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Formation of Isopenillic Acid Derivatives in the Reaction of Benzylpenicillin with Phosphorus Pentachloride

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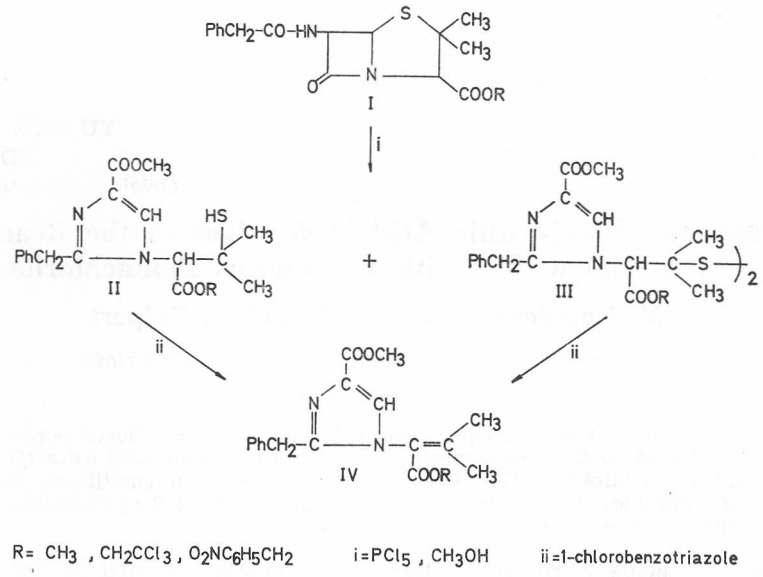
Treatment of benzylpenicillin ester (I) with phosphorus pentachloride at 60 °C gives a mixture of benzylisopenillic acid ester (II) and its disulphide (III). Under the same reaction conditions, 6--phthalimidopenicillinate ester (V) yields α-methyl 6-phthalimidopenicilloate ester (VIII).

Isopenillic acids were one of the first products obtained in the study of the penicillin structure and its degradation products[1]. Their structure was proved by synthesis from D-penicillamine via thiazolidine derivatives[2]. Not much attention was given to these structures, since isopenillic acids did not exhibit antibacterial activity. Recently, we isolated isopenillic acid derivatives in the reaction of penicillin esters with phosphorus pentachloride; this result is reported here.

Phosphorus pentachloride has been used for the removal of *N*-acyl side chains in penicillins and some cephalosporins, since it gives a nearly complete conversion of the amide group into an iminochloride even at temperatures below 0 °C [3]. However, phenoxy- and phenylacetamidodeacetoxycephalosporin esters require heating to 60—80 °C to form iminochloride with good yield[4].

When benzylpenicillin ester (I; R=CH_2CCl_3) was treated with phosphorus pentachloride at 60 °C, two products were isolated, after the addition of alcohol and water, which were different from the 6-aminopenicillanic acid ester. The presence of some groups, like =C—OCH_3, —C=N—CH=CH—, and HS—$C(CH_3)_2$—CH, indicated by data from NMR, IR and UV spectra, stimulated our interest in the structures of these products. Although data from ^{13}C NMR also suggested an enethiolate as one of the possible structures, this was not probable given their chemical properties, such as stability under hydrolysis and hydrogenation[5]. Since recent X-ray crystallographic analysis has established the α-(4-carbomethoxy-2-benzyl-5-imidazolyl)-β,β-dimethylacrylate ester structure of the compound obtained by desulphurisation of these two products, the parent compounds should possess the structure of an isopenillic acid ester[6]. Dimethyl ester (II; R=CH_3), prepared later by the same procedure, had a melting point in the range expected, although the value of optical rotation was higher than recorded for the natural or synthetic product[7].

SCHEME I



R= CH_3 , CH_2CCl_3 , $O_2NC_6H_5CH_2$ i=PCl_5 , CH_3OH ii=1-chlorobenzotriazole

Isopenillic acid ester (II), obtained in this reaction, was the product with the higher R_f (c. 0.60) and was isolated from the reaction mixture by crystallization or by chromatography. The second product had a lower R_f value (c. 0.30) and was obtained by chromatography of the mother liquor or further elution of a chromatography column. It was identified as III, a disulphide form of II, on the basis of its spectroscopic data and chemical reactions. The ^1H NMR spectrum of III resembles one recorded of II, except for the S—H band at δ 2.1, which was missing. This product also did not show the S—H band at 2225 cm^{-1} in its IR spectrum which compound II did. Treatment of II or III with 1-chlorobenzotriazole, according to the procedure described by Kukolja[8], gave an olefinic product in high yield, which was later identified by X-ray analysis as IV[6]. The same olefin product was obtained in the reaction of III with Raney nickel or by treatment with acetic anhydride. The dimethyl ester of IV, obtained in this reaction from II or III, was described in the literature as being prepared by the esterification of the product obtained by pyrolysis of methyl benzylpenicilloate[9]. It is noteworthy that the same product was obtained in an attempt to hydrolyse trichloroethyl ester II with sodium hydroxide in methanol.

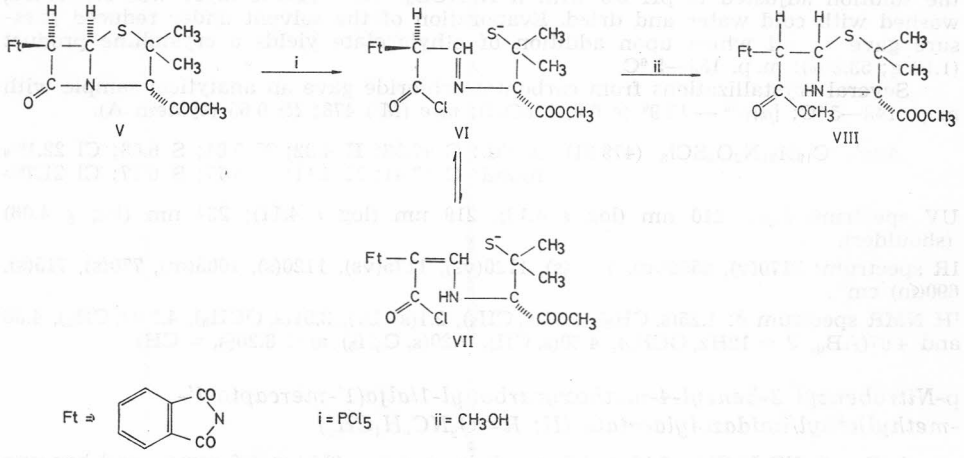
According to the methods reported so far in the literature, isopenillic acids can be obtained from penicillin by a stepwise procedure with penillic acid as an intermediate. In the first step, penicillin yields penillic acid in acid solution (pH 2—3); in a second reaction, penillic acid rearranges into isopenillic acid when stood in alkaline solution or acetic acid or by heated in organic solvents[10,11].

In the reaction of benzylpenicillin ester with phosphorus pentachloride, isopenillic acid derivatives were obtained in a one-step procedure; a penillic acid derivative may be one of the possible intermediates. However, there are some indications that penillic acid is one of the less probable intermediates in

this reaction. Namely, no traces of dimethylpenillate, but only I, II and III have been detected by TLC, in the course of the reaction of benzylpenicillin methyl ester and phosphorus pentachloride. Moreover, no dimethyl benzylisopenillate was formed when benzylpenillic acid was treated with phosphorus pentachloride and methanol under the same reaction conditions.

On the other hand, 6-phthalimidopenicillinate ester (V) treated with phosphorus pentachloride under the same reaction conditions gave C-5 and C-6 isomers of α-methyl 6-phthalimidopenicilloate ester (VIII). A similar mixture of C-5 and C-6 isomers of benzylpenicilloate was obtained when benzylpenicilloamides were heated in organic solvents without the presence of phosphorus halide[11].

SCHEME II



The isolation of C-5 epimers of VIII and the detection of the presence of C-6 isomers indicate the opening of the thiazolidine ring in benzylpenicilloate intermediates in the course of this reaction.

The yield of thiole II and disulphide III was found to depend on the phosphorus halide used. When phosphorus trichloride was used in the reaction instead of pentachloride, no disulphide III was obtained but only thiol II, isolated in low yield (c. 10%). The disulphide III was obviously not formed by atmospheric oxidation of II since the reaction was carried out under nitrogen. One explanation for the formation of disulphide may be that thiol II is oxidized into III by phosphorus pentachloride in the course of the reaction, since III was also obtained when II was heated in the presence of phosphorus pentachloride.

EXPERIMENTAL

Melting points are uncorrected.

The UV spectra were recorded in methanol with a SP8-100 Unicam spectrometer. The IR spectra were recorded on potassium bromide plates, unless otherwise stated, with a Model 257G Perkin-Elmer spectrometer. The PMN measurements were made with a EM-360 Varian in $CDCl_3$ with TMS as internal standard. The mass spectrum was determined using a CEC 21-110 B spectrometer operating at 70 eV.

TLC was conducted on original plates (Merck, Kieselgel HF_{254}) followed by detection using iodine vapour and water or by UV absorption in solvent systems as follows:

(A) dichloromethane : ether (4 : 1)
(B) benzene : acetone (9 : 1)

Optical rotations were measured on an Opton 372 149 polarimeter at ambient temperature.

2',2',2'-Trichloroethyl 2-benzyl-4-methoxycarbonyl-1/alfa(1'-mercapto-1'--methyl)ethyl/imidazolylacetate (II; R=CH_2CCl_3)

To a solution of I (R = CH_2CCl_3; 2.14 g, 4.6 mmol) in pyridine (0.54 g, 6.8 mmol) and benzene (120 ml), phosphorus pentachloride (1.4 g, 6.8 mmol) was added in portions over 15 minutes. The reaction mixture was stirred under nitrogen at 60 °C for 1 hour and then cooled to + 10 °C. Methanol (200 ml) was added and stirring continued for a further 2 hours. The solvent was evaporated under reduced pressure and the residue dissolved in ethylacetate (30 ml) and water (20 ml), and the pH of the solution adjusted to pH 6.5 with n $NaHCO_3$. The organic layer was separated, washed with cold water and dried. Evaporation of the solvent under reduced pressure gave an oil which upon addition of ethylacetate yields a crystalline product (1.19 g; 53.8%): m. p. 133—5 °C.

Several crystallizations from carbontetrachloride gave an analytical sample with m. p. 143—5 °C; $[\alpha]_D^{20}$ — 13.9° (*c* 0.5, MeOH); *m/e* (M^+) 478; R_f 0.65 (system A).

Anal. $C_{19}H_{21}N_2O_4SCl_3$ (479.81) calc'd.: C 47.56; H 4.32; N 5.84; S 6.68; Cl 22.1%
found: C 47.41; H 4.11; N 5.77; S 6.77; Cl 21.7%

UV spectrum λ_{max}: 210 nm (log ε 4.13), 219 nm (log ε 4.11); 234 nm (log ε 4.06) (shoulder).

IR spectrum: 3170(v), 2550(m), 1757(s), 1720(vs), 1175(vs), 1120(s), 1003(m), 770(s), 715(s), 690(m) cm^{-1}.

^1H NMR spectrum δ: 1.25(s, CH_3), 1.51(s, CH_3), 2.1(s, SH), 3.91(s, OCH_3), 4.23(s, CH_2), 4.38 and 4.67(AB_q, J = 12Hz, OCH_2), 4.80(s, CH), 7.20(s, C_6H_5) and 8.20(s, = CH).

p-*Nitrobenzyl 2-benzyl-4-methoxycarbonyl-1/alfa(1'-mercapto-1'--methyl)ethyl/imidazolylacetate (II; R=$O_2NC_6H_4CH_2$)*

I (R = $O_2NC_6H_4CH_2$; 2.16 g, 4.6 mmol) in pyridine (0.54 g, 6.8 mmol) and benzene (120 ml) was treated with phosphorus pentachloride as described above. An oily product was adsorbed on a silicagel column in methylenechloride. Elution with methylenechloride : ether (4 : 1) afforded an oily fraction (0.655 g; 32.4%) which crystallized upon the addition of ether: m. p. 127—9 °C; $[\alpha]_D^{20}$ — 15° (*c* 0.5, MeOH); R_f 0.62 (system A).

Anal. $C_{24}H_{25}N_3O_6S$ (438.5) calc'd.: C 59.61; H 5.21; N 8.69%
found: C 59.40; H 4.98; N 8.45%

UV spectrum λ_{max}: 204 nm (log ε 4.49), 242 nm (log ε 4.27).

IR spectrum: 3162(vw), 2940(m), 2525(w), 1750(vs), 1720(vs), 1604(w), 1520(s), 1340(vs), 1193(s), 1180(s), 1165(s), 1120(s), 832(s) cm^{-1}.

^1H NMR spectrum δ: 1.27(s, CH_3), 1.47(s, CH_3), 1.93(s, SH), 3.90(s, OCH_3), 4.10 and 4.43(AB_q, J = 16Hz, OCH_2) 4.80(s, CH), 5.03(s, CH_2), 7.20(s, C_6H_5), 7.20 and 8.17(2d, J = = 9Hz, C_6H_4), 8.18(s, =CH).

Methyl 2-benzyl-4-methoxycarbonyl-1/alfa(1'-mercapto-1'-methyl)ethyl/imidazolylacetate (II; R=CH_3)/Dimethyl benzylisopenillate/

I (R = CH_3; 1.6 g, 4.6 mmol) in pyridine and benzene was treated with phosphorus pentachloride as described above. An oily product was adsorbed on a silicagel column in methylenechloride. Elution with methylenechloride : ether (4 : 1) afforded an oily fraction (0.157 g; 9.4%) which crystallized upon the addition of ether, m. p.

120—1 °C; $[\alpha]_D^{22}$ — 30° (*c* 0.5, MeOH); R_f 0.58 (system A.)/Lit.[7] m. p. 111—2 °C and 127—9 °C; $[\alpha]_D^{22}$ — 9.4° (*c* 1.4, MeOH).

UV spectrum λ_{max}: 212 nm (log ε 4.07), 220 nm (log ε 4.03), 236 nm (log ε 4.05) (shoulder).

IR spectrum: 3150(m), 2560(v), 1760(vs), 1715(s), 1430(m), 1205(s), 730(s), 695(m) cm^{-1}.

^1H NMR spectrum δ: 1.16(s, CH_3), 1.43(s, CH_3), 1.95(s, SH), 3.54(s, OCH_3), 3.90(s, OCH_3), 4.23(s, CH_2), 4.70(s, CH), 7.20(s, C_6H_5), 8.21 (s, =CH).

2',2',2'-Trichloroethyl 2-benzyl-4-methoxycarbonyl-1/alfa (1'-thio-1'--methyl)ethyl/ imidazolylacetate disulfide (III; R=CH_2CCl_3)

The filtrate after the isolation of II (R = CH_2CCl_3) was evaporated to an oily residue (0.85 g; 38.7%) with R_f 0.25 (system A).

For analysis the oily product was adsorbed on a silicagel column. Elution with methylenechloride : ether : methanol (90 : 9 : 1) gave the product as a foam: $[\alpha]_D^{20}$ — — 106.3° (c 0.5, MeOH); R_f 0.25 (system A).

UV spectrum λ_{max}: 210 nm (log ε 4.44), 219 nm (log ε 4.42), 234 nm (log ε 4.37).

IR spectrum (CH_2Cl_2): 3150(v), 1760(s), 1720(vs), 1385(v), 1325(m), 1220(s), 1175(s), 1118(s) cm^{-1}.

^1H NMR spectrum δ: 1.15(s, CH_3), 1.40(s, CH_3), 3.90(s, OCH_3), 4.18(s, CH_2), 4.33 and 4.67(AB_q, J = 12 Hz, OCH_2), 4.77(s, CH), 7.21(s, C_6H_5), 8.21(s, =CH).

p-Nitrobenzyl 2-benzyl-4-methoxycarbonyl-1/alfa(1'-thio-1'-methyl)ethyl/ imidazolylacetate disulfide (III; R=$O_2NC_6H_4CH_2$)

a) After elution of II (R = $O_2NC_6H_4CH_2$), the silicagel column was eluted with methylenechloride : ether : methanol (90 : 9 : 1).

Evaporation of the solvent yielded an oily product (0.92 g; 46%) with R_f 0.27 (system A); $[\alpha]_D^{22}$ — 110° (c 0.5, MeOH).

UV spectrum λ_{max}: 205 nm (log ε 5.17), 241 nm (log ε 4.88), 270 nm (log ε 4.60) (shoulder).

IR spectrum (CH_2Cl_2): 3170(w), 1750(s), 1725(vs), 1530(s), 1355(s), 1205(s), 1185(s), 1015(m), 850(m) cm^{-1}.

^1H NMR spectrum δ: 1.22(s, CH_3), 1.40(s, CH_3), 3.92(s, OCH_3), 4.00 and 4.40(AB_q, J = 16Hz, OCH_2), 4.73(s, CH), 4.97(s, CH_2), 7.17(s, C_6H_5), 7.32 and 8.10(2d, J = 11, C_6H_4), 8.07(s, =CH).

b) To a solution of II (R = $O_2NC_6H_4CH_2$; 0.15 g, 0.3 mmol) in benzene (15 ml), phosphorus pentachloride (0.065 g, 0.3 mmol) was added and the solution heated to 60 °C under nitrogen for 1 hour. To the cooled solution methanol (15 ml) was added and stirred for 30 minutes. Evaporation of the solvent under reduced pressure gave a residue which was dissolved in methylenechloride and washed with water with n $NaHCO_3$ and dried. When the solvent was evaporated an oily residue was chromatographed on a silicagel column according to the procedure described above.

The fraction with R_f 0.27 (system A) (0.050 g; 33%) was identical with the product obtained under a).

Methyl 2-benzyl-4-methoxycarbonyl-1/alfa(1'-thio-1'-methyl)ethyl/ imidazolylacetate disulfide (III; R=CH_3)

After elution of II (R = CH_3) the silicagel column was eluted with methylenechloride : ether : methanol (90 : 9 : 1). After evaporation of the solvent an only residue was obtained as a foam (0.974 g; 58%); $[\alpha]_D^{22}$ — 110° (*c* 0.5, MeOH); R_f 0.27 (system A)

UV spectrum λ_{max}: 212 nm (log ε 4.41), 220 (log ε 4.41), 236 nm (log ε 4.37).

IR spectrum: 3150(w), 1740(vs), 1710(s), 1540(m), 1430(s), 1200(vs), 1110(m), 728(s) 696(m) cm^{-1}.

^1H NMR spectrum δ: 1.13(s, CH_3), 1.30(s, CH_3), 3.46(s, OCH_3), 3.87(s, OCH_3), 3.96 and 4.34 (AB_q, J = 16 Hz, CH_2), 4.60(s, CH), 714(s, C_6H_5), 8.0(s, =CH).

2',2',2'-Trichloroethyl 2-benzyl-4-methoxycarbonyl-1(alfa-izopropylidene) imidazolylacetate (IV; R=CH_2CCl_3)

a) To a solution of II (R = CH_2CCl_3; 0.48 g, 1 mmol) in methylenechloride (10 ml) and triethylamine (0.1 g, 1 mmol), 1-chlorobenzotriazole (0.15 g, 1 mmol) was added. The reaction solution was stirred at 25 °C for 5 hours. The solvent was evaporated under reduced pressure and the residue suspended in benzene. The traces of undissolved material were filtered and the filtrate evaporated. The oily residue was adsorbed on a silicagel column and eluted with methylenechloride : ether (4 : 1). Evaporation of the solvent gave the product (0.417 g; 93%), which crystallized upon the addition of ether, m. p. 111—2 °C; R_f 0.72 (system A).

Anal. $C_{19}H_{19}N_2O_4Cl_3$ (445.72) calc'd.: C 51.19; H 4.29; N 6.28; Cl 23.86%
found: C 51.10; H 4.00; N 6.56; Cl 23.70%

UV spectrum λ_{max}: 219 nm (log ε 4.20), 236 nm (log ε 4.11) (shoulder).
IR spectrum: 3110(w), 2938(w), 1685—1735(b, vs), 1630(m), 1530(m), 1220(vs), 1190(vs), 1110(s), 765(s), 726(s), 717(s) cm^{-1}.
^1H NMR spectrum δ: 1.23(s, CH_3), 2.27(s, CH_3), 3.92(s, OCH_3), 4.0(s, CH_2), 4.40 and 4.63 (AB_q, J = 12Hz, OCH_2), 7.20(s, C_6H_5), 7.43(s, =CH).

b) To a solution of III (R = CH_2CCl_3; 1.59 g, 1.66 mmol) in methylenechloride (20 ml), 1-chlorobenzotriazole (0.61 g, 3.98 mmol) was added and the solution stirred at 25 °C for 30 minutes. The solvent was evaporated and an oily residue adsorbed on a silicagel column. Elution with methylenechloride : ether (4 : 1) afforded an oily product (0.739 g; 50.2%), which crystallized upon the addition of ether: m. p. 111—2 °C; R_f 0.72 (system A).

UV, IR and ^1H NMR spectra were identical with those obtained for the product under a).

p-Nitrobenzyl 2-benzyl-4-methoxycarbonyl-1(alfa-izopropylidene) imidazolylacetate (IV; R=$O_2NC_6H_4CH_2$)

a) II (R = $O_2NC_6H_4CH_2$; 0.967 g, 2 mmol) in methylenechloride and triethylamine was treated with 1-chlorobenzotriazole as described above. The oily product was adsorbed on a silicagel column. Elution with methylenechloride : ether (4 : 1) gave a product which crystallized upon the addition of ether (0.795 g; 88.3%): m. p. 87—90 °C; R_f 0.65 (system A).

Anal. $C_{24}H_{23}N_3O_6$ (449.45) calc'd.: C 64.13; H 5.16; N 9.35%
found: C 63.93; H 5.21; N 9.44%

UV spectrum λ_{max}: 210 nm (log ε 4.48), 218 nm (log ε 4.48), 238 nm (log ε 4.34) (shoulder), 270 nm (log ε 4.08).
IR spectrum: 3150(m), 2940(w), 1700—1730(b, vs), 1630(m), 1605(m), 1520(s), 1340(s), 1225(s), 1185(s), 1090(s), 830(s), 768(s), 730(vs) cm^{-1}.
^1H NMR spectrum δ: 1.33(s, CH_3), 2.27(s, CH_3), 3.93(s, OCH_3), 4.72 and 5.07 (AB_q, J = 14Hz, OCH_2), 7.17(s, C_6H_5), 7.17 and 8.10(2d, J = 9Hz, C_6H_4) and 7.43(s, = CH).

b) III (R = $O_2NC_6H_4CH_2$; 0.289 g, 0.29 mmol) was dissolved in acetic anhydride (5 ml) and heated at 60 °C for 12 hours. The solvent was evaporated under reduced pressure and the residue dissolved in methylenechloride (5 ml) and water (5 ml). The organic layer was separated, washed with water, dried and evaporated. An oily residue was adsorbed on a silicagel column and eluted with methylenechloride : : ether (4 : 1). After evaporation of the solvent, the product crystallized from ether (0.112 g; 42%), m. p. 87—90 °C; R_f 0.65 (system A).

UV, IR and NMR spectral data were identical with those obtained under a).

Methyl 2-benzyl-4-methoxycarbonyl-1-(alfa-izopropylidene) imidazolylacetate (IV; R=CH_3)

a) II (R = CH_3; 0.362 g, 1 mmol) in methylenechloride and triethylamine was treated with 1-chlorobenzotriazole as described above. The oily residue was adsorbed on a silicagel column and eluted with methylenechloride : ether (4 : 1). Evaporation

of the solvent gave an oily product (0.268 g; 82%) with R_f 0.55 (system A), which crystallized upon the addition of n-hexane : acetone; m. p. 115—7 °C. (Lit.[9] m. p. 117 °C).

UV spectrum λ_{max}: 220 nm (log ε 4.37), 236 nm (log ε 4.26).
IR spectrum (liquid film): 3130(w), 2942(m), 1700—1750(b, vs), 1637(w), 1545(m), 1435(m), 1222(s), 1195(s), 725(s), 692(m) cm^{-1}.

^1H NMR spectrum δ: 1.25(s, CH_3), 2.25(s, CH_3), 3.45(s, OCH_3), 3.92(s, OCH_3, CH_2), 7.22 (s, C_6H_5), 7.42(s, =CH).

b) III (R = CH_3; 0.34 g, 0.47 mmol) was dissolved in abs. ethanol (15 ml), Raney nickel added (1 ml) and the reaction mixture stirred at 80 °C for 2 hours. The catalyst was filtered and the filtrate evaporated to an oily residue, which was adsorbed on a silicagel column. Elution with methylenechloride : ether (4 : 1) afforded an oily product (0.237 g; 77%) with R_f 0.55 (system A), crystallized with n-hexane : acetone; m. p. 115—7 °C. UV, IR and NMR spectral data were identical to those reported under a).

c) II (R = CH_2CCl_3; 0.070 g, 0.16 mmol) was dissolved in methanol (5 ml) and 10% methanolic NaOH (0.5 ml) added. The reaction solution was stirred at 25 °C for 1 hour and then neutralized with 20% HCl (pH 6). The solvent was evaporated and the residue dissolved in ether (10 ml) and water (10 ml). The organic layer was separated, washed with water and dried. Evaporation of the solvent gave an oily residue (0.050 g; 95%) with R_f 0.55 (system A), crystallized with *n*-hexane : acetone; m. p. 115—7 °C. UV, IR and NMR spectral data were identical to those reported under a).

Methyl (3-carbomethoxy-2,2-dimethyl-5-thiazolidyl)-phthalimidoacetate (VIII)

To a solution of V (0.826 g, 2.3 mmol) and pyridine (0.182 g, 2.3 mmol) in benzene (60 ml) phosphorus pentachloride (0.478 g, 2.3 mmol) was added at 25 °C with stirring. The solution was heated at 60 °C for 1 hour and then cooled. Methanol was added and stirring continued for a further 1 hour. The solvent was evaporated under reduced pressure and ethylacetate (20 ml) and water (20 ml) added. The organic layer was washed with n $NaHCO_3$ (10 ml), with water (20 ml) and dried. Evaporation of the solvent gave an oily residue with spots on TLC having R_f 0.69, 0.59, 0.51 and 0.45 (system B).

a) *5R, 6R isomer.*

The oily residue was dissolved in benzene and adsorbed on a silicagel column. Elution with benzene: acetone (94 : 4) gave a product (0.326 g; 38%) with R_f 0.69 (system B); $[\alpha]_D^{22} - 2^0$ (*c* 1, MeOH). (Lit.[12] R_f 0.67 (system B); $[\alpha]^{22}{}_D - 2^0$ (*c* 1, MeOH)).
IR spectrum: 3335, 1780, 1715, 1745, 1212, 715 cm^{-1}.

(Lit.[12]: 3340 (NH), 1780, 1715 (imide), 1740, 1215 (ester), 725 (phenyl).

^1H NMR spectrum δ: 1.17(s, CH_3), 1.64(s, CH_3), 3.10(br, NH), 3.70(s, OCH_3), 3.72(s, OCH_3), 3.73(s, H-3), 4.88(d, J = 10 Hz, H-6), 5.27(d, J = 10 Hz, H-5), 7.5—7.95 (m, C_6H_4).

(Lit.[12]: 1.17, 1.64; 3.2; 3.71, 3.73; 3.78; 4.93, 5.31; 7.6—8.0).

b) *5S, 3R isomer*

Further elution of the silicagel column with benzene: acetone (96 : 5) yielded a product (0.243 g; 26.3%) with R_f 0.45 (system B); $[\alpha]_D^{22} - 35^0$ (*c* 1, MeOH).
(Lit.[12]: R_f 0.48 (system B)).

IR spectrum (CH_2Cl_2): 3310(w), 2960(m), 1785(m), 1750(s), 1730(vs), 1440(w), 1390(s), 1210(m), 1110(m), 1090(m), 1020(m), 920(w) cm^{-1}.

^1H NMR spectrum δ: 1.25(s, CH_3), 1.55(s, CH_3), 3.6(br, NH), 3.72(s, H-3), 3.77(s, OCH_3), 3.79(s, OCH_3), 5.06(s, J = 7 Hz, H-6), 5.50(s, J = 7 Hz, H-5), 7.55—8.0(m, C_6H_4).
(Lit.[12]: 1.26, 1.55; 3.5; 3.66; 3.75—3.80; 5.15, 5.85; 7.6—8.0).

Spots with R_f 0.59 and 0.51 were ascribed to the traces of 5R,6S and 5S,6S isomers present in the reaction mixture.
(Lit.[12]: R_f 0.53 and 0.51 (system B)).

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SAŽETAK

Nastajanje derivata izopenilinske kiseline u reakciji benzilpenicilina sa fosforpentakloridom

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Esteri benzilpenicilina (I) reagiraju sa fosforpentakloridom na 60 °C dajući estere benzilizopenilinske kiseline (II) i disulfida izopenilinske kiseline (III). 6-Ftalimidopenicilinat esteri (V) u jednakim reakcionim uvjetima daju odgovarajuće estere α-metil benzilpenicilojeve kiseline (VIII).

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