SYNTHESIS OF SPIRO(PIPERIDINE-4,6'-DIBENZ[*b*,*e*]--1,4-OXATHIEPIN) AND ITS 1-METHYL DERIVATIVE AS POTENTIAL ANTIDEPRESSANT AGENTS

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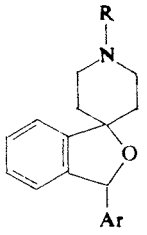
Received June 12th, 1984

Starting from 2-chloronitrobenzene and 2-fluorothiophenol, the synthesis of 2-bromo-2'-fluorodiphenyl sulfide (*X*) was carried out in three steps. The product was converted to the Grignard reagent which reacted with 1-ethoxycarbonyl-4-piperidone and gave the alcohol *XIII*. Cyclization of this compound with sodium hydride in dimethylformamide afforded 1-ethoxycarbonylspiro(piperidine-4,6'-dibenz[*b*,*e*]-1,4-oxathiepin) (*V*) which was hydrolyzed to the title compound *IV*. Reduction of compound *V* with sodium dihydridobis(2-methoxyethoxy)aluminate afforded the 1-methyl derivative *III* which exhibited antireserpine activity and showed the pharmacological profile of a potential antidepressant.

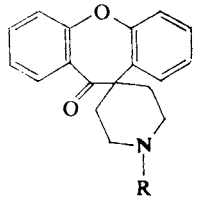
Spiro(isobenzofuranpiperidines) of the general formula *I* (ref.[1-4]), the analogous spiro(benzo[*c*]thiophenepiperidines) (ref.[5]), spiro(indoline-3,4'-piperidines) (ref.[6,7]) and the isomeric spiro(benzofuranpiperidines) (ref.[8,9]) were described as compounds exhibiting interesting pharmacodynamic properties, in the first line effects typical for potential antidepressants. For spiro(dibenz[*b*,*f*]oxepin-10,4'-piperidines) of type *II* analgetic[10] and anticonvulsant activity[11] were given. Our own previous investigation of synthesis of 6*H*-dibenz[*b*,*e*]-1,4-oxathiepin derivatives[12-15] led us now to preparing compounds *III*–*VII*, derived from a new skeleton of spiro(piperidine-4,6'--dibenz[*b*,*e*]-1,4-oxathiepin), which show some structural relation to compounds *I* and *II*, and for which, therefore, some useful pharmacodynamic properties could also be expected.

Our synthesis was started by reaction of 2-fluorothiophenol[16] with 2-chloronitrobenzene in boiling ethanol in the presence of sodium hydroxide leading to 2-fluoro--2'-nitrodiphenyl sulfide (*VIII*) in a good yield. Its reduction to the amine *IX* proceeded almost quantitatively with hydrazine hydrate in boiling ethanol in the presence of a small amount of ferric chloride and active carbon (method[17]). Transformation to 2-bromo-2'-fluorodiphenyl sulfide (*X*) was carried out by making use of the Sandmeyer reaction. After conversion of compound *X* to the Grignard reagent in tetrahydrofuran, an attempt at reaction with 1-methyl-4-piperidone was made; amino alcohol *XII* was obtained in a very low yield and for proving its identity the

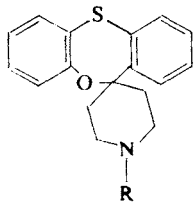
mass and IR spectra were used in addition to analysis. The main product to be isolated was 2-fluorodiphenyl sulfide (*XI*) (*cf.*[18]) resulting from the hydrolysis of the unreacted Grignard reagent. Previously, we already met with the fact that 1-alkyl-4-piperidones react rather uneasily with Grignard reagents while similar reactions with 1-acyl-4-piperidones proceed smoothly[19]. For this reason, a reaction of 2-(2-fluorophenylthio)phenylmagnesium bromide with 1-ethoxycarbonyl-4-piperidone[19] in



I



II

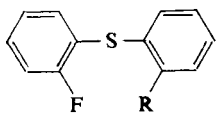


III, R = CH_3
IV, R = H
V, R = $COOC_2H_5$

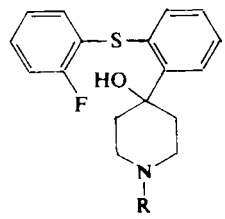
VI, R = $CHCH_2C_6H_5$ (CH_3)
VII, R = CHO

tetrahydrofuran was carried out and the resulting crude carbamate alcohol *XIII* was subjected – without characterization – to cyclization (method[12–15]) by treatment with sodium hydride in dimethylformamide at 90°C. Chromatography of the crude product gave again a considerable quantity of 2-fluorodiphenyl sulfide (*XI*) as the least polar component of the mixture. There was then eluted in a moderate yield a homogeneous oily substance which was identified by analysis and spectra as the desired spirocyclic compound *XIII*. Its reduction with sodium dihydridobis-(2-methoxyethoxy)aluminate in benzene afforded the oily base *III* which was transformed to the maleate. Its identity was proven by the mass spectrum. The carbamate was further hydrolyzed with a concentrated potassium hydroxide solution in ethanol at the boiling point of the mixture and the secondary amine *IV* was obtained in a high yield; it was analyzed in the form of hydrogen maleate. An attempt at the reductive amination of 1-phenylpropan-2-one with the amine *IV* by heating with 98% formic acid to 170°C (method, *cf.*[20]) was not successful and instead of the desired base

VI, the neutral N-formyl derivative *VII* was obtained as the only product. The base *VI* was then prepared in a very low yield by alkylation of the secondary amine *IV* with 2-chloro-1-phenylpropane[21] in dimethyl sulfoxide at 120°C using sodium hydride as the base.



VIII, R = NO_2
IX, R = NH_2
X, R = Br
XI, R = H



XII, R = CH_3
XIII, R = H

Compounds *III* and *IV* were pharmacologically evaluated as potential antidepressants. Acute toxicity in mice on oral administration, LD_{50} in mg/kg: *III*, 183; *IV*, 96 In the test of influencing reserpine ptosis in mice both compounds were administered in an oral dose of 25 mg/kg; while compound *III* antagonized the ptosis significantly, compound *IV* was without a significant effect. In the test of influencing the formation of reserpine gastric ulcers in rats both compounds were administered in an oral dose of 50 mg/kg: compound *III* effected a significant inhibition of the ulcer formation in 50% of the animals used in the experiment and for the rest it was lethal; compound *IV* did not show a significant effect. In an oral dose of 10 mg/kg, compound *III* did not reveal an anticonvulsant effect in the electroshock in mice. Both compounds exhibited only low affinity to "imipramine receptors" in the rat hypothalamus: concentration inhibiting the binding of [^{3}H]imipramine by 50% (IC_{50}) in both cases is higher than 500 nmol l^{-1} (for amitriptyline, IC_{50} = 20·2 nmol l^{-1}).

Compound *IV* was also tested for antimicrobial activity *in vitro*: minimum inhibitory concentrations in μg/ml are given (unless they exceed 100 μg/ml): *Streptococcus β-haemolyticus*, 100; *Streptococcus faecalis*, 50; *Staphylococcus pyogenes aureus*, 25; *Escherichia coli* 50; *Proteus vulgaris*, 50.

EXPERIMENTAL

The melting points of analytical samples were determined in a Mettler FP-5 melting point recorder. The samples were dried *in vacuo* of about 60 Pa over P_2O_5 at room temperature or at 77°C. UV spectra (in methanol) were recorded with a Unicam SP 8000 spectrophotometer, IR spectra (in Nujol unless stated otherwise) with a Perkin Elmer 298 spectrophotometer, the ^{1}H NMR spectra (in C^2HCl_3) with a Tesla BS 487C (80 MHz) spectrometer and the mass spectra with the spectrometers MCH-1320 and/or Varian MAT 44S. The homogeneity of the compounds and composition of the mixtures were checked by thin-layer chromatography on silica gel (Silufol).

The extracts were processed by drying with $MgSO_4$ or K_2CO_3, filtration and evaporation of the filtrates under reduced pressure on a rotating evaporator.

2-Fluoro-2'-nitrodiphenyl Sulfide (*VIII*)

2-Fluorothiophenol[16] (57·5 g) was added to a solution of 19·8 g NaOH in 350 ml ethanol and the solution formed was treated with 70·8 g 2-chloronitrobenzene, diluted with 150 ml ethanol and refluxed for 6 h. Ethanol was evaporated *in vacuo* and the residue was distributed between 200 ml water and 500 ml chloroform. The organic layer was washed with water, 250 ml 1M-NaOH, water, 250 ml 5% hydrochloric acid and again with water, dried and evaporated, The residue was crystallized from 300 ml ethanol; 79·2 g crude product, m.p. 74–76°C. Processing of the mother liquor gave further 12·3 g substance, m.p. 68–74°C; the total yield was 91·5 g (82%) crude *VIII*. Analytical sample, m.p. 75–75·5°C (ethanol). UV spectrum: λ_{max} 239 nm (log ε 4·16), 271 nm (3·86), 276 nm (3·85), 364 nm (3·62). IR spectrum: 734, 755 (4 adjacent Ar—H), 1 305, 1 330, 1 563 ($ArNO_2$), 1 470, 1 563, 1 590, 3 055, 3 100 cm^{-1}(Ar). ^1H NMR spectrum: δ 8·19 (m, 1 H, 3'-H), 7·00–7·70 (m, 6 H, 3,4,5,6,4',5'-H_6), 6·80 (m, 1 H, 6'-H). For $C_{12}H_8FNO_2S$ (249·3) calculated: 57·82% C, 3·23% H, 7·62% F, 5·62% N, 12·87% S; found: 57·41% C, 3·21% H, 7·85% F, 5·33% N, 12·87% S.

2-Amino-2'-fluorodiphenyl Sulfide (*IX*)

A solution of 84·6 g *VIII* in 800 ml ethanol was stirred and treated with 16·0 g active carbon, 61 ml 100% $N_2H_4.H_2O$ and over 15 min with a solution of 4·0 g $FeCl_3.6\,H_2O$ in 80 ml ethanol, added dropwise. The mixture was refluxed for 10 h, filtered, the filtrate was evaporated *in vacuo*, the residue was diluted with 420 ml water, acidified with acetic acid and the product was filtered after cooling and standing for 1 h; 70·9 g (95%), m.p. 42–44°C. Analytical sample, m.p. 43–44°C (ethanol). UV spectrum: λ_{max} 241 nm (log ε 3·95), 306 nm (3·61). IR spectrum: 755 (4 adjacent Ar—H), 1 476, 1 565, 1 601, 3 060 (Ar), 3 355, 3 472 cm^{-1} (NH_2). ^1H NMR spectrum: δ 6·50 to 7·50 (m, 8 H, ArH), 4·28 (bs, 2 H, NH_2). For $C_{12}H_{10}FNS$ (219·3) calculated: 65·73% C, 4·60% H, 8·66% F, 6·39% N, 14·62% S; found: 65·90% C, 4·65% H, 8·97% F, 6·30% N, 14·38% S.

2-Bromo-2'-fluorodiphenyl Sulfide (*X*)

A) A mixture of 76·4 g *IX*, 105 ml 48% hydrobromic acid and 200 ml water was heated to 100°C and then cooled with stirring to −3°C. The stirred suspension of the hydrobromide was diazotized by a slow addition of a solution of 24·5 g $NaNO_2$ in 45 ml water at −3 to +2°C. The obtained suspension was added over 30 min to a stirred mixture of 28 ml 48% hydrobromic acid and 27·5 g CuBr which was heated to 70°C. It was stirred for 2 h at 70°C, allowed to stand overnight at room temperature and extracted with benzene. The extract was filtered and evaporated. The residue was washed three times with 15 ml H_2SO_4, with water and 40 ml 5% NaOH, it was diluted with 100 ml benzene, the solution was dried and distilled; 33·0 g (34%), b.p. 144°C/40 Pa, m.p. 41–43°C (light petroleum). IR spectrum: 743, 751 (4 adjacent Ar—H), 1 470, 1 580, 1 592, 3 055, 3 070 cm^{-1} (Ar). ^1H NMR spectrum: δ 6·70–7·60 (m, ArH). For $C_{12}H_8BrFS$ (283·2) calculated: 50·90% C, 2·85% H, 28·22% Br, 6·71% F, 11·32% S; found: 50·94% C, 2·79% H, 28·48% Br, 7·02% F, 11·49% S.

B) Nitrosylsulfuric acid was prepared by the slow addition of 28·0 g $NaNO_2$ to 175 ml stirred H_2SO_4 at 5–10°C, by heating the mixture to 70°C and cooling to 15–20°C. At this temperature it was treated under stirring over 45 min with a solution of 70·8 g *IX* in 315 ml acetic acid. The mixture was stirred for 3 h at room temperature and then dropped into a stirred mixture of 125 ml

48% hydrobromic acid and 56 g CuBr, heated to 70°C. The stirring and heating to 70°C was continued for 2 h and the mixture was allowed to stand overnight. It was then poured into 1·3 l water and extracted with 900 ml benzene. The extract was washed with 50 ml H_2SO_4, water and 250 ml 8% NaOH, dried and distilled; 66·9 g (73%) *X*, b.p. 142—144°C/40 Pa, m.p. 41—43°C.

4-[2-(2-Fluorophenylthio)phenyl]-1-methylpiperidin-4-ol (*XII*)

Grignard reagent was prepared from 3·0 g Mg and 14·2 g *X* in 60 ml tetrahydrofuran (a small amount of 1,2-dibromoethane was used for starting the reaction); the mixture was refluxed for 1·5 h. After cooling, a solution of 5·6 g 1-methyl-4-piperidone in 10 ml tetrahydrofuran was added dropwise under stirring over 15 min, the mixture was refluxed for 30 min, allowed to stand overnight, decomposed by the addition of 20% NH_4Cl and water, and extracted with ether. Processing of the extract gave 10·4 g oily residue from which cyclohexane induced to crystallize 0·60 g (4%) *XII*, m.p. 141—150°C. Recrystallization from benzene gave 0·48 g 3 : 1 solvate with benzene, m.p. 151—152°C. Mass spectrum, *m/z* (composition): 317 (M^+ corresponding to $C_{18}H_{20}FNOS$), 299 ($C_{18}H_{18}FNS$), 298, 267 ($C_{18}H_{18}FN$), 190 ($C_{12}H_{16}NO$), 187, 71, 70, IR spectrum (KBr): 730, 750, 770 (4 adjacent Ar—H), 1 155 (R_3C—OH), 1 570, 1 580, 1 592, 3 060 (Ar), 2 800, 2 830 (N—CH_3), 3 100 cm^{-1} (OH). For $C_{18}H_{20}FNOS + 1/3\ C_6H_6$ (343·5) calculated: 69·94% C, 6·46% H, 5·53% F, 4·08% N, 9·33% S; found: 69·60% C, 6·44% H, 5·51% F, 4·55% N, 9·16% S.

The mother liquor was washed with dilute hydrochloric acid, dilute NH_4OH and water, dried and distilled; 8·45 g (83%) 2-fluorodiphenyl sulfide (*XI*), b.p. 154—156°C/0·53 kPa. IR spectrum (film): 690, 750 (5 and 4 adjacent Ar-H), 1 470, 1 570, 1 580, 3 060 cm^{-1} (Ar). ^1H NMR spectrum: δ 6·80—8·00 (m, ArH). For $C_{12}H_9FS$ (204·3) calculated: 70·56% C, 4·44% H, 9·30% F, 15·70% S; found: 70·53% C, 4·28% H, 9·14% F, 15·48% S. The literature[18] gave a rather different boiling point (142°C/2·13 kPa).

1-(Ethoxycarbonyl)spiro(piperidine-4,6′-dibenz[*b*,*e*]-1,4-oxathiepin) (*V*)

Grignard reagent was prepared from 9·0 g Mg and 48·1 g *X* in 150 ml tetrahydrofuran and the mixture was refluxed for 1 h. Under stirring it was treated over 5 min with a solution of 29·1 g 1-ethoxycarbonyl-4-piperidone[19] in 40 ml tetrahydrofuran and the mixture was refluxed for 5·5 h. It was then diluted with ether and decomposed with 20% NH_4Cl and water. The organic layer was dried (K_2CO_3) and evaporated. The residue, consisting mainly of *XIII*, was dissolved in 500 ml dimethylformamide, the solution was treated with 8·0 g 80% suspension of NaH in oil and the mixture was stirred and heated for 5 h to 100°C. It was poured into 2·5 l water, acidified with hydrochloric acid and extracted with ether. The extract was processed and the oily residue was chromatographed on 200 g silica gel. Benzene eluted first 23·0 g *XI*, b.p. 140—150°C/50 Pa. The chromatography was continued by elution with a mixture of benzene and chloroform which led to 14·0 g (23%) oily *V*. IR spectrum (film): 760 (4 adjacent Ar—H), 1 220, 1 240 (C—O), 1 560, 3 055 (Ar), 1 690 cm^{-1} (NCOOR). ^1H NMR spectrum: δ 6·80—7·50 (m, 8 H, ArH), 4·18 (q, J = 7·0 Hz, 2 H, OCH_2), *c.* 4·15 (m) and 3·40 (dt) (2 + 2 H, CH_2NCH_2), 1·90—2·50 (m, 4 H, remaining 2 CH_2 of piperidine), 1·25 (t, J = 7·0 Hz, 3 H, CH_3 in ethyl). For $C_{20}H_{21}NO_3S$ (355·5) calculated: 67·58% C, 5·96% H, 3·94% N; found: 67·64% C, 6·11% H, 3·37% N.

1-Methylspiro(piperidine-4,6′-dibenz[*b*,*e*]-1,4-oxathiepin) (*III*)

A stirred solution of 2·4 g *V* in 40 ml benzene was treated dropwise over 10 min with 12 ml 50% solution of sodium dihydridobis(2-methoxyethoxy)aluminate in benzene and the mixture was

heated to 60°C for 5 h. After cooling it was decomposed with water and 20% NaOH, the organic layer was dried with K_2CO_3 and evaporated. The oily residue (1·88 g crude *III*) was dissolved in ether and neutralized with maleic acid in ether; 2·14 g (77%) hydrogen maleate, m.p. 192—195°C (ethanol). Mass spectrum, *m/z* (%): 297·1136 (M^+ corresponding to $C_{18}H_{19}NOS$, calculated 297·1188, 77%), 265, 239, 191, 190 (52), 161 (59), 147 (100), 128 (50), 72 (47), 57 (80). For $C_{22}.H_{23}NO_5S$ (413·5) calculated: 63·90% C, 5·61% H, 3·39% N, 7·75% S; found: 63·96% C, 5·72% H, 2·99% N, 7·57% S.

Spiro(piperidine-4,6′-dibenz[*b*,*e*]-1,4-oxathiepin) (*IV*)

A mixture of 13·8 g *V*, 15 ml ethanol and 15 g KOH was refluxed for 3 h in a bath heated to 130°C. After cooling it was diluted with water and extracted with benzene. The extract was shaken with an excess of 10% hydrochloric acid, the oily hydrochloride was combined with the acid aqueous layer, made alkaline with NH_4OH and extracted with benzene. Processing of the extract gave 10·2 g (93%) crude oily *IV*. Neutralization of a sample with maleic acid in acetone gave the hydrogen maleate, m.p. 177—178·5°C (aqueous ethanol–ether). For $C_{21}H_{21}NO_5S$ (399·5) calculated: 63·14% C, 5·30% H, 3·51% N, 8·03% S; found: 63·11% C, 5·47% H, 3·49% N, 7·98% S.

1-(1-Phenyl-2-propyl)spiro(piperidine-4,6′-dibenz[*b*,*e*]-1,4-oxathiepin) (*VI*)

A solution of 2·95 g *IV* in 50 ml dimethyl sulfoxide was treated with 0·3 g 80% NaOH, the mixture was stirred for 15 min at 60°C, 9·2 g 2-chloro-1-phenylpropane[21] were added and the mixture was stirred for 3·5 h at 120°C. After cooling it was distributed between benzene and 5% NaOH, the benzene solution was washed with 5% hydrochloric acid and water. The acid aqueous solution contained only 2·3 g of the starting *IV* in the form of hydrochloride. The hydrochloride of the desired *VI* remained in the benzene layer and was obtained by evaporation and crystallization from the residue, which was induced by a little ether; 0·20 g (19% per conversion) hydrochloride monohydrate, m.p. 246—252°C (ethanol–ether). Mass spectrum, *m/z* (%): 401 (M^+ corresponding to $C_{26}H_{27}NOS$, proven only by the chemical ionization technique), 310·1274 ($C_{19}H_{20}NOS$, calculated 310·1269, 100%), 173 (10), 155 (10), 147 (7), 91 (18), 56 (75). For $C_{26}H_{28}ClNOS + H_2O$ (456·0) calculated: 68·47% C, 6·63% H, 7·78% Cl, 3·07% N, 7·03% S; found: 68·17% C, 6·36% H, 7·60% Cl, 3·39% N, 7·33% S.

1-Formylspiro(piperidine-4,6′-dibenz[*b*,*e*]-1,4-oxathiepin) (*VII*)

A mixture of 3·0 g *IV*, 2 ml 98% formic acid and 3·0 ml 1-phenylpropan-2-one was heated for 15 h to 170°C, after cooling dissolved in benzene and the benzene layer was shaken with dilute hydrochloric acid. Processing of the acid aqueous layer did not lead to any basic product. The original benzene solution was washed with water, dried and evaporated. The residue was chromatographed on 100 g silica gel. Elution with a mixture of benzene and chloroform recovered 2·8 g starting 1-phenylpropan-2-one. Continued elution with chloroform gave an oily substance which crystallized from a mixture of benzene and cyclohexane; 1·70 g (52%) *VII*, m.p. 148—149·5°C. Mass spectrum, *m/z* (%): 311·0978 (M^+ corresponding to $C_{18}H_{17}NO_2S$, calculated 311·0980, 50%), 282, 266, 253, 252, 251, 239 (100), 217 (24), 161 (26), 160 (47), 147 (25), 128 (23). IR spectrum: 766, 780, 785 (4 adjacent Ar—H), 1 220 (Ar—O—R), 1 561, 1 570, 1 586, 3 053, 3 070 (Ar), 1 659 cm^{-1} (NCHO). ^1H NMR spectrum: δ 8·10 (s, 1 H, NCHO), 6·80—7·60 (m, 8 H, ArH), 4·48 (bd, J = 13·0 Hz) and 3·00—4·00 (m) (1 + 3 H, CH_2NCH_2), 1·80—2·70 (m, 4 H, remaining 2 CH_2 of piperidine). For $C_{18}H_{17}NO_2S$ (311·4) calculated: 69·43% C, 5·50% H, 4·50% N, 10·30% S; found: 69·92% C, 5·64% H, 4·60% N, 10·50% S.

The authors thank Mrs A. Hrubantová for the help with the syntheses, Mrs A. Kargerová, Miss A. Vykulilová and Miss J. Křikavová for the pharmacological experimental work, Dr V. Holá (Microbiological department of the institute) for the microbiological data, Drs E. Svátek, M. Ryska, I. Koruna and Mrs A. Hrádková (Physico-chemical department) for the UV, IR *and a part of the mass spectra, and finally Mrs A. Komancová, Mrs V. Šmídová and Mr M. Čech (Analytical department) for carrying out the analyses.*

REFERENCES

1. Bauer V. J., Duffy B. J., Hoffman D., Klioze S. S., Kosley R. W. jr, McFadden A. R., Martin L. L., Ong H. H.: J. Med. Chem. *19*, 1 315 (1976).
2. Klioze S. S., Bauer V. J., Geyer H. M. III: J. Med. Chem. *20*, 610 (1977).
3. Klioze S. S., Novick W. J. jr.: J. Med. Chem. *21*, 400 (1978).
4. Allen R. C., Bauer V. J., Kosley R. W. jr, McFadden A. R., Shutske G. M., Confeldt M. L., Fielding S., Geyer H. M. III, Wilker J. C.: J. Med. Chem. *21*, 1 149 (1978).
5. Ong H. H., Profitt J. A., Anderson V. B., Kruse H., Wilker J. C., Geyer H. M. III: J. Med. Chem. *24*, 74 (1981).
6. Ong H. H., Profitt J. A., Fortunato J., Glamkowski E. J., Ellis D. B., Geyer K. H. III, Wilker J. C., Burghard H.: J. Med. Chem. *26*, 981 (1983).
7. Glamkowski E. J., Fortunato J. M., Ong. H. H., Allen R. C., Wilker J. C., Geyer H. M. III: J. Med. Chem. *27*, 81 (1984).
8. Effland R. C., Gardner B. A., Strupczewski J.: J. Heterocycl. Chem. *18*, 811 (1981).
9. Ong H. H., Agnew M. N.: J. Heterocycl. Chem. *18*, 815 (1981).
10. Ong H. H., Profitt J. A., Spaulding T. C., Wilker J. C.: J. Med. Chem. *22*, 834 (1979).
11. Nagai Y., Uno H.: Chem. Pharm. Bull. *27*, 2 056 (1979).
12. Šindelář K., Holubek J., Svátek, E., Ryska M., Dlabač A., Protiva M.: This Journal *47*, 1 367 (1982).
13. Šindelář K., Metyšová J., Holubek J., Svátek E., Protiva J., Protiva M.: This Journal *47*, 3 077 (1982).
14. Šindelář K., Holubek J., Svátek E., Ryska M., Dlabač A., Metyšová J., Protiva M.: This Journal *47*, 3 114 (1982).
15. Šindelář K., Holubek J., Ryska M., Dlabač A., Valchář M., Metyšová J., Protiva M.: This Journal *49*, 2531 (1984).
16. Červená I., Metyšová J., Bártl V., Protiva M.: This Journal *44*, 2 139 (1979).
17. Hirashima T., Manabe O.: Chem. Lett. *1975*, 259; Nippon Kagaku Kaishi *1975*, 1 223; Chem. Abstr. *83*, 131 252 (1975).
18. Benati L., Montevecchi P. C.: J. Org. Chem. *42*, 2 025 (1977).
19. Šindelář K., Rajšner M., Červená I., Valenta V., Jílek J. O., Kakáč V., Holubek J., Svátek E., Mikšík F., Protiva M.: This Journal *38*, 3 879 (1973).
20. Novelli A.: Anales Assoc. Quím. Argentina *27*, 169 (1939); Chem. Abstr. *34*, 1 627 (1940).
21. Baddeley G., Williamson R.: J. Chem. Soc. *1956*, 4 647.

Translated by the author (M. P.).