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Research Article

Two-dimensional NMR experiments (^{13}C-^{1}H HSQC and ^{1}H-^{1}H COSY) for *N*-[(*R*)-(+)-*α*-ethylbenzyl]-*P*,*P*-diphenylphosphinic amide

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ABSTRACT

The NMR experiments (^{1}H, $^{13}C\{^{1}H\}$, $^{31}P\{^{1}H\}$, DEPT), IR spectrum and X-ray crystallography of $(C_6H_5)_2P(O)[NH$-*R*-$(+)CH(C_2H_5)(C_6H_5)]$ were previously studied. Here, two-dimensional NMR spectra (^{13}C-^{1}H HSQC and ^{1}H-^{1}H COSY) are investigated. The ^{1}H-^{1}H COSY shows the most shielded aromatic protons, appeared as overlapped peaks, only correlate with themselves and associate to the phenyl ring of chiral amine. The assignments for the phenyl ring directly attached to phosphorus are done considering the number of cross-peaks; typically the *meta*-proton shows correlation with three proton signals (belonging to the *ortho*- and *para*-protons, besides oneself). The ^{13}C-^{1}H HSQC experiment shows the correlations between each carbon atom and directly attached proton (where it exists). This experiment shows the doublets assigned to the diastereotopic *ortho*-carbon atoms have lower values of phosphorus-carbon coupling constants (^{2}J) with respect to the doublets assigned to the *meta*-carbon atoms (^{3}J).

Keywords: NMR; ^{13}C-^{1}H HSQC; ^{1}H-^{1}H COSY; Phosphinamide

1. Introduction

Nuclear magnetic resonance (NMR) spectroscopy represents perhaps the most important analytical tool for structural elucidation formula of compounds [1,2]. In this domain, the development of new tools for computational analysis of the spectra have increased the scope of NMR spectroscopy and opened new lines of scientific inquiry in natural products chemistry and chemical biology [3].

Two-dimensional NMR (2D NMR) spectra, such as ^{1}H-^{1}H correlation spectroscopy (COSY) and ^{13}C-^{1}H heteronuclear single-quantum correlation (HSQC), have most frequently used by chemists. The first technique shows which protons are coupled to each other and the second illustrates the relationship between ^{13}C and the hydrogen that is directly attached to it [3].

In previous studies, these techniques were used for the NMR assignment of some phosphoric triamides, typically ^{13}C-^{1}H HSQC experiment for (4-F-$C_6H_4C(O)NH)P(O)(NH)_2C_5H_{10}$ [4] and ^{1}H-^{1}H COSY for $(C_6H_5NH)(C_6H_5CH_2NH)_2P(O)$ [5]. Here, we report on the ^{13}C-^{1}H HSQC and ^{1}H-^{1}H COSY spectra for *N*-[(*R*)-(+)-α-ethylbenzyl]-*P*,*P*-diphenylphosphinic amide, $(C_6H_5)_2P(O)[NH$-*R*-$(+)CH(C_2H_5)(C_6H_5)]$.

2. Experimental

The title compound was prepared according to the published method [6], from a reaction between $(C_6H_5)_2P(O)Cl$, NH_2-*R*-$(+)CH(C_2H_5)(C_6H_5)$ and $N(C_2H_5)_3$ (1:1:1 molar ratio) in dry chloroform at 0 °C. After removing the solvent in a vacuum, the solid obtained was washed with distilled water to remove the $(C_2H_5)_3NHCl$ salt. NMR spectra were recorded on a Bruker Avance 400 spectrometer.

3. Results and discussion

In a recently published paper [6], the NMR experiments (^{1}H, $^{13}C\{^{1}H\}$, $^{31}P\{^{1}H\}$, DEPT), IR spectrum and X-ray crystallography of $(C_6H_5)_2P(O)[NH$-*R*-$(+)CH(C_2H_5)(C_6H_5)]$ were investigated. Due to the presence of chiral segment, the two phenyl rings directly attached to phosphorus are diastereotopic and two sets of associated proton and carbon signals are observed in the ^{1}H NMR and $^{13}C\{^{1}H\}$ NMR spectra.

The ^{13}C-^{1}H HSQC of this compound is represented in Figure 1. The carbon signals at 11.60, 32.62, 57.10, 126.87, 126.97, 128.45 and 145.50 ppm associate to the chiral $NHCH(C_2H_5)(C_6H_5)$ segment. The correlation of ^{1}H and ^{13}C signals in the aliphatic region is shown in Figure 2. The proton signals of triplet at 0.79 ppm, two multiplets at 1.69/1.82 ppm and the multiplet at 3.84 ppm respectively correlate with the carbon signals of 11.60, 32.62

and 57.10 ppm. As a result, in this region, the frequency orders of signals for protons and associated carbons are the same; *i.e.* the proton with a peak at lower frequency binds to the carbon which also appears a signal at lower frequency, and the same is true for the higher frequency.

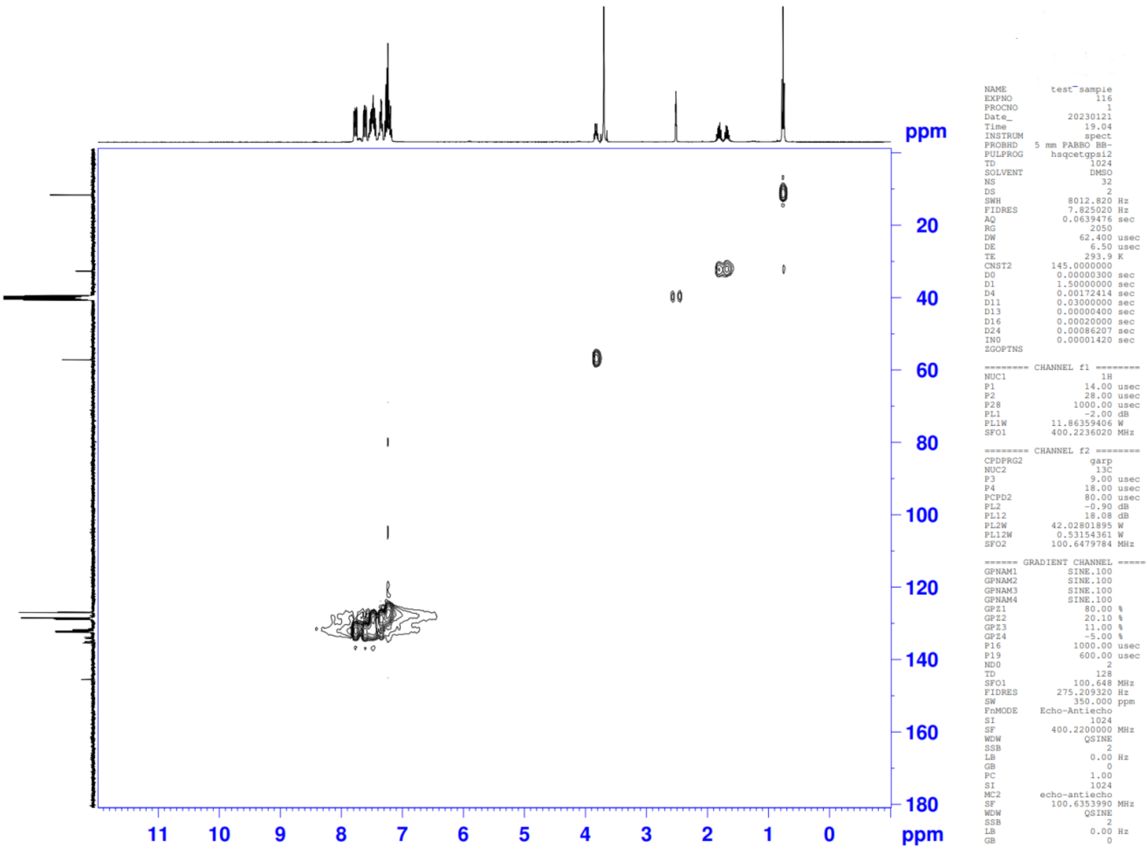

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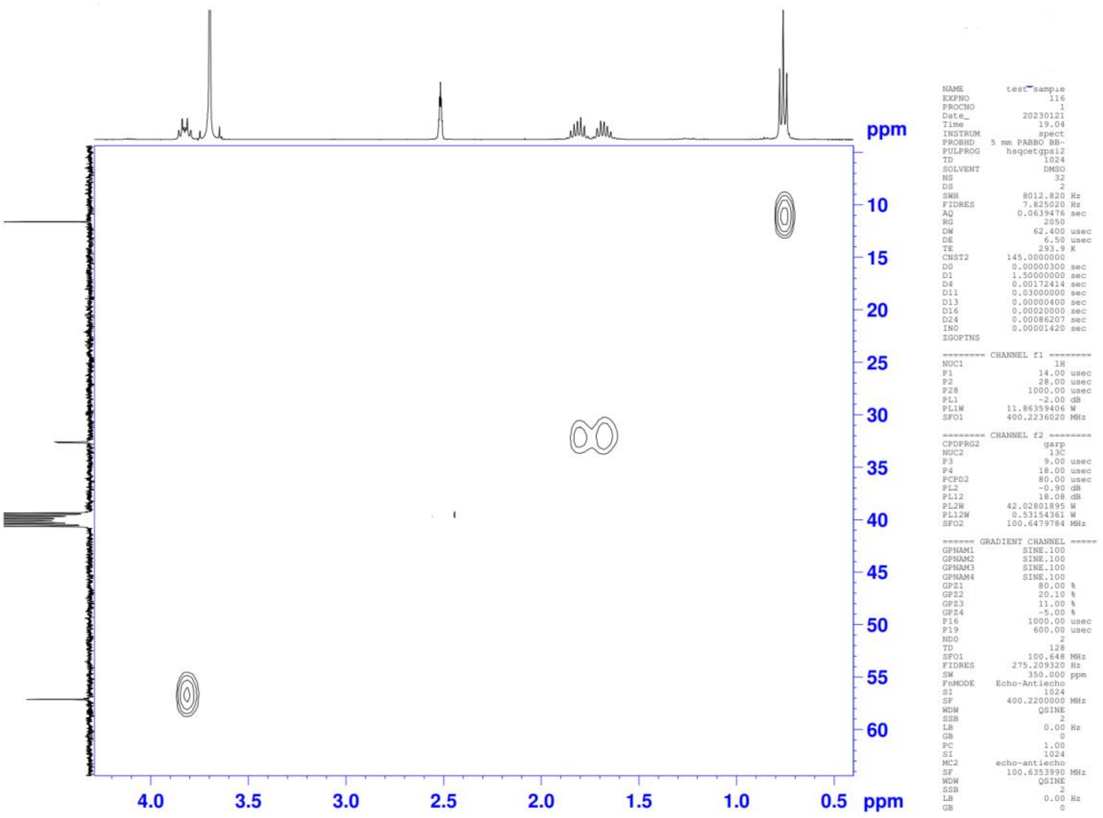
Figure 1. ^{13}C-^{1}H HSQC of the title compound. The ^{1}H and $^{13}C\{^{1}H\}$ NMR and ^{13}C-^{1}H HSQC spectra were recorded in DMSO-d_6/D_2O.



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P2                28.00 usec
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SFO1        400.2236020 MHz

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GPZ4              -5.00 %
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FIDRES       275.209320 Hz
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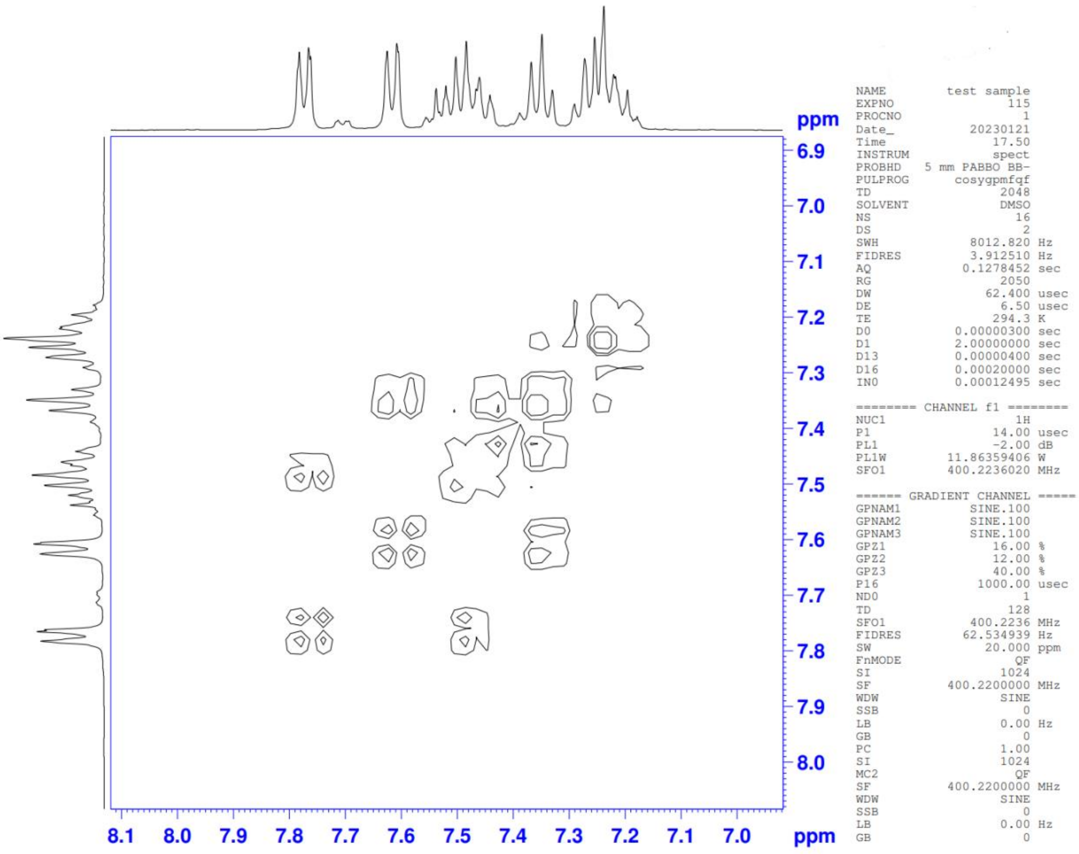
Figure 2. ^{13}C-^{1}H HSQC in the aliphatic region.

Aromatic region of ^{1}H NMR spectrum showed the signals at 7.26, 7.37, 7.50, 7.64 and 7.79 ppm, all of them as a multiplet (or overlapped peaks) with the integrations in accordance with five, two, four, two and two protons, respectively. The ^{1}H-^{1}H COSY (Figure 3) shows the overlapped peaks centered at 7.26 ppm only correlate with themselves; thus, these signals belong to the phenyl ring of chiral amine. These are the most shielded aromatic protons of the title compound.



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SFO1          400.2236020 MHz

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Figure 3. ^{1}H-^{1}H COSY in the aromatic region.

An estimation of chemical shifts for the proton signals with ChemDraw program confirms the upfield proton signals for the phenyl group of chiral amine (Figure 4). This scheme cannot discriminate between the diastereotopic phenyl rings directly attached to phosphorus; thus, these phenyl rings appear to have the same chemical shifts in this estimation. The ^{1}H NMR spectra of two analogous compounds, $(C_6H_5)_2P(O)(NH\text{-}\textit{cyclo}\text{-}C_7H_{13})$ and $(C_6H_5)_2P(O)(NH\text{-}\textit{cyclo}\text{-}C_6H_{11})$ show the peaks of aromatic protons centered at 7.40 ppm (6H)/7.92 (4H) and 7.47 (6H)/7.78 (4H), respectively [7]. These data show that the protons of the phenyl rings directly attached to phosphorus appear at relatively high frequency, as observed in the title structure.

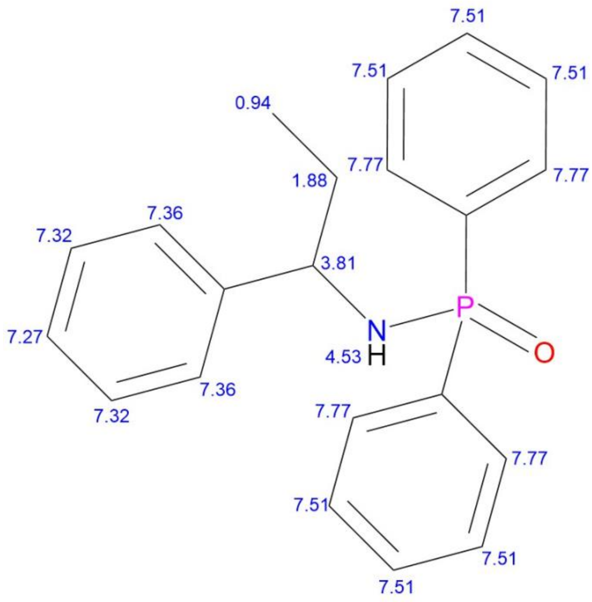
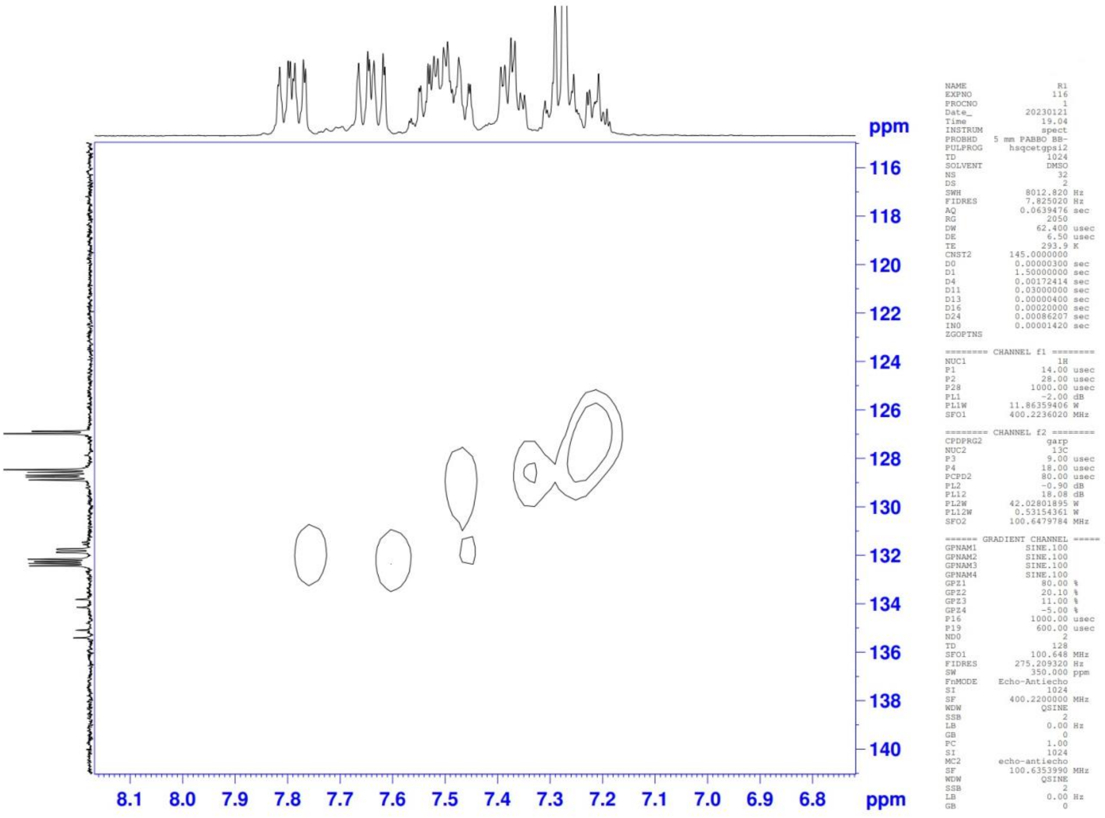


Figure 4. An estimation of chemical shifts for the proton signals with ChemDraw program.

The ^{13}C-^{1}H HSQC in the aromatic region (Figure 5) shows the correlation of overlapped peaks centered at 7.26 ppm with the three first carbon signals (upfield), *i.e*. 126.87, 126.97 and 128.45 ppm, which associate to the phenyl ring of chiral amine. The assignment of the *ipso* carbon atom of this phenyl ring is simple, as it appears as a doublet (the last downfield signal in the spectrum), which does not any correlation with the proton' signal. The shape of these overlapped contours comes to mind the correlation of proton' signals from low to high frequencies with the carbon' signals from low to high frequencies, respectively.



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DS                   2
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D1          1.50000000 sec
D4          0.00172414 sec
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D13         0.00000400 sec
D16         0.00020000 sec
D24         0.00086207 sec
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ZGOPTNS

======== CHANNEL f1 ========
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P1               14.00 usec
P2               28.00 usec
P28            1000.00 usec
PL1              -2.00 dB
PL1W       11.86359406 W
SFO1       400.2236020 MHz

======== CHANNEL f2 ========
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NUC2               13C
P3                9.00 usec
P4               18.00 usec
PCPD2            80.00 usec
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GPZ4             -5.00 %
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P19             600.00 usec
ND0                  2
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FIDRES      275.209320 Hz
SW             350.000 ppm
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SSB                  2
LB                0.00 Hz
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PC                1.00
SI                1024
MC2     echo-antiecho
SF         100.6353990 MHz
WDW              QSINE
SSB                  2
LB                0.00 Hz
GB                   0
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Figure 5. ^{13}C-^{1}H HSQC in the aromatic region.

The two doublets at 132.20 (J = 9.4 Hz) and 132.38 (J = 9.5 Hz) show correlations with two last aromatic signals at high frequencies, centered at 7.64 and 7.79 ppm, with an almost “ddd” pattern (doublet of doublets of doublets). This pattern is arisen from geminal (^{2}J) P-H and vicinal (^{3}J) H-H couplings with together H-H coupling with four bonds separation (^{4}J), and the signals associate to the *ortho*-carbon/proton atoms. The overlapped peaks centered at 7.50 ppm seem to associate with three different hydrogen atoms. The middle section of these overlapped peaks seems to have the shape similar to the peak centered at 7.37 ppm (with integration related to two protons for both these signals). The isolated peak at 7.37 ppm is apparent as a triplet of doublets. The correlation of these two proton’ peaks with a similar fine structure with the doublet carbon’ signals of 128.62 (J = 12.2 Hz) and 128.82 ppm (J = 12.1 Hz) is seen. According to Figure 3, a correlation of multiplet centered at 7.37 ppm with the signal at 7.64 ppm and a section of the overlapped peaks centered at 7.50 ppm proposes that this multiplet associates to the *meta*-protons of phenyl ring directly attached to phosphorus.

References

[1] K. Gholivand, M. Pourayoubi and Z. Shariatinia, Polyhedron 26 (2007) 837–844.

[2] K. Gholivand, Z. Shariatinia and M. Pourayoubi, Z. Anorg. Allg. Chem. 631 (2005) 961–967.

[3] T. D. W. Claridge, High-Resolution NMR Techniques in Organic Chemistry (2016), Chapter 7, 243–294, Elsevier.

[4] A. Tarahhomi, M. Pourayoubi, A. L. Rheingold and J. A. Golen, Struct. Chem. 22 (2010) 201–210.

[5] M. Pourayoubi, M. Toghraee, J. Zhu, M. Dušek, P. J. Bereciartua and V. Eigner, CrystEngComm 16 (2014) 10870–10887.

[6] F. Eslami, M. Pourayoubi, F. Sabbaghi, E. Skořepová, M. Dušek and S. Baniyaghoob, Acta Cryst. E 79 (2023) 769–776.

[7] F. Hamzehee, M. Pourayoubi, A. Farhadipour and D. Choquesillo-Lazarte, Phosphorus, Sulfur, Silicon Relat. Elem. 192 (2017) 359–367.