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4,8-Dimethyl-2-phenyl-1,3,6,2-dioxaselenaphosphocane 2-selenide **6** was synthesized by the condensation of dichlorophenylphosphine and 4-selenaheptane-2,6-diol **8** followed by oxidation with selenium. The conformations of **6** and related 2-(*p*-methylphenoxy)-1,3,6,2-dioxaselenaphosphocane 2-oxide **7** in the solid state and in solution were studied through X-ray diffraction and NMR spectroscopy. The asymmetric boat–chair conformation in both solid state and solution was established for the eight-membered heterocycles.

We have recently synthesized 2-substituted 1,3,6,2-dioxaselenaphosphocane 2-oxides, sulfides and selenides^{1,2} and been interested in the elucidation of their conformation in comparison with the reported conformations of similar 8-membered 1,3,6,2-trioxaphosphocanes, 1,3,6,2-dioxasulfaphosphocanes and 1,3,6,2-dioxazaphosphocanes.³ A chair–chair conformation was suggested for 2-methyl-1,3,6,2-trioxaphosphocane **1** and its 2-sulfide **2** in solution⁴ and a crown conformation with the sulfur atom axial and the methyl group equatorial on the phosphorus atom was found for the molecule **2** in the crystal state.⁵ An equilibrium between two twisted chair–chair conformations **3a** and **3b** was proposed for 2-methyl-1,3,6,2-dioxasulfaphosphocane 2-oxide **3** and an equilibrium between two chair–chair conformations **4a** and **4b** for 2,6-dimethyl-1,3,6,2-dioxazaphosphocane **4** in solution (Chart 1 and Scheme 1).⁶ It was shown that *N*-acyl-4,4,8,8-tetramethyl-

1,3,6,2-dioxazaphosphocanes **5** exhibit a boat–chair conformation or a crown conformation depending upon the nature of the acyl group.⁷ Thus, *N*-trifluoroacetyl derivative **5a** was shown to have a crown conformation by NMR analysis whereas the conformation of *N*-benzoyl derivative **5b** was established as boat–chair by X-ray crystallography. These results indicate that there are a variety of conformations depending upon the nature of the atoms at the 6-position of the 1,3,6,2-dioxaphosphocane ring.

The above reports prompted us to investigate the conformation of newly synthesized 4,8-dimethyl-2-phenyl-1,3,6,2-dioxaselenaphosphocane 2-selenide **6** and 2-(*p*-methylphenoxy)-1,3,6,2-dioxaselenaphosphocane 2-oxide **7**.² Conformational analyses of **6** and **7** have been carried out by NMR spectroscopy and X-ray crystallography and led to the conclusion that both compounds exhibit asymmetric boat–chair conformations in solution and in the crystal state.

Results and discussion

4-Selenaheptane-2,6-diol **8** was synthesized in 97% yield from selenium powder by reduction with Rongalite (CH₂O·NaHSO₂·2H₂O) followed by treatment with epoxypropane. This method has the advantages of preparation at ambient temperature, use of a simple operation and higher yield over the electrochemical method.⁸ Although trisubstituted heterocycle **6** was not obtained by the method at 0 °C for synthesizing mono-substituted heterocycle **7**,¹ it was prepared in 10% yield by the reaction of compound **8** with phenyldichlorophosphine in pyridine at the lower temperature of –15 °C followed by oxidation with selenium (Scheme 2). Compound **6** was obtained as

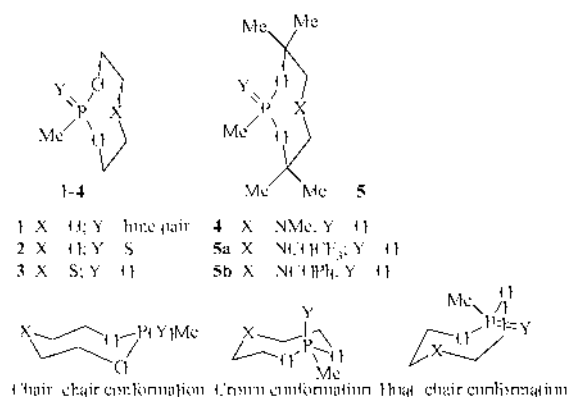
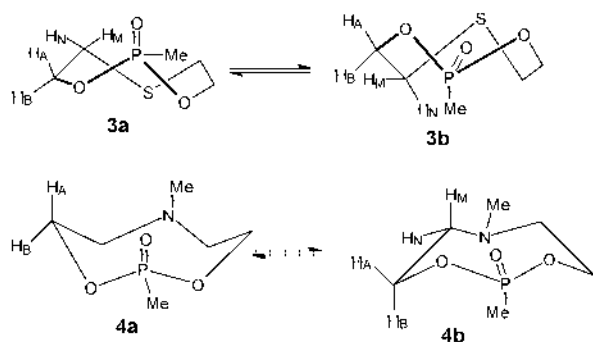
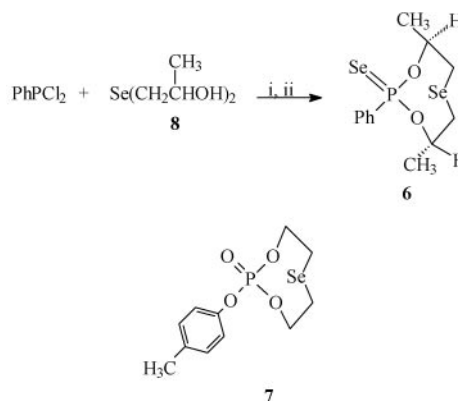


Chart 1



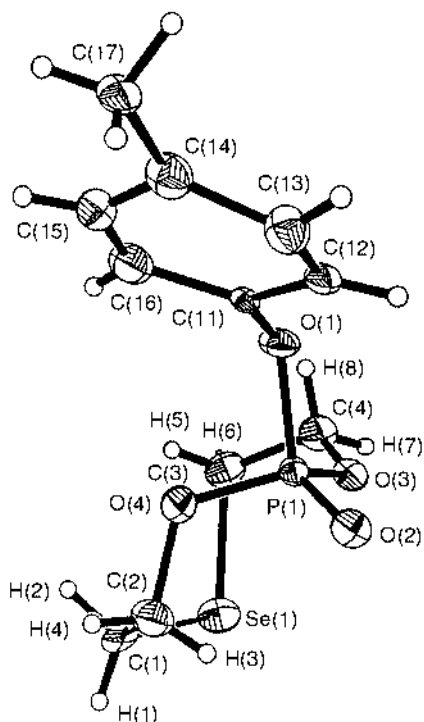
Scheme 1



Scheme 2 Reagents: (i) Py–ice–salt bath. (ii) Se.

Table 1 ^1H and ^{31}P NMR spectral parameters of **7** in CDCl_3

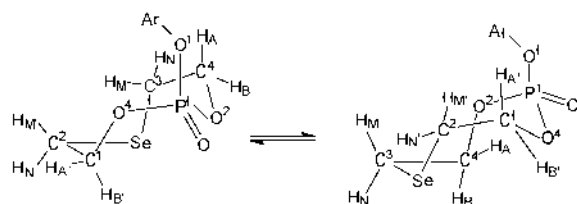
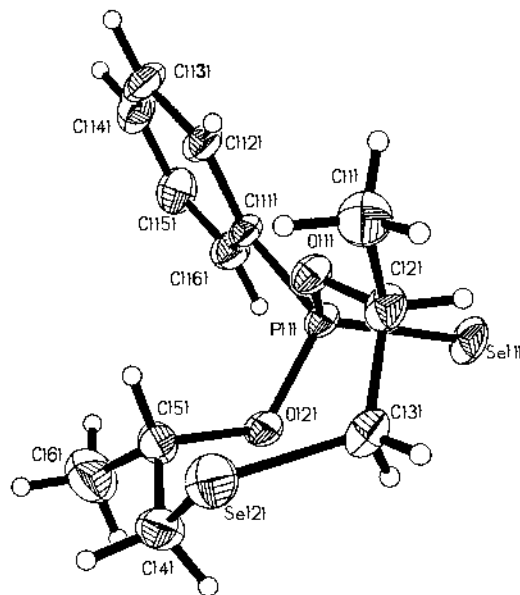
| Chemical shifts (ppm) | | | | | Coupling constants/Hz | | | | | | | |
|-----------------------|------------|------------|------------|------------|-----------------------|------------|------------|------------|------------|------------|------------|------------|
| δ_A | δ_B | δ_M | δ_N | δ_P | $^3J_{AP}$ | $^3J_{BP}$ | $^2J_{MN}$ | $^2J_{AB}$ | $^3J_{AM}$ | $^3J_{AN}$ | $^3J_{BM}$ | $^3J_{BN}$ |
| 4.69 | 4.35 | 3.12 | 2.86 | -7.72 | 10.9 | 18.6 | -14.7 | -18.9 | 3.1 | 5.3 | 9.3 | 2.6 |

**Fig. 1** The molecular structure of compound **7**. Reprinted from ref. 2 with kind permission of the Chinese Chemical Society.

colourless crystals and its stereochemistry was finally confirmed by X-ray crystallographic analysis (see below). As previously reported,² the X-ray crystal structure of compound **7** (Fig. 1) shows that the eight-membered heterocycle exists in an asymmetric boat-chair conformation with the ArO group axial and the P=O bond equatorial in the solid state. It is noticeable that the distance between the non-bonded atoms P and Se is 3.824 Å, shorter than the equilibrium distance corresponding to the sum of van der Waals radii (3.90 Å), which indicates that a weak transannular P...Se interaction exists in this eight-membered ring.

In solution, the ethylene portions of the ^1H NMR spectrum of compound **7** were analyzed as an ABMNY system (Y is the phosphorus atom). The resonances of H_A , H_B , H_M and H_N were well separated, giving the chemical shifts and coupling constants shown in Table 1.

Supposing compound **7** in solution also existed in an asymmetric boat-chair conformation like that in the solid state, H_A and H_B should have different chemical shifts. There must exist a fast equilibrium between two such conformations (Scheme 3); thus the NMR spectrum of compound **7** falls into the time-average result of the above equilibrium. Since H_8 and H_5 (Fig. 1) interact with the lone pair p electrons of O1 and O4

**7**, Ar = 4-MePh-
Scheme 3**Fig. 2** The molecular structure of compound **6**.

respectively, they should appear downfield. Thus, H_8 , H_7 , H_5 and H_6 (Fig. 1) are assigned to be H_A , H_B , H_M and H_N (Scheme 3), respectively. H_A with the larger chemical shift is *trans* to the P=O bond and H_B with the smaller chemical shift is *cis* to the P=O bond. The coupling constants (Table 2) of **7** estimated from POCH⁹ and HCCH¹⁰ dihedral angles are basically consistent with those obtained experimentally, which confirms that **7** exists in an equilibrium between two asymmetric boat-chair conformations as shown in Scheme 3 in solution.

Fig. 2 shows the crystal structure of **6**. It is very clear that the eight-membered ring has an asymmetric boat-chair conformation with P=Se axial and phenyl and both methyl groups equatorial. Although both **6** and **7** have an asymmetric boat-chair conformation, the orientations of substituents on phosphorus are very different. The P=O group is equatorial in **7**, while the P=Se bond is axial in **6**. In addition, the two methyl groups are both equatorial and *trans* to each other in **6**. H_5A and H_2A are both axial, but *trans* and *cis*, respectively, to P=Se. H_5A is located spatially near the C1 methyl group. The dihedral angle of 82.9° between C4-H4A and C5-H5A is close to 90°. The intracyclic O-P-O and C-Se-C bond angles are 106.3 and 102.2° respectively. P1-O1-C2 and P1-O2-C5 angles are 123.2 and 121.6° respectively, which implies that O1 and O2 are sp^2 hybridised. Similarly, bond angles of Se2-C4-C5 and Se2-C3-C2 are 116.8 and 117.4° respectively, bigger than the sp^3 bond angle of 109° 28', implying that the heterocycle is squashed at the C4 and C3 ends and puckered at the P1 and Se2 ends. In addition, the non-bonded distance of 4.063 Å between P1 and Se2 is larger than the equilibrium distance corresponding to the sum of van der Waals radii (3.90 Å), which leads to the conclusion that a transannular P...Se interaction does not exist.

In the 200 MHz ^1H NMR spectrum of **6**, the aliphatic protons are separated into two groups. Group 1 comprises H_A , H_M , H_N and H_X , and Group 2 comprises H_A' , H_M' , H_N' and H_X' . Group 1 is located downfield relative to Group 2. The coupling relationships between them were determined by double irradiation experiments. The ^1H , ^{13}C and ^{31}P NMR parameters of **6** are listed in Tables 3 and 4.

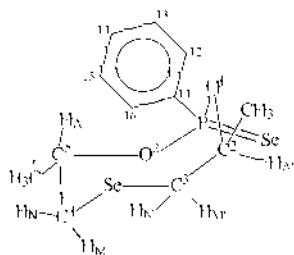


Fig. 3 Conformation of **6** in CDCl_3 .

First of all, each proton on a carbon in the eight-membered ring has a different chemical shift, which implies that the eight-membered ring possesses an asymmetric conformation and that a fast equilibrium does not exist between the different conformations. Secondly, both H_N and H_N' appear as doublets and double irradiation experiments show that they are split only by geminal protons H_M and H_M' , respectively, not by the vicinal protons H_A and H_A' , respectively. According to the Karplus equation, it could be deduced that the dihedral angles between H_A and H_N , H_A' and H_N' are close to 90° . Thirdly, during double irradiation experiments, H_A is enhanced greatly, not only by the irradiation of H_X but also by the irradiation of H_X' . This fact implies that H_A is spatially close to both methyl groups and thus the two methyl groups are *trans* to each other. Furthermore, in the ^{13}C NMR spectrum of **6**, all the carbon atoms except for C3 (Fig. 3) appear as doublets, which suggests that there is no coupling between C3 and P ($^3J_{\text{P-C3}} = 0$ Hz). The large differences between $^3J_{\text{P-C3}}$ (0 Hz) and $^3J_{\text{P-C4}}$ (19.8 Hz), $^2J_{\text{P-C2}}$ (11.4 Hz) and $^2J_{\text{P-C5}}$ (5.3 Hz) show that the C2–C3 and C5–C4 bonds, which have the same chemical environment, possess large spatial differentiation in the solution conformation of **6**. The NMR data for selenide **6** support a boat–chair conformation, however it has some differences compared with the actual chair–boat in the solid.

Table 2 The estimated coupling constants from the dihedral angle ($^\circ$) of **7** in the crystal state

| Atoms | Dihedral angle/ $^\circ$ | $^3J/\text{Hz}$ | Average | $^3J_{\text{exp}}/\text{Hz}$ |
|-----------|--------------------------|-----------------|------------------------|------------------------------|
| P(1) H(8) | 57.55 | 10 | $^3J_{\text{PA}} = 11$ | 10.9 |
| P(1) H(3) | 125.80 | 12 | | |
| P(1) H(7) | 177.18 | 22 | $^3J_{\text{PB}} = 19$ | 18.6 |
| P(1) H(4) | 6.85 | 16 | | |
| H(2) H(4) | –178.79 | 10 | $^3J_{\text{BM}} = 9$ | 9.3 |
| H(5) H(7) | –162.94 | 8 | | |
| H(1) H(3) | –56.09 | 6 | $^3J_{\text{AN}} = 5$ | 5.3 |
| H(6) H(8) | 73.13 | 4 | | |

Table 3 ^1H NMR Chemical shifts (ppm) and coupling constants (Hz) of **6**

| H_A | H_A' | H_M | H_M' | H_N | H_N' | H_X | H_X' |
|---------------------|----------------------|---------------------|----------------------|---------------------|----------------------|---------------------|----------------------|
| 5.30 | 4.26 | 3.48 | 2.94 | 2.89 | 2.44 | 1.44 | 1.06 |
| J_{AM} | J_{AX} | J_{MN} | $J_{\text{A'M'}}$ | $J_{\text{A'X'}}$ | $J_{\text{M'N'}}$ | | |
| 3.88 | 6.32 | –14.51 | 8.57 | 6.41 | –14.25 | | |

Table 4 ^{31}P , ^{13}C NMR Chemical shifts (ppm) and coupling constants (Hz) of **6**

| C11 | C12 | C13 | C14 | C15 | C16 | C2 | C3 | C4 | C5 | C6 | C1 |
|-------------------|----------------------|----------------------|----------------------|----------------------|----------------------|---------------------|---------------------|---------------------|---------------------|---------------------|---------------------|
| 131.84 | 128.30 | 130.09 | 134.16 | 129.86 | 128.02 | 72.75 | 29.42 | 31.26 | 79.43 | 23.18 | 21.10 |
| δ_P | $^1J_{\text{P-C11}}$ | $^2J_{\text{P-C12}}$ | $^3J_{\text{P-C13}}$ | $^3J_{\text{P-C15}}$ | $^2J_{\text{P-C16}}$ | $^2J_{\text{P-C2}}$ | $^3J_{\text{P-C3}}$ | $^3J_{\text{P-C4}}$ | $^2J_{\text{P-C5}}$ | $^3J_{\text{P-C6}}$ | $^3J_{\text{P-C1}}$ |
| 81.78 | 26.2 | 13.7 | 13.8 | 11.0 | 12.6 | 11.4 | 0 | 19.8 | 5.3 | 8.5 | 11.7 |

In conclusion, we have studied the conformation of 1,3,6,2-dioxaselenaphosphocanes and established the asymmetric boat–chair conformation of **6** in the solid state by X-ray diffraction study. The NMR study in solution revealed that **6** also has a boat–chair conformation, and that **7** exists in the equilibrium between two asymmetric boat–chair conformations. These boat–chair conformations of the dioxaselenaphosphocanes are different from those of other types of dioxaphosphocanes such as **1–4** having –O–, –NR– or –S– within the ring instead of –Se–. Most of these dioxaphosphocanes have a chair–chair or crown conformation with the exception of *N*-trifluoroacetyl-1,3,6,2-dioxazaphosphocane **5a** which has been shown to have a boat–chair conformation.⁷

Experimental

The melting points are uncorrected. IR spectra were measured as KBr pellets. ^1H , ^{13}C and ^{31}P NMR spectra were recorded on a Bruker ACP-200 spectrometer using tetramethylsilane as internal standard for ^1H and ^{13}C and 85% phosphoric acid as external standard for ^{31}P , respectively. Mass spectra were recorded at an ionizing voltage of 70 eV. Elemental analyses were determined on a Yanaco CHN CORDER MT-3 analyzer. Phenylidichlorophosphine was synthesized according to the literature.¹⁰

Synthesis of 4-selenaheptane-2,6-diol **8**

A 500 mL four-necked flask was charged with 12.5 g (0.16 mol) of selenium powder, 60.8 g (0.38 mol) of Rongalite ($\text{CH}_2\text{O} \cdot \text{NaHSO}_2 \cdot 2\text{H}_2\text{O}$), 35.0 g (0.87 mol) of sodium hydroxide and 260 mL of water. The reaction was exothermic with the temperature reaching 60°C under stirring. Then 25.0 mL (0.36 mol) of epoxypropane was added over a period of 50 minutes while keeping the temperature at $50\text{--}60^\circ\text{C}$. The mixture was stirred for another 10 hours at room temperature and then extracted with chloroform (2×50 mL). The combined chloroform solutions were dried with anhydrous magnesium sulfate. After removal of the solvent, compound **8** was obtained as a colorless oil in 97% yield as tested to show one spot on TLC. ^1H NMR (CDCl_3) δ 3.88 (2H, m), 2.80 (2H, m), 2.57 (2H, m), 2.41 (2H, s), 1.25 (6H, d, $J = 6.0$ Hz); MS: 198 (M^+ , 28), 180 ($\text{M}^+ - \text{H}_2\text{O}$, 2), 172 ($\text{M}^+ - 2 \times \text{H}_2\text{O}$, 0.5), 154 ($\text{M}^+ - \text{CH}_3\text{-CHO}$, 27), 121 ($\text{CH}_2=\text{CH}-\text{CH}_2=\text{Se}^+$, 48), 110 ($\text{M}^+ - 2 \times \text{CH}_3\text{-CHO}$, 65), 94 ($\text{CH}_2=\text{Se}^+$, 79), 59 [$\text{CH}_2\text{CH}(\text{OH})-\text{CH}_3$, 100], 45 (CH_3CHOH , 100).

Synthesis of 4,8-dimethyl-2-phenyl-1,3,6,2-dioxaselenaphosphocane 2-selenide **6**

To a 100 mL Schlenk flask 1.97 g (0.010 mol) of 4-selenaheptane-2,6-diol **8** and 20 mL of pyridine were added and cooled to between -17 and -15°C with an ice–salt bath. Phenylidichlorophosphine (0.010 mol) was added slowly over 1 h to the magnetically stirring solution while maintaining the temperature at -15°C and the mixture was kept stirring at this temperature for another hour. The mixture was then stirred for 20 h at room temperature. The selenium powder (0.010 mol) and 20 mL of toluene were then added and the mixture was kept stirring for 20 h at room temperature. The precipitated salt was removed by filtration and washed with benzene. The

combined filtrate and washings were evaporated *in vacuo* (<40 °C) and the residual oil was dissolved in 20 mL of chloroform and washed consecutively with 20 mL of 1 M hydrochloric acid, 20 mL of saturated sodium bicarbonate and 20 mL of saturated sodium chloride aqueous solution, and then dried with magnesium sulfate. The product was purified with flash chromatography. Colorless crystals, 9.9% yield, mp 105–107 °C; ¹H NMR (CDCl₃) δ 7.94–7.45 (5H, m), 5.29 (1H, m), 4.30 (1H, m), 3.48 (1H, dd), 2.93 (2H, m), 2.44 (1H, d), 1.44 (3H, d), 1.05 (3H, d); ³¹P NMR (CDCl₃) δ 81.78; MS: 384 (M⁺, 24), 342 (M⁺ – CH₃ – CH=CH₂, 8), 300 (M⁺ – 2 × CH₃ – CH=CH₂, 15), 121 (CH₃ – CH=CH – Se⁺, 46), 93 (CH=Se⁺, 32), 77 (Ph, 96), 41 (C₃H₅, 85). Anal. Calcd. for C₁₂H₁₇O₂PSe₂ (*M* 382.16): C, 37.72; H, 4.48. Found: C, 37.50; H, 4.46%. For X-ray data of **6**, see ref. 11.

2-(*p*-Methylphenoxy)-1,3,6,2-dioxaselenaphosphocane 2-oxide **7**

Compound **7** was prepared according to the literature method.² ¹H NMR (CDCl₃) δ 7.11 (s, 4H), 4.69 (dodecet, 2H), 4.35 (tridecet, 2H), 3.12 (octet, 2H), 2.86 (octet, 2H), 2.27 (s, 3H); ³¹P NMR (81 MHz, CDCl₃) δ –7.72 (ddd, *J* = 10.9 Hz, *J* = 18.6 Hz, *J* = 32.8 Hz). ¹³C NMR (CDCl₃) δ 20.7, 24.2, 70.3 (d, *J*_{P-C} = 6.8 Hz), 102.5, 102.8, 119.6, 119.7, 130.2, 134.9. For other spectral data and the detailed crystal data, see the previous report.²

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References

- 1 J. L. Li, B. Tian, C. Q. Zhao, Y. M. Wang, T. Matsuura and J. B. Meng, *Pol. J. Chem.*, 1998, **72**, 534.
- 2 J. L. Li, B. Tian, C. Q. Zhao, Y. M. Wang and J. B. Meng, *Chin. J. Chem.*, 1998, **15**, 450.
- 3 R. P. Arshinova, *Phosphorus, Sulfur Silicon*, 1992, **68**, 155.
- 4 J. P. Dutasta and J. B. Robert, *J. Am. Chem. Soc.*, 1978, **100**, 1925.
- 5 A. Grand, *Cryst. Struct. Commun.*, 1982, **11**, 569.
- 6 K. S. Ravinder, K. Sampath and R. Vaidyanathaswamy, *J. Chem. Res. (S)*, 1980, 12.
- 7 D. Houalla, K. Elabed, Z. Bounja and R. Wolf, *Phosphorus, Sulfur Silicon*, 1992, **69**, 13.
- 8 A. M. Akhmedov, Sh. R. Ashurova and E. Sh. Mamedov, *Azerb. Khim. Zh.*, 1987, 118.
- 9 D. G. Gorenstein, *Phosphorus-31 NMR Principles and Applications*, Academic Press, Inc., San Diego, CA, USA, 1984, p. 45.
- 10 Y. X. Zhao and X. Y. Sun, *Guangpu Jiexi Yu Youji Jiegou Jianding*, Chinese Science and Technology Press, Beijing, 1992, p. 256.
- 11 X-Ray data for **6**: C₁₂H₁₇O₂PSe₂, 382.15, orthorhombic, *Pbca* (No. 61), *μ* = 5.092 mm⁻¹, *R* = 0.1179, *wR* = 0.1298, *a* = 9.270, *b* = 16.083, *c* = 19.858 Å, *V* = 2960.6(10) Å³, *T* = 293(2) K, *Z* = 8, measured/independent reflections = 2589/2589 [*R*(int) = 0.0000]. CCDC reference number 169302. See <http://www.rsc.org/suppdata/p2/b0/b008294p/> for crystallographic files in .cif or other electronic format.

