SPIROCYCLIZATION OF ISATIN WITH CHIRAL α-AMINOTHIOLS: DIASTEREOSELECTIVE SYNTHESIS OF (–)- AND (+)-4′-(METHOXYCARBONYL)SPIRO[INDOLINE-3,2′-THIAZOLIDIN]-2-ONE

Peter KUTSCHY[a1,*], Mojmír SUCHÝ[a2], Milan DZURILLA[a3], Pavel PAZDERA[b], Mitsuo TAKASUGI[c] and Vladimír KOVÁČIK[d]

[a] *Department of Organic Chemistry, Faculty of Natural Sciences, P. J. Šafárik University, Moyzesova 11, 041 67 Košice, Slovak Republic; e-mail: [1] kutschy@kosice.upjs.sk, [2] suchymo@kosice.upjs.sk, [3] dzurilla@kosice.upjs.sk*

[b] *Department of Organic Chemistry, Faculty of Natural Sciences, Masaryk University, Kotlářská 2, 61 137 Brno, Czech Republic; e-mail: pazdera@chemi.muni.cz*

[c] *Division of Material Sciences, Graduate School of Environmental Earth Science, Hokkaido University, Sapporo 060-0810, Japan; e-mail: mtaka@ees.hokudai.ac.jp*

[d] *Institute of Chemistry, Slovak Academy of Sciences, Dúbravská cesta 9, 842 38 Bratislava, Slovak Republic; e-mail: chemkov@savba.savba.sk*

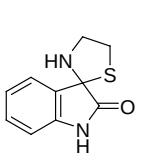
Received January 24, 2000
Accepted March 6, 2000

Reactions of isatin with chiral α-aminothiols have been studied. With L-cysteine, only decomposition products were formed under various reaction conditions, whereas D- and L-penicillamine afforded mixtures of diastereomeric 4′-carboxy-5′,5′-dimethylspiro[indoline-3,2′-thiazolidin]-2-ones (**4a** and **4b** or **5a** and **5b**) in the ratio 1 : 1. The reaction of isatin with methyl L- and D-cysteinates under mild reaction conditions (methanol–benzene, room temperature) proceeded diastereoselectively with the formation of (–)- and (+)-4′-(methoxycarbonyl)spiro[indoline-3,2′-thiazolidin]-2-one (**6a** and **8**) in 38 and 30% yields, respectively. Optically inactive 4′-(methoxycarbonyl)spiro[indoline-3,2′-([2′,5′]dihydrothiazol)]-2-one (**7**) was isolated as a side product in 7 and 3% yield, respectively. Structure of the obtained products was determined by spectral methods, including NOE difference measurements and by X-ray crystallography.

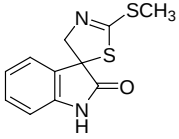
Key words: Phytoalexins; Indoles; Thiazolidines; Diastereoselective spirocyclization; Cysteine; Penicillamine.

In the framework of our continuing interest in the synthesis of indole phytoalexins and congeneric indoles[1], we have also decided to prepare derivatives of spiro[indoline-3,2′-thiazolidin]-2-one (**1**) as a compounds, related to indole phytoalexin spirobrassinin (**2**; ref.[2]). Compound **1** has been previously prepared as hydrochloride by treatment of isatin with cysteamine hydrochloride in propan-2-ol[3a] or ethanol[3b]. Of derivatives of **1**, a large number of spiro[indoline-3,2′-thiazolidin]-2,4′-diones (**3**) were synthe-

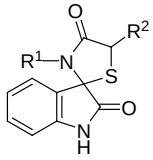
sized by the reactions of 3-(arylimino)indoline-2-ones with sulfanylacetic acid[4] (R^2 = H), 2-sulfanylpropanoic acid[5] (R^2 = CH_3), sulfanylsuccinic acid[6] (R^2 = CH_2COOH) and some other α-sulfanyl acids[7] in refluxing benzene, toluene, or dioxane in 20–80% yields. Another approach to these derivatives is the reaction of spiro[indoline-3,2′-[1,3]oxathiolane]- 2,5′-dione (prepared from isatin and sulfanylacetic acid) with amines[8]. All these compounds were prepared by non-stereoselective reactions and, consequently, the obtained spirooxindoles are racemates. Compounds of type **3** are much investigated, because of their antibacterial[4f,4g,4j,4k,7b], antifungal[4i,4l,7b], insecticidal[7b] and antileukemic[7a] activities.



1



2



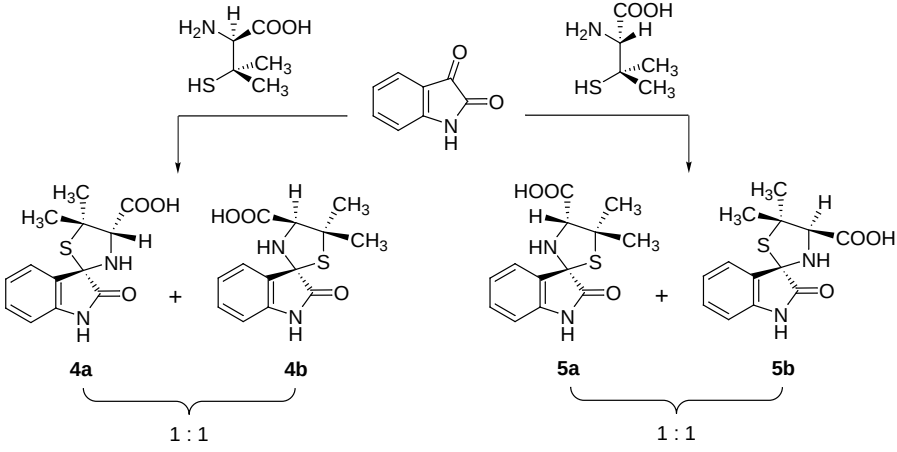
3

The aim of the present study was to investigate the reactions of isatin with chiral α-aminothiols (L- and D-cysteine, D- and L-penicillamine, methyl L- and D-cysteinate) and to assess a possibility of diastereoselective synthesis of spiro[indoline-3,2′-thiazolidin]-2-one derivatives (**1**). We were interested in whether the specific structure features of isatin as a cyclic 1,2-dicarbonyl compound could support asymmetric induction in its reactions with chiral α-aminothiols. To our knowledge, except for the reaction with cysteamine[3], no reaction of isatin with α-aminothiols has been described to date.

Reactions of L-cysteine in ethanol–water or its methyl ester in methanol–benzene, or D-penicillamine in ethanol–water with aldehydes and ketones were previously described to proceed with the formation of a 1 : 1 mixture of diastereomeric thiazolidines, containing the original amino acid chirality (*e.g.*, *R* for L-cysteine) at C-4 of the thiazolidine ring and *R* or *S* chirality on a new stereogenic center at C-2, the C-atom of the former carbonyl group[9].

Although there appeared a paper, describing the diastereoselective formation of 3-acetyl-2-(4-tolyl)thiazolidine-4-carboxylic acid from L-cysteine and 4-methylbenzaldehyde[10], it was later shown that in this case and in the case of some analogous derivatives, the original product was a mixture of diastereomers, which epimerized during subsequent acetylation to a single diastereomer[11]. We have started our study by the reaction of isatin with L-cysteine hydrochloride monohydrate in a mixture of ethanol–water[9]. At

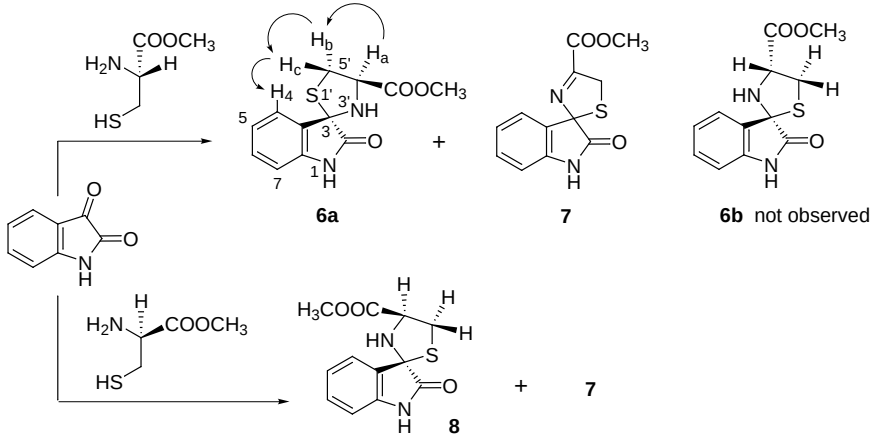
various temperatures (from room temperature to 90 °C), only highly polar decomposition products, less chromatographically mobile, were formed and no isolable product was observed by monitoring the reaction by TLC. The same results were obtained under nitrogen atmosphere. A similar situation occurred with D-penicillamine. We have found that the reaction of D-penicillamine with isatin can be successfully performed in a mixture of ethanol–water, in the presence of sodium acetate and hydrochloric acid at room temperature, whereas with L-cysteine, only decomposition products were formed. These reaction conditions were previously used for the preparation of 4-carboxy-5,5-dimethyl-2-(2-pyridyl)thiazolidine from D-penicillamine and pyridine-2-carbaldehyde[9a]. However, under these conditions, with D-penicillamine we have obtained an inseparable mixture of diastereomers (**4a** and **4b**) in the 1 : 1 ratio (Scheme 1).



SCHEME 1

In the reaction of isatin with L-penicillamine under the same conditions, again an inseparable mixture of diastereomers (**5a** and **5b**) in the 1 : 1 ratio was obtained. The products resulting from D- or L-penicillamine exhibited identical spectral data and melting points. In ^{1}H NMR spectra the signals of methyl protons at 1.49 and 1.54, as well as those at 1.78 and 1.83 ppm (1 : 1 : 1 : 1 ratio) and the signals of CH protons at 4.32 and 4.71 ppm (1 : 1) evidence the presence of two diastereomers of **4** and **5**. Analogously, the signals of all carbon atoms in ^{13}C NMR spectra are doubled. To avoid possible epimerization in the reaction mixture, we turned our attention to the reaction of isatin with methyl L- and D-cysteinates, enabling the use of mild reaction conditions. Using the methyl cysteinate hydrochloride and a mix-

ture of benzene– methanol as a solvent, the free ester was liberated by addition of triethylamine to the reaction mixture according to the previously described procedure for the reactions of aldehydes with methyl L-cysteinate hydrochloride[9a]. The reaction of methyl L-cysteinate afforded under these conditions two products (**6a**, 30% and **7**, 7%; Scheme 2) separable by column chromatography. We have found that if an equimolar quantity of reagents is used, some amount of isatin remains unreacted and chromatographic separation of products is complicated, because isatin appears as impurity eluting from the column together with products. Subsequent purification by crystallization resulted in low yields of pure products. The best yields of pure **6a** and **7** were obtained if only 0.79 equivalents of isatin was used. Compounds **6a** and **7** were accompanied by highly polar decomposition products, strongly adsorbed on silica gel. The major product **6a** showed optical activity ($[\alpha]_D^{25}$ –53.0 (*c* 0.19, methanol)), whereas the minor (**7**) appeared to be optically inactive.



Both products exhibited in ^{13}C NMR spectra quaternary atoms signals at 75.38 (**6a**) and 89.18 (**7**) confirming the presence of spiro atoms. The structure of compound **6a** was determined by NOE difference measurements, using the signal of CH proton at 4.73 ppm, two signals of diastereotopic CH_2 protons at 3.41 and 3.93 ppm and the signal of aromatic proton H-4 at 7.47 ppm. The signals of aromatic protons have been assigned by analogy with spirobrassinin (**2**; ref.[2]) and confirmed by decoupling experiments. Irradiation of H_a at 4.73 ppm resulted in enhancement of the intensity of H_b at 3.93 ppm by 11%, and thus the signal at 3.41 ppm has been assigned to H_c

(enhanced by irradiation of H_b by 31%). Irradiation of H_c resulted in enhancement of aromatic proton H-4 at 7.47 ppm by 3%. With respect to the known absolute configuration (*R*), at C-4′ originating from methyl L-cysteinate we have assigned to **6a** the structure of (3*S*,4′*R*)-4′-(methoxycarbonyl)spiro[indoline-3,2′-thiazolidin]-2-one. In the mass spectrum of **6a**, the presence of molecular ion at *m*/*z* 264 (13%) corresponds to the expected molecular weight. The minor reaction product (**7**) was expected to be the other diastereomer (**6b**). However the mass spectrum revealed that its molecular weight is by two mass units lower than that corresponding to **6b**, indicating that two hydrogen atoms are missing in **7** compared with **6b**. Therefore the structure of spirothiazoline **7** was proposed for this compound. The structure of **7** was confirmed by the presence of a singlet of CH_2 protons at 4.64 ppm in ^{1}H NMR spectrum, whereas the signals of CH and NH protons are missing.

The way of the formation of **7** is unclear and will be further studied in our laboratory, preferably by using 1-substituted isatin derivatives. To check the stereospecificity of diastereoselective spirocyclization of isatin with methyl L-cysteinate we performed the same reaction with methyl D-cysteinate. As a result, we have isolated two products (Scheme 2). The optically inactive compound (**7**; 3%), identical with a minor product obtained from methyl L-cysteinate and (3*R*,4′*S*)-4′-(methoxycarbonyl)spiro[indoline-3,2′-thiazolidin]-2-one (**8**; $[\alpha]_D^{25}$ +55.8 (*c* 0.19, methanol)), the enantiomer of **6a**, thus confirming the stereospecificity of the studied spirocyclization. Compound **8** exhibited spectral data identical with those for **6a**. Because in the case of **6a**, the NOE difference measurements showed only 3% NOE between H_c and H-4, structure of **8** was also studied by 2D NMR spectroscopy. ^{1}H NMR NOESY spectrum of **8** exhibited all the expected NOEs, except for

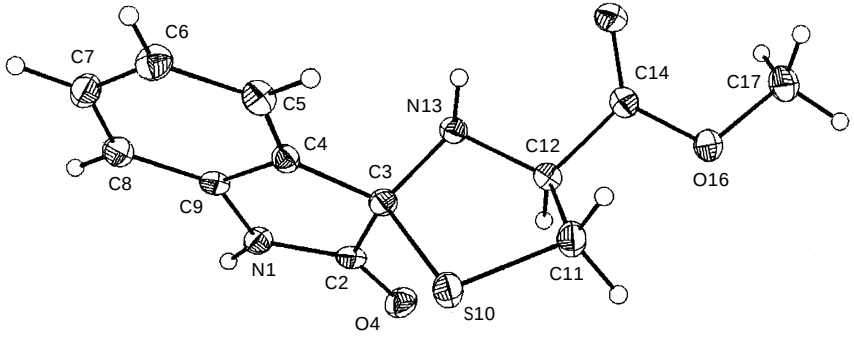


FIG. 1
ORTP diagram of **8** showing the crystallographic atom numbering scheme

the NOE between H_c and H-4. Therefore, it was decided to prove the structure of **8** by X-ray crystallography. We have succeeded in growing suitable crystals by slow diffusion of hexane into a saturated dichloromethane solution, and the structure of **8** was unambiguously proved by X-ray analysis (Fig. 1).

Antifungal activity of compounds **6a** and **8** was examined, using the fungus *Bipolaris leersiae* and compared with phytoalexin brassinin, which completely inhibited the conidial germination of the fungus at concentration 0.1 mmol l^{-1} (ref.[1b]). None of the studied isomers showed any significant antifungal activity.

EXPERIMENTAL

Infrared absorption spectra were recorded on an IR 75 spectrometer (Zeiss, Jena) in chloroform, the wavenumbers are given in cm^{-1}. ^1H and ^{13}C NMR spectra were measured on Bruker AMX-200 (200 MHz), AMX 400 (400 MHz), Bruker Avance DRX-500 (500 MHz) and Varian Gemini 2000 (300 MHz) spectrometers in hexadeuterioacetone (compounds **4** and **5**) and deuteriochloroform (compounds **6**–**8**). Chemical shifts (δ) are reported in ppm downfield from tetramethylsilane, coupling constants (*J*) in Hz. Microanalyses were performed with a Perkin–Elmer, Model 2400 analyzer. The mass spectra were recorded on a JMS-100D spectrometer (Jeol) using the electron impact method at ionization energy 70 eV. The optical rotation was determined on digital polarimeter POLAR L-mP (IBZ Messtechnik). Specific rotations are given in 10^{-1} deg cm^2 g^{-1}. The reaction course was monitored by thin layer chromatography, using Silufol plates (Kavalier). Preparative column chromatography was performed on Kieselgel Merck, Typ 9383, 230–400 mesh. Antifungal activity was examined by the previously reported procedure[1b]. Isatin (Fluka), L-cysteine hydrochloride monohydrate (Fluka), D-cysteine hydrochloride monohydrate (Aldrich), D- and L-penicillamine (Aldrich) were used as obtained without further purification. Methyl L- and D-cysteinate hydrochlorides were prepared by literature procedure[12].

Reaction of Isatin with D- and L-Penicillamine

To a solution of D- or L-penicillamine (149 mg, 1 mmol), sodium acetate trihydrate (136 mg, 1 mmol) and concentrated hydrochloric acid (0.1 ml, 1.2 mmol) in water (2 ml), a solution of isatin (147 mg, 1 mmol) in ethanol (14 ml) was added and the reaction mixture was stirred for 48 h at room temperature. After evaporation of ethanol, the crystalline precipitate was filtered with suction and dried. Analytical samples were obtained by crystallization from acetone–hexane.

(3S,4′S)- (**4a**) *and (3R,4′S)-4′-Carboxy-5′,5′-dimethylspiro[indoline-3,2′-thiazolidin]-2-one* (**4b**) *(1 : 1 mixture).* Yield 220 mg (79%), m.p. 146–148 °C. For $C_{13}H_{14}N_2O_3S$ (278.3) calculated: 56.10% C, 5.07% H, 10.07% N; found: 55.89% C, 5.22% H, 9.91% N. IR: 3 459 (N–H); 2 400–3 400 $(COOH)_{assoc}$; 1 613, 1 727 (C=O). ^1H NMR: 1.49 s, 1.54 s, 1.78 s, 1.83 s (1 : 1 : 1 : 1), 6 H (2 × CH_3); 4.31 s, 4.71 s (1 : 1), 1 H (H-4′); 6.91–6.95 m, 1 H (H-7); 7.03–7.11 m, 1 H (H-6); 7.20–7.33 m, 1 H (H-5); 7.55–7.60 m, 1 H (H-4); 9.41 s, 9.62 s (1 : 1), 1 H (NH). ^{13}C NMR: 26.76, 27.03, 28.48, 29.45 (CH_3); 61.79, 62.09 (C-5′); 73.26, 76.01 (C-4′); 74.47, 75.44

(C-spiro); 110.91, 111.22, 123.47, 123.87, 125.84, 126.26, 129.12 (q), 130.16, 131.30, 135.47 (q), 141.33 (q), 142.97 (q) (-C_6H_4-); 170.37, 170.84, 178.83, 179.05 (C=O). MS, *m*/*z* (%): 278 (M^+, 10), 250 (85), 205 (20), 191 (16), 158 (25), 150 (100), 118 (22), 44 (80).

(3R,4′R)- (**5a**) *and (3S,4′R)-4′-Carboxy-5′,5′-dimethylspiro[indoline-3,2′-thiazolidin]-2-one* (**5b**) *(1 : 1 mixture).* Yield 220 mg (79%), m.p. 146–148 °C. For $C_{13}H_{14}N_2O_3S$ (278.3) calculated: 56.10% C, 5.07% H, 10.07% N; found: 55.81% C, 5.24% H, 9.93% N. All spectral data are identical with those for the mixture of **4a** and **4b**.

Reaction of Isatin with Methyl L- and D-cysteinate Hydrochloride

To a solution of methyl L- or D-cysteinate hydrochloride (0.5 g, 2.9 mmol) in a mixture of methanol (1.2 ml) and benzene (2.4 ml), triethylamine (293 mg, 0.4 ml, 2.9 mmol) and isatin (338 mg, 2.3 mmol) were added. The reaction mixture was stirred at room temperature for 30 h, the solvent evaporated and the residue chromatographed on 100 g of silica gel (eluent cyclohexane–acetone 5 : 1). After evaporation and two crystallizations from dichloromethane–hexane, pure products **6a** and **7**, or **8** and **7**, were obtained.

(–)-(3S,4′R)-4′-(Methoxycarbonyl)spiro[indoline-3,2′-thiazolidin]-2-one (**6a**). Yield 231 mg (38%), m.p. 162–164 °C; $[\alpha]_D^{25}$ –53.0 (*c* 0.19, methanol), –57.7 (*c* 0.19, dichloromethane). For $C_{12}H_{12}N_2O_3S$ (264.3) calculated: 54.53% C, 4.58% H, 10.60% N; found: 54.66% C, 4.51% H, 10.48% N. IR: 3 443, 3 323 (N–H); 1 737, 1 617 (C=O). ^{1}H NMR: 3.21 d, 1 H, *J* = 9.10 (NH); 3.41 dd, 1 H, *J* = 10.71, 6.15 (H_c); 3.48 s, 3 H (CH_3); 3.93 dd, 1 H, *J* = 10.71, 7.50 (H_b); 4.73 ddd, 1 H, *J* = 6.16, 7.50, 9.10 (H_a); 6.87 d, 1 H, *J* = 7.50 (H-7); 7.11 ddd, 1 H, *J* = 1.07, 7.50, 7.50 (H-5); 7.30 ddd, 1 H, *J* = 1.34, 7.74, 7.74 (H-6); 7.47 d, *J* = 7.50 (H-4); 7.90 s, 1 H (NH). ^{13}C NMR: 37.94 (CH_2); 51.90 (OCH_3); 63.55 (CH); 75.38 (C-spiro); 109.61, 121.70, 123.60, 126.66 (q), 129.58, 141.26 (q) (-C_6H_4-); 171.35, 177.58 (C=O). MS, *m*/*z* (%): 264 (M^+, 13), 236 (77), 177 (100), 118 (10).

4′-(Methoxycarbonyl)spiro[indoline-3,2′-([2′,5′]dihydrothiazol)]-2-one (**7**). Yield 42 mg (7%) from L-, 18 mg (3%) from D-methyl cysteinate hydrochloride, m.p. 148–150 °C. For $C_{12}H_{10}N_2O_3S$ (262.3) calculated: 54.95% C, 3.84% H, 10.68% N; found: 55.02% C, 3.71% H, 10.88% N. IR: 3 433 (N–H); 1 732, 1 617 (C=O); 1 640 (C=N). ^{1}H NMR: 3.94 s, 3 H (OCH_3); 4.64 s, 2 H (CH_2); 6.90 d, 1 H, *J* = 7.69 (H-7); 7.09 ddd, 1 H, *J* = 7.69, 7.65, 1.10 (H-5); 7.27–7.34 m, 2 H (H-4, H-6). ^{13}C NMR: 45.36 (CH_2); 53.63 (OCH_3); 89.18 (C-spiro); 110.78, 123.67, 126.31, 129.00 (q), 130.98, 140.68 (q) (-C_6H_4-); 161.57, 167.10, 175.44 (C=N, 2 × C=O). MS, *m*/*z* (%): 262 (M^+, 66), 230 (47), 162 (100).

(+)-(3R,4′S)-4′-(Methoxycarbonyl)spiro[indoline-3,2′-thiazolidin]-2-one (**8**). Yield 182 mg (30%), m.p. 159–161 °C; $[\alpha]_D^{25}$ +55.8 (*c* 0.19, methanol), +60.4 (*c* 0.19, dichloromethane). For $C_{12}H_{12}N_2O_3S$ (264.3) calculated: 54.53% C, 4.58% H, 10.60% N; found: 54.71% C, 4.39% H, 10.75% N. All spectral data for compound **8** are identical with those for **6a**.

X-Ray Crystal Structure Analysis of Compound **8**

Formula $C_{12}H_{12}N_2O_3S$, *M* = 264.30, orthorhombic, space group $P2_12_12_1$, *a* = 5.867(1) Å, *b* = 8.305(1) Å, *c* = 23.952(2) Å, *V* = 1 167.1(3) Å, *F*(000) = 552, *Z* = 4, D_{calc} = 1.504 mg m^{-3}, μ = 0.279 mm^{-1}. A colourless cube of the dimensions 0.50 × 0.50 × 0.50 mm (from dichloromethane–hexane) was measured at 150(2) K (MoKα radiation, λ = 0.71073 Å). From total of 7 924 reflections collected with a KUMA KM-4 kappa four-circle diffractometer, θ range from 2.98 to 27.49°, *h* = –12 to 7, *k* = –10 to 10, *l* = –18 to 30; 2 573 reflections were independent

(R_{int} = 0.0223). The structure was solved by direct methods using SHELXS86 (ref.[13]) and refined on F^2 for all reflections using SHELXL93 (ref.[14]). The hydrogen atoms were placed in calculated positions (those of methyl group were allowed freely to rotate) and their thermal parameters were tied with the thermal parameter of the parent atoms, all other atoms were refined anisotropically. Final R indices were: $R1$ = 0.0258, $wR2$ = 0.0625 for observed [$I > 2\sigma(I)$] and $R1$ = 0.0268, $wR2$ = 0.0639 for all data, goodness-of-fit on F^2 = 1.138. The absolute structure was considered during refinement, the final orientation yielded a Flack parameter –0.04(6). The final difference map was featureless, the extreme values of the hole and peak were –0.180 and 0.223 e Å^{-3}, respectively. Crystallographic data for the structure **8** reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC-139283. Copies of the data can be obtained free of charge on application to CCDC, e-mail: deposit@ccdc.cam.ac.uk.

We thank Dr A. Solladie-Cavallo (Ecole Européene des Hautes Etudes des Industries Chimiques de Strasbourg) for valuable discussions regarding the structure of compound ***6a****, Prof. Z. Žák (Department of Inorganic Chemistry, Masaryk University, Brno) for X-ray crystallographic analysis of compound* ***8****, Dr R. Marek (Laboratory of NMR Spectroscopy, Masaryk University, Brno) for 2D NMR spectra of compound* ***8****, the Grant Agency for Science of the Slovak Republic (grants No. 1/3229/96 and No. 1/6080/99) and the Grant Agency of the Czech Republic (projects No. 203/96/0111 and No. 203/98/0676) for financial support of this work.*

REFERENCES

1. a) Kutschy P., Achbergerová I., Dzurilla M., Takasugi M.: *Synlett* **1997**, 289; b) Kutschy P., Dzurilla M., Takasugi M., Török M., Achbergerová I., Homzová R., Rácová M.: *Tetrahedron* **1998**, *54*, 3549; c) Dzurilla M., Kutschy P., Tewari J., Ružinský M., Ševnický S., Kováčik V.: *Collect. Czech. Chem. Commun.* **1998**, *63*, 94; d) Kutschy P., Dzurilla M., Takasugi M., Sabová A.: *Collect. Czech. Chem. Commun.* **1999**, *64*, 348; e) Dzurilla M., Ružinský M., Kutschy P., Tewari J. P.: *Collect. Czech. Chem. Commun.* **1999**, *64*, 1448.
2. Takasugi M., Monde K., Katsui N., Shirata A.: *Chem. Lett.* **1987**, 1631.
3. a) Sweetman B. J., Bellas M., Field L.: *J. Med. Chem.* **1969**, *12*, 888; b) Wolf M., Mascitti A. A. (American Home Corp.): U.S. 3 458 525; *Chem. Abstr.* **1970**, *72*, 21715.
4. a) Otomasu H., Ohniya S. (Kohjin Co., Ltd): *Japan 75 140 441; Chem. Abstr.* **1976**, *85*, 32991; b) Hassan Kh. M., El-Shafei A. K., El-Kashef H. S.: *Z. Naturforsch., B* **1978**, *33*, 1515; c) Hassan Kh. M., Khalil Z. H.: *Z. Naturforsch., B* **1979**, *34*, 621; d) Hassan Kh. M., Khalil Z. H.: *Z. Naturforsch., B* **1979**, *34*, 1326; e) Joshi K. C., Patni R., Chand P.: *Heterocycles* **1981**, *16*, 1555; f) Piscopo E., Diurno M. V., Mazzoni O., Ciaccio A. M.: *Boll. Soc. Ital. Biol. Sper.* **1990**, *66*, 1181; g) Piscopo E., Diurno M. V., Mazzoni O., Ciaccio A. M.: *Boll. Soc. Ital. Biol. Sper.* **1990**, *66*, 1187; h) Jain R., Vajpei S.: *Phosphorus, Sulfur Silicon Relat. Elem.* **1992**, *70*, 63; i) Singh K., Tiwari N., Nizamuddin: *Indian J. Chem., Sect. B: Org. Chem. Incl. Med. Chem.* **1993**, *32*, 1086; j) Diurno M. V., Mazzoni O., Piscopo E., Bolognese A.: *Farmaco* **1993**, *48*, 435; k) Mogiliah K., Rao R. B.: *Indian J. Chem., Sect. B: Org. Chem. Incl. Med. Chem.* **1998**, *37*, 894; l) Khan M. H., Tewari S., Begum K., Nizamuddin: *Indian J. Chem., Sect. B: Org. Chem. Incl. Med. Chem.* **1998**, *37*, 1075.
5. Rajopadhye M., Popp F. D.: *J. Heterocycl. Chem.* **1984**, *21*, 289.

6. Popp F. D., Rajopadhye M., Brown D., Waddington D., Barrie C. U.: *J. Heterocycl. Chem.* **1987**, *24*, 261.
7. a) Rajopadhye M., Popp F. D.: *J. Heterocycl. Chem.* **1987**, *24*, 1637; b) Dandia A., Kaur V., Singh P.: *Indian J. Pharm. Sci.* **1993**, *55*, 129.
8. Al-Thebeiti M. S., El-Zohry M. F.: *Phosphorus, Sulfur Silicon Relat. Elem.* **1994**, *88*, 251.
9. a) Brunner H., Becker R., Riepl G.: *Organometalics* **1984**, *3*, 1354; b) Tronchet J. M. J., Kovács I., Barballat-Ray F., Holm M. V.: *Nucleosides Nucleotides* **1998**, *17*, 1115.
10. Parthasarathy R., Paul B., Korytnyk W.: *J. Am. Chem. Soc.* **1976**, *98*, 6634.
11. a) Silágyi L., Györgydeák Z.: *J. Am. Chem. Soc.* **1979**, *101*, 427; b) Ando W., Igarashi Y., Huang L.: *Chem. Lett.* **1987**, 1364; c) Inaba A., Inami K., Kimodo Y., Yamada R., Miwa Y., Taga T., Bessho K.: *Chem. Pharm. Bull.* **1995**, *43*, 1601; d) Altenbach H.-J., Roth P. R., Brauer D. J.: *Liebigs Ann. Chem.* **1995**, 1427.
12. Brit. 797 508; *Chem. Abstr.* **1959**, *53*, 4157.
13. Sheldrick G. M.: *Acta Crystallogr., Sect. A: Fundam. Crystallogr.* **1990**, *46*, 467.
14. Sheldrick G. M.: *SHELXL93. Program for Crystal Structure Refinement.* University of Göttingen, Göttingen 1993.