alpha]_D^{20} = +10.0^\circ$  (0.9 c,  $\text{CHCl}_3$ ).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 9.51 (s, 1H,  $H_2$ ), 8.61 (d,  $J = 7.6$  Hz, 1H,  $H_7$ ), 7.63 (t,  $J = 1.8$  Hz, 1H,  $H_4$ ), 7.40 (t,  $J = 1.8$  Hz, 1H,  $H_3$ ), 5.48 (d,  $J = 4.0$  Hz, 2H,  $H_5$ ), 4.27 (dd,  $J = 8.0, 4.4$  Hz, 1H,  $H_8$ ), 4.12 (dq,  $J = 7.2, 7.0$  Hz, 1H,  $H_{13}$ ), 4.11 (dq,  $J = 7.0, 7.0$  Hz, 1H,  $H_{13}$ ), 4.01 (s, 3H,  $H_1$ ), 2.21 (qqd,  $J = 6.6, 6.8, 4.4$  Hz, 1H,  $H_9$ ), 1.22 (t,  $J = 7.0$  Hz, 3H,  $H_{14}$ ), 0.98 (d,  $J = 6.8$  Hz, 3H,  $H_{10/11}$ ), 0.91 (d,  $J = 6.8$  Hz, 3H,  $H_{10/11}$ ).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 171.40 (CO,  $C_{12}$ ), 165.26 (CO,  $C_6$ ), 137.60 (NCHN,  $C_2$ ), 123.82 (NCH,  $C_4$ ), 122.73 (NCH,  $C_3$ ), 61.25 ( $\text{OCH}_2$ ,  $C_{13}$ ), 58.76 (CH,  $C_8$ ), 50.30 (NCH<sub>2</sub>,  $C_5$ ), 36.74 (NCH<sub>3</sub>,  $C_1$ ), 30.37 (CH,  $C_9$ ), 19.09 (CH<sub>3</sub>,  $C_{10/C11}$ ), 18.36 (CH<sub>3</sub>,  $C_{10/C11}$ ), 14.19 (CH<sub>3</sub>,  $C_{14}$ ). IR (neat) ( $\text{cm}^{-1}$ ) 3047 (b), 2967 (w), 1733 (s), 1682 (vs), 1544 (s), 1198 (s), 1173 (s), 1150 (s). MS ( $m/z$ ) Found  $[\text{M}-\text{Br}]^+$  268.1657,  $\text{C}_{13}\text{H}_{22}\text{N}_3\text{O}_3^+$  requires 268.1655



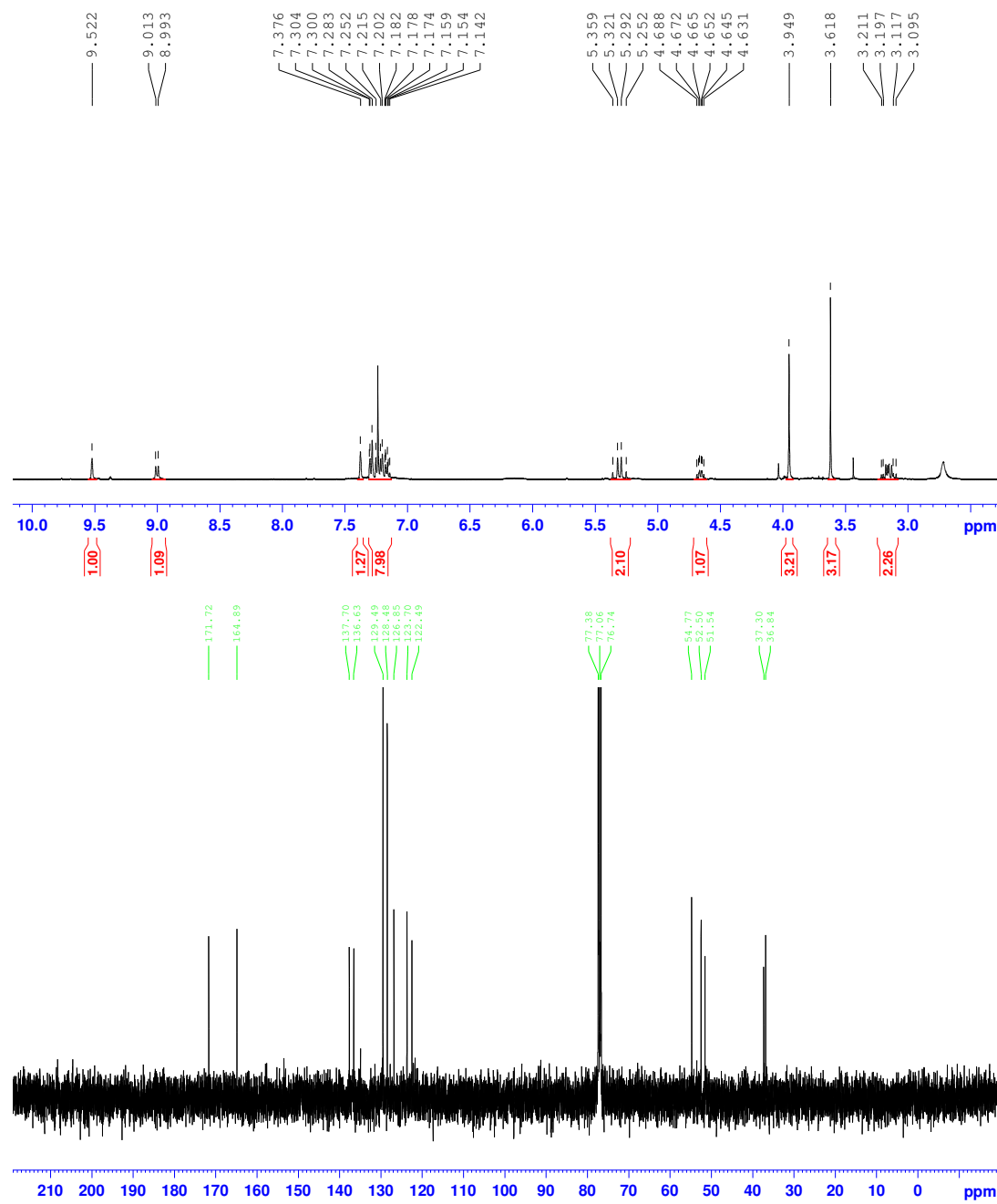
<sup>1</sup>H and <sup>13</sup>C NMR Spectra (**10c**)

### 3-Methyl-1-D-phenylalanine methyl ester imidazolium bromide-11c



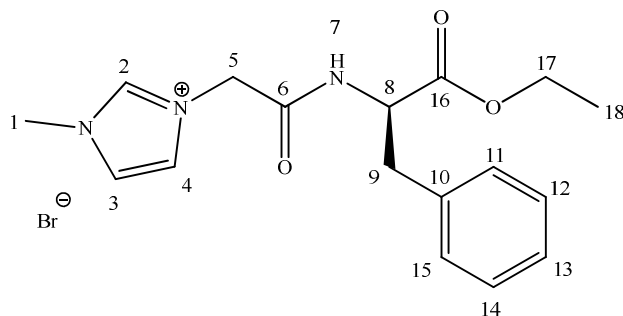
The title compound (**11c**) was prepared from 1-methylimidazole (0.432 g, 5.25 mmol) and D-phenylalanine methyl ester bromoacetate (**11b**) (1.881 g, 6.30 mmol) according to the general procedure as an off white solid in 87 % yield (1.753 g, 4.59 mmol).

m.p. 56-58 °C,  $[\alpha]_D^{20} = -19.0^\circ$  (1.0 c, CHCl<sub>3</sub>). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 9.52 (s, 1H, *H*2), 9.01 (d, *J* = 7.6 Hz, 1H, *H*7), 7.38 (s, 1H, *H*4), 7.30-7.14 (m, 6H, *H*3, *H*11-15), 5.28 (d, *J* = 10.0 Hz, 2H, *H*5), 4.64 (ddd, *J* = 7.4, 5.6, 5.6 Hz, 1H, *H*8), 3.95 (s, 3H, *H*1), 3.62 (s, 3H, *H*17), 3.20 (dd, *J* = 13.6, 6.0 Hz, 1H, *H*9), 3.10 (dd, *J* = 13.0, 6.6 Hz, 1H, *H*9). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 171.72 (CO, *C*16), 164.89 (CO, *C*6), 137.70 (NCHN, *C*2) 136.63 (ArC, *C*10), 129.49 (ArCH), 128.48 (ArCH), 126.85 (ArCH, *C*13), 123.70 (NCH, *C*4), 122.49 (NCH, *C*3), 54.77 (CH, *C*8), 52.50 (NCH<sub>2</sub>, *C*5), 51.54 (OCH<sub>3</sub>, *C*17), 37.30 (NCH<sub>3</sub>, *C*1), 36.84 (CH<sub>2</sub>, *C*9). IR (neat) (cm<sup>-1</sup>) 3194 (w), 3025 (m), 1736 (s), 1672 (vs), 1529 (m), 1220 (s), 1174 (vs), 1111 (m), 765 (m), 701 (m). MS (*m/z*) Found [M-Br]<sup>+</sup> 302.1500, C<sub>16</sub>H<sub>20</sub>N<sub>3</sub>O<sub>3</sub><sup>+</sup> requires 302.1499



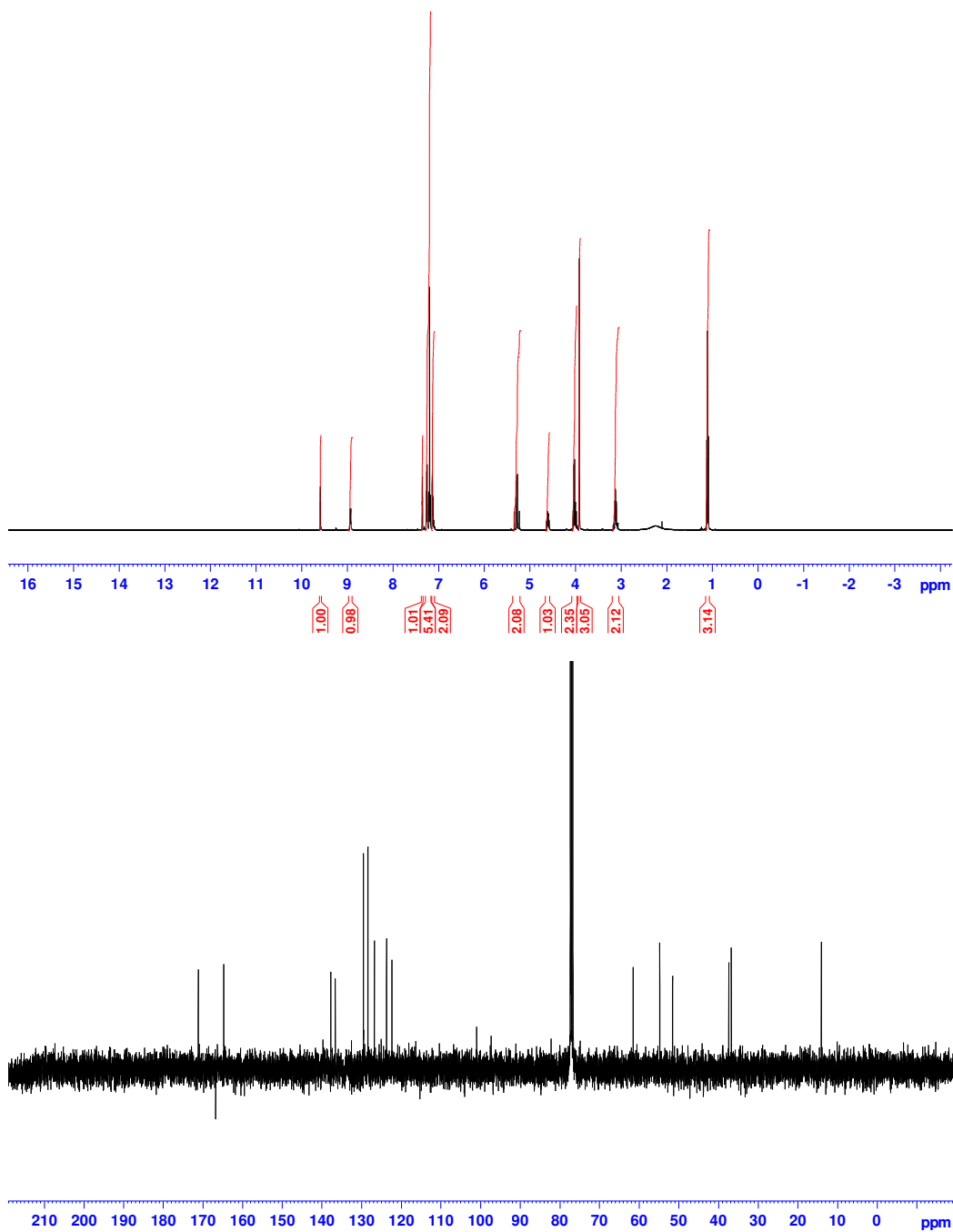
<sup>1</sup>H and <sup>13</sup>C NMR Spectra (**11c**)

### 3-Methyl-1-D-phenylalanine ethyl ester imidazolium bromide-12c



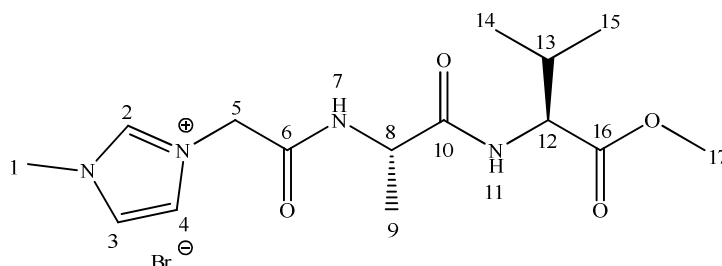
The title compound (**12c**) was prepared from 1-methylimidazole (0.381 g, 4.65 mmol) and D-phenylalanine ethyl ester bromoacetate (**12b**) (1.753 g, 5.60 mmol) according to the general procedure as a white solid in 84 % yield (1.549 g, 3.91 mmol).

m.p. 63-65 °C  $[\alpha]_D^{20} = -15.5^\circ$  (0.8 c, CHCl<sub>3</sub>). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 9.54 (s, 1H, *H*2), 8.98 (d, *J* = 8.0 Hz, 1H, *H*7), 7.35 (s, 1H, *H*4), 7.30-7.07 (m, 6H, *H*3, *H*11-15), 5.42 (d, *J* = 24.1 Hz, 2H, *H*5), 4.61 (ddd, *J* = 8.0, 6.0, 6.0 Hz, 1H, *H*8), 4.05 (dq, *J* = 7.2, 7.2 Hz, 1H, *H*17), 4.05 (dq, *J* = 7.2, 7.2 Hz, 1H, *H*17), 3.92 (s, 3H, *H*1), 3.17 (dd, *J* = 13.6, 6.0 Hz, 1H, *H*9), 3.07 (dd, *J* = 13.0, 6.6 Hz, 1H, *H*9), 1.11 (t, *J* = 7.2 Hz, 3H, *H*18). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 171.24 (CO, *C*16), 164.82 (CO, *C*6), 137.72 (NCHN, *C*2) 136.67 (ArC, *C*10), 129.54 (ArCH), 128.43 (ArCH), 126.81 (ArCH, *C*13), 123.67 (NCH, *C*4), 122.49 (NCH, *C*3), 61.52 (OCH<sub>2</sub>, *C*17), 54.84 (CH, *C*8), 51.54 (NCH<sub>2</sub>, *C*5), 37.41 (NCH<sub>3</sub>, *C*1), 36.80 (CH<sub>2</sub>, *C*9), 14.08 (CH<sub>3</sub>, *C*18). IR (neat) (cm<sup>-1</sup>) 3201 (w), 3027 (m), 2937 (w), 1732 (s), 1675 (vs), 1527 (m), 1373 (m), 1218 (s), 1177 (vs), 1108 (s), 749 (s), 703 (s). MS (*m/z*) Found [M-Br]<sup>+</sup> 316.1655, C<sub>17</sub>H<sub>22</sub>N<sub>3</sub>O<sub>3</sub><sup>+</sup> requires 316.1655



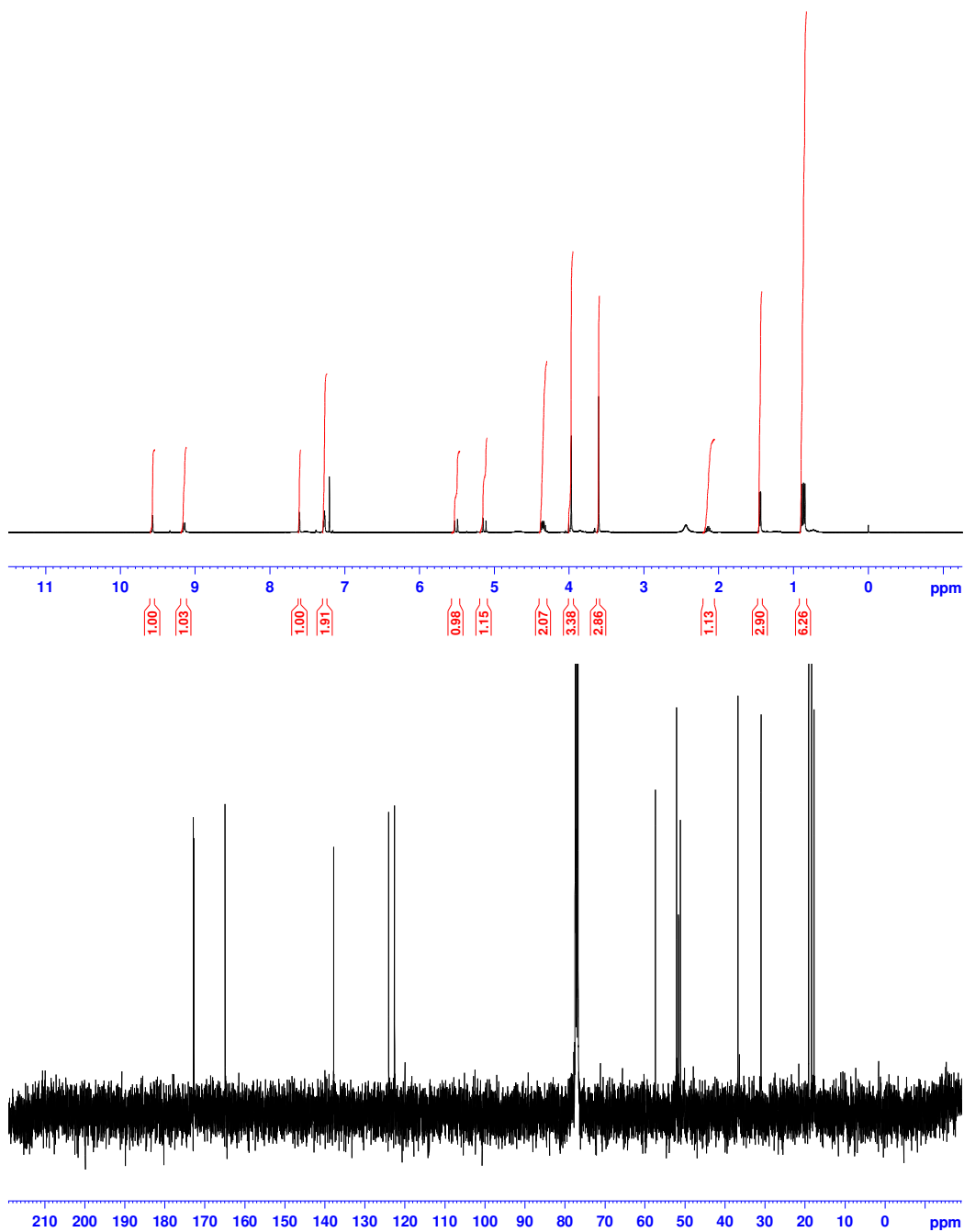
$^1\text{H}$  and  $^{13}\text{C}$  NMR Spectra (**12c**)

### 3-Methyl-1-L-alanine-L-valine methyl ester imidazolium bromide-13c



The title compound (**13c**) was prepared from 1-methylimidazole (0.261 g, 3.35 mmol) and L-alanine-L-valine methyl ester bromoacetate (**13b**) (1.290 g, 4.00 mmol) according to the general procedure as a pale yellow viscous liquid in 97 % yield (1.320 g, 3.26 mmol).

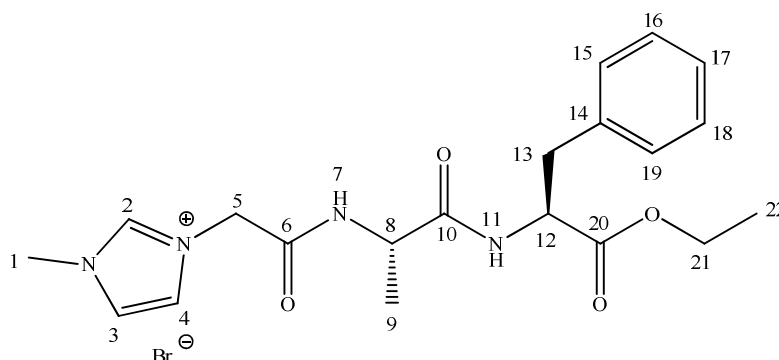
$[\alpha]_D^{20} = -23.5^\circ$  (0.7 c,  $\text{CHCl}_3$ ).  $^1\text{H NMR}$  (600 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 9.65 (s, 1H, *H*2), 9.24 (d,  $J = 7.6$  Hz, 1H, *H*7), 7.59 (t,  $J = 1.8$  Hz, 1H, *H*4), 7.25-7.20 (m, 2H, *H*3, *H*1), 5.58 (d,  $J = 15.2$  Hz, 1H, *H*5), 5.01 (d,  $J = 15.2$  Hz, 1H, *H*5), 4.37 (dd,  $J = 8.8, 4.8$  Hz, 1H, *H*12), 4.32 (dq,  $J = 7.2, 7.2$  Hz, *H*8), 3.97 (s, 3H, *H*1), 3.10 (s, 3H, *H*17), 2.17 (qqd,  $J = 7.0, 7.0, 4.8$  Hz, 1H, *H*13), 0.94 (d,  $J = 6.8$  Hz, 3H, *H*9), 0.89 (d,  $J = 7.2$  Hz, 3H, *H*14/*H*15), 0.85 (d,  $J = 7.2$  Hz, 3H, *H*14/*H*15).  $^{13}\text{C NMR}$  (150 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 172.97 (CO, *C*16), 172.66 (CO, *C*10), 164.83 (CO, *C*6), 137.84 (NCHN, *C*2), 124.06 (NCH, *C*4), 122.47 (NCH, *C*3), 57.28 (CH, *C*12), 52.01 (NCH<sub>2</sub>, *C*5), 51.73 (CH, *C*8), 51.28 (OCH<sub>3</sub>, *C*17), 36.74 (NCH<sub>3</sub>, *C*1), 31.06 (CH, *C*13), 19.09 (CH<sub>3</sub>, *C*14/*C*15), 18.33 (CH<sub>3</sub>, *C*14/*C*15), 17.69 (CH<sub>3</sub>, *C*9). IR (neat) ( $\text{cm}^{-1}$ ) 3220 (b), 3053 (w), 2966 (w), 1737 (m), 1661 (vs), 1534 (s), 1206 (s), 1173 (vs). MS ( $m/z$ ) Found  $[\text{M}-\text{Br}]^+$  325.1861,  $\text{C}_{15}\text{H}_{25}\text{N}_4\text{O}_4^+$  requires 325.1870



$^1\text{H}$  and  $^{13}\text{C}$  NMR Spectra (**13c**)

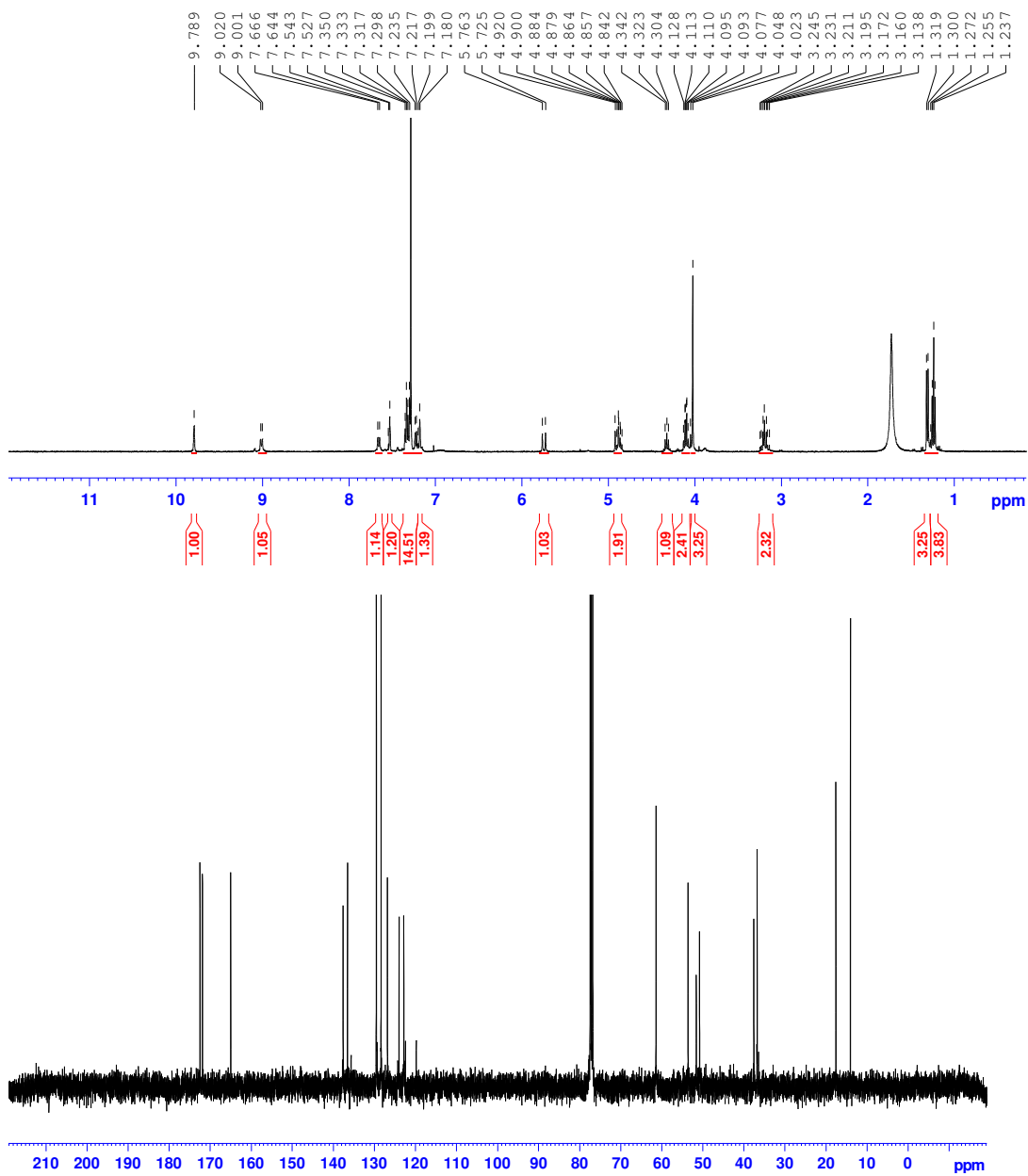


### 3-Methyl-1-L-alanine-L-phenylalanine ethyl ester imidazolium bromide -14c



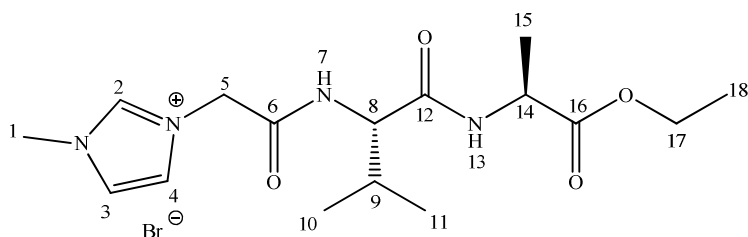
The title compound (**14c**) was prepared from 1-methylimidazole (0.298 g, 3.65 mmol) and L-alanine-L-phenylalanine ethyl ester bromoacetate (**14b**) (1.673 g, 4.35 mmol) according to the general procedure as a pale yellow hygroscopic semi-solid in 84 % yield (1.440 g, 3.08 mmol).

$[\alpha]_D^{20} = -11.4^\circ$  (0.6 c,  $\text{CHCl}_3$ ).  $^1\text{H NMR}$  (600 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 9.69 (s, 1H, *H*2), 8.94 (d,  $J = 7.0$  Hz, 1H, *H*7), 7.57 (d,  $J = 8.0$  Hz, 1H, *H*11), 7.46 (d,  $J = 1.4$  Hz, 1H, *H*4), 7.27-7.17 (m, 6H, *H*3,15-19), 5.66 (d,  $J = 14.8$  Hz, 1H, *H*5), 4.89 (d,  $J = 14.4$  Hz, 1H, *H*5), 4.73 (ddd,  $J = 8.0, 6.0, 6.0$  Hz, 1H, *H*12), 4.62 (d,  $J = 14.4$  Hz, 1H, *H*5), 4.24 (dq,  $J = 7.2, 7.2$  Hz, 1H, *H*8), 4.11 (q,  $J = 6.8$  Hz, 2H, *H*21), 3.92 (s, 3H, *H*1), 3.15 (dd,  $J = 14.0, 6.0$  Hz, 1H, *H*13), 3.05 (dd,  $J = 13.8, 6.4$  Hz, 1H, *H*13), 1.24 (d,  $J = 7.2$  Hz, 3H, *H*9), 1.12 (t,  $J = 7.0$  Hz, 3H, *H*22).  $^{13}\text{C NMR}$  (150 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 172.50 (CO,*C*20), 171.93 (CO,*C*10), 165.05 (CO,*C*6), 137.62 (NCHN,*C*2), 136.57 (ArC,*C*14), 129.53 (ArCH), 128.38 (ArCH), 126.81 (ArCH,*C*17), 123.98 (NCH,*C*4), 122.83 (NCH,*C*3), 61.37 ( $\text{OCH}_2$ ,*C*21), 53.58 (CH,*C*12), 51.58 ( $\text{NCH}_2$ ,*C*5), 50.79 (CH,*C*8), 37.57 ( $\text{CH}_2$ ,*C*13), 36.75 ( $\text{NCH}_3$ ,*C*1), 17.60 ( $\text{CH}_3$ ,*C*9), 14.08 ( $\text{CH}_3$ ,*C*22). IR (neat) ( $\text{cm}^{-1}$ ) 3423 (w), 3301 (w), 2983 (w), 1751 (s), 1679 (vs), 1650 (vs), 1532 (vs), 1212 (m), 1175 (vs), 749 (m), 699 (m). MS ( $m/z$ ) Found  $[\text{M}-\text{Br}]^+$  387.2018,  $\text{C}_{20}\text{H}_{27}\text{N}_4\text{O}_4^+$  requires 387.2026



$^1\text{H}$  and  $^{13}\text{C}$  NMR Spectra (**14c**)

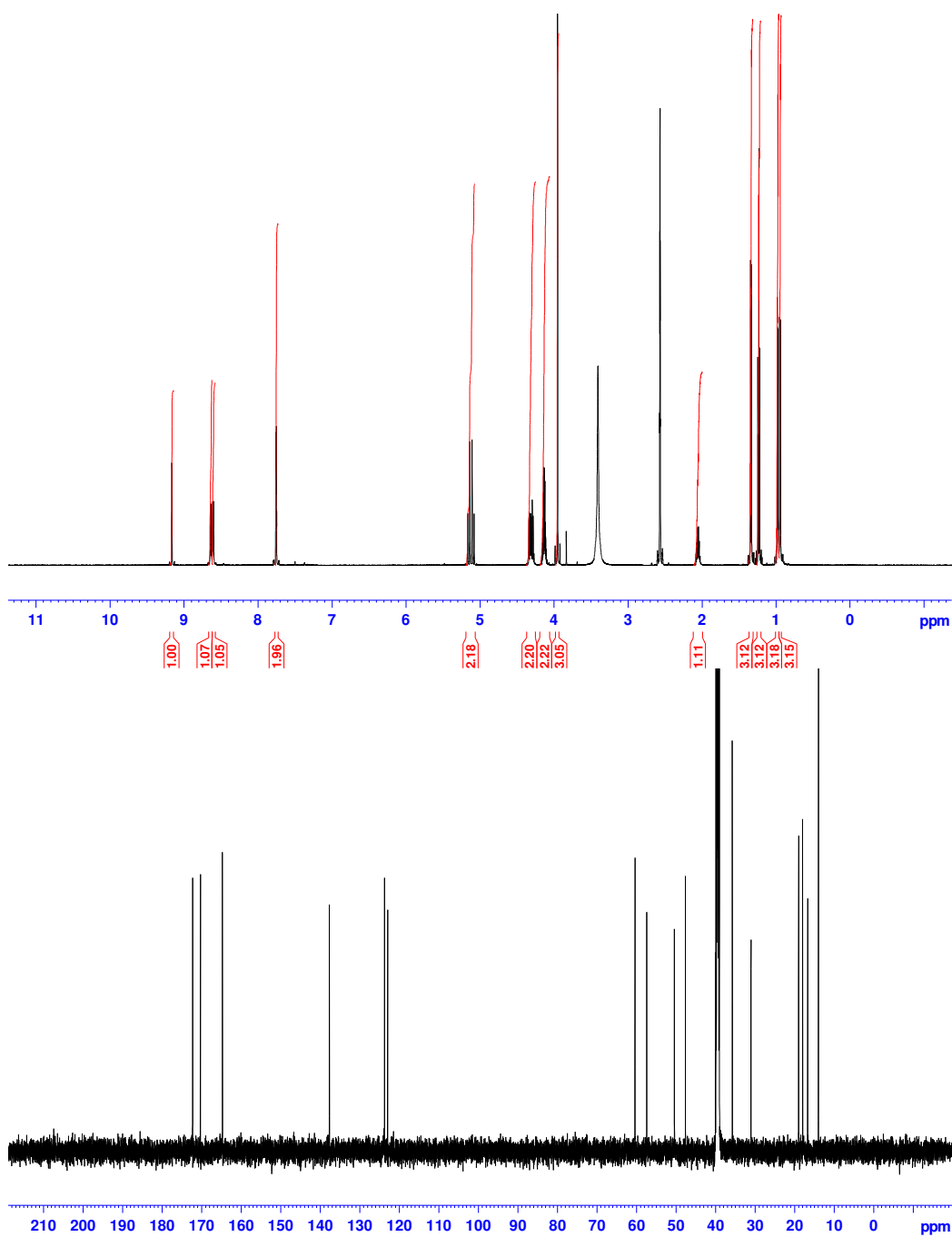
### 3-Methyl-1-L-valine-L-alanine ethyl ester imidazolium bromide-15c



The title compound (**15c**) was prepared from 1-methylimidazole (0.101 g, 1.32 mmol) and L-valine-L-alanine ethyl ester bromoacetate (**15b**) (0.579 g, 1.72 mmol) according to the general procedure as a white solid in 95 % yield (0.526 g, 1.25 mmol).

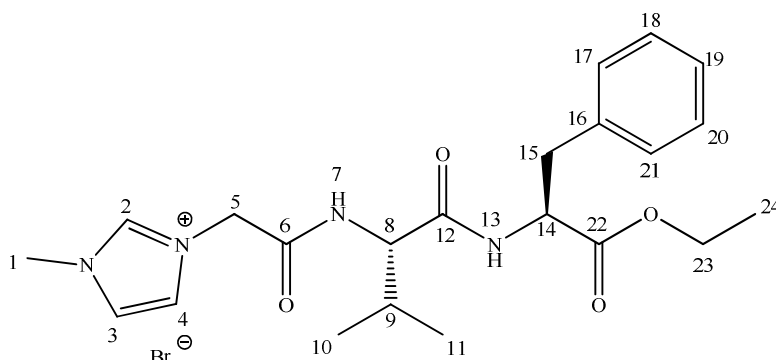
m.p. 130-132 °C [ $\alpha$ ]<sub>D</sub><sup>20</sup> = -46.2 ° (0.5 c, CHCl<sub>3</sub>)

<sup>1</sup>H NMR (600 MHz, DMSO-d<sub>6</sub>)  $\delta$  (ppm) 9.16 (s, 1H, H2), 8.63 (d, *J* = 9.0 Hz, 1H, H7), 8.57 (d, *J* = 6.6 Hz, 1H, H13), 7.76 (t, *J* = 1.8 Hz, 1H, H4), 7.73 (t, *J* = 1.8 Hz, 1H, H3), 5.14 (d, *J* = 16.2 Hz, 2H, H5), 4.32 (dd, *J* = 8.4, 6.0 Hz, 1H, H8), 4.28 (dq, *J* = 7.2, 7.2 Hz, 1H, H14), 4.14 (dq, *J* = 7.2, 7.2 Hz, 1H, H17), 4.13 (dq, *J* = 7.2, 7.2 Hz, 1H, H17), 3.95 (s, 3H, H1), 2.06 (qqd, *J* = 6.8, 6.8, 5.6 Hz, 1H, H9), 1.33 (d, *J* = 7.2 Hz, 3H, H15), 1.24 (t, *J* = 7.2 Hz, 3H, H18), 0.97 (d, *J* = 6.6 Hz, 3H, H10/11), 0.94 (d, *J* = 6.6 Hz, 3H, H10/11). <sup>13</sup>C NMR (150 MHz, DMSO-d<sub>6</sub>)  $\delta$  (ppm) 172.29 (CO, C16), 170.29 (CO, C12), 164.76 (CO, C6), 137.70 (NCHN, C2), 123.73 (NCH, C4), 122.95 (NCH, C3), 60.41 (OCH<sub>2</sub>, C17), 57.45 (CH, C8), 50.44 (NCH<sub>2</sub>, C5), 47.62 (CH, C14), 35.78 (NCH<sub>3</sub>, C1), 31.07 (CH, C9), 19.01 (CH<sub>3</sub>, C10/C11), 17.99 (CH<sub>3</sub>, C10/C11), 16.72 (CH<sub>3</sub>, C15), 13.98 (CH<sub>3</sub>, C18). IR (neat) (cm<sup>-1</sup>) 3280 (m), 3258 (m), 2964 (w), 1727 (m), 1669 (m), 1646 (vs), 1557 (s), 1219 (s), 1174 (s). MS (*m/z*) Found [M-Br]<sup>+</sup> 339.2024, C<sub>16</sub>H<sub>27</sub>N<sub>4</sub>O<sub>4</sub><sup>+</sup> requires 339.2026



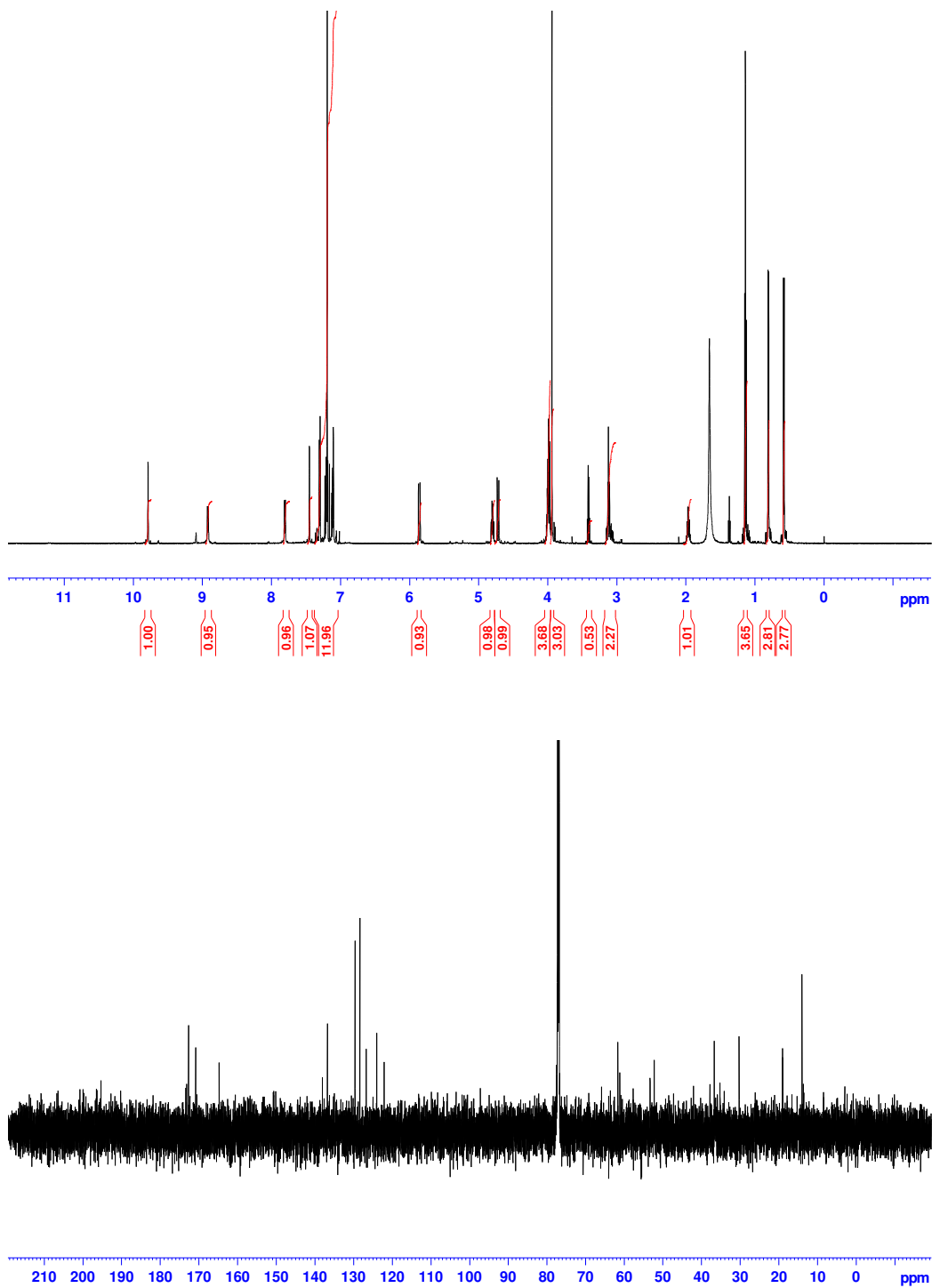
$^1\text{H}$  and  $^{13}\text{C}$  NMR Spectra (**15c**)

### 3-Methyl-1-L-valine-L-phenylalanine ethyl ester imidazolium bromide-16c



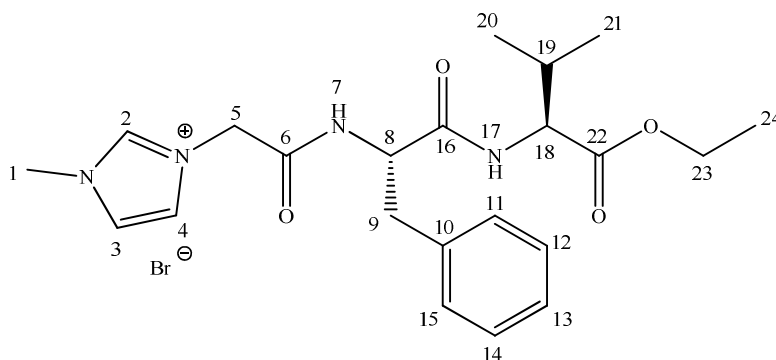
The title compound (**16c**) was prepared from 1-methylimidazole (0.245 g, 3.00 mmol) and L-valine-L-phenylalanine ethyl ester bromoacetate (**16b**) (1.481 g, 3.60 mmol) according to the general procedure as a pale yellow hygroscopic semi-solid in 98 % yield (1.450 g, 2.93 mmol).

$[\alpha]_D^{20} = -20.7^\circ$  (0.9 c,  $\text{CHCl}_3$ ).  $^1\text{H NMR}$  (600 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 9.68 (s, 1H, *H*2), 8.88 (d, *J* = 6.8 Hz, 1H, *H*13), 7.76 (d, *J* = 8.8 Hz, 1H, *H*7), 7.49 (t, *J* = 1.6 Hz, 1H, *H*4), 7.39-7.23 (m, 6H, *H*3,17-21), 5.78 (d, *J* = 14.8 Hz, 1H, *H*5), 4.89 (d, *J* = 14.8 Hz, 1H, *H*5), 4.75 (ddd, *J* = 8.0, 6.4, 6.4 Hz, 1H, *H*14), 4.06-3.94 (m, 3H, *H*8,23), 3.92 (s, 3H, *H*1), 3.16-3.06 (m, 2H, *H*15), 2.16 (qqd, *J* = 6.8, 6.8, 4.4 Hz, 1H, *H*9), 1.13 (t, *J* = 7.2 Hz, 3H, *H*24), 0.82 (d, *J* = 6.8 Hz, 3H, *H*10/11), 0.58 (d, *J* = 6.8 Hz, 3H, *H*10/11).  $^{13}\text{C NMR}$  (150 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 172.13 (CO,*C*22), 171.26 (CO,*C*12), 165.37 (CO,*C*6), 137.68 (NCHN,*C*2), 136.70 (ArC,*C*16), 129.43 (ArCH), 128.56 (ArCH), 126.77 (ArCH,*C*19), 123.95 (NCH,*C*4), 122.80 (NCH,*C*3), 65.82 (OCH<sub>2</sub>,*C*23), 61.29 (CH,*C*8), 53.67 (CH,*C*14), 51.72 (NCH<sub>2</sub>,*C*5), 37.51 (CH<sub>2</sub>,*C*15), 36.69 (NCH<sub>3</sub>,*C*1), 30.31 (CH,*C*9), 19.06 (CH<sub>3</sub>,*C*10/*C*11), 18.95 (CH<sub>3</sub>,*C*10/*C*11), 15.25 (CH<sub>3</sub>,*C*24). IR (neat) ( $\text{cm}^{-1}$ ) 3055 (w), 2963 (w), 1731 (m), 1659 (vs), 1535 (s), 1173 (vs), 745 (m), 700 (s). MS (*m/z*) Found  $[\text{M}-\text{Br}]^+$  415.2339,  $\text{C}_{17}\text{H}_{29}\text{N}_4\text{O}_4^+$  requires 415.2339



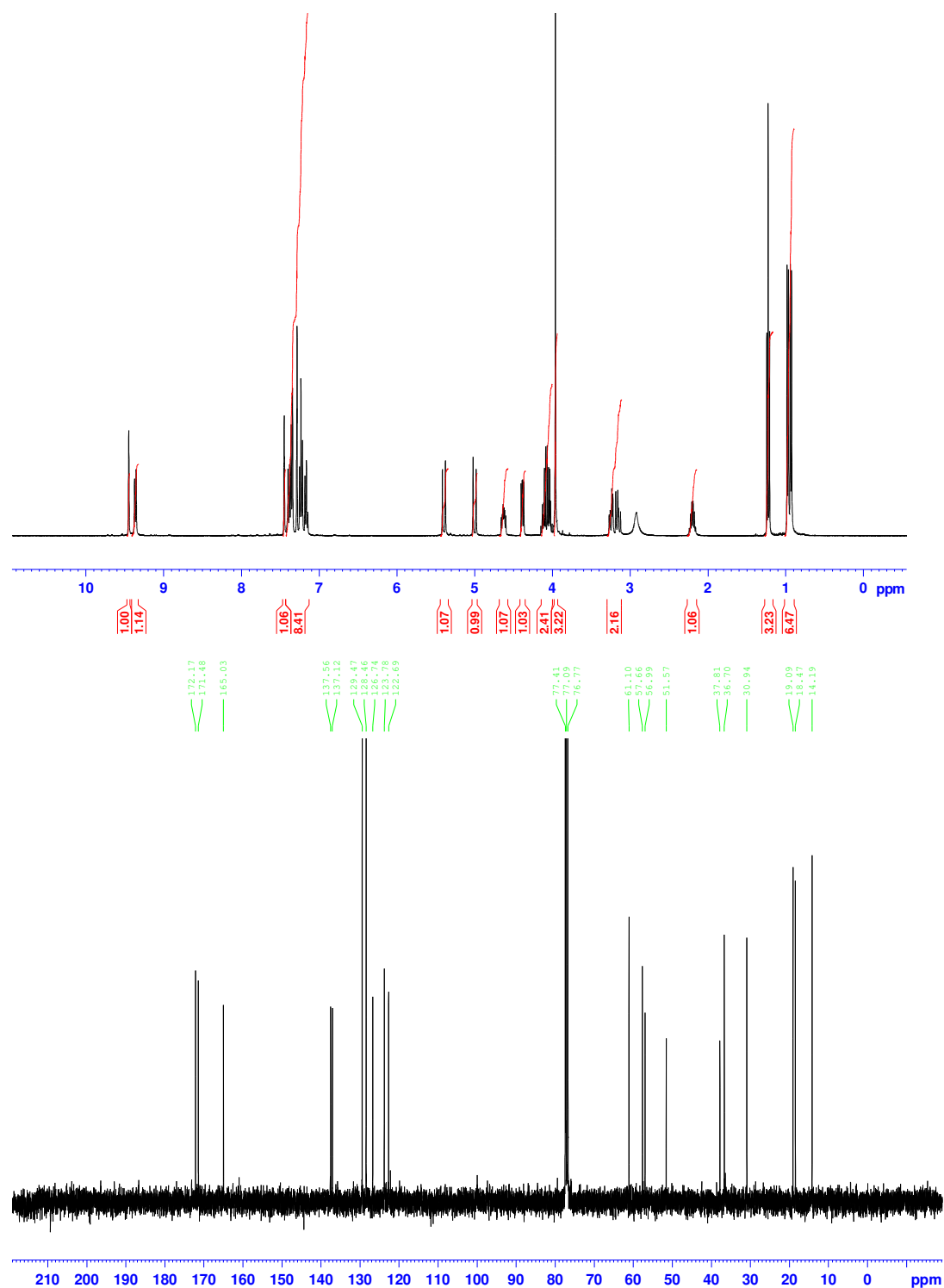
$^1\text{H}$  and  $^{13}\text{C}$  NMR Spectra (**16c**)

### 3-Methyl-1-L-phenylalanine-L-valine ethyl ester imidazolium bromide-17c



The title compound was prepared from 1-methylimidazole (0.266 g, 3.25 mmol) and L-phenylalanine-L-valine ethyl ester bromoacetate (**17b**) (1.592 g, 3.87 mmol) according to the general procedure as a pale yellow hygroscopic semi-solid in 96 % yield (1.544 g, 3.12 mmol).

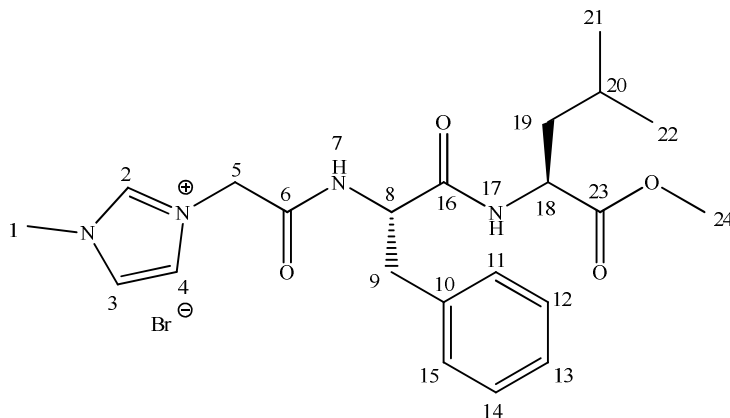
$[\alpha]_D^{20} = -22.0^\circ$  (0.8 c,  $\text{CHCl}_3$ ).  $^1\text{H NMR}$  (600 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 9.61 (s, 1H, *H*2), 9.42 (d,  $J = 8.0$  Hz, 1H, *H*7), 7.69 (d,  $J = 8.4$  Hz, 1H, *H*17), 7.46-7.09 (m, 8H, *H*3,4,11-15), 5.47 (d,  $J = 14.4$  Hz, 1H, *H*5), 5.01 (d,  $J = 14.4$  Hz, 1H, *H*5), 4.74 (ddd,  $J = 8.0, 6.4, 6.4$  Hz, 1H, *H*8), 4.37 (dd,  $J = 8.4, 4.8$  Hz, 1H, *H*18), 4.17-4.07 (m, 2H, *H*23), 3.96 (s, 3H, *H*1), 3.34 (dd,  $J = 13.6, 4.0$  Hz, 1H, *H*9), 3.08 (dd,  $J = 14.0, 7.6$  Hz, 1H, *H*9), 2.15 (qqd,  $J = 6.8, 6.8, 4.4$  Hz, 1H, *H*19), 1.19 (t,  $J = 7.2$  Hz, 3H, *H*24), 0.89 (dd,  $J = 8.4, 6.8$  Hz, 6H, *H*20,21).  $^{13}\text{C NMR}$  (150 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 172.17 (CO,*C*22), 171.48 (CO,*C*16), 165.03 (CO,*C*6), 137.56 (NCH<sub>2</sub>,*C*2), 137.12 (ArC,*C*10), 129.47 (ArCH), 128.46 (ArCH), 126.74 (ArCH,*C*13), 123.78 (NCH,*C*4), 122.69 (NCH,*C*3), 61.10 (OCH<sub>2</sub>,*C*23), 57.66 (CH,*C*18), 56.99 (CH,*C*8), 51.57 (NCH<sub>2</sub>,*C*5), 37.81 (CH<sub>2</sub>,*C*9), 36.70 (NCH<sub>3</sub>,*C*1), 30.94 (CH,*C*19), 19.09 (CH<sub>3</sub>,*C*20/*C*21) 18.47 (CH<sub>3</sub>,*C*20/*C*21), 14.19 (CH<sub>3</sub>,*C*24). IR (neat) ( $\text{cm}^{-1}$ ) 3210 (b), 3044 (w), 2965 (w), 1730 (m), 1658 (s), 1534 (m), 1172 (s), 1206 (m), 744 (m), 701 (m). MS ( $m/z$ ) Found  $[\text{M}-\text{Br}]^+$  415.2236,  $\text{C}_{22}\text{H}_{31}\text{N}_4\text{O}_4^+$  requires 415.2239



$^1\text{H}$  and  $^{13}\text{C}$  NMR Spectra (**17c**)

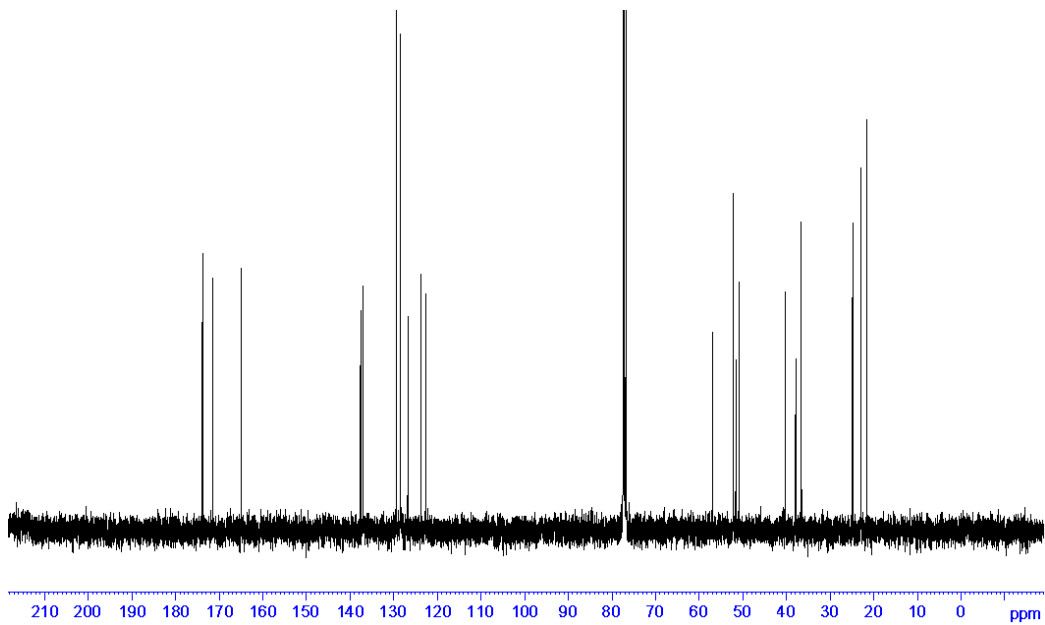
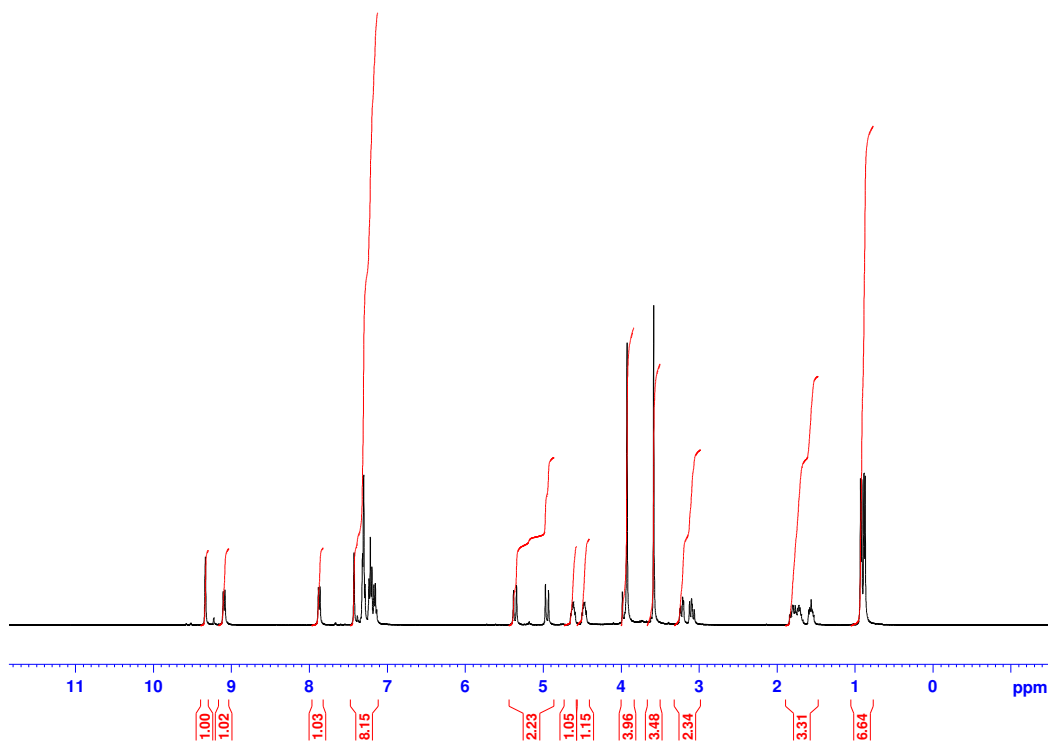


### 3-Methyl-1-L-phenylalanine-L-leucine methyl ester imidazolium bromide-18c



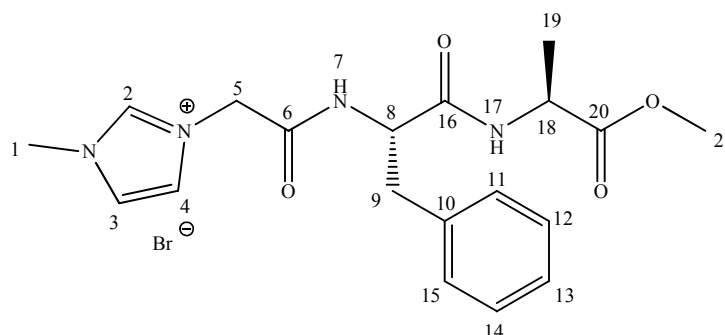
The title compound (**18c**) was prepared from 1-methylimidazole (0.242 g, 2.95 mmol) and L-phenylalanine-L-leucine methyl ester bromoacetate (**18b**) (1.451 g, 3.55 mmol) according to the general procedure as a pale yellow hygroscopic semi-solid in 75 % yield (1.091 g, 2.20 mmol).

$[\alpha]_D^{20} = -44.9^\circ$  (0.8 c,  $\text{CHCl}_3$ ).  $^1\text{H NMR}$  (600 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 9.38 (s, 1H, *H*2), 9.15 (d,  $J = 8.4$  Hz, 1H, *H*7), 7.87 (d,  $J = 8.0$  Hz, 1H, *H*17), 7.44 (s, 1H, *H*4), 7.40-7.24 (m, 7H, *H*3,11-15), 5.42 (d,  $J = 15.2$  Hz, 1H, *H*5), 4.95 (d,  $J = 15.6$  Hz, 1H, *H*5), 4.58 (ddd,  $J = 8.0, 6.0, 6.0$  Hz, 1H, *H*8), 4.47 (ddd,  $J = 8.0, 8.0, 5.6$  Hz, 1H, *H*18), 3.94 (s, 3H, *H*1), 3.61 (s, 3H, *H*24), 3.26 (dd,  $J = 9.0, 5.2$  Hz, 1H, *H*9), 3.11 (dd,  $J = 10.4, 6.0$  Hz, 1H, *H*9), 1.86-1.58 (m, 3H, *H*19,20), 0.94 (d,  $J = 6.4$  Hz, 3H, *H*21/22), 0.88 (d,  $J = 6.4$  Hz, 3H, *H*21/22).  $^{13}\text{C NMR}$  (150 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 173.87 (CO,*C*23), 171.59 (CO,*C*17), 165.04 (CO,*C*6), 137.59 (NCHN,*C*2), 137.00 (ArC,*C*10), 129.45 (ArCH), 128.47 (ArCH), 126.79 (ArCH,*C*13), 123.83 (NCH,*C*4), 122.70 (NCH,*C*3), 56.97 (CH, *C*8), 52.20 (CH,*C*18), 51.61 (NCH<sub>2</sub>,*C*5), 50.91 (OCH<sub>3</sub>,*C*24), 40.33 (CH<sub>2</sub>,*C*19), 37.88 (CH<sub>2</sub>,*C*9), 36.69 (NCH<sub>3</sub>,*C*1), 24.86 (CH,*C*20), 22.93 (CH<sub>3</sub>,*C*21/*C*22), 21.51 (CH<sub>3</sub>,*C*21/*C*22). IR (neat) ( $\text{cm}^{-1}$ ) 3196 (w), 3037 (w), 2956 (w), 1738 (m), 1660 (vs), 1537 (s), 1436 (m), 1202 (s), 1171 (vs), 745 (m), 700 (s). MS ( $m/z$ ) Found  $[\text{M}-\text{Br}]^+$  415.2339,  $\text{C}_{22}\text{H}_{31}\text{N}_4\text{O}_4^+$  requires 415.2339



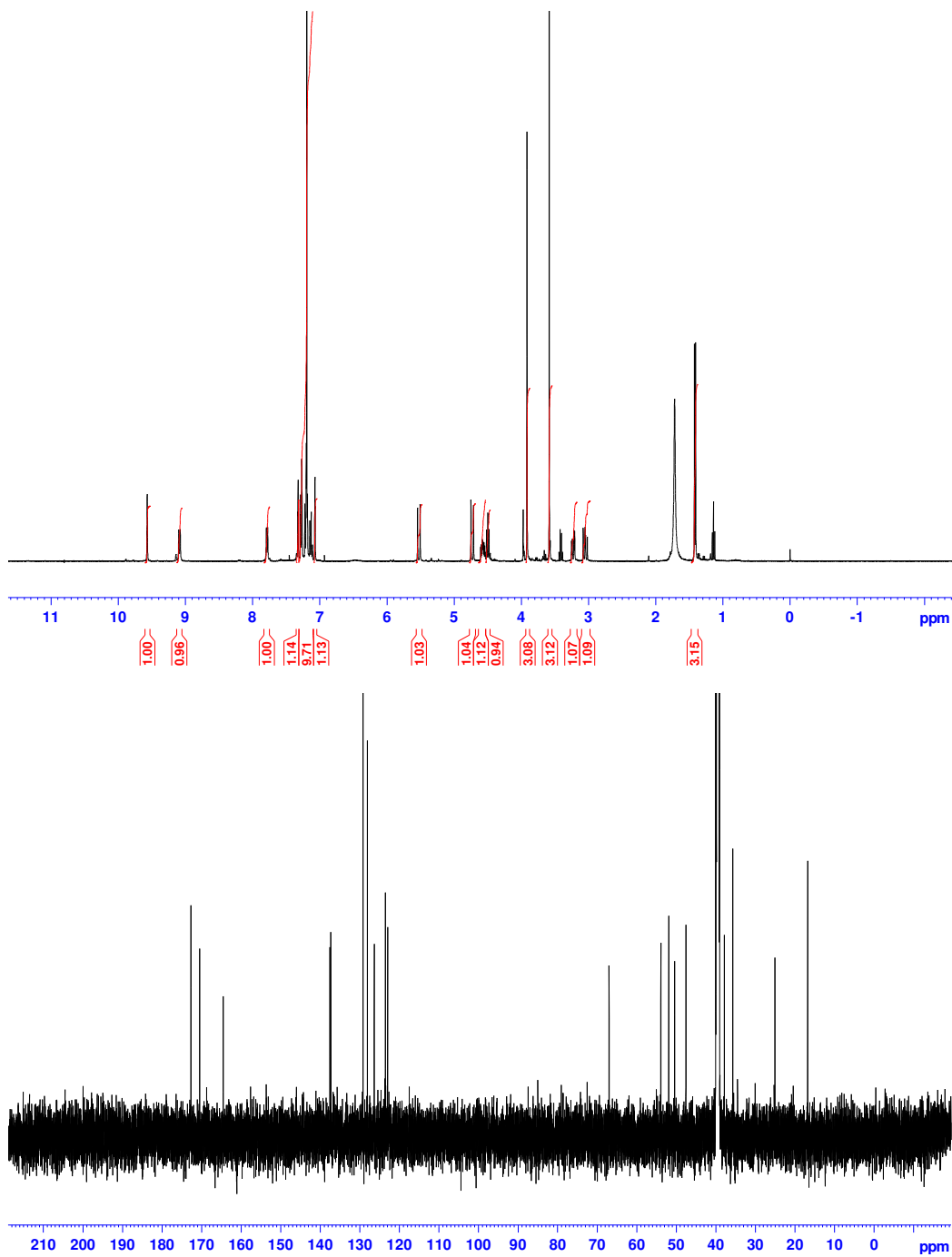
$^1\text{H}$  and  $^{13}\text{C}$  NMR Spectra (**18c**)

### 3-Methyl-1-L-phenylalanine-L-alanine methyl ester imidazolium bromide-19c



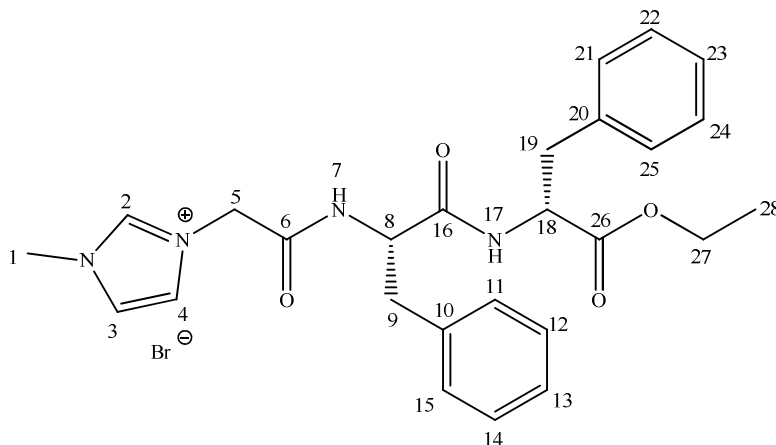
The title compound (**19c**) was prepared from 1-methylimidazole (0.272 g, 3.31 mmol) and L-phenylalanine-L-alanine methyl ester bromoacetate (**19b**) (1.594 g, 4.31 mmol) according to the general procedure as a white hygroscopic semi-solid in 97 % yield (1.455 g, 3.21 mmol).

$[\alpha]_D^{20} = -22.7^\circ$  (0.8 c,  $\text{CHCl}_3$ ).  $^1\text{H NMR}$  (600 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 9.56 (s, 1H, *H*2), 8.96 (d,  $J = 8.4$  Hz, 1H, *H*7), 7.77 (d,  $J = 7.2$  Hz, 1H, *H*17), 7.34 (t,  $J = 1.6$  Hz, 1H, *H*4), 7.32-7.12 (m, 6H, *H*3, *H*11-15), 5.35 (d,  $J = 10.8$  Hz, 1H, *H*5), 4.88 (d,  $J = 10.6$  Hz, 1H, *H*5), 4.59 (ddd,  $J = 8.0, 5.6, 5.6$  Hz, 1H, *H*8), 4.42 (dq,  $J = 7.2, 7.2$  Hz, 1H, *H*18), 3.89 (s, 3H, *H*1), 3.57 (s, 3H, *H*21), 3.18 (dd,  $J = 13.8, 4.8$  Hz, 1H, *H*9), 3.02 (dd,  $J = 14.4, 10.2$  Hz, 1H, *H*9), 1.38 (d,  $J = 7.2$  Hz, 3H, *H*19).  $^{13}\text{C NMR}$  (150 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 173.75 (CO, *C*20), 171.75 (CO, *C*16), 164.85 (CO, *C*6), 137.11 (ArC, *C*10), 137.08 (NCHN, *C*2), 129.46 (ArCH), 128.48 (ArCH), 126.74 (ArCH, *C*13), 123.86 (NCH, *C*4), 122.36 (NCH, *C*3), 56.69 (CH, *C*8), 52.57 (OCH<sub>3</sub>, *C*21), 51.79 (NCH<sub>2</sub>, *C*5), 48.13 (CH, *C*18), 37.93 (CH<sub>2</sub>, *C*9), 36.70 (NCH<sub>3</sub>, *C*1), 17.79 (CH<sub>3</sub>, *C*19). IR (neat) ( $\text{cm}^{-1}$ ) 3198 (b), 3046 (w), 2952 (w), 1737 (m), 1659 (vs), 1537 (s), 1210 (s), 1169 (s), 726 (m), 701 (m). MS ( $m/z$ ) Found  $[\text{M}-\text{Br}]^+$  373.1862,  $\text{C}_{19}\text{H}_{25}\text{N}_4\text{O}_4^+$  requires 373.1870.



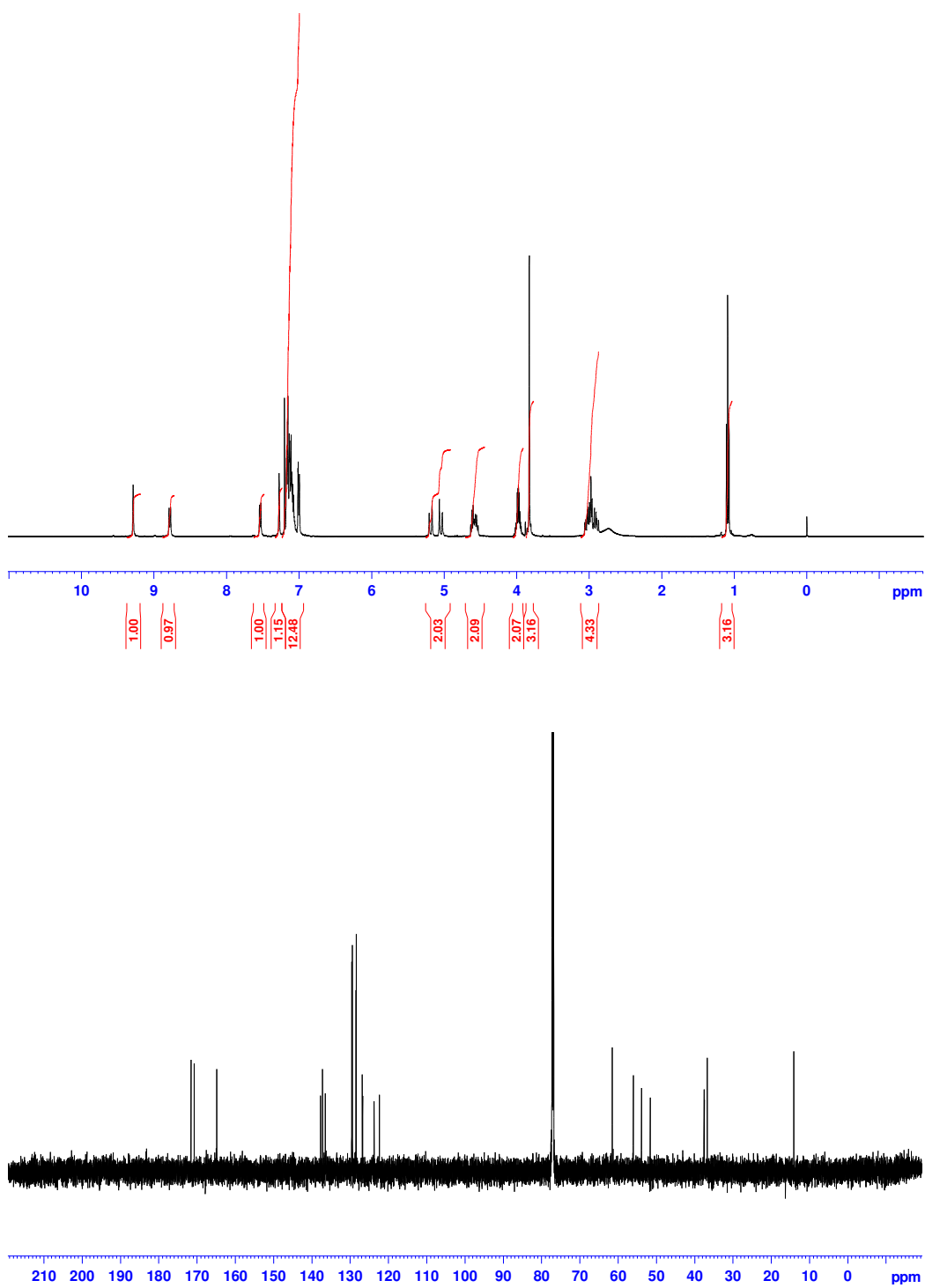
$^1\text{H}$  and  $^{13}\text{C}$  NMR Spectra (**19c**)

### 3-Methyl-1-L-phenylalanine-D-phenylalanine ethyl ester imidazolium bromide-20c



The title compound (**20c**) was prepared from 1-methylimidazole (0.170 g, 2.05 mmol) and L-phenylalanine-D-phenylalanine ethyl ester bromoacetate (**20b**) (1.151 g, 2.50 mmol) according to the general procedure as a white solid in 98 % yield (1.098 g, 2.02 mmol).

m.p. 93-95 °C  $[\alpha]_D^{20} = -23.7^\circ$  (0.7 c, CHCl<sub>3</sub>). <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 9.31(s, 1H, *H*2), 8.85 (d, *J* = 8.4 Hz, 1H, *H*7), 7.56 (d, *J* = 9.0 Hz, 1H, *H*17), 7.34 (s, 1H, *H*4), 7.31-6.98 (m, 11H, *H*3, *H*11-15, *H*21-25), 5.36 (d, *J* = 15.3 Hz, 1H, *H*5), 5.06 (d, *J* = 15.3 Hz, 1H, *H*5), 4.63 (ddd, *J* = 8.0, 6.0, 6.0 Hz, 1H, *H*8), 4.52 (ddd, *J* = 8.8, 5.6, 5.6 Hz, 1H, *H*18), 4.41 (dq, *J* = 7.2, 7.2 Hz, 1H, *H*27), 4.00 (dq, *J* = 7.2, 7.2 Hz, 1H, *H*27), 3.85 (s, 3H, *H*1), 3.18-2.94 (m, 4H, *H*9, *H*19), 1.11 (t, *J* = 7.2 Hz, 3H, *H*28). <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 171.34 (CO, *C*26), 170.40 (CO, *C*16), 164.42 (CO, *C*6), 137.54 (NCHN, *C*2), 137.12 (ArC, *C*10/*C*20), 136.99 (ArC, *C*10/*C*20), 129.19 (ArCH), 129.17 (ArCH), 128.21 (ArCH), 128.01 (ArCH), 126.61 (ArCH, *C*13/*C*23), 126.32 (ArCH, *C*13/*C*23), 123.51 (NCH, *C*4), 122.97 (NCH, *C*3), 66.99 (OCH<sub>2</sub>, *C*27), 60.64 (CH, *C*8), 53.87 (CH, *C*18), 50.44 (NCH<sub>2</sub>, *C*5), 38.14 (CH<sub>2</sub>, *C*9/*C*19), 36.99 (NCH<sub>3</sub>, *C*1), 35.77 (CH<sub>2</sub>, *C*9/*C*19), 13.93 (CH<sub>3</sub>, *C*28). IR (neat) (cm<sup>-1</sup>) 3300 (m), 1736 (s), 1677 (m), 1645 (vs), 1536 (s), 1219 (s), 1181 (s), 746 (m), 695 (s). MS (*m/z*) Found [M-Br]<sup>+</sup> 463.2338, C<sub>26</sub>H<sub>31</sub>N<sub>4</sub>O<sub>4</sub><sup>+</sup> requires 463.2339



$^1\text{H}$  and  $^{13}\text{C}$  NMR Spectra (**20c**)