

a, R = CH₃; **b**, R = *i*-C₃H₇; **c**, R = *t*-C₄H₉

case of **11b** and **11c**, we distilled off **5** (kugelrohr distillation at 0.005 torr, room temperature) and isolated **11b** and **11c** by low-pressure chromatography^[8] in 63 and 72% yield, respectively, and with ee > 95% in each case.^[9] In the case of **11a**, after the hydrolysis, we acetylated the mixture of **5**·HCl and **11a**·HCl on nitrogen,^[10] separated *N*-acetyl-**5** by chromatography, and obtained (*R*)-*N*-acetyl-**11a**. This compound has already been prepared in racemic form.^[11] For (optically pure) (*R*)-*N*-acetyl-**11a**, we found [α]_D²⁰ = -86.9 (c = 2.0, methanol).

β-Carboxyaspartic acid (Asa) is—presumably in the (*S*) form **12**—a constituent of ribosomal bacterial proteins.^[11] Syntheses of the racemic triesters of Asa have been described,^[11, 12] but no asymmetric syntheses are known.

With the bislactim ether of cyclo(*D*-Val-Gly),^[13] the (*S*) enantiomer **11** is obtained.

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[1] Reviews: U. Schöllkopf, *Pure Appl. Chem.* 55 (1983) 1799; *Chem. Scr.* 25 (1985) 105; H. Prinzbach, G. Schill in K. Streith (Ed.): *Organic Synthesis: An Interdisciplinary Challenge*. Blackwell Scientific Publications, Oxford 1985, p. 101 ff.

[2] For achiral cationic amino acid synthons, see D. Ben-Ishai, S. Hirsch, *Tetrahedron Lett.* 24 (1983) 955 and earlier publications of this group; T. Shono, *Tetrahedron* 40 (1984) 811; R. Kober, W. Hammes, W. Steglich, *Angew. Chem.* 94 (1982) 213; *Angew. Chem. Int. Ed. Engl.* 21 (1982) 203; *Angew. Chem. Suppl.* 1982, 542; C. G. Shin, Y. Sato, H. Ohmatsu, J. Yoshimura, *Bull. Soc. Chem. Pharm. Jpn.* 54 (1981) 1137; W. D. Bennet, M. J. O'Donell, R. L. Polt, *Tetrahedron Lett.* 26 (1985) 695; for chiral cationic amino acid synthons, see R. Kober, K. Papadopoulos, W. Miltz, D. Enders, W. Steglich, H. Reuter, H. Puff, *Tetrahedron* 41 (1985) 1693.

[3] U. Schöllkopf, U. Groth, C. Deng, *Angew. Chem.* 93 (1981) 793; *Angew. Chem. Int. Ed. Engl.* 20 (1981) 798.

[4] In the reaction of **2** with **3**, *trans*-**4** is the main diastereomer formed. Accordingly, the reactions of **2** with electrophiles and the chlorination take place via different mechanisms. For the chlorination, a radical pathway is likely; for the reactions with electrophiles, a polar one [1].

[5] Typical experiment for the in-situ preparation of **8**: **1** (0.92 g, 5.0 mmol) was lithiated according to [3]: the solution of **2** (in THF) was injected at -78°C under nitrogen into a solution of hexachloroethane (1.42 g, 6.0 mmol). In one experiment, **8** was isolated and characterized [6].

[6] H.-J. Neubauer, *Dissertation*, Universität Göttingen 1984.

[7] Determined by capillary GC (WCOT Chrompack column, 50 m, 210°C).—The diastereomeric ratio of **10** differs from that of **8** since the sodium dialkyl malonate causes elimination of HCl to a different extent from *trans*-**8** (in competition with the S_N reaction).

[8] Silica gel 60; ether/ethanol = 50 : 1.

[9] Determined by ¹H-NMR spectroscopy with Eu(ffc)₃ (up to 40 mol-%, shifting but no splitting of the OCH₃ signal). **11b**: oil, ¹H-NMR (CDCl₃): δ = 1.28 (d, CH(CH₃)₂), 1.84 (s, br, NH₂), 3.74 (s, OCH₃), 3.83 (d, OCCHCO), 3.05 (d, HC-N), 5.8 (h, CH(CH₃)₂). **11c**: m.p. = 63–64°C; [α]_D²⁵ + 0.4 (c = 1.0, methanol); ¹H-NMR (CDCl₃): δ = 1.48 (s, C(CH₃)₃), 2.0 (s, br, NH₂), 3.66 (s, OCH₃), 3.75 (d, OCCHCO), 3.99 (d, HC-N). The two amino acid triesters were also isolated as Boc derivatives by allowing the mixture of **5**·HCl and **11**·HCl (obtained by hydrolysis) to react with di(*tert*-butyl) dicarbonate in dimethylformamide and separating the Boc derivatives of **5** and **11** by fractional kugelrohr distillation.

[10] Acetic anhydride, pyridine, a small amount of 4-dimethylaminopyridine, dichloromethane.

[11] M. R. Cristy, R. M. Barkley, T. H. Koch, J. J. van Buskirk, W. M. Kirsch, *J. Am. Chem. Soc.* 103 (1981) 3935.

[12] D. H. Rich, M. K. Dhaon, *Tetrahedron Lett.* 24 (1983) 1671; E. B. Henson, P. M. Gallop, P. V. Hauschka, *Tetrahedron* 37 (1981) 2561.

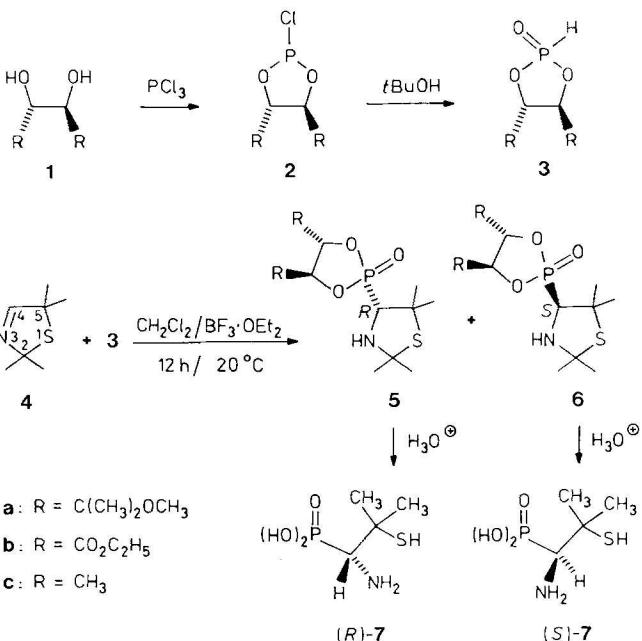
[13] Bislactim ethers of type **1** with *L*- and *D*-valine as the inducing centers are obtainable from Merck-Schuchardt.

Asymmetric Addition of a Chiral Cyclic Phosphite to a Cyclic Imine—Synthesis of Phosphonic Acid Analogues of *D*- and *L*-Penicillamine**

By *Inga Hoppe*,* *Ulrich Schöllkopf*, *Martin Nieger*, and *Ernst Egert**

Dedicated to Professor Hans Musso on the occasion of his 60th birthday

α-Amino phosphonic acids,^[1] the phosphonic acid analogues of α-amino carboxylic acids, are of interest owing to their potential biological activity. Only a few asymmetric syntheses for this class of compounds have been reported so far.^[2] Thus, for example, only the racemate of the analogue **7** of penicillamine (obtained by addition of



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an achiral phosphorous acid derivative to 2,5-dihydro-2,2,5,5-tetramethylthiazole **4**) has been described.^[3] We report here a procedure that makes accessible both of the enantiomers, (*R*)-**7** and (*S*)-**7**.

Reaction of the diol^[4] **1a** (synthesized from diethyl (*R,R*)-2,3-O-isopropylidenetartrate) with PCl_3 and *tert*-butanol^[5] affords the enantiomerically pure cyclic phosphite (*-*)-**3a**^[6] in 90% yield, which undergoes addition to **4**^[7] with BF_3 catalysis. The diastereomers (*-*)-**5a**^[8] and (+)-**6a**^[8] are thereby obtained in a ratio of 2:1 (yield 82%) and can be easily separated on silica gel.^[9] An X-ray structure determination^[10] gave the (*4R*) configuration for the diastereomer (*-*)-**5a**, which is present in excess (Fig. 1).

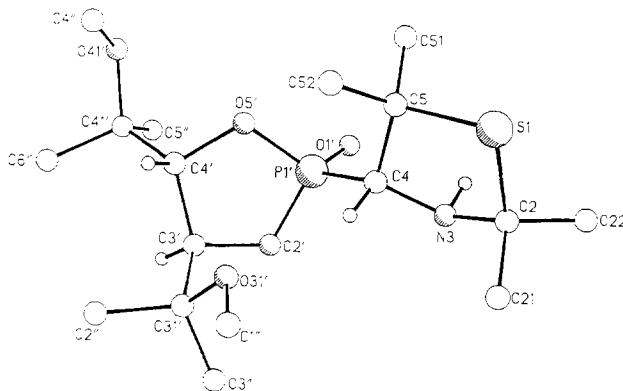


Fig. 1. Crystal structure of (*-*)-**5a**.

Hydrolysis of (*-*)-**5a** (48% HBr or conc. HCl, reflux^[3b]) gives 52% (*R*)-(*-*)-**7**,^[11] which corresponds to L-penicillamine, while 48% of the enantiomer (*S*)-(+)-**7** is obtained from (+)-**6a**.

With the phosphites **3b** (from diethyl (*R,R*)-tartrate) or **3c** (from (*R,R*)-2,3-butanediol^[12]), unsatisfactory results were obtained since the adducts **5b** and **6b** as well as **5c** and **6c** undergo extensive decomposition on chromatographic separation.

The chiral phosphite (*-*)-**3a** is stable upon storage. It can be added to a variety of prochiral C=N or C=O groups,^[13] thus opening up a general route to optically active α -amino and α -hydroxy phosphonic acids.

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- [4] a) **1a** prepared from diethyl (*R,R*)-2,3-O-isopropylidenetartrate [4b]: 1) 5 equiv. $\text{MeMgBr}/\text{Et}_2\text{O}/\text{reflux}$, 2 h (98%); 2) $\text{NaH}/\text{tetrahydrofuran}/\text{CH}_3\text{I}/\text{reflux}$, 24 h (90%); 3) $\text{CH}_3\text{OH}/8\text{N H}_2\text{SO}_4$ (2:1), RT, 48 h (92%). B.p. = 90°C/0.01 torr, $[\alpha]_{D}^{20} = -8.5$ ($c = 1.55$, CHCl_3); b) J. A. Musich, H. Rapoport, *J. Am. Chem. Soc.* 100 (1978) 4865.
- [5] A. Zwierzak, *Can. J. Chem.* 45 (1967) 2501.
- [6] (*-*)-**3a**: b.p. = 160°C/0.01 torr; m.p. = 51–52°C; $[\alpha]_{D}^{20} = -50.4$ ($c = 1.48$, CHCl_3); $^1\text{H-NMR}$ (CDCl_3): $\delta = 4.39, 4.25$ (each dd, $J(\text{P},\text{H}) = 16$ Hz, $J(4,5) = 2.5$ Hz, CH); 3.25, 3.22 (each s, OCH_3), 1.28, 1.27, 1.11 (each s, CH_3); $^{31}\text{P-NMR}$ (CDCl_3 , standard H_3PO_4): $\delta = 25.4$.
- [7] F. Asinger, W. Schäfer, G. Herkelmann, H. Römgens, B. D. Reintges, G. Scharein, A. Wegerhoff, *Justus Liebigs Ann. Chem.* 672 (1964) 156.

- [8] (*-*)-**5a**: $R_f(\text{Et}_2\text{O}) = 0.18$; m.p. = 126°C; $[\alpha]_{D}^{20} = -67.4$ ($c = 1.2$, CHCl_3); $^1\text{H-NMR}$ (CDCl_3): $\delta = 4.43, 4.29$ (each s, CH), 3.92 (d, $J(\text{P},\text{H}) = 20$ Hz, 4-H), 3.26, 3.24 (each s, OCH_3), 3.2 (br., NH), 1.69, 1.64, 1.55, 1.35, 1.31, 1.10 (each s, CH_3); $^{31}\text{P-NMR}$ (CDCl_3): $\delta = 44.7$; (+)-**6a**: $R_f(\text{Et}_2\text{O}) = 0.27$; m.p. = 118°C; $[\alpha]_{D}^{20} + 12.2$ ($c = 1.7$, CHCl_3); $^1\text{H-NMR}$ (CDCl_3): $\delta = 4.55$ –4.15 (m, CH), 3.61 (d, $J(\text{P},\text{H}) = 18$ Hz, 4-H), 3.34 (br., NH), 3.23 (s, OCH_3), 1.69, 1.59, 1.55, 1.32, 1.11 (each s, CH_3); $^{31}\text{P-NMR}$ (CDCl_3): $\delta = 45.0$.

[9] Eluted with diethyl ether.

- [10] (*-*)-**5a**: $P_2\text{I}_2\text{C}_1$, $a = 1130.3(1)$, $b = 1212.5(1)$, $c = 1546.7(1)$ pm, $V = 2.120$ nm^3 , $Z = 4$, $\mu = 0.24$ mm^{-1} (MoK_{α}), 3870 measured intensities (hkl and $\bar{h}\bar{k}\bar{l}$), $2\theta_{\max} = 50^\circ$, 3461 symmetry independent reflections with $|F|/3\sigma_F$ used for structure solution (Patterson and Fourier methods) and refinement. Non-hydrogen atoms refined anisotropically. H atoms localized by difference electron density determination and refined using a "riding" model, $R = 0.036$ ($R_w = 0.038$, $w^{-1} = \sigma_F^2 + 0.0005 F^2$), absolute configuration confirmed by η -refinement. Further details of the crystal structure investigation are available on request from the Fachinformationszentrum Energie, Physik, Mathematik GmbH, D-7514 Eggenstein-Leopoldshafen 2, by quoting the depository number CSD 51585, the names of the authors, and the journal citation.

- [11] (*R*)-**7**: decomp. point = 221°C; $[\alpha]_{D}^{20} = -10.8$ ($c = 0.64$, 1*n* NaOH); $^1\text{H-NMR}$ (D_2O): $\delta = 3.21$ (d, $J(\text{P},\text{H}) = 15$ Hz, CH), 1.49, 1.43 (each s, CH_3); $^{31}\text{P-NMR}$ ($\text{CF}_3\text{CO}_2\text{H}/\text{CDCl}_3$): $\delta = 14.3$; (*S*)-**7**: decomp. point = 219°C; $[\alpha]_{D}^{20} + 10.0$ ($c = 0.72$, 1*n* NaOH).

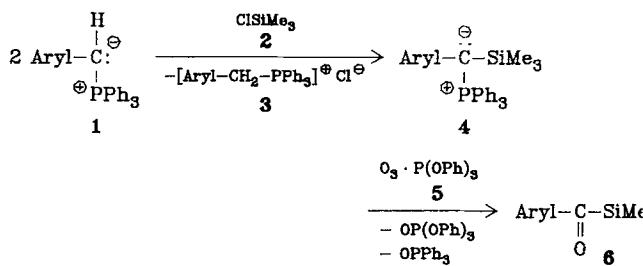
- [12] **1c**: R. C. Anderson, M. J. Shapiro, *J. Org. Chem.* 49 (1984) 1304.

- [13] I. Hoppe, unpublished.

Acylsilanes via Oxidation of Phosphonium Ylides: The First Synthesis of Bis(trimethylsilyl)kétone and Its Use as a $\text{CO}^{2\ominus}$ Equivalent

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Hans Jürgen Bestmann*

Acylsilanes, which are employed as nucleophilic acylation reagents, are a preparatively interesting class of compounds.^[1,2] We have found that aromatic acylsilanes **6** can be easily synthesized from phosphonium ylides **1**.



a. Aryl = C_6H_5 ; **b.** Aryl = $p\text{-Br-C}_6\text{H}_4$; **c.** Aryl = $p\text{-CH}_3\text{O-C}_6\text{H}_4$

Upon reaction of **1** with chlorotrimethylsilane **2** in a molar ratio of 2:1, the silylated ylides **4**,^[3] along with the phosphonium salts **3**, are formed by trans-ylidation. Oxidation of **4** with the adduct **5**, formed from ozone and triphenylphosphite (5% less than the stoichiometric amount

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