Mendeleev Commun., 2000, 10(6), 216–217

Diastereomeric transformations in the series of 3-cyano-2-oxo-1,2-thiaphosphorinanes

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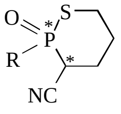
10.1070/MC2000v010n06ABEH001378

A mechanism of mutual diastereomeric transformations in the series of 3-cyano-2-oxo-1,2-thiaphosphorinanes was suggested, which is based on the elimination–attachment of a rather acidic hydrogen atom at the 3-position of the heterocycle.

Previously,[1] we have reported the synthesis of the first functionalised 1,2-thiaphosphacyclanes, namely, 3-cyano-2-oxo-1,2-thiaphosphorinanes **1a**,**b**. They were formed *via* the intramolecular S-alkylation of 3-halopropyl-substituted thiophosphorylacetonitriles, which proceeds either on the distillation of parent compounds *in vacuo* (Hlg = Cl) or on refluxing in acetonitrile (Hlg = I). Compounds **1a**,**b**, which were obtained as a statistical mixture of diastereomers **A** (*trans*, 2*R**, 3*S**) and **B** (*cis*, 2*R**, 3*R**)[†] transform in the absence of solvent to an individual diastereomer that is favourable in terms of the generalised anomeric effect; that is, diastereomer **B** with the axial ethoxy group and diastereomer **A** with the axial oxygen atom of the P=O group were formed for compounds **1a** and **1b**, respectively. Both compounds slowly (during 3 months) undergo a reverse transformation of individual diastereomers to an equilibrium mixture with the initial diastereomer ratio in benzene solutions.

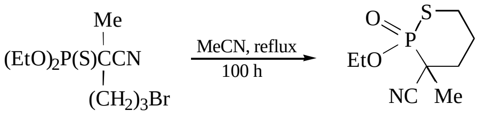


1a,**b**

A *trans*, 2*R**,3*S**
B *cis*, 2*R**,3*R**

a R = OEt
b R = Me

It was suggested that diastereomeric transformations occur *via* the opening of the six-membered ring (at either the P–S or the S–C bond), the inversion of the asymmetric phosphorus atom and the repeated closure of a ring. Under such a mechanism, similar transformations must be inherent in the series of 3-cyano-2-oxo-1,2-thiaphosphorinanes, including their 3-alkyl derivatives. To test this hypothesis, we synthesised a 3-alkyl-substituted analogue of the above compounds, namely, 3-cyano-3-methyl-2-oxo-1,2-thiaphosphorinane **3**. Compound **3** was obtained[‡] in 75% yield (according to ^{31}P NMR data) as a result of refluxing of 3-bromopropyl(diethoxythiophosphoryl)methylacetonitrile **4** in an acetonitrile solution for 100 h. The diastereomer ratio in the reaction product was **A**:**B** ≈ 4:6.



4 **3**

A *trans*, 2*R**,3*S**
B *cis*, 2*R**,3*R**

The fractional crystallization of the reaction mixture produced one diastereomer (*cis*-**B**, 2*R**,3*R**), which was examined by single-crystal X-ray diffraction.[§] We found that the bond lengths and angles in **3**(**B**) (Figure 1) are close to the corresponding values in **1a**(**B**), and the introduction of a methyl group at the 3-position of the ring resulted only in small changes in the molecular geometry. The six-membered ring is characterised by a slightly distorted chair conformation, wherein the oxygen atom of the P=O group and the methyl group in the 3-position are equatorial, and OEt and CN groups are axial. The torsion angle O(1)–P (1)–C (4)–C(6) is –55. 2°. Thus, the mutual orientation of the P(1)=O(1) and P(1)–OEt in respect to the lone electron pairs of the sulfur atom and, as a consequence, the *n*– * interaction in **3**(**B**) and **1a**(**B**) are nearly the same. The P(1)=O(1) and P(1)–S (1) bond lengths in **3**(**B**) are elongated up to 1.469(1) and 2.0558(7) Å, respectively, that is by approximately 0.01 Å longer in comparison with similar bond lengths in **1a**(**B**), which are equal to 1.456(2) and 2.044(2) Å. The elongation of the P(1)–C(4) and S(1)–C (1) bonds in **3**(**B**) is observed along with the nearly equal P(1)–O (2) bond lengths in **1a**(**B**) and **3**(**B**). Thus, the electron-donating effect of the -alkyl substituent leads to the elongation of all bonds formed by the phosphorus atom with the exception of the P–OEt bond.

We also found that the storage of a diastereomer mixture of **3** without solvent remained the initial **A**:**B** ratio unchanged; that is, a diastereomeric transformation to a thermodinamically preferred isomer does not take place. Moreover, individual dia-

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[†] An isomer having a downfield-shifted signal in the ^{31}P NMR spectrum was designated arbitrarily as diastereomer **A**; *cis*- and *trans*-isomers are indicated on the basis of the mutual orientation of the phosphoryl-group oxygen and the cyano group in relation to the ring plane; each diastereomer presents a racemic mixture of enantiomers.

[‡] *Synthesis of* **3**: 3-bromopropyl(dietoxythiophosphoryl)methylacetonitrile **4** was obtained by the reaction of dietoxythiophosphorylacetonitrile with 1,3-dibromopropane under phase-transfer catalysis conditions (solid KOH/MeCN/TEBA) according to ref. 2. Compound **4** was refluxed in an acetonitrile solution for 100 h (according to the ^{31}P NMR data, further heating did not increase the yield of **4**). Upon cooling, the reaction mixture was concentrated *in vacuo*, diethyl ether was added and solid **3** was isolated as a mixture of isomers (**A**:**B** = 38:62). Recrystallization from Et$_2$O gave pure **3**(**B**). Evaporation of the mother liquor gave **3** with the ratio **A**:**B** = 70:30. For both portions of **3**, satisfactory elemental analysis data were obtained.

Selected data for **3**. Mixture **A**:**B** = 70:30, mp 94–9 5 °C. Diastereomer **B**: mp 107–108 °C. ^{13}C NMR (CDCl$_3$) δ: 19.56 (Me, $^3J_{PC}$ 6.0 Hz), 25.07 (SCH$_2$*C*H$_2$, $^3J_{PC}$ 5.0 Hz), 31.05 [–C(CN)(Me)*C*H$_2$, $^2J_{PC}$ 3.4 Hz], 37.93 (SCH$_2$, $^2J_{PC}$ 4.8 Hz), 39.51 [P*C*(CN), $^1J_{PC}$ 103.7 Hz], 118.85 (CN). ^{31}P NMR, δ: 41.51 (in CDCl$_3$), 41.04 (in MeCN). IR (KBr, ν/cm^{-1}): 2235 (CN), 1245 (PO), 1035 (POC). Diastereomer **A**: ^{31}P NMR, δ: 43.93 (in CDCl$_3$), 43.70 (in MeCN).

[§] *Crystallographic data for* **3**(**B**): C$_8$H$_{14}$NO$_2$PS, *M* 219.23, monoclinic, space group $P2_1/n$, a = 7.781(2), b = 10.955(2) and c = 13.176(3) Å, β = = 106.98(2)°, V = 1074.1(5) Å^3, d_{calc} = 1.356 g cm^{-3}, μ = 4.20 cm^{-1}, Z = 4. Intensities of 3659 reflections (R_{int} = 0.031) were measured at 153 K with a Siemens P3/PC diffractometer using MoK radiation (λ = 0.71073 Å, $\theta/2\theta$ scan, $\theta \leq 30°$). The structure was solved by the direct method and refined by the full-matrix least squares against F^2 in the anisotropic (H-atoms isotropic) approximation. All hydrogen atoms were located from the electron density difference synthesis and were included in the refinement in the isotropic approximation. The refinement for **3**(**B**) converged to wR_2 = 0.1254 and GOF = 1.117 for 3404 independent reflections [R_1 = 0.0438 was calculated against F for the 2697 observed reflections with $I > 2\sigma(I)$]. The number of the refined parameters was 174 (the ratio of the refined parameters for observed reflections was 15.5). All calculations were performed using the SHELXTL PLUS 5 on an IBM PC/AT. Atomic coordinates, bond lengths, bond angles and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre (CCDC). For details, see 'Notice to Authors', *Mendeleev Commun.*, Issue 1, 2000. Any request to the CCDC should quote the full literature citation and the reference number 1135/73.

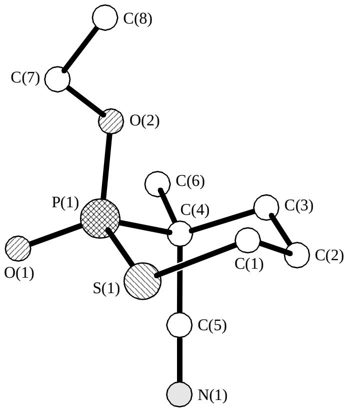

Figure 1 Molecular structure of compound **1**. Selected bond lengths (Å): S(1)–P(1) 2.0558(7), S(1)–C (1) 1.832(2), P(1)–O(1) 1.469(1), P(1)–O(2) 1.572(1), P(1)–C(4) 1.836(1); selected bond angles (°): C(1)–S(1)–P(1) 99.54(8), O(1)–P(1)–O (2) 116.56(8), O(1)–P (1)-C(4) 115.74(8), O(2)–P (1)–C(4) 99.25(7), O(1)–P(1) –S(1) 110. 22(7), O(2)–P(1)–S (1) 108.27(6), C(4)–P(1)–S(1) 105.79(5), C(7)–O(2)–P(1) 118.7(12), C(2)–C(1)–S(1) 114.0(1), C(3)–C (4)–P(1) 111.1(1).

stereomer *cis*-**B** does not transform to an equilibrium mixture of **A** and **B** on storage in a benzene solution for at least 1.5 years. Thus, we suggested that the mechanism of the mutual diastereomeric transformations in the series of 3-cyano-2-oxo-1,2-thiaphosphorinanes is related to the presence of an acidic hydrogen atom at the 3-position of the ring. That is, the diastereomeric transformations of **1a**,**b** appear to proceed *via* the dissociation of the above hydrogen atom, the formation of a flat carbanion and the attachment of a proton with the configuration inversion of the asymmetric 3-carbon atom.

This work was supported by the Russian Foundation for Basic Research (grant nos. 99-03-33014 and 00-03-32807a).

References

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Received: 25th September 2000; Com. 00/1704