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Research Article

Spectroscopic study of diphenyl [(S)-(–)-1-phenylpropanamido]-phosphate: differences of diastereotopic groups

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ABSTRACT

The synthesis and crystal structure of diphenyl [(*S*)-(–)-1-phenylpropanamido]-phosphate, $(C_6H_5O)_2P(O)[NH\text{-}(S)\text{-}(–)CH(C_2H_5)(C_6H_5)]$, was previously reported. Here, the spectroscopic features (^{1}H-NMR, ^{13}C{^{1}H}-NMR, ^{31}P{^{1}H}-NMR and IR) are investigated. In the ^{1}H-NMR and ^{13}C{^{1}H}-NMR spectra, the diastereotopic C_6H_5O groups show two sets of signals. Typically, in the ^{13}C{^{1}H}-NMR spectrum, the doublets at 151.08/151.20 ppm and 120.52/120.55 ppm, with $^2J_{CP}$ = 6.5/6.6 Hz for the first pair and $^3J_{CP}$ = 4.9/4.7 Hz for the second pair are associated to the diastereotopic *ipso*-C atoms and diastereotopic *ortho*-C atoms. In the ^{1}H-NMR spectrum, the signals related to diastereotopic phenyl groups overlap with those of phenyl group of chiral amine. The *ipso*-carbon atom of chiral amine fragment appears a doublet signal at 144.85 ppm ($^3J_{CP}$ = 2.7 Hz). The phosphorus signal (^{31}P{^{1}H}-NMR) appears at –0.49 ppm.

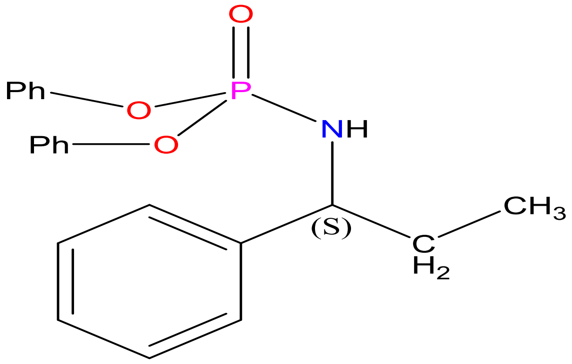
Keywords: Amidophosphodiester; IR; NMR; Phosphorus-carbon coupling constant.

1. Introduction

Phosphoramides can be introduced by the P(O)(X)(W)(NR^{1}R^2) formula, where R^1 and R^2 refer to organic groups or H atom, and X and W may be either amide/amine fragment, OR, OH or halogen. These compounds are well-known for their rules in various chemical reactions and synthetic processes, for example designing of ligands and catalysts [1]. A subset of phosphoramide, amidophosphodiester, with the $(O)_2P(O)(N)$ skeleton, is interesting for application in manufacturing of drugs [2, 3].

The chiral moieties make some valuable usages in compounds bearing them, and are widely employed in asymmetric catalysis [4]. The chiral compounds facilitate enantioselective reactions, allowing the production of a single-enantiomer of a desired product [5]. The selective actions of chiral phosphorus-containing compounds to interact with different molecules have been studied, with different usages in pharmaceuticals and agrochemicals [6]. In compounds with the $(RO)_2P(O)(NHCHR'R'')$ formula ($NHCHR'R''$ is a chiral fragment), two RO groups have a diastereotopic relation, and show some differences in reactivity and structural/spectroscopic features [7].

In a previous work, the crystal structure of $(C_6H_5O)_2P(O)[NH$-*S*-(–)$CH(C_2H_5)(C_6H_5)]$ was reported [8]. Here, we continue with the study of its spectroscopic features (NMR and IR), with focusing on the differences of NMR parameters related to diastereotopic C_6H_5O groups. The NMR/IR parameters of the title compound are compared with those of its enantiomer, $(C_6H_5O)_2P(O)[NH$-*R*-(+)$CH(C_2H_5)(C_6H_5)]$ [9].



Scheme 1. Chemical structure of $(C_6H_5O)_2P(O)[NH$-(*S*)-(–)$CH(C_2H_5)(C_6H_5)]$.

2. Experimental

2.1. Synthesis and Identification

The title compound was prepared according to the method reported in a previously published paper with a few modification [8], as follows: to a solution of $(C_6H_5O)_2P(O)Cl$ in dry chloroform, a solution of S-(–)-1-phenylpropylamine and triethylamine (1:1:1 mole ratio) in the same solvent was added at 273 K. After 4 h of stirring, the solvent was removed in a vacuum and the obtained solid was washed with distilled water to remove $(C_2H_5)_3NHCl$. Colorless crystals were obtained in $CHCl_3/CH_3CN$ (1:2 v/v) after slow evaporation at room temperature. Analytical data: IR (KBr, ν, cm^{-1}): 3267, 2934, 1591, 1490, 1452, 1421, 1247, 1199, 1168, 1123, 1111, 1073, 1055, 1021, 1006, 943, 902, 823, 773, 750, 687, 634, 582, 554, 523, 503, 465, 453. ^1H-NMR (400.22 MHz, DMSO-d_6): δ = 7.37 – 7.13 (m, 12H), 7.02 (d, J = 8.4 Hz, 2H), 6.41 (dd, J = 13.6 Hz, 10.4 Hz, 1H), 4.17 (m, 1H), 3.36 (overlapped with HOD/H_2O signal of solvent, 1H, NH), 1.64 (m, 2H), 0.74 (t, J = 7.4 Hz, 3H). $^{13}C\{^1H\}$-NMR (100.64 MHz, DMSO-d_6): δ = 151.20 (d, J = 6.6 Hz), 151.08 (d, J = 6.5 Hz), 144.85 (d, J = 2.7 Hz), 130.11 (s), 129.99 (s), 128.48 (s), 127.10 (s), 126.92 (s), 125.08 (s), 125.02 (s), 120.55 (d, J = 4.7 Hz), 120.52 (d, J = 4.9 Hz), 58.07 (s), 31.90 (d, J = 8.7 Hz), 11.57 (s). $^{31}P\{^1H\}$-NMR (162.01 MHz, DMSO-d_6): δ = –0.49 (s*)*.

3. Results and discussion

3.1. NMR spectroscopy

The $^{31}P\{^1H\}$-NMR spectrum shows the high purity of the synthesized compound, and the phosphorus signal appears at –0.49 ppm in DMSO-d_6 (Fig. 1). The NMR spectrum of the *R*-(+) enantiomer of the title compound was previously reported in $CDCl_3$ solvent, which reveals a phosphorus signal at –2.16 ppm [9]. The relatively high magnetic field for the phosphorus nucleus in the amidophosphoester including an arene ring is related to displacing the phosphorus atom towards the zone of ring where a higher magnetic field is needed, as the phosphorus is separated by an ester oxygen atom from ring.

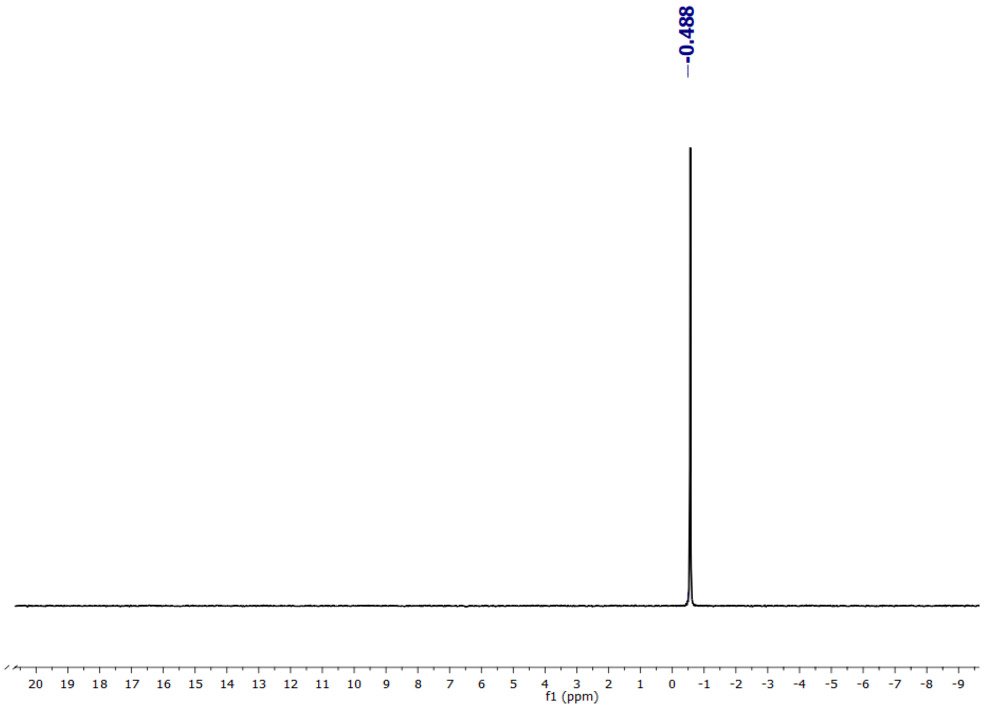


Figure 1. $^{31}P\{^{1}H\}$ NMR spectrum of $(C_6H_5O)_2P(O)[NH$-(*S*)-(–)$CH(C_2H_5)(C_6H_5)]$.

In the ^{1}H-NMR spectrum, the N—H proton overlaps with the signal related to HOD/H_2O of DMSO-d_6 solvent. Similar signal in *R*-(+) enantiomer is revealed as a triplet at 3.84 ppm (apparent $J = 10.8$ Hz) [9], due to geminal phosphorus-hydrogen ($^{2}J_{HP}$) and vicinal hydrogen-hydrogen ($^{3}J_{HH}$) couplings. The two C_6H_5O groups bonded to phosphorus are diastereotopic, and two sets of peaks are observed for them in the aromatic region, which are mixed with the signals of hydrogen atoms of the other phenyl ring in the compound. The triplet and two multiplets at 0.74 ($^{3}J_{HH} = 7.4$ Hz), 1.64 and 4.17 ppm associate to CH_3, CH_2 and CH groups (Fig. 2 and Fig. 3).

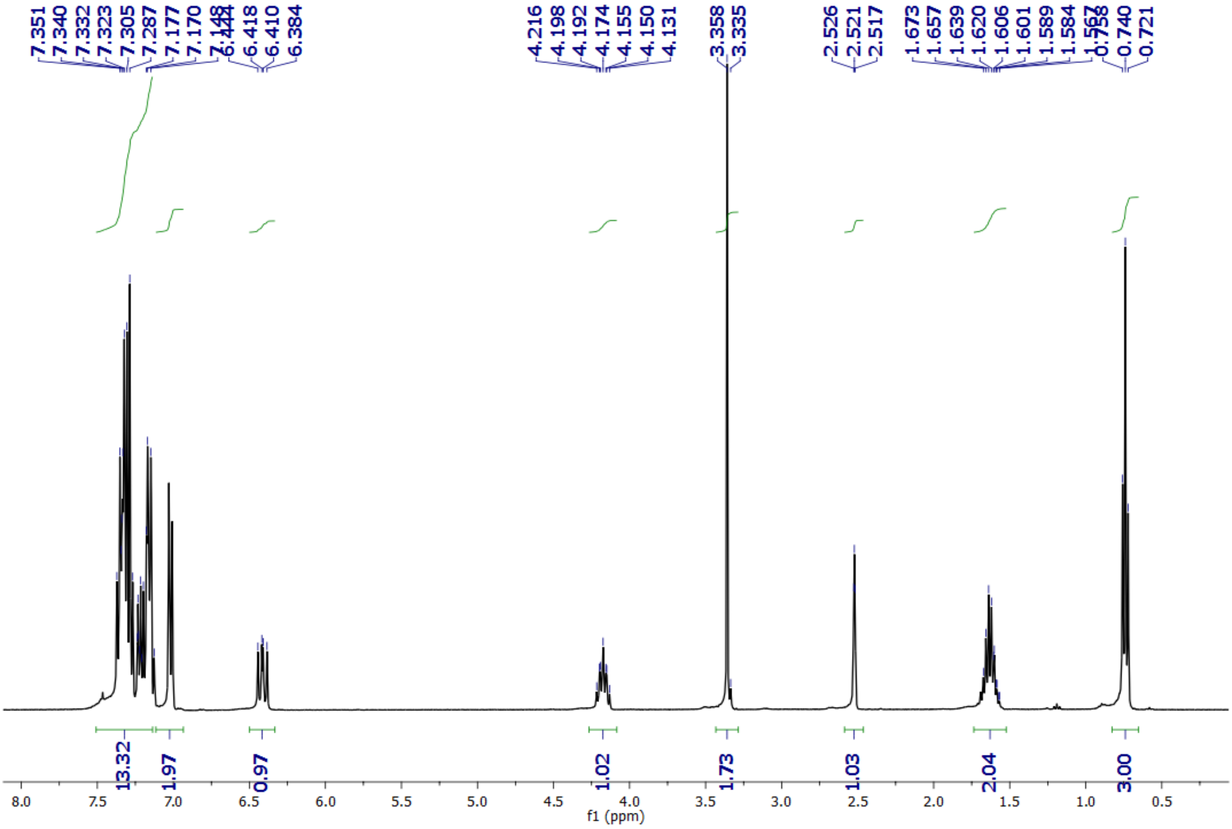


Figure 2. ^{1}H-NMR spectrum of $(C_6H_5O)_2P(O)[NH$-(*S*)-(–)$CH(C_2H_5)(C_6H_5)]$.

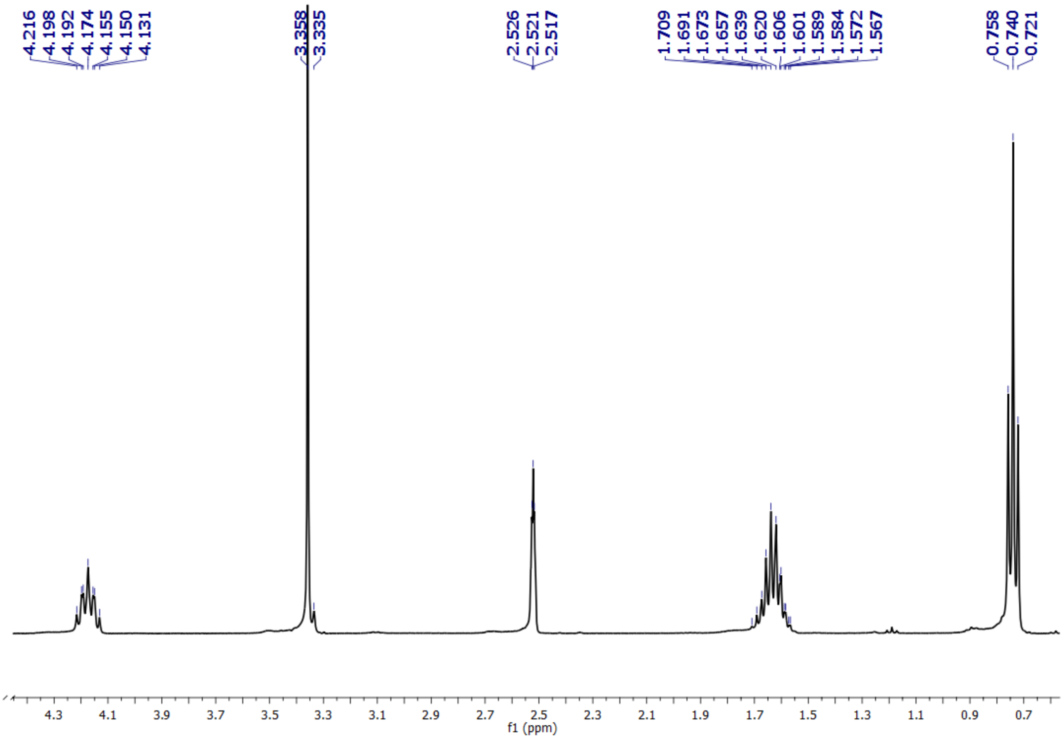


Figure 3. ^{1}H NMR spectrum in the range of 0.7 to 4.3 ppm showing the signals related to CH_3, CH_2, NH and CH groups).

In the $^{13}C\{^{1}H\}$-NMR spectrum (Fig. 4), the doublet signal at 31.90 ppm corresponds to the CH_2 group ($^{3}J_{CP}$ = 8.7 Hz), in comparing with the doublet at 31.80 ppm (J = 8.1 Hz, $CDCl_3$) in *R*-(+) enantiomer [9]. The dissymmetric carbon atom does not show coupling with phosphorus, and the *ipso*-C atom attached to it (with a three-bond separation from phosphorus), shows a doublet at 144.85 ppm ($^{3}J_{CP}$ = 2.7 Hz). For the two diastereotopic C_6H_5O groups, two sets of carbon signals are observed. For example, the diastereotopic *ortho*-C atoms reveal four lines (belonging to a pair of doublets) at 120.50, 120.52, 120.54 and 120.57 ppm. To show which two lines belong to a doublet, an analogous achiral published amidophosphoester (*i.e.* $(C_6H_5O)_2P(O)(NC_4H_8N)P(O)(OC_6H_5)_2$) is given with the value of 4.7 Hz for the corresponding *ortho*-carbon atom [10]. In this compound, two phenyl rings attached to phosphorus atom are magnetically equivalent.

The evaluation of centers of two doublets in the title compound and measuring the related coupling constants were done by considering the lines 1 and 3 for one doublet and lines 2 and 4 for the other doublet. Thus, the diastereotopic *ortho*-C atoms appear doublets at 120.52 ($^{3}J_{CP}$ = 4.9 Hz) and 120.55 ppm ($^{3}J_{CP}$ = 4.7 Hz) (Fig. 5 and Fig. 6). Moreover, the diastereotopic *ipso*-C atoms appear doublets at 151.08 ($^{2}J_{CP}$ = 6.5 Hz) and 151.20 ppm ($^{2}J_{CP}$ = 6.6 Hz), in comparing with 6.4 Hz for the noted literature compound. In the *R*-(+) enantiomer of the title compound [9], the diastereotopic *ortho*-C atoms and diastereotopic *ipso*-C atoms are revealed as doublets at 120.12/120.23 ppm (J = 4.0 Hz for both) and at 150.74/150.92 ppm (J = 7.0 Hz for both) in $CDCl_3$.

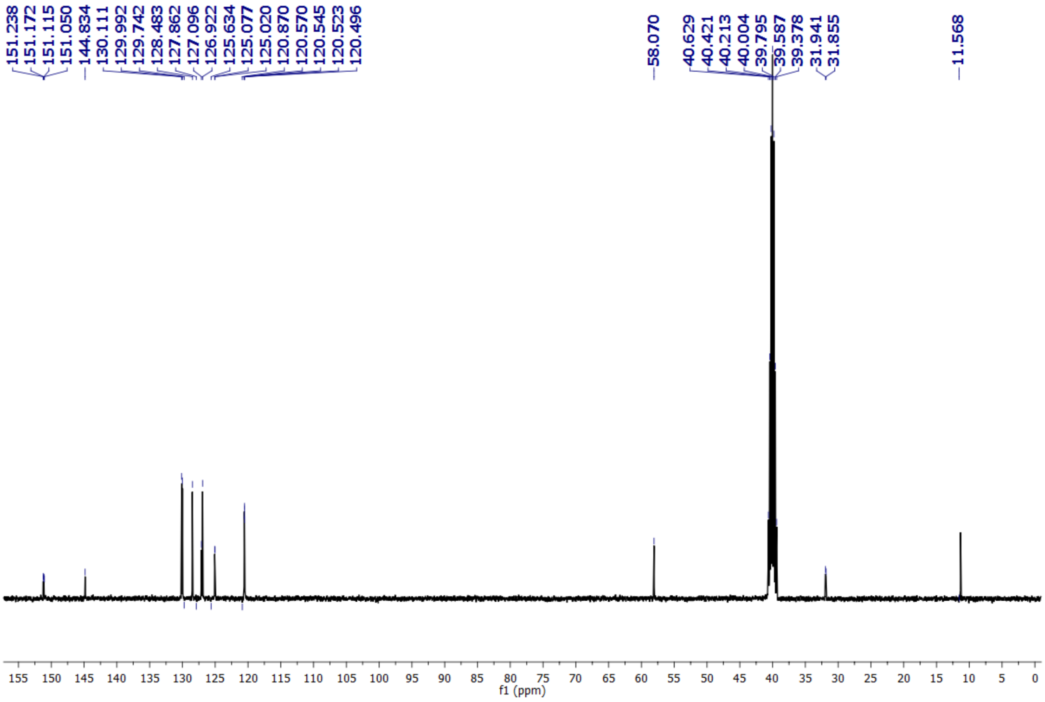


Figure 4. $^{13}C\{^1H\}$ NMR spectrum of $(C_6H_5O)_2P(O)[NH\text{-}(S)\text{-}(–)CH(C_2H_5)(C_6H_5)]$.

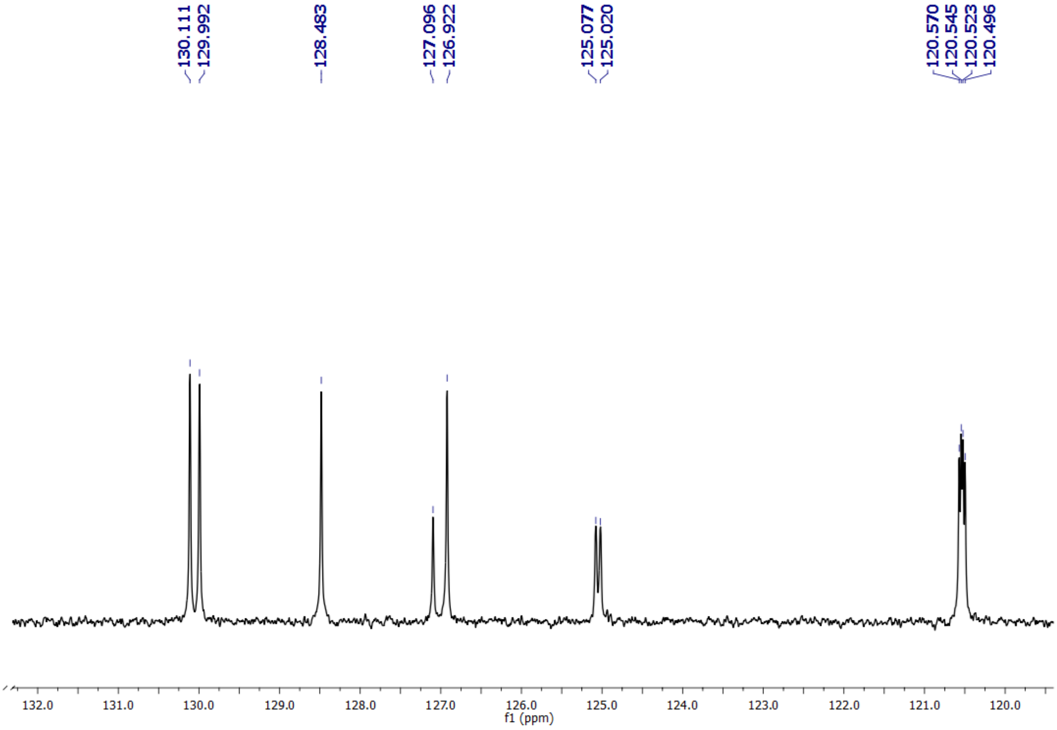


Figure 5. $^{13}C\{^1H\}$ NMR spectrum of $(C_6H_5O)_2P(O)[NH\text{-}(S)\text{-}(–)CH(C_2H_5)(C_6H_5)]$ in the range of 120 to 131 ppm. The two doublets at about 120 ppm are related to the diastereotopic *ortho*-carbon atoms. The two close singlet signals at 125.02/125.08 ppm and at 129.99/130.11 ppm are related to diastereotopic phenyl rings (a pair for diastereotopic *meta* and the other pair for diastereotopic *para* carbon atoms). The signals at 126.92, 127.10, 128.48 (singlets) and 144.85 (doublet, see figure 6) ppm are related to the phenyl ring of chiral amine.

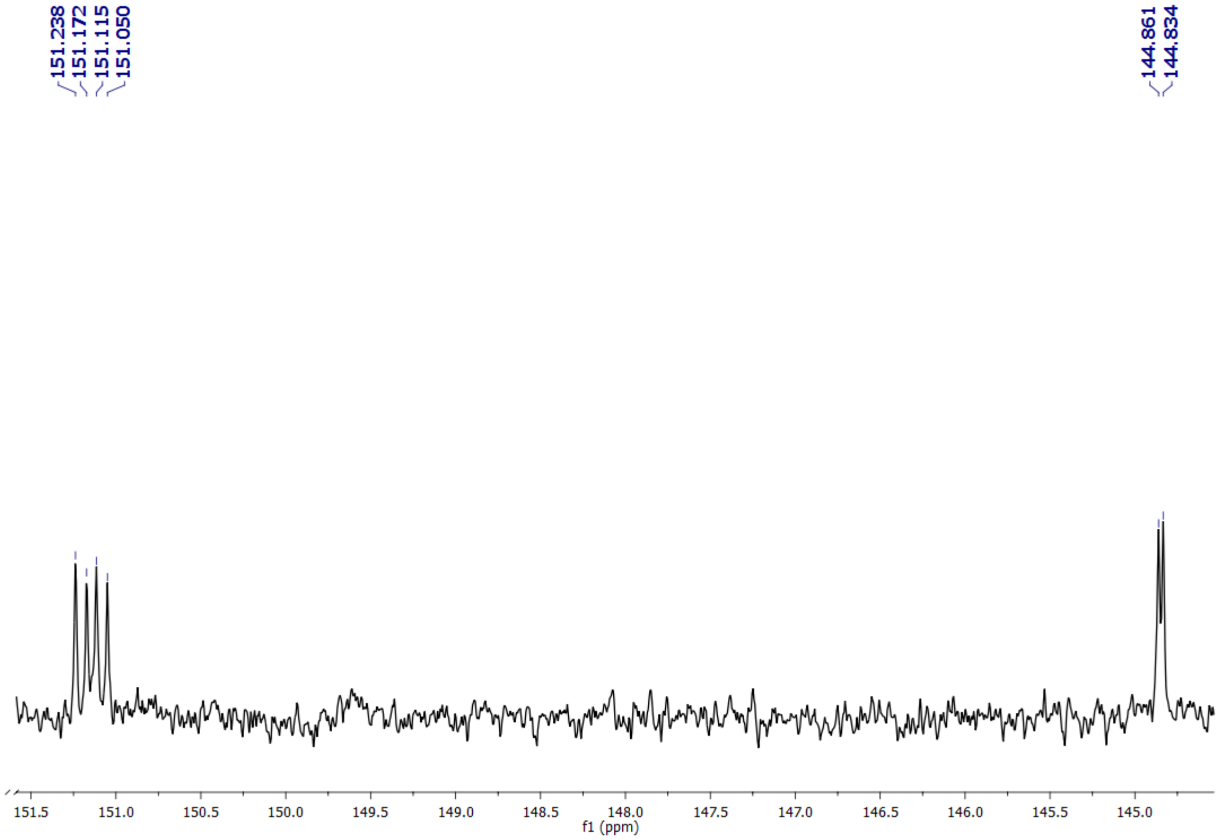


Figure 6. $^{13}C\{^1H\}$ NMR spectrum of $(C_6H_5O)_2P(O)[NH$-(*S*)-(–)$CH(C_2H_5)(C_6H_5)]$ in the range of 144 to 152 ppm. The two doublets within 151.05 to 151.24 ppm are related to the diastereotopic *ipso*-carbon atoms. The doublet at 144.85 ppm is related to the phenyl ring of chiral amine.

3.2. Infrared spectroscopy

The band centered at 3267 cm^{-1} associate to the NH stretching vibrations, which takes part in a relatively weak N—H…O hydrogen bond. This is supported with the N…O distance of 3.077(3) Å examined by the X-ray crystallography of the compound [8]. The band at 1247 cm^{-1} is assigned to the P═O vibration (Fig. 7).

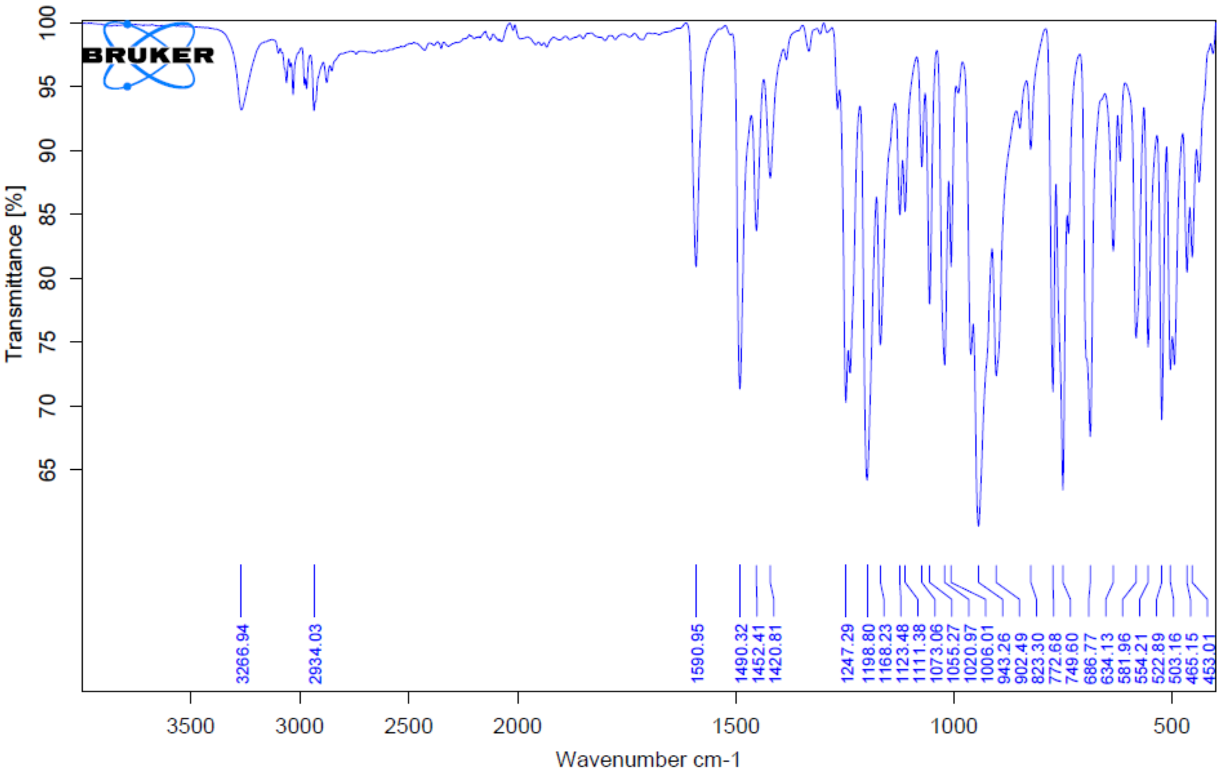


Figure 7. IR spectrum of $(C_6H_5O)_2P(O)[NH\text{-}(S)\text{-}(–)CH(C_2H_5)(C_6H_5)]$ (KBr).

4. Conclusion

Spectroscopic features of $(C_6H_5O)_2P(O)[NH\text{-}(S)\text{-}(–)CH(C_2H_5)(C_6H_5)]$ were studied and compared with its enantiomer $(C_6H_5O)_2P(O)[NH\text{-}(R)\text{-}(+)CH(C_2H_5)(C_6H_5)]$. In the ^{1}H-NMR and ^{13}C{^{1}H}-NMR spectra, the diastereotopic C_6H_5O groups show two sets of signals, and the differences in chemical shifts and coupling constants are significant in the ^{13}C{^{1}H} NMR spectrum.

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