Monatshefte für Chemie 124, 763–773 (1993)

Monatshefte für Chemie
Chemical Monthly

A New Heteroannulation Method to 2-Cyclohexenone, Mediated by Phosphonate Auxiliaries. Synthesis of 4,5,6,7-Tetrahydrobenzothiazole Derivatives

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Summary. Dimethyl (1,2-epoxy-3-oxocyclohex-1-yl)phosphonate **7**, easily available from 2-cyclohexen-1-one, affords the new (tetrahydrobenzothiazolyl)phosphonates **10** upon reaction with thiocarboxamides **8**. This cyclocondensation proceeds with regioselective conjunction of the bisnucleophile **8** to carbonyl group and adjacent oxirane carbon of the epoxide precursor. On treatment with alkali the 5,6-dihydro-7(4*H*)benzothiazolones **12** are obtained from compounds **10**, or from the intermediately formed bicyclic dihydroxy derivatives **9**. Reaction of the corresponding cyclopentylphosphonate **14** with thiobenzamide (**8b**) yields the cyclopentathiazole derivative **15** as a single isomer, the dihydro-thiazole moiety being now annulated regio- and *cis*-stereoselectively to both oxirane carbons of the epoxyphosphonate.

Keywords. (1,2-Epoxy-3-oxo-cyclohex-1-yl)phosphonate; 5,6-Dihydro-7(4*H*)benzothiazolones, 2-substituted; Heteroannulation with thiocarboxamides; (4,5,6,7-Tetrahydrobenzothiazol-7-yl)phosphonates; Thiocarboxamides.

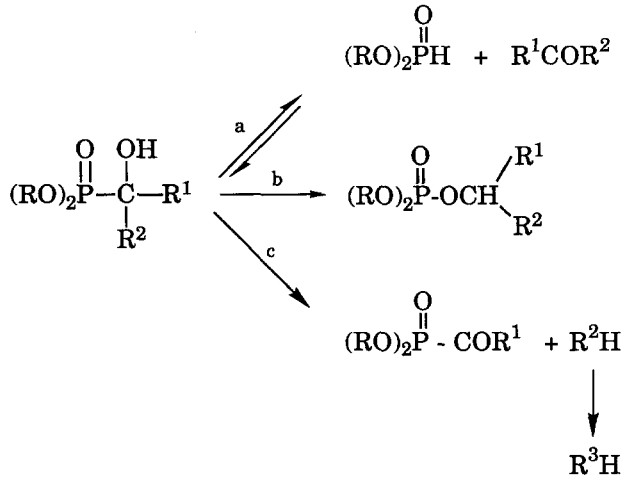
Eine neue, durch Phosphonat-Synthone gesteuerte Methode zur Heteroanellierung an 2-Cyclohexenon. Synthese von 4,5,6,7-Tetrahydrobenzthiazol-Derivaten

Zusammenfassung. Umsetzung des aus 2-Cyclohexen-1-on leicht zugänglichen (1,2-Epoxy-3-oxocyclohex-1-yl)phosphonats **7** mit den Thioamiden **8** liefert die neuen (Tetrahydrobenzthiazolyl)phosphonate **10**. Dabei wird der Thiazolring regioselektiv an Carbonylgruppe und benachbarten Oxirankohlenstoff des Epoxyphosphonats anelliert. Mit Alkali werden sowohl die α-Hydroxyphosphonate **10** als auch die intermediär gebildeten Dihydroxyverbindungen **9** zu den 5,6-Dihydro-7(4*H*)benzthiazolonen **12** gespalten. Im Gegensatz dazu reagiert das Cyclopentylphosphonat **14** mit Thiobenzamid **8b** zu einem Cyclopentathiazol-Derivat **15**, bei dem der Dihydrothiazolring regio- und *cis*-stereoselektiv mit den beiden früheren Oxiran-Kohlenstoffen verknüpft ist.

Introduction

The behaviour of α-hydroxyphosphonates to basic reagents depends on the substituents R^1 and R^2 (Scheme 1). Thus strong bases in aqueous solutions cause the breakdown of the P–C-bond with formation of carbonyl compounds and dialkyl-

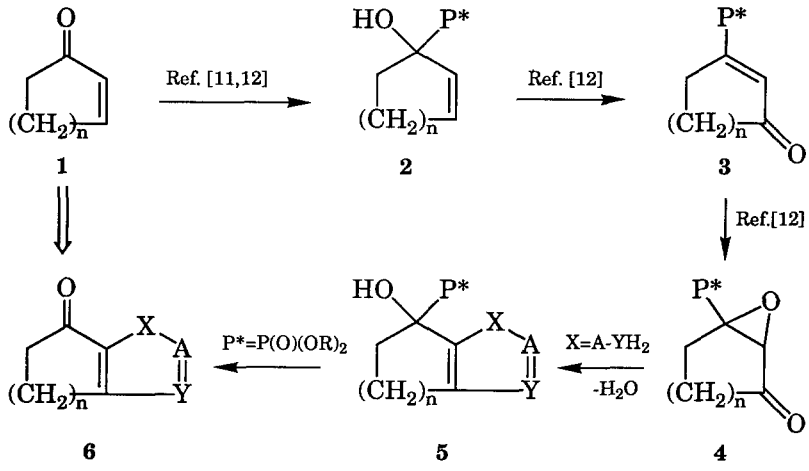
phosphites, when $R^1, R^2 = H$, alkyl [1] (way a). If one of the substituents is an electron attracting group able to stabilize a carbanionic intermediate, rearrangement to a phosphate derivative will occur [2] (way b). Occasionally, cleavage of the β-C–C-bond has been observed, particularly if this step was accompanied by subsequent aromatization ($R^2H \rightarrow R^3H$) of the leaving group (way c) [3].



Scheme 1

During the last years acylic (1,2-epoxy-3-oxoalkyl)phosphonates, and the homologous 2,3-epoxy-4-oxo derivatives have been shown in our group to be versatile intermediates for the synthesis of phosphorus and non-phosphorus bearing heterocycles [4–8]. The 1,2-biselectrophilic behaviour exhibited by these compounds was manifested by a series of regioselective cyclocondensation reactions with their polarity complements, 1,3-bidentate nucleophiles $X = A–YH_2$ (Scheme 2): Thiocarboxamides, activated α-picolines, and 2-aminopyri(mi)dines, reagents for the well established heterocyclization reactions with α-haloketones leading to thiazoles [9], indolizines [10], and imidazo[1,2-a]pyri(mi)dines [10], respectively, have been reacted analogously with the acyclic epoxyphosphonates **4** to yield (α-hydroxy-α-heteroaryl)-[4,5], or (β-hydroxy-β-heteroaryl)alkylphosphonates [6] (monocyclic compounds of the general type **5**). The hydroxy group adjacent to the heterocycle, generated by regioselective epoxide opening by the more nucleophilic part of the bisnucleophile, can be used for various further transformations [4–6, 8]. Especially the heteroaryl-substituted α-hydroxyphosphonates, upon treatment with alkali have been transformed to a series of acylsubstituted heterocycles according to way a, Scheme 1 (R^1 = H, alkyl, R^2 = thiazol-5-yl, indolizin-3-yl, imidazo[1,2-a]pyri(mi)din-3-yl) [5].

Recently we found a convenient route to the new (1,2-epoxy-3-oxo-cycloalkyl) phosphonates and the homologous cycloalkylmethyl derivatives **4** [P* = $P(O)(OR)_2$, and $CH_2P(O)(OR)_2$, respectively]. This synthesis (regioselective 1,2-addition of the required phosphorus nucleophiles to cycloalkenones **1** [11, 12], followed by oxidative 1,3-transposition of the tertiary allylic hydroxy group with chromium(VI) reagents,



P* = $P(O)(OR)_2$, $CH_2P(O)(OR)_2$

Scheme 2

and subsequent epoxidation [12], Scheme 2) centered around the expectation to develop a new heteroannulation procedure to the double bond of cycloalkenones **1** following the pathway presented in Scheme 2, the key step being the regioselective conjunction of the epoxyphosphonates **4** with bisnucleophiles of the general type $X = A\text{–}YH_2$. In the next step elimination of the auxiliary dialkyl phosphite from the heterocyclic α-hydroxyphosphonate **5** [P* = $P(O)(OR)_2$] would regenerate the carbonyl group of the cycloalkenone precursor **1**.

This paper presents the first results gained upon cyclocondensation of the epoxyphosphonates **7** (and **14**) with a series of thiocarboxamides **8**.

Results and Discussion

Reaction of the cyclohexyl phosphonate **7** with thiocarboxamides **8** in boiling ethanol afforded satisfactory yields of the desired bicyclic annulation products **10**, using the thioamides **8b**, **8c**, and **8f** (R = Ph, 3-pyridyl, and CO_2Et, respectively). The derivative **10e**, which was found to decompose in boiling ethanol, was also obtained in good yield, when **7** was reacted with thiourea at room temperature (Table 1). Upon condensation of **7** with the 4-pyridyl derivative **8d**, the α-hydroxyphosphonate **10d** was formed sluggishly (yield 29%), partial deprotection of the phosphonate ester, and formation of ketone **12d** being observed by TLC monitoring. However, an intermediate cyclization product was isolated after a short reaction time and before decomposition was apparent, whose ^{13}C-NMR data suggested the dihydrothiazole structure **9d** (1:1 mixture of two isomeric compounds, yield 66%), depicted in Scheme 3. This dihydroxy compound, after the usual treatment with alkali (0.5 *N* NaOH, room temp.) afforded the benzothiazolone derivative **12d** in

Table 1. Cyclocondensation product(s) from epoxyphosphonate **7** with the thiocarboxamides **8**, and phosphorus-free cleavage products **12**

Thioamide	Reaction time (h)	Temp. (°C)	Product(s)	Yield[a] (%)	M.p. (°C)	Cleavage method[b]	Reaction time (min)	Product	Yield[a] (%)	M.p. (°C)
8a	1.5	80	–	–	–	B	30	**12a**	60	–[c]
8b	9	80	**10b**	88	139–142	A	20	**12b**	95	114–115
8c	12.5	80	**10c**	55	131–134	A	30	**12c**	97	114–115
8d	1	80	**9d**[d]	66	–	A	15	**12d**	95	155–157
8d	1	80	–	–	–	B	15	**12d**	74	–
8d	22	80	**10d**	29	148 dec.	A	15	**12d**	98	–
8e	7d	20	**10e**[e]	69	158–160[e]	A	20	**12e**[e]	95	272[e]
			13e[e]	6	57–60[e]					
8e	7d	20	–	–	–	B	20	**12e**[e]	83	–
8f	24	80	**10f**	67	138–140	C	100	**12f**	78	85–87

[a] Yields of isolated crystalline compounds

[b] Method A: crystalline **10** (**9**) + 0.5 *N* NaOH, room temp.; Method B (one pot procedure): 1., **7** + **8** (ethanol), 2., 0.5 *N* NaOH, room temp.; Method C: satd aq. $NaHCO_3$, room temp.

[c] Oil, b.p. 80–85 °C (oven temp. at Kugelrohr distillation) at 0.01 Torr, Ref. [14] 85–87 °C/0.2 Torr

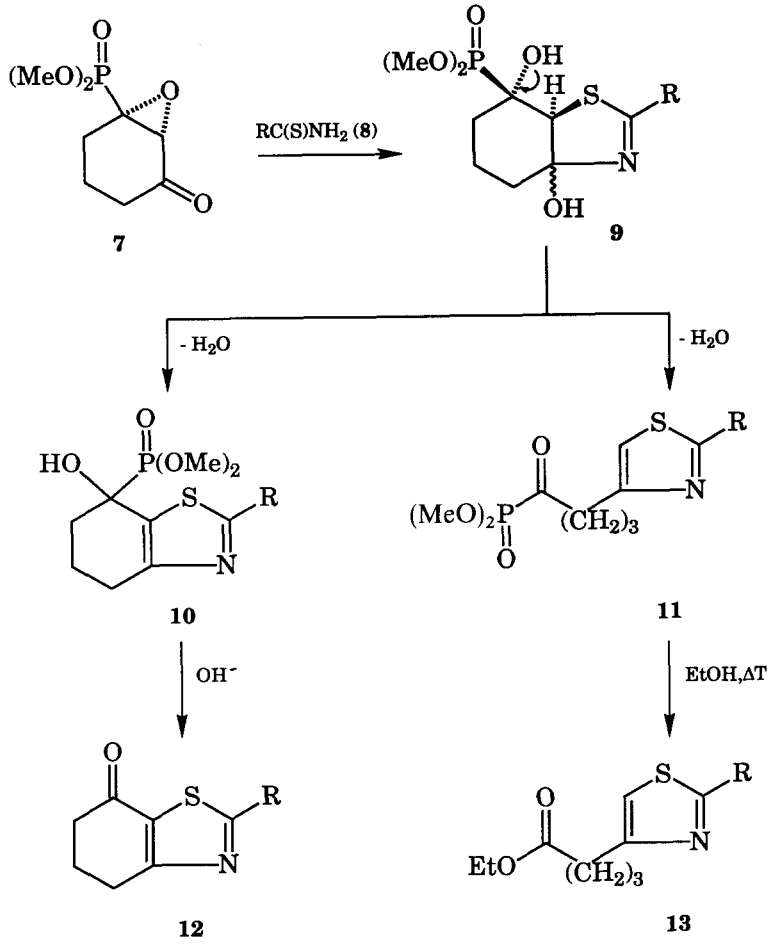
[d] 1:1 – Mixture of isomers

[e] N-Acetyl derivative

very good yield. Similar results have been obtained performing cyclization of **7** with **8d** and cleavage of the intermediate **9d** in an one pot procedure (Table 1).

Thioacetamide **8a**, which with acyclic epoxyphosphonates has been found to give only poor results [5], yielded also the carbonyl derivative **12a** in 60% overall yield upon application of the one pot procedure.

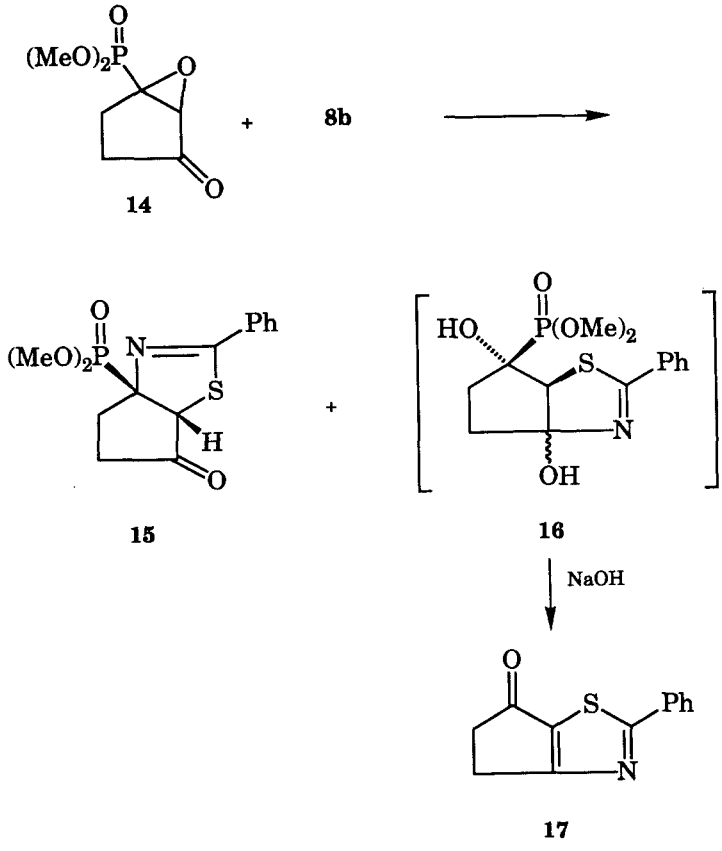
The formation of the open chain thiazole derivative **13e**, which was isolated as byproduct reacting epoxide **7** with thiourea under various reaction conditions, can also be explained assuming a dihydrothiazole intermediate **9e**: Retroaldol reaction at C-7a and subsequent dehydration, which parallels way c, Scheme 1, would lead to the thiazolyl-substituted acylphosphonate **11e**, which then is solvolyzed to generate the ethylester derivative **13e** observed.



8 - 12	a	b	c	d	e	f
R	Me	Ph	3-Pyr	4-Pyr	NH_2	CO_2Et

Scheme 3

Under analogous reaction conditions, condensation of dimethyl (1,2-epoxy-3-oxo-cyclopent-1-yl)phosphonate **14** with thiobenzamide **8b** afforded no (or only traces) of an α-hydroxyphosphonate. Instead, an isomeric compound was isolated with high yield, whose spectral data suggest the bicyclic structure **15** shown in Scheme 4: The IR spectrum exhibits no OH-absorption, but a strong absorption at 1752 cm^{-1}, which is typical for cyclopentanones. The base peak of the mass spectrum was found to be 216 ($M-109$), as compared with the spectra of compounds **10**, which uniformely exhibited no molecular peaks, but an intensive fragmentation, caused by the loss of dimethylphosphite ($M-110$). Further evidence for structure and *cis*-stereochemistry of compound **15** is found in the ^{1}H-NMR (doublet of a CH-signal at $\delta = 4.45$ ppm with a *vicinal* ^{31}**P**–C–C–**H** coupling, $^3J_{PH} = 16.4$ Hz, which suggests the *cis*-relation) and also in the ^{13}C-NMR-spectrum (CO-signal at $\delta = 211.91$ ppm with a high *vicinal* ^{31}**P**–C–C–**CO** coupling, $^3J_{PC} = 15.2$ Hz, which is also in accordance with the geometry given in the scheme) [13].



Scheme 4

The formation of compound **15**, which regioselectively integrates the both oxirane carbons of the precursor **14** in the dihydrothiazole moiety with the carbonyl group being unchanged, parallels the annulation type previously observed in our laboratory, upon the condensation of acyclic epoxyphosphonates with some 2-mercaptoazoles [7]. There, the generation of acyl-substituted dihydrothiazoles

has been explained by regioselective oxirane opening by the sulfur group, subsequent dehydration, and intramolecular Michael addition (5-*endo* trig cyclization) of the nitrogen part of the bisnucleophile to the α-enone formed intermediately.

Experimental Part

Melting points were determined with a Kofler apparatus and are uncorrected. IR-spectra (CH_2Cl_2) were recorded on a Perkin-Elmer 377 Infrared spectrophotometer. ^1H- and *J*-modulated ^{13}C-NMR spectra were recorded on a Bruker WM 250 spectrometer. TLC was performed on Merck silica gel 60 F_{254} plates with visualization by UV light (254 nm) and/or by iodine vapour. Flash-chromatography was performed on glass columns packed with Merck silica gel 60 (230–400 mesh). The epoxy phosphonates **7** and **14** were prepared according to the literature protocol [12].

Dimethyl [4,5,6,7,3a,7a-Hexahydro-3a,7-dihydroxy-2-(4-pyridyl)benzothiazol-7-yl]phosphonate (**9d**)

A solution of **7** and **8d** (each 1.0 mmol) in dry EtOH (5 ml) was refluxed, the reaction being monitored by TLC (EtOAc/MeOH, 5:1) to avoid the formation of **10d**. After 1 h the solution, which was shown to contain unreacted starting materials and a substance slightly more polar than **10d** (**9d**: $R_f = 0.26$, TLC-visualization at 254 nm; **10d**: $R_f = 0.29$, visualization at 254 and 366 nm) was evaporated. The residue was subjected to flash-chromatography (EtOAc/MeOH, 5:1) to yield subsequently a mixture of **7** and **8d** ($R_f \approx 0.75$, 160 mg), and **9a** (182 mg), colorless crystals, not soluble in CH_2Cl_2 and $CHCl_3$. The above procedure was repeated with unreacted material to give further 56 mg of **9a**. Total yield: 238 mg (66%). ^{13}C-NMR (*DMSO-d*$_6$): $\delta = 14.17$ ($^3J_{PC} = 10.0$), 15.06 ($^3J_{PC} = 11.5$ Hz) [C-5], 26.49, 28.58, 31.78, 33.75 (4s, C-4, C-6), 53.40, 53.52, 53.66, 53.79 (4d, $J_{PC} = 8.2$, 8.2, 8.3, and 6.8 Hz, $POCH_3$), 57.63 (s), 61.29 (d, $^2J_{PC} = 5.1$ Hz) [C-7a], 71.61, 71.73 (2d, $^1J_{PC} = 167.3$, and 172.1 Hz, C-7), 104.94, 105.20 (2d, $^3J_{PC} = 13.7$, and 12.0 Hz, C-3a), 121.09, 121.58 (C-3′, C-5′), 139.77, 140.01 (C-4′), 150.41, 150.52 (C-2′, C-6′), 161.00, 165.43 (C-3) [diastereomeric ratio ≈ 1:1]. $C_{14}H_{19}N_2O_5PS$ (358.4). Calc. C 46.91, H 5.35, N 7.82, S 8.95; found C 46.72, H 5.43, N 7.71, S 8.60.

Synthesis of 2-Substituted Dimethyl [(4,5,6,7-Tetrahydro-7-hydroxy)benzothiazol-7-yl]phosphonates **10** *(General Procedure)*

A solution of epoxyphosphonate **7** (220 mg, 1.0 mmol) and thioamide **8** (1.0 mmol) in dry EtOH (5 ml) is refluxed (compounds **8b**, **8c**, **8d**, **8f**) or reacted at room temp. (compound **8e**) under Ar, the reaction being monitored by TLC. After complete consumption of **7** and the polar intermediates primarily formed (reaction time given in Table 1), the solution is evaporated and the residue purified by flash-chromatography on silica gel (recrystallization of compounds **10** should be avoided, as upon heating, tertiary α-hydroxyphosphonates are partially cleaved to the corresponding carbonyl derivatives and dialkylphosphite).

Dimethyl [(4,5,6,7-Tetrahydro-7-hydroxy-2-phenyl)benzothiazol-7-yl]phosphonate (**10b**)

Flash-chromatography (CH_2Cl_2/acetone, 4:1, $R_f = 0.18$), yield 300 mg (88%), colorless crystals, m.p. 139–142 °C. IR(CH_2Cl_2): $\nu = 3560\,cm^{-1}$, 3270 (OH), 1235 (P=O), 1060, 1038 (P–OC). ^1H-NMR ($CDCl_3$): $\delta = 1.95$–2.30 (m, 4H, H-5, H-6), 2.70–3.00 (m, 2H, H-4), 3.78, 3.82 (2d, $J_{HP} = 10.0$ Hz, each 3H, $POCH_3$), 4.08 (br d, $J_{HP} \approx 5.5$ Hz, 1H, D_2O-exchange, OH), 7.40 (m, $3H_{arom}$), 7.90 (m, $2H_{arom}$). $C_{15}H_{18}NO_4PS$ (339.4). Calc. C 53.08, 5.36, N 4.12, S 9.45; found C 53.03, H 5.37, N 4.16, S 9.49.

Dimethyl {[4,5,6,7-Tetrahydro-7-hydroxy-2-(3-pyridyl)]benzothiazol-7-yl}phosphonate (**10c**)

Flash-chromatography (EtOAc/MeOH, 19:1, $R_f = 0.21$), yield 188 mg (55%), m.p. 131–134 °C. ^1H-NMR ($CDCl_3$): $\delta = 1.96$–2.37 (m, 4H, H-5, H-6), 2.70–3.03 (m, 2H, H-4), 3.80, 3.81 (2d, $J = 10.0$ Hz,

each 3H, $POCH_3$), ≈ 4.75 (br s, 1H, D_2O-exchange, OH), 7.34 (dd, 1H, H-5'), 8.15 (td, 1H, H-4'), 8.59 (dd, 1H, H-6'), 9.07 (d, 1H, H-2') [$J_{4',5'} = 8.1$, $J_{5',6'} = 5.0$, $J_{4',6'} \approx J_{2',4'} \approx 1.5$ Hz]. $C_{14}H_{17}N_2O_4PS$ (340.4). Calc. C 49.40, H 5.04, N 8.23, S 9.42; found C 49.48, H 5.09, N 8.11, S 8.97.

Dimethyl {[4,5,6,7-Tetrahydro-7-hydroxy-2-(4-pyridyl)]benzothiazol-7-yl}phosphonate (**10d**)

Flash-chromatography (EtOAc/MeOH, 5:1, $R_f = 0.29$); yield 103 mg (29%), m.p. 148 °C (dec.) from EtOAc. Compound **10d** is not stable in solution, ketone **12d** and a polar decomposition product being detected by TLC after a few hours. ^{1}H-NMR ($CDCl_3$): $\delta = 1.91$–2.35 (m, 4H, H-5, H-6), 2.67–3.00 (m, 2H, H-4), 3.75, 3.76 (2d, $J_{HP} = 10.3$ and 10.4 Hz, each 3H, $POCH_3$), ≈ 5.1 (br s, 1H, D_2O-exchange, OH), 7.68 (d, 2H, H-3', H-5'), 8.54 (d, 2H, H-2', H-6'). $C_{14}H_{17}N_2O_4PS$ (340.4). Calc. C 49.40, H 5.04, N 8.23, S 9.42; found C 49.17, H 5.01, N 8.21, S 9.39.

N-[(7-Dimethoxyphosphoryl-4,5,6,7-tetrahydro-7-hydroxy)benzothiazol-2-yl]acetamide (Ac-**10e**)

A solution of **7** (2.20 g, 10.0 mmol) and thiourea (760 mg, 10.0 mmol) in dry EtOH (50 ml) was stirred under argon at room temp. After 3 h crystals started to deposit. Stirring was continued for 7 days, then **10e** (860 mg) was filtered off. The mother liquor was evaporated, the dark residue treated with EtOAc to crystallize another portion (630 mg) of **10e**. The residue obtained from the filtrate was subjected to flash-chromatography (EtOAc/MeOH, 19:1) to isolate subsequently **13e** ($R_f = 0.75$, 138 mg, 6%), and 415 mg **10e** (total yield: 1.905 g, 69%, $R_f = 0.24$) as yellowish crystals.

For analysis, both compounds have been reacted with Ac_2O at room temp. to give the corresponding N-acetyl derivatives.

Ac-**10e**: M.p. 158–160 °C (MeOH/EtOAc). ^{1}H-NMR (*DMSO-d*$_6$): $\delta = 1.77$–2.11 (m, 4H, 2xCH_2), 2.11 (s, 3H, $COCH_3$), 2.42–2.69 (m, 2H, CH_2), 3.67, 3.71 (2d, $J = 10.0$ Hz, each 3H, $POCH_3$), 6.07 (d, $^3J_{HP} \approx 13$ Hz, 1H, exchange with D_2O, OH), ≈ 12.0 (br s, 1H, exchange with D_2O, NH). ^{13}C-NMR (*DMSO-d*$_6$): $\delta = 17.44$ ($^3J_{PC} = 6.8$ Hz, C-5), 21.89 ($COCH_3$), 25.69, 32.70 (C-4, C-6), 52.81, 52.97 ($^2J_{PC} = 7.4$, and 7.5 Hz, $POCH_3$), 68.96 ($^1J_{PC} = 176.9$ H, PC), 121.26 (C-7a), 147.43 ($^3J_{PC} = 10.0$ Hz, C-3a), 157.53 (C-2), 167.65 (NHCO). MS (70 eV): *m/z* (%) = 320 (1) [M^+], 302 (50) [$M-H_2O$], 260 (100) [$M-H_2O-CH_2CO$]. $C_{11}H_{17}N_2O_5PS$ (320.3). Calc. C 41.24, H 5.36, N 8.75, S 10.01; found C 41.69, H 5.48, N 8.28, S 9.89.

N-[4-(3-Ethoxycarbonyl)propyl-thiazol-2-yl]acetamid (Ac-**13e**)

M.p. 57–60 °C (ether/petroleum ether, b.p. 40 °C). ^{1}H-NMR ($CDCl_3$): $\delta = 1.26$ (t, 3H, OCH_2CH_3), 2.00 (quint, $CH_2CH_2CH_2$), 2.24 (s, 3H, $COCH_3$), 2.35, 2.70 (2t, each 2H, $CH_2-CH_2-CH_2$), 4.14 (q, 2H, $CO_2CH_2CH_3$), 6.58 (s, 1H, H-5). ^{13}C-NMR ($CDCl_3$): $\delta = 14.25$ ($CO_2CH_2CH_3$), 23.18 ($COCH_3$), 24.12 ($CH_2-CH_2-CH_2$), 30.47, 33.53 ($CH_2-CH_2-CH_2$), 60.39 (CO_2CH_2), 108.13 (C-5), 149.96 (C-4), 158.26 (C-2), 167.80 (NHCO), 173.34 (CO_2). MS (70 eV): *m/z* (%) = 256 [M^+], 211 (15) [M–OEt], 169(85), 127(100). $C_{11}H_{16}N_2O_3S$ (256.4). Calc. C 51.52, H 6.30, N 10.93, S 12.51; found C 51.28, H 6.28, N 11.07, S 12.63.

Ethyl [7-Dimethoxyphosphoryl-4,5,6,7-tetrahydro-7-hydroxy-benzothiazol-2-yl]carboxylate (**10f**)

Flash-chromatography (EtOAc/MeOH, 19:1, $R_f = 0.56$); yield 225 mg (67%), colorless crystals, m.p. 138–140 °C (Et_2O). ^{1}H-NMR ($CDCl_3$): $\delta = 1.40$ (t, $J = 7.0$ Hz, 3H, $CO_2CH_2CH_3$), 1.92–2.38 (m, 4H), 2.71–3.08 (m, 2H) [H-4, H-5, H-6], 3.75, 3.82 (2d, $J_{HP} = 10.4$ Hz, each 3H, $POCH_3$), 4.45 (q, $J = 7.0$ Hz, $CO_2CH_2CH_3$), 4.80 (d, $J = 3.7$ Hz, 1H, D_2O-exchange, OH). $C_{12}H_{18}NO_6PS$ (335.4). Calc. C 42.98, H 5.42, N 4.18, S 9.56; found C 43.01, H 5.37, N 4.14, S 9.37.

Synthesis of 5,6-Dihydro-7(4H)benzothiazolones **12**

a) From α-Hydroxyphosphonates **10** *(General Procedure)*: A suspension of **10** (1.0 mmol) in 10 ml 0.5 *N* aq. NaOH (compounds **10a–10e**), or 10 ml satd. aq. $NaHCO_3$ (**10f**) is stirred at room temp. for the time given in Table 1 (work up is given below).

b) From **7** *and* **8** *(One Pot Procedure)*: A solution of **7** and **8** (each 1.0 mmol) in dry EtOH (5 ml) is reacted under the conditions given in Table 1, and then evaporated. To the dry residue 0.5 *N* NaOH (10 ml) is added with stirring at room temp. (work up is given below).

5,6-Dihydro-2-methyl-7(4H)benzothiazolone (**12a**) *(One Pot Procedure)*

The dark aqueous solution was extracted with CH_2Cl_2, the dry (Na_2SO_4) extracts were evaporated and the residue purified by Kugelrohr distillation (oven temp. 80–85 °C, 0.01 Torr, Ref. [14] b.p. 85–87 °C/0.2 Torr) to yield **12a** (101 mg, 60%) as a colorless oil, $R_f = 0.40$ (CH_2Cl_2/EtOAc, 9:1). – ^{1}H-NMR ($CDCl_3$): $\delta = 2.09$ (quint, $J = 6.0$ Hz, 2H, H-5), 2.49 (br t, $J \approx 6$ Hz, 2H, H-4), 2.62 (s, 3H, CH_3), 2.90 (t, $J = 6.0$ Hz, 2H, H-6).

5,6-Dihydro-2-phenyl-7(4H)benzothiazolone (**12b**) *from* **10b**

The reaction mixture was cooled to 5 °C, **12b** was filtered off, washed with cold H_2O, and dried at 0.01 Torr. Yield 217 mg (95%), colorless crystals, m.p. 114–115 °C (ether, petroleum ether b.p. 40 °C), Ref. [14] m.p. 121–123 °C. IR (CH_2Cl_2): $\nu = 1668\,cm^{-1}$ (CO). ^{1}H-NMR ($CDCl_3$): $\delta = 2.24$ (quint, $J = 6.0$ Hz, 2H, H-5), 2.64 (t, $J = 6.0$ Hz, 2H, H-4), 3.09 (t, $J = 6.0$ Hz, 2H, H-6), 7.45 (m, $3H_{arom}$), 7.96 (m, $2H_{arom}$). MS (70 eV): *m/z* (%) = 229 (26) [M^+], 201 (40) [*M*–CO], 70 (100). $C_{13}H_{11}NOS$ (229.3). Calc. C 68.09, H 4.85, N 6.11, S 13.98; found C 67.85, H 4.86, N 6.10, S 13.81.

5,6-Dihydro-2-(3-pyridyl)-7(4H)benzothiazolone (**12c**) *from* **10c**

The aqueous reaction mixture was extracted with CH_2Cl_2. The residue, obtained from the dried (Na_2SO_4) extracts was purified by flash-chromatography (CH_2Cl_2/ EtOAc, 3:7) to yield **12c** (223 mg, 97%) as colorless crystals m.p. 114–115 °C (Et_2O). IR (CH_2Cl_2): $\nu = 1670\,cm^{-1}$ (CO). ^{1}H-NMR ($CDCl_3$): $\delta = 2.24$ (quint, $J = 6.0$ Hz, 2H, H-5), 2.63 (t, $J = 6.0$ Hz, 2H, H-4), 3.10 (t, $J = 6.0$ Hz, 2H, H-6), 7.38 (dd, 1H, H-5'), 8.23 (td, 1H, H-4'), 8.68 (br dd, 1H, H-6'), 9.18 (br d, 1H, H-2') [$J_{4',5'} = 8.0$, $J_{5',6'} = 5.0$, $J_{2',4'} \approx J_{4',6'} \approx 1.5$ Hz]. $C_{12}H_{10}N_2OS$ (230.3). Calc. C 62.58, H 4.39, N 12.17, S 13.92; found C 62.83, H 4.25, N 12.12, S 13.70.

5,6-Dihydro-2-(4-pyridyl)-7(4H)benzothiazolone (**12d**)

a) From **10d**: Work up analogously to **12c** afforded **12d** (225 mg, 98%) as colorless crystals, m.p. 155–157 °C (Et_2O). ^{1}H-NMR ($CDCl_3$): $\delta = 2.26$ (quint, $J = 6.0$ Hz, 2H, H-5), 2.66 (t, $J = 6.0$ Hz, 2H, H-4), 3.07 (t, $J = 6.0$, 2H, H-6), 7.80 (d, $J = 5.5$ Hz, 2H, H-3', H-5'), 8.74 (d, $J = 5.5$ Hz, 2H, H-2', H-6'). MS (70 eV): *m/z* (%) = 230 (76) [M^+], 202 (66) [*M*–CO], 70 (100). $C_{12}H_{10}N_2OS$ (230.3). Calc. C 62.58, H 4.39, N 12.17, S 13.92; found C 62.44, H 4.39, N 11.93, S 13.90.

b) From **7** and **8d** (One Pot Procedure): **12d** was extracted with CH_2Cl_2 and purified by flash-chromatography (CH_2Cl_2/EtOAc, 3:7). Yield 171 mg (74%).

c) From **9d**: **9d** (100 mg, 0.28 mmol) was reacted with 0.5 *N* NaOH according to the protocol given for the conversion of **10d** to **12d**. Yield 61 mg (95%).

N-[(4,5,6,7-Tetrahydro-7-oxo)benzothiazol-2-yl]acetamide (Ac-**12e**) *(One Pot Procedure)*

A solution of **7** and **8e** (each 1.0 mmol) in dry EtOH (5 ml) was reacted at room temp. as given for the synthesis of **10e** and then evaporated. To the residue was added 0.5 *N* aq. NaOH (10 ml) with stirring at room temp. After 30 min the reaction mixture was brought to $pH = 7$ with 1 *N* HCl and then evaporated to dryness. The residue was purified by flash-chromatography (EtOAc/MeOH, 19:1, $R_f = 0.47$) to yield 141 mg (83%) **12e**, yellowish crystals m.p. 278–280 °C (Ref. [14] m.p. 280–282 °C). Acetylation with Ac_2O at room temp. afforded, after usual work up Ac-**12e**: m.p. 272 °C (MeOH). ^{1}H-NMR (*DMSO-d*$_6$): $\delta = 2.09$ (m, 2H, H-5), 2.18 (s, 3H, $COCH_3$), 2.50 (t, 2H, H-4), 2.85 (t, 2H, H-6),

12.6 (br s, 1H, D_2O-exchange, NH). ^{13}C-NMR: $\delta = 22.58$ ($COCH_3$ + C-5), 26.32 (C-4), 37.15 (C-6), 123.22 (C-7a), 162.71, 163.97 (C-2, C-3a), 169.17 (NHCO), 191.85 (CO). $C_9H_{10}N_2O_2S$ (210.3). Calc. C 51.41, H 4.80, N 15.25; found C 50.73, H 4.69, N 14.53.

Ethyl (4,5,6,7-Tetrahydro-7-oxobenzothiazol-2-yl)carboxylate (**12f**) *from* **10f**

Purification by flash-chromatography (CH_2Cl_2/EtOAc, 3:7, $R_f = 0.67$), yield 175 mg (78%), yellowish crystals, m.p. 85–87 °C (ether/petroleum ether, b.p. 40 °C). ^{1}H-NMR ($CDCl_3$): $\delta = 1.40$ (t, $J = 7.0$ Hz, 3H, $CO_2CH_2CH_3$), 2.20 (quint, $J = 6.0$ Hz, 2H, H-5), 2.61 (t, $J = 6.0$ Hz, 2H, H-4), 3.10 (t, $J = 6.0$ Hz, 2H, H-6), 4.45 (q, $J = 7.0$ Hz, 2H, CO_2CH_2). MS (70 eV): m/z (%) = 225 (18) [M^+], 197 (19) [M–CO], 153 (100). $C_{10}H_{11}NO_3S$ (225.3). Calc. C 53.31, H 4.93, N 6.22, S 14.23; found C 53.88, H 5.12, N 6.10, S 14.20.

Dimethyl [3a,5,6,6a-Tetrahydro-6-oxo-2-phenyl-3a(4H)cyclopentathiazolyl]phosphonate **15**

A solution of **14** (206 mg) and **8b** (137 mg) (each 1.0 mmol) in dry EtOH (5 ml) was refluxed, the reaction being monitored by TLC (CH_2Cl_2/acetone, 4:1). The starting thioamide ($R_f \approx 0.75$) was consumed after 1–2 h, the primary reaction products ($R_f \leq 0.1$) being slowly converted to a less polar compound ($R_f = 0.38$). After 15 h the dark solution was evaporated. The residue, on flash-chromatography over silica gel (20 g) afforded 267 mg (82%) **15**, colorless crystals, m.p. 80–81 °C (ether/petroleum ether, b.p. 40 °C). IR (CH_2Cl_2): $\nu = 1753$ cm^{-1} (CO), 1248 (P=O), 1058, 1030 (P–OC). MS (70 eV): m/z (%) = 325 (2.4) [M^+], 216 (100) [M–P(O)(OMe)$_2$]. ^{1}H-NMR ($CDCl_3$): $\delta = 2.30$–2.86 (m, 4H, $2CH_2$), 3.80, 3.84 (2d, $J = 10.0$ Hz, each 3H, $POCH_3$), 4.45 (d, $^3J_{HP} = 16.4$ Hz, CH), 7.34–7.52 (m, $3H_{arom}$), 7.82 (m_c, $2H_{arom}$). ^{13}C-NMR ($CDCl_3$): $\delta = 30.37$ (s), 34.75 ($J_{PC} = 5.1$ Hz) [CH_2], 53.79, 54.00 ($^2J_{PC} = 6.8$, and 7.2 Hz, $POCH_3$), 56.78 ($^2J_{PC} = 4.3$ Hz, CH), 88.15 ($^1J_{PC} = 168.5$ Hz, P–C), 128.47 ($4CH_{arom}$), 131.69 ($^4J_{PC} = 2.6$ Hz, i-C_{arom}), 131.90 (p-CH_{arom}), 169.12 ($^3J_{PC} = 14.3$ Hz, C-2), 211.91 ($^3J_{PC} = 15.2$ Hz, CO). $C_{14}H_{16}NO_4PS$ (325.4). Calc. C 51.86, H 4.97, N 4.31, S 9.85; found C 51.58, H 4.92, N 4.33, S 9.90.

5,6-Dihydro-2-phenyl-6(4H)cycopentathiazolone **17**

A small amount of polar reaction products was collected by further elution (EtOAc/MeOH, 5:1) of the column after the isolation of **15**. This was treated with 0.5 *N* NaOH (2 ml) for 15 min. Then the solution was extracted with CH_2Cl_2. Flash-chromatography of the dried (Na_2SO_4) solution (CH_2Cl_2/EtOAc, 1:1) afforded **17** (25 mg, 12%, colorless crystals with $R_f = 0.80$), m.p. 150–151 °C (ether/petroleum ether, b.p. 40 °C). IR (CH_2Cl_2): $\nu = 1700$ cm^{-1}, 1378, 1298. MS (70 eV): m/z (%) = 215 (55) [M^+], 84 (100). ^{1}H-NMR ($CDCl_3$): $\delta = 3.02$, 3.19 (2 m_c, each 2H, $2CH_2$), 7.48 (m, $3H_{arom}$), 8.00 (m_c, $2H_{arom}$). $C_{12}H_9NOS$ (215.3). Calc. C 66.95, H 4.22, N 6.59, S 14.89; found C 67.11, H 4.37, N 6.46, S 14.14.

Acknowledgements

The author wants to thank Miss S. Kotzinger for excellent technical assistance and Mag. J.-P. Polsterer for measuring the NMR spectra.

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Received October 12, 1992. Accepted November 11, 1992