Synthesis of Phenyl-substituted 2*H*-3,4-Dihydro-3-aminomethyl-1,4-benzoxazines. Intermediates for 1*H*-2,3,3a,4-Tetrahydroimidazo-[5,1-*c*][1,4]benzoxazin-1-one Derivatives. Part II.

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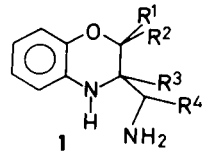
The synthesis of 2*H*-3,4-dihydro-3-aminomethyl-1,4-benzoxazines substituted by one phenyl group in the 2, 3 or α-position is reported. The two diastereoisomers of the 2-phenyl-derivative were independently synthesized from ethyl *trans*-3-phenylglycidate by a stereospecific route. A previous attempt at the synthesis of these same compounds gave rise to an unexpected aliphatic-aromatic ketone rearrangement.

J. Heterocyclic Chem., **20**, 259 (1983).

In part I we reported the synthesis of some imidazo-[5,1-*c*][1,4]benzoxazin-1-one derivatives of the base compound **1a** (1,2). Two of them were found to have good activity as selective, reversible MAO-type A inhibitors. As a further development we prepared the compounds **1b-g**, containing a phenyl group in position 2, 3 or α as intermediates for the corresponding 2,3 and α-imidazo[5,1-*c*][1,4]-benzoxazin-1-one derivatives.



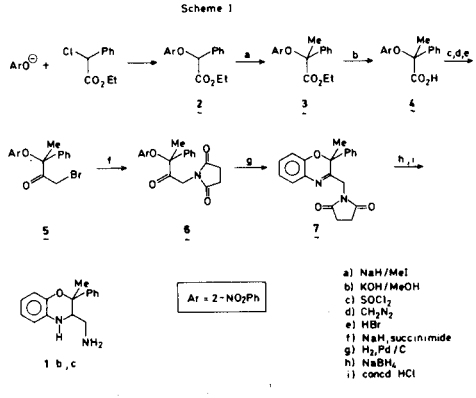
1

	R^1	R^2	R^3	R^4
a	H	H	H	H
b,c	Ph	Me	H	H
d,e	Ph	H	H	H
f	H	H	Ph	H
g	H	H	H	Ph

Synthesis of **1b, c**.

Little is known about the chemistry of the phenyl 1,4-benzoxazine derivatives (3) except for the 2- or 3-benzoxazinones and 2*H*-3-phenyl-1,4-benzoxazine (4). Therefore for the synthesis of **1b, c** we successfully used the route shown in Scheme I previously used by us for the synthesis of 2*H*-3,4-dihydro-3-aminomethyl-2,2-dimethyl-1,4-benzoxazine (1). Also in this case catalytic reduction of the nitroketone **6** stopped at the cyclic imine derivative **7** which was converted to final products **1b, c** by reduction with sodium borohydride followed by acidic hydrolysis. The diastereoisomers were separated by column chromatography, but no assignment of the relative configuration was attempted.

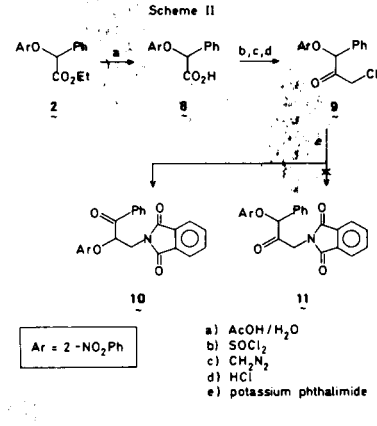
Scheme I



Synthesis of **1d, e**.

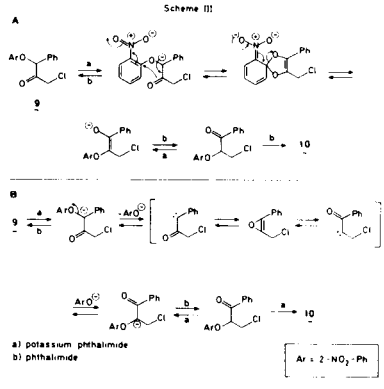
The synthesis of **1d, e** was more difficult than expected. The same route as for **1b, c** was first attempted (Scheme II). Unexpectedly the major product obtained in 25% yield from the reaction of **9** with potassium phthalimide was not the compound **11** deriving from a direct nucleophilic substitution of chlorine, but the rearranged compound **10**. Reaction of **9** with either sodium azide or hexamethylenetetramine [Delépine reaction (5)] did not give the desired products.

Scheme II



Two possible mechanisms are proposed in Scheme III for the rearrangement, one involving an intramolecular reaction and the other one the isomerization of a ketocarbene through an oxirene as demonstrated by Sammes (6) in the case of photochemical decomposition of diazoketones.

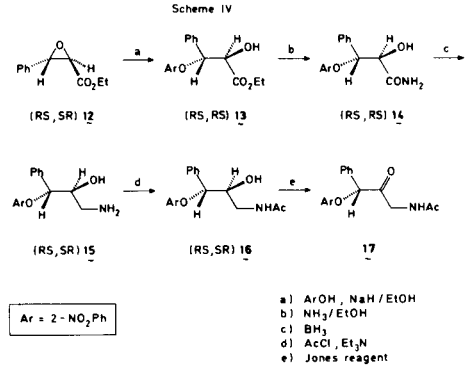
Scheme III



Whatever the mechanism, the formation of the benzylic anion is the first step and formation of an aromatic ketone is the driving force of the rearrangement.

Owing to the difficulties encountered in the preparation of the intermediate **11**, the synthesis of **1d, e**, through the equivalent intermediate **17** was attempted, according to Scheme IV, which however failed since **17**, obtained from **16** either by Jones or Moffat oxidation, proved too unstable to be isolated.

Scheme IV

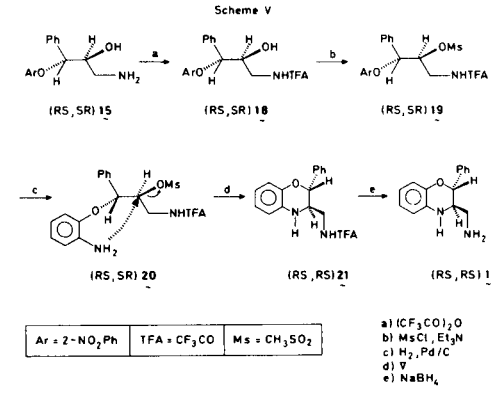


We want nevertheless to stress the fact that the reaction of sodium 2-nitrophenoxide with ethyl *trans*-3-phenylglycidate **12** was regio and stereospecific. In fact only **13** was isolated and no traces of isomers could be detected, as confirmed by nmr and ms spectroscopy.

Finally **1d** was obtained according to Scheme V.

From the chemical and stereochemical view point the crucial step in the synthesis was the cyclization of **20** to **21**. The reaction was very slow and the yield moderate, but it was observed to be stereospecific and **21** was obtained without contamination of the other isomer. Its structure was confirmed by spectroscopic data: the nmr confirmed

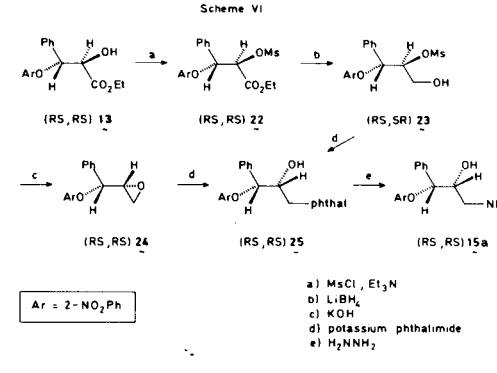
Scheme V



the *trans* configuration of **21** previously attributed to the product on the basis of the configuration assigned to the starting material **15** and of the known stereochemistry of the reactions involved (see Experimental).

As the route of Scheme V was stereospecific it gave the possibility of synthesizing also compound **1e** provided that the diastereoisomer of **15** (which we shall call **15a**) was available. The compound **15a** was prepared according to Scheme VI and was used for the same sequence of reactions that is for the preparation of **18a, 19a**, *etc.* (see Experimental). Unfortunately the ring closure **20a** → **21a**

Scheme VI



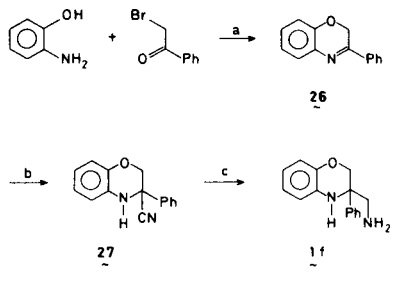
gave a very poor yield. In Scheme VI the very neat inversion of configuration passing from compound **23** to compound **25** was achieved *via* S_N2 closure and opening of an epoxide. We later found that isolation of **24** was not necessary since **25** could be directly obtained from **23** and potassium phthalimide.

Synthesis of **1f**.

For the synthesis of **1f** (see Scheme VII) we started from 2*H*-3-phenyl-1,4-benzoxazine (**26**).

This compound was prepared by Lellmann and Donner (7) by reduction of α-(2-nitrophenoxy)acetophenone and by Tischenko (4) by hydrolysis of α-(2-acetamidophenoxy)-acetophenone. As it is known that 2-aminophenol reacts with equimolecular amounts of α-dicarbonyl compounds to give 2-hydroxy-1,4-benzoxazines (8-11) it may be expec-

Scheme VII



a) NaH ; b) $NaHSO_3$, KCN ; c) H_2 , Ra/Ni , NH_3 /EtOH

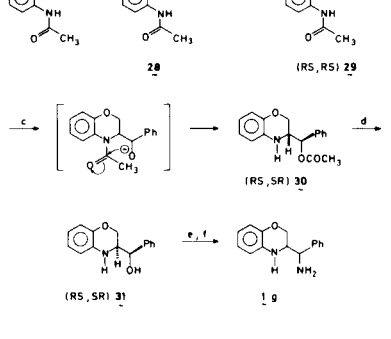
ted to condense also with α-bromoacetophenone to give **26** directly (12). This did actually occur and **26** was obtained in 85% yield.

The introduction of the aminomethyl group in position 3 of the benzoxazine ring was achieved by reduction of the nitrile **27** obtained by addition of hydrocyanic acid to **26** in weakly basic conditions using sodium bisulfite and potassium cyanide in aqueous DMF, a procedure that avoids handling liquid hydrocyanic acid or potassium cyanide/-hydrochloric acid (13).

Synthesis of **1g**.

In the synthesis of **1g** (see Scheme VIII) the dihydrobenzoxazine ring was formed in step **29** → **30** by an intramolecular reaction between an epoxide and an amide, similar to Potter's route to 2*H*-3,4-dihydro-3-hydroxymethyl-1,4-benzoxazine (14).

Scheme VIII



a) cinnamylchloride ,NaH ; b) MCPBA , c) NaH , d) KOH/MeOH , e) $SOCl_2$, f) NH_3/EtOH

In the cyclization **29** → **30** the acetyl group migrated from the nitrogen to the oxygen even though the reverse process usually occurs. This can be explained taking into account the reaction conditions used (0.1 equivalent of sodium hydride was used instead of the nearly 9 equivalents used by Potter) and considering the acid-base equilibria involved in the process. The whole synthesis is stereospecific, but we could not assign the configuration to **1g**, single diastereoisomer from that of compound **31** of known configuration because the stereochemistry of the reaction is uncertain and no attempt was made to prepare the other diastereoisomer.

Compounds **1b-f** were cyclised with urea to imidazo-[5,1-*c*][1,4]benzoxazin-1-one derivatives which were alkylated with chloroacetamide. The compounds tested on mice displayed CNS activity although not as interesting as that for the compounds reported in Part I.

EXPERIMENTAL

Melting points were taken on a Büchi melting point apparatus and are uncorrected. Infrared spectra were recorded on a Perkin-elmer 297 spectrophotometer. The nmr spectra indictated as nmr* were registered on Bruker-90 MHz spectrometer and the others on Perkin-Elmer R 24B and are reported in parts per million downfield from internal tetramethylsilane. Mass spectra were recorded on a CH-7 Varian MAT spectrometer. Elemental analyses are fully reported in Experimental.

Ethyl α-(2-Nitrophenoxy)phenylacetate (**2**).

To a stirred solution of 32.2 g (0.2 mole) of sodium 2-nitrophenoxide in 120 ml of anhydrous DMA was added dropwise a solution of 43.8 g (0.22 mole) of ethyl α-chlorophenylacetate in 50 ml of DMA at 70° under nitrogen. After 1 hour the solution was cooled, poured into cold water and extracted thoroughly with diethyl ether. The extracts were washed with brine, dried over anhydrous sodium sulfate and concentrated under vacuum. The residue was solidified in pentane and recrystallized from cyclohexane to give 31.4 g of **2** (yield 52%), mp 63-65°; ir (nujol): ν max cm^{-1} 1740 (C=O), 1530, 1370 (NO_2); nmr* (deuteriochloroform): δ 1.17 (t, 3H, OCH_2CH_3), 4.17 (q, 2H, OCH_2CH_3), 5.76 (s, 1H, PhC*H*).

Anal. Calcd. for $C_{16}H_{15}NO_5$: C, 63.78; H, 5.02; N, 4.65. Found: C, 63.88; H, 5.01; N, 4.59.

Ethyl 2-(2-Nitrophenoxy)-2-phenylpropanoate (**3**).

To a suspension of 4.4 g (0.093 mole) of 50% sodium hydride in 90 ml of anhydrous DMF, 20 g (0.66 mole) of **2** and 30 ml (0.5 mole) of methyl iodide were quickly added at 0° under vigorous stirring in a nitrogen stream. After 1 hour at 0° and 5 hours at 15-18° the mixture was filtered and concentrated to small volume *in vacuo*. The residue was poured into excess water and the solution extracted with ethyl acetate. After thorough washing with water, treatment with charcoal and drying over sodium sulfate the solvent was eliminated *in vacuo*. The oily residue was solidified with *n*-pentane and crystallized from acetone-water mixture to give 17.2 g (82%) of **3**, mp 41-43°.

Anal. Calcd. for $C_{17}H_{17}NO_5$: C, 64.76; H, 5.43; N, 4.44. Found: C, 64.58; H, 5.35; N, 4.37.

2-(2-Nitrophenoxy)-2-phenylpropanoic Acid (**4**).

Ten g (0.032 mole) of **3** was hydrolized with 6.2 g (0.094 mole) of 85% potassium hydroxide in 30 ml of methanol for 24 hours at room temperature. After the usual work-up 7.6 g (84%) of **4** was obtained, mp 110-112°; nmr* (deuteriochloroform): δ 1.90 (s, 3H, CH_3), 10.0 (s, 1H, COOH).

Anal. Calcd. for $C_{15}H_{13}NO_5$: C, 62.71; H, 4.56; N, 4.87. Found: C, 62.74; H, 4.64; N, 4.77.

1-Bromo-3-(2-nitrophenoxy)-3-phenyl-2-butanone (**5**).

A mixture of 50 g (0.175 mole) of **4** and 340 ml of thionyl chloride was kept at 60° for 5 hours. After elimination of the excess thionyl chloride the oily residue (53 g) was diluted with 400 ml of diethyl ether and added dropwise at 0° to a solution of 25 g (0.6 mole) of diazomethane in 1000 ml of diethyl ether. After 2 hours the solution was warmed to 35° to remove the excess diazomethane, 100 ml of 95% ethanol was added and then 500 ml of 48% hydrobromic acid. After 16 hours at room tempera-

ture and under stirring the two layers were separated and the aqueous phase extracted twice with diethyl ether. After evaporation of the ether the oily residue was solidified with absolute ethanol to give 26 g (41%) of **5**, mp 82-84°.

Anal. Calcd. for $C_{16}H_{14}BrNO_4$: C, 52.78; H, 3.87; N, 3.84; Br, 21.94. Found: C, 53.18; H, 3.95; N, 3.83; Br, 22.27.

1-Succinimido-3-(2-nitrophenoxy)-3-phenyl-2-butanone (**6**).

A mixture of 67 g (0.184 mole) of **5**, 22 g (0.22 mole) of succinimide and 11 g (0.23 mole) of 50% sodium hydride dispersion in 1000 ml of DMA was kept under stirring at room temperature for 24 hours. After concentration *in vacuo* to a small volume, the solution was diluted with water and extracted with ethyl acetate. After normal work-up, **6** was obtained as a solid which was purified by grinding in absolute ethanol, 42 g, (60%), mp 156-168°.

Anal. Calcd. for $C_{20}H_{18}N_2O_6$: C, 62.82; H, 4.74; N, 7.32. Found: C, 63.06; H, 4.84; N, 7.10.

2*H*-2-Methyl-2-phenyl-3-succinimidomethyl-1,4-benzoxazine (**7**).

Thirty-five g (0.092 mole) of **6** dissolved in 800 ml of absolute ethanol and 200 ml of DMF were hydrogenated at 3-3.5 atmospheres with 10% Pd/C as catalyst. The reaction was complete in 5 hours. After filtration, the solvent was concentrated to a small volume from which 21 g (70%) of **7** crystallized as a white solid, mp 156-158°; nmr* (deuteriochloroform): δ 1.98 (s, 3H, CH_3), 2.88 (s, 4H, CH_2CH_2), 4.1 (d, 1H, $J_{A,B}$ = 19 Hz, CH_AH_B-N), 4.34 (d, 1H, CH_AH_BN).

Anal. Calcd. for $C_{20}H_{18}N_2O_3$: C, 71.84; H, 5.42; N, 8.38. Found: C, 71.66; H, 5.45; N, 8.37.

2*H*-3,4-Dihydro-3-aminomethyl-2-methyl-2-phenyl-1,4-benzoxazine (**1b, c**).

To a suspension of 21 g (0.063 mole) of **7** in 200 ml of *p*H 6.4 buffered solution diluted with 200 ml of dioxane, 10.5 g (0.284 mole) of sodium borohydride was added portionwise, maintaining the temperature at approximately 20°. The mixture was stirred for 24 hours then diluted with water and extracted with ethyl acetate. After evaporation to dryness the residue was taken up with 200 ml of 37% hydrochloric acid and refluxed for 1 hour. After dilution with water and washing with diethyl ether, the solution was made basic with 10% sodium hydroxide and extracted with ether. The ether extract was washed with water, dried over anhydrous sodium sulfate and evaporated to dryness. The residue was separated on a silica gel column (chloroform:methanol:ammonium hydroxide 190:10:0.5), to tive 3.5 g of **1b** (Rf>) and 2.5 of **1c**(Rf<) in 40% overall yield.

Compound **1b**.

This compound had mp 96-97°; nmr* (deuteriochloroform): δ 1.54 (s, 3H, CH_3), 2.3-2.9 (m, 2H, CH_2), 3.29 (dd, 1H, CH).

Anal. Calcd. for $C_{16}H_{16}N_2O$: C, 75.56; H, 7.13; N, 11.02. Found: C, 75.22; H, 7.16; N, 10.79.

Compound **1c**.

This compound had mp 113-115°; nmr* (deuteriochloroform): δ 1.62 (s, 3H, CH_3), 2.4 (m, 2H, CH_2), 3.36 (dd, 1H, CH).

Anal. Calcd. for $C_{16}H_{16}N_2O$: C, 75.56; H, 7.13; N, 11.02. Found: C, 75.68; H, 7.28; N, 10.79.

α-(2-Nitrophenoxy)phenylacetic Acid (**8**).

A solution of 6 g (0.02 mole) of **2** in 110 ml of 75% acetic acid was refluxed for 60 hours, then poured into an excess of ice-water. The mixture was extracted with diethyl ether, the ether washed to neutrality and evaporated to dryness after drying over anhydrous sodium sulfate. The residue was crystallized from toluene/petroleum ether to give 4.16 g (76%) of **8**, mp 95-97°; nmr* (deuteriochloroform): δ 5.77 (s, 1H, PhCH), 10.3 (b, 1H, CO_2H).

Anal. Calcd. for $C_{14}H_{11}NO_5$: C, 61.54; H, 4.06; N, 5.13. Found: C, 61.54; H, 4.07; N, 5.08.

3-Chloro-1-(2-nitrophenoxy)-1-phenyl-2-propanone (**9**).

A mixture of 15 g (0.055 mole) of **8** in 75 ml of thionyl chloride was refluxed for 30 minutes and the excess thionyl chloride was evaporated under reduced pressure. The residue crystallized from petroleum ether (40-70°) to yield 14.9 g (0.051 mole) (93%) of acid chloride (mp 61-63°) which was dissolved in 130 ml of anhydrous diethyl ether and added dropwise to a solution of 4.2 g (0.1 mole) of diazomethane in diethyl ether under stirring at 0°. The solution was allowed to stand and the temperature raised to room temperature during 2 hours. After cooling again at 5° gaseous hydrogen chloride was bubbled in for 40 minutes and then 200 ml of water was added. The organic layer was separated, the aqueous solution was extracted twice again with diethyl ether and the mixed extracts were washed with a 5% sodium bicarbonate solution and finally with water to neutrality. The ether was dried and concentrated *in vacuo* to yield 14 g (90%) of **9** as a bright yellow syrup; nmr* (deuteriochloroform): δ 4.63 (d, 1H, CH_AH_B), 4.70 (d, 1H, CH_AH_B), 5.94 (s, 1H, PhC*H*).

Anal. Calcd. for $C_{15}H_{12}ClNO_4$: C, 58.91; H, 3.96; N, 4.58; Cl, 11.60. Found: C, 58.52; H, 4.06; N, 4.63; Cl, 11.28.

2-(2-Nitrophenoxy)-3-phthalimido-1-phenyl-1-propanone (**10**).

Into a suspension of 1.4 g (8.0 mmoles) of potassium phthalimide in 30 ml of DMA, 2.4 g (8.0 mmoles) of **9** dissolved in 50 ml of DMA was dropped in under stirring. After 3 hours at room temperature the mixture was diluted with 20 ml of water and extracted with diethyl ether:ethyl acetate, 1:1. The extracts were washed with water, made anhydrous, treated with charcoal and concentrated *in vacuo*. The residue was ground in diisopropyl ether to yield 1.2 g of a crude product. Crystallization from ethanol 95° gave 0.8 g (25%) of **10**, mp 161-162°; ir (nujol): ν max 1775 and 1710 cm^{-1} (cyclic imide), 1695 (arom CO); nmr* (deuteriochloroform): δ 4.38 (m, 2H, CH_2), 5.97 (dd, 1H, CH-CO).

Anal. Calcd. for $C_{23}H_{16}N_2O_6$: C, 61.95; H, 4.38; N, 7.61. Found: C, 62.11; H, 4.42; N, 7.31.

Ethyl (*RS,RS*)-2-Hydroxy-3-(2-nitrophenoxy)-3-phenylpropanoate (**13**).

To a solution of 28.83 g (0.15 mole) of ethyl (*RS,SR*)-*trans*-3-phenyl glycidate **12** and 27.13 g (0.195 mole) of 2-nitrophenol in 500 ml of absolute ethanol, 1.96 g (0.045 mole) of 55% sodium hydride were slowly added. The mixture was refluxed under stirring for 5 days. The solvent was evaporated under reduced pressure and the residue taken up with 500 ml chloroform. The organic solution was washed with sodium carbonate solution until the nitrophenol was completely removed and then with water to neutrality. After evaporation of the solvent the residue was crystallized from diethyl ether to yield 25.8 g (52%) of **13**, mp 130-132°; nmr (DMSO-d_6): δ 1.13 (t, 3H, CH_3), 4.08 (q, 2H, CH_2), 4.26 (dd, 1H, C*H*-OH), 5.55 (d, 1H, PhC*H*), 6.02 (d, 1H, OH); ms: (70 eV) m/z 228 (M-HOCHCOOC_2H_5, 30).

Anal. Calcd. for $C_{17}H_{16}NO_6$: C, 61.62; H, 5.17; N, 4.23. Found: C, 61.38; H, 5.11; N, 4.16.

(*RS,RS*)-2-Hydroxy-3-(2-nitrophenoxy)-3-phenylpropanamide (**14**).

A solution of 40 g (0.12 mole) of (*RS,RS*)-**13** and 150 ml of liquid ammonia in 1 ℓ of methanol was heated 8 hours at 55° in an autoclave. After evaporation of the methanol the residue was crystallized from diethyl ether to yield 28.3 g (78%) of **14**, mp 127-129°; nmr* (DMSO-d_6): δ 4.40 (1H, C*H*-OH), 5.84 (d, 1H, PhC*H*), 5.90 (d, 1H, OH).

Anal. Calcd. for $C_{15}H_{14}N_2O_5$: C, 59.60; H, 4.67; N, 9.27. Found: C, 59.59; H, 4.72; N, 9.35.

(*RS,SR*)-2-Hydroxy-3-(2-nitrophenoxy)-3-phenyl-1-propylamine (**15**).

Into the solution of 7.5 g (0.025 mole) of (*RS,RS*)-**14** in 120 ml of anhydrous THF, 63 ml of 1*M* borane in THF was added dropwise. The solution was refluxed for 3 hours and then 15 ml of methanol and 5 ml of 14% hydrochloric acid in ethanol were cautiously added. After 30 minutes at reflux temperature and evaporation to dryness the residue was taken up with chloroform. After the usual work-up 7 g (97%) of **15** as a crude oil was obtained which did not solidify and was too hydroscopic as the hydrochloride to be filtered. It was used as a crude oil for the next

step.

(*RS,SR*)-*N*-Acetyl-2-hydroxy-3-(2-nitrophenoxy)-3-phenyl-1-propylamine (**16**).

A solution of 4.7 g (0.016 mole) of crude (*RS,SR*)-**15** and 10 ml of 2*N* sodium hydroxide in 50 ml of dichloromethane was added dropwise at 0° to a solution of 1.34 ml (0.019 mole) of acetyl chloride in 8 ml of dichloromethane. After a normal work-up the solid obtained was crystallized from ethyl acetate to yield 2.6 g (52%) of **16**, mp 150-152° (recrystallized from ethyl acetate).

Anal. Calcd. for $C_{17}H_{18}N_2O_5$: C, 61.81; H, 5.49; N, 8.48. Found: C, 62.11; H, 5.62; N, 8.28.

N-Acetyl-3-(2-nitrophenoxy)-2-oxo-3-phenyl-1-propylamine (**17**).

To a solution of 1.65 g (5 mmoles) of **16** in 25 ml of acetone, 5.5 ml of Jones reagent was slowly dropped in at 10°. The solution was stirred at this temperature for 4 hours and then poured into crushed ice and the excess chromium trioxide decomposed with sodium bisulphite. The mixture was extracted with ethyl acetate, the organic solution washed with water, made anhydrous and evaporated to dryness at reduced pressure. The residual oil (1.4 g) was of limited purity (70% on tlc) and decomposed extensively on a silica-gel column. The 2,4-dinitrophenylhydrazone of the crude **17** was prepared and crystallized from 95% ethanol mp 140-145° dec. The sample was insufficent from a recrystallization. Inorganic residue was 1.35%, thus a more satisfactory value of C was not obtained.

Anal. Calcd. for $C_{23}H_{20}N_6O_8 \cdot H_2O$: C, 52.47; H, 4.21; N, 15.96. Found: C, 51.57; H, 4.00; N, 15.52.

(*RS,SR*)-2-Hydroxy-3-(2-nitrophenoxy)-3-phenyl-*N*-trifluoroacetyl-1-propylamine (**18**).

Into a solution of 2.9 g (0.01 mole) of (*RS,SR*)-**15** and 1.61 ml (0.011 mole) of triethylamine in 40 ml of chloroform, 1.55 ml (0.011 mole) of trifluoroacetic anhdyride was added dropwise under stirring at -5°. When the addition was complete the solution was stirred again for 30 minutes, then poured into 100 ml of water. The organic layer was washed, dried and evaporated to dryness under reduced pressure to give quantitatively (*RS,SR*)-**18** as colorless oil; ir (film): ν max 1710 cm^{-1} (C=O).

(*RS,RS*)-2-Hydroxy-3-(2-nitrophenoxy)-3-phenyl-*N*-trifluoroacetyl-1-propaylamine (**18a**).

Following the same procedure from (*RS,RS*)-**15a**, compound **18a** was obtained as a colourless oil, 90% yield; ir (film): ν max 1710 cm^{-1} (C=O).

(*RS,SR*)-2-Mesyloxy-3-(2-nitrophenoxy)-3-phenyl-*N*-trifluoroacetyl-1-propylamine (**19**).

To a solution of 3.8 g (0.01 mole) of crude (*RS,SR*)-**18** and 1.74 ml (0.012 mole) of triethylamine in 40 ml anhydrous dichloromethane, 0.92 ml (0.011 mole) of mesyl chloride in 5 ml of anhydrous dichloromethane was added dropwise at -5°. After 30 minutes at -5° the mixture was poured in water (100 ml) and after the usual work-up the solid obtained was crystallized from diethyl ether to give 2.55 g (56.6%) of (*RS,SR*)-**19**, mp 176-178°; ir (nujol): ν max 3290 (NH), 1720, 1570 (C=O), 1520, 1345 (NO_2), 1360, 1170 cm^{-1} (CH_3SO_3); nmr (DMSO-d_6): δ 3.03 (s, 3H, CH_3SO_3), 3.55 (m, 2H, CH_2N), 5.12 (m, 1H, C*H*CH_2), 5.95 (d, 1H, PhC*H*).

Anal. Calcd. for $C_{18}H_{17}F_3N_2O_7S$: C, 46.75; H, 3.71; N, 6.06. Found: C, 46.85; H, 3.63; N, 5.98.

(*RS,RS*)-2-Mesyloxy-3-(2-nitrophenoxy)-3-phenyl-*N*-trifluoroacetyl-1-propylamine (**19a**).

Following the same procedure crude (*RS,RS*)-**18a** gave **19a** (78%) mp 163-165°; ir (chloroform): θ max 3420 (NH), 1720, 1570 (CF_3CONH), 1345, 1520 (NO_2), 1350 and 1170 cm^{-1} (CH_3SO_3); nmr* (deuteriochloroform/DMSO-d_6): δ 2.77 (s, 3H, CH_3SO_3), 3.64 (dd, 2H, CH_2N), 5.24 (m, 1H, PhCHC*H*), 5.88 (d, 1H, PhC*H*), 9.44 (t, 1H, -NHCO).

Anal. Calcd. for $C_{18}H_{17}F_3N_2O_7S$: C, 46.75; H, 3.71; N, 6.06; S, 6.93. Found: C, 47.00; H, 3.37; N, 6.02; S, 6.78.

(*RS,SR*)-3-(2-Aminophenoxy)-2-mesyloxy-3-phenyl-*N*-trifluoroacetyl-1-propylamine (**20**).

A solution of 4.6 g (0.01 mole) of (*RS,SR*)-**19** in 80 ml of DMF was hydrogenated at 2 atmospheres and room temperature on a Parr apparatus in presence of 0.4 g of 10% Pd/C as catalyst. When the theoretical amount of hydrogen was absorbed, the solution was filtered and the solvent evaporated under reduced preessure. The solid residue was crystallized from diethyl ether to give 3.86 g (86%) of (*RS,SR*)-**20**, mp 175-178°; nmr (DMSO-d_6): δ 3.05 (s, 3H, CH_3SO_3), 3.2-3.5 (m, 2H, CH_2N), 4.80 (broad, 2H, $ArNH_2$), 5.1 (m, 1H, C*H*CH_2), 5.55 (d, 1H, PhC*H*).

Anal. Calcd. for $C_{18}H_{19}F_3N_2O_5S$: C, 49.99; H, 4.47; N, 6.48; S, 7.41. Found: C, 49.68; H, 4.47; N, 6.37; S, 7.30.

(*RS,RS*)-3-(2-Aminophenoxy)-2-mesyloxy-3-phenyl-*N*-trifluoroacetyl-1-propylamine (**20a**).

Following the same procedure, (*RS,RS*)-**19a** gave **20a** (78%), mp 164-166°.

Anal. Calcd. for $C_{18}H_{19}F_3N_2O_5S$: C, 49.99; H, 4.47; N, 6.48; S, 7.41. Found: C, 49.99; H, 4.29; N, 6.42; S, 7.13.

(*RS,RS*)-2*H*-3,4-Dihydro-2-phenyl-3-trifluoroacetamidomethyl-1,4-benzoxazine (**21**).

A mixture of 4.23 g (0.01 mole) of (*RS,SR*)-**20** and 1.64 g (0.02 mole) of sodium acetate in 200 ml of toluene was refluxed under nitrogen for 24 hours. After cooling, the inorganic salts were filtered out and the solvent evaporated under reduced pressure. The residue was purified on a column of silica gel (chloroform:ethanol 300:10 as eluant) to give 2.4 g of crude material which after crystallization from diisopropyl ether yielded 2.15 g (64%) of (*RS,RS*)-**21**, 99-101°; ir (chloroform): ν max 3420 cm^{-1} (NH), 1720 (C=O), 1540 (ArNH and CONH); nmr* (deuteriochloroform): δ 3.1-3.8 (m, 3H, N-C*H*-C*H*$_2$-N), 4.05 (bs, 1H, Ar-NH), 4.84 (d, 1H, J = 7 Hz, CH-O), 6.39 (bt, 1H, $NHCOCF_3$); ms: m/z 336 (M^+), 210 ([M-$CH_2NHCOCF_3$]$^+$).

Anal. Calcd. for $C_{17}H_{15}F_3N_2O_2$: C, 60.71; H, 4.50; N, 8.33. Found: C, 60.55; H, 4.57; N, 8.16.

(*RS,SR*)-2*H*-3,4-Dihydro-2-phenyl-3-trifluoroacetamidomethyl-1,4-benzoxazine (**21a**).

The same procedure was used for preparation of **21a** from **20a** but refluxed for 9 days and the residue purified on a silica gel column (chloroform:ethyl acetate 180:20 as eluant). The product isolated was crystallized from methanol to give (*RS,SR*)-**21a** (18%), mp 171-174°; ir (chloroform): ν max 3420 cm^{-1} (NH), 1720 (CF_3CONH), 1540 (ArNH and bending NH of sec amide); nmr* (deuteriochloroform): δ 3.0-3.7 (m, 2H, CH_2), 3.89 (bt, 1H, C*H*NHAr), 4.22 (bs, 1H, ArNH), 5.24 (d, 1H, J = 2 Hz, CH-O), 6.30 (bt, 1H, $NHCOCF_3$); ms: m/z 336 (M^+), 210 ([M-$CH_2NHCOCF_3$]$^+$, 100), 182 (210-CO).

Anal. Calcd. for $C_{17}H_{15}F_3N_2O_2$: C, 60.71; H, 4.50; N, 8.33. Found: C, 60.92; H, 4.62; N, 8.07.

(*RS,RS*)-2*H*-3,4-Dihydro-3-aminomethyl-2-phenyl-1,4-benzoxazine (**1d**).

To the solution of 1.4 g (4.0 mmoles) of (*RS,RS*)-**21** in 20 ml of ethanol, 0.46 g (12.0 mmoles) of sodium borohydride was added during 1 hour. After further stirring for an hour, the solution was diluted with 100 ml of ice-water and acetic acid was added to decompose the excess sodium borohydride. The solution was made alkaline by 8% sodium hydroxide and extracted thoroughly with dichloromethane. The combined extracts were washed with brine, dried over anhydrous sodium sulfate and evaporated. The residue was crystallized from diethyl ether to give 0.7 g (74%) of (*RS,RS*)-**1d**, mp 135-136° (recrystallized from diethyl ether); nmr* (deuteriochloroform): δ 1.00-2.00 (broad, 2H, NH_2), 2.51 (dd, 1H, J_{AB} = 13 Hz, J_{AC} = 8 Hz, CH_AH$_B$NH$_2$), 2.71 (dd, 1H, J_{BC} = 4 Hz, $CH_AH_BNH_2$), 3.33 (m, 1H, CH_CCH$_A$H$_B$), 3.49 (s, 1H, ArNH), 4.76 (d, 1H, J = 7 Hz, PhC*H*).

Anal. Calcd. for $C_{15}H_{16}N_2O$: C, 74.97; H, 6.71; N, 11.66. Found: C, 75.11; H, 6.63; N, 11.33.

(*RS,SR*)-2*H*-3,4-Dihydro-3-aminomethyl-2-phenyl-1,4-benzoxazine (**1e**).

Following the same procedure (*RS,SR*)-**21a** gave **1e**. The product was purified by flash chromatography (eluant chloroform:methanol:ammonium hydroxide 170:30:2). The product was precipitated as a mono-hydrochloride from an ethereal solution, yield 24%, mp 268-274°; nmr* (DMSO-d_6): δ 2.50 (m, 2H, CH_2NH$_2$), 3.97 (m, 1H, CHCH$_2$N), 5.20 (d, 1H, J = 2 Hz, PhCHCH), 8.16 (broad, 4H, NH_3^+ + NH); ms: m/z 240 (M^+), 210 ([M-CH$_2$NH$_2$]$^+$), 182 (210-CO).

Anal. Calcd. for $C_{15}H_{16}N_2O$·HCl: C, 65.09; H, 6.19; N, 10.12; Cl, 12.81. Found: C,64.93; H, 6.25; N, 9.79; Cl, 13.16.

Ethyl (*RS,RS*)-2-Mesyloxy-3-(2-nitrophenoxy)-3-phenylpropanoate (**22**).

Into a solution of 6.60 g (0.02 mole) of (*RS,RS*)-**13** and 3.34 ml (0.024 mole) of triethylamine in 70 ml of dichloromethane, 1.76 ml (0.022 mole) of mesyl chloride in 5 ml of dichloromethane was slowly added under stirring at 3-5°. After 15 minutes, the mixture was washed with water, dried over anhydrous sodium sulfate and evaporated to dryness under reduced pressure. The solid residue was crystallized from diethyl ether to give 7.6 g (93%) of (*RS,RS*)-**22**, mp 108-110°; ir (chloroform): ν max 1735 cm^{-1} (C=O), 1520 and 1360 (ArNO_2), 1350 and 1170 (CH_3SO_3); nmr (deuteriochloroform): δ 1.23 (t, 3H, CH_3), 3.00 (s, 3H, CH_3SO_3), 4.25 (q, 2H, OCH_2), 5.39 (d, 1H, CHOMs), 5.78 (d, 1H, PhCH).

Anal. Calcd. for $C_{16}H_{19}NO_6S$: C, 52.80; H, 4.68; N, 3.42; S, 7.83. Found: C, 52.41; H, 4.67; N, 3.45. S, 7.85.

(*RS,SR*)-2-Mesyloxy-3-(2-nitrophenoxy)-3-phenyl-1-propanol (**23**).

To the solution of 8.2 g (0.02 mole) of (*RS,RS*)-**22** in 200 ml of anhydrous THF, 1.13 g (0.03 mole) of sodium borohydride, 5 g (0.03 mole) potassium iodide and 1.27 g (0.03 mole) of lithium chloride were added at room temperature under vigorous stirring. The mixture was stirred for 24 hours then poured into 500 ml of water. After acidification with acetic acid and extraction wtih ethyl acetate the solvent was evaporated to dryness to obtain 7 g of a crude oil. After crystallization from diethyl ether, 5.9 g (81%) of (*RS,SR*)-**23** was obtained, mp 129-134°; nmr (deuteriochloroform): δ 2.5 (broad 1H, OH), 3.03 (s, 3H, CH_3SO_3), 4.0 (m, 2H, CH_2OH), 4.89 (m, 1H, CH-OMs), 5.65 (d, 1H, PhCH).

Anal. Calcd. for $C_{16}H_{17}NO_7S$: C, 52.31; H, 4.66; N, 3.81; S, 8.73. Found: C, 52.29; H, 4.65; N, 3.76; S, 8.70.

(*RS,RS*)-3-(2-Nitrophenoxy)-3-phenyl-1-propene-1,2-oxide (**24**).

To a solution of 33.5 g (0.091 mole) of (*RS,SR*)-**23** in 300 ml of dioxane, 136.7 ml of 2*N* sodium hydroxide was added at room temperature in 20 minutes. After 24 hours the mixture was poured into 2 ℓ of water and extracted twice with ethyl acetate. After normal work-up 23.6 g (96%) of (*RS,RS*)-**24** were obtained, mp 72-75° (recrystallized from methanol); nmr (deuteriochloroform): δ 2.76 (d, 2H, CH_2O), 3.4 (m, 1H, CH-CH_2), 5.0 (d, 1H, PhCH).

Anal. Calcd. for $C_{15}H_{13}NO_4$: C, 66.41; H, 4.83; N, 5.16. Found: C, 66.47; H, 4.80; N, 4.79.

(*RS,RS*)-3-(2-Nitrophenoxy)-3-phenyl-1-phthalimido-2-propanol (**25**).

a) A mixture of 3.67 g (0.01 mole) of (*RS,SR*)-**23**, 2.22 g (0.012 mole) of potassium phthalimide in 100 ml of anhydrous DMA was kept 30 hours under stirring at 80°. Water (400 ml) was added and the aqueous solution was extracted three times with ethyl acetate. After normal work up and crystallization from absolute ethanol, 2.43 g (58%) of (*RS,RS*)-**25** was obtained, mp 153-155°.

b) To a solution of 2 g (7.4 mmoles) of (*RS,RS*)-**24** in 30 ml of DMF, 2.03 g (11 mmoles) of potassium phthalimide was added. The mixture was heated at 100° for 6 hours. The solvent was evaporated under reduced pressure, the residue was taken up with dichloromethane and the organic solution washed with 4% sodium hydroxide than with water to neutrality. After evaporation to dryness the residue was crystallized from absolute ethanol to give 2.1 g (69%) of (*RS,RS*)-**25**, mp 151-154°; nmr* (deuteriochloroform): δ 3.53 (d, 1H, OH), 3.78 (dd, 1H, N-CH_AH_B), 3.97 (dd, 1H, N-CH_AH_B), 4.65 (m, 1H, CH-OH), 5.3 (d, 1H, PhCH).

Anal. Calcd. for $C_{23}H_{18}N_2O_6$: C, 66.02; H, 4.34; N, 6.69. Found: C, 65.74; H, 4.26; N, 6.68.

(*RS,RS*)-2-Hydroxy-3-(2-nitrophenoxy)-3-phenyl-1-propylamine (**15a**).

A solution of 5.1 g (0.012 mole) of (*RS,RS*)-**25** and 7.2 ml of 85% hydrazine hydrate in 120 ml of dioxane was heated to reflux for 10 minutes. The solvent was evaporated under reduced pressure, the residue was taken up with chloroform, the chloroform was washed with diluted sodium hydroxide solution, then with water and evaporated after drying over anhydrous sodium sulfate. The residue was dissolved in diethyl ether:ethyl acetate 20:1, 2.5 ml of 14% ethanol hydrochloric acid was added and the precipitate was filtered. There was obtained 2.9 g (75%) of (*RS,RS*)-**15a** as the hydrochloride, mp 190-193°.

Anal. Calcd. for $C_{15}H_{16}N_2O_4$·HCl: C, 55.47; H, 5.27; N, 8.63; Cl, 10.92. Found: C, 55.56; H, 5.32; N, 8.58; Cl, 11.01.

2*H*-3-Phenyl-1,4-benzoxazine (**26**).

To a solution of 44 g (0.40 mole) of 2-aminophenol in 500 ml of anhydrous DMA, 13.8 g (0.46 mole) of 80% sodium hydride was added under stirring in 10 minutes and under a stream of nitrogen. A solution of 80 g (0.40 mole) of α-bromoacetophenone in 250 ml of anhydrous DMA was added dropwise in 40 minutes to the dark red solution, keeping the temperature below 30° by cooling with ice-wate. After 10 hours at room temperature the mixture was poured into ice-water and the precipitate was filtered and washed with water. After crystallization from water:acetone 1:1, 72.0 g (85.6%) of **26** was obtained, mp 111-112° [lit 111° (4)]; nmr (deuteriochloroform): 4.94 (s, 2H, OCH_2), 6.9 (m, 3H), 7.3 (m, 4H), 7.8 (m, 2H, H 2′ and H 6′).

Anal. Calcd. for $C_{14}H_{11}NO$: C, 80.35; H, 5.30; N, 6.70. Found: C, 80.19; H, 5.45; N, 6.66.

2*H*-3,4-Dihydro-3-cyano-3-phenyl-1,4-benzoxazine (**27**).

A mixture of 11.8 g (0.056 mole) of **26**, 11.6 g (0.11 mole) of sodium bisulfite and 11 g (0.17 mole) of potassium cyanide in 350 ml of DMF and 120 ml of water was stirred at 50° for 4 hours and then at room temperature for 40 hours. The suspension was filtered and the solid washed with 1 ℓ of diethyl ether. The organic layer of mixed filtrates was separated, washed thoroughly with water, dried over anhydrous sodium sulfate and evaporated to dryness *in vacuo*. The solid residue was crystallized from petroleum ether 40-70° to yield 11.75 g (88%) of **27**, mp 95-98°; ir (chloroform): ν max 3450 cm^{-1} (NH), 2240 cm^{-1} (-CN); nmr* (deuteriochloroform): δ 4.01 (d, 1H, OCH_AH_B), 4.40 (m, 2H, OCH$_A$H$_B$ and ArNH).

Anal. Calcd. for $C_{15}H_{12}N_2O$: C, 76.25; H, 5.12; N, 11.86. Found: C, 76.31; H, 5.13; N, 11.84.

2*H*-3,4-Dihydro-3-aminomethyl-3-phenyl-1,4-benzoxazine (**1f**).

Thirty-nine g (0.16 mole) of **27** in 1 ℓ of 5% ammonia in ethanol was hydrogenated at 3-4 atmospheres at room temperature over Raney/Ni. When the theoretical amount of hydrogen was absorbed the catalyst was filtered and the solution evaporated to dryness under reduced pressure. The residue was crystallized from diethyl ether to yield 20.6 g (53%) of **1f**, mp 88-90°; nmr* (deuteriochloroform): δ 0.93 (s, 2H, NH_2), 2.91 (d, 1H, CH_AH_BNH$_2$), 3.28 (d, 1H, CH$_A$H$_B$NH$_2$), 4.10 (d, 1H, OCH_AH_B), 4.20 (d, 1H, OCH$_A$H$_B$), 4.86 (s, 1H, -NH).

Anal. Calcd. for $C_{15}H_{16}N_2O$: C, 74.97; H, 6.71; N, 11.66. Found: C, 75.15; H, 6.80; N, 11.61.

3-(2-Acetamidophenoxy)-1-phenylpropene (**28**).

To a stirred solution of 3.02 g (0.02 mole) of 2-acetamidophenol and 2.76 g (0.02 mole) of anhydrous potassium carbonate in 40 ml of DMF, 3.3 g (0.022 mole) of cinnamyl chloride in 10 ml of DMF was slowly added at 60°. After 2 hours the DMF was evaporated *in vacuo* (0.3 mm Hg) and the residue was treated wtih 100 ml of ice-water. The precipitate was filtered and crystallized from ethanol to yield 4 g (74%) of **28**, mp 136-138°.

Anal. Calcd. for $C_{17}H_{17}NO_2$: C, 76.38; H,6.41; N, 5.24. Found: C, 76.20; H, 6.27; N, 5.11.

(*RS,RS*)-3-(2-Acetamidophenoxy)-1-phenylpropene-1,2-oxide (**29**).

To a solution of 13.4 g (0.068 mole) of 85% *m*-chloroperbenzoic acid in

300 ml of dichloromethane, a solution of 16.5 g (0.060 mole) of **28** in 200 ml of dichloromethane was added dropwise and the reaction mixture was stirred at room temperature overnight. After decomposing the excess of peracid with 10% solution of sodium bisulfite the solid was filtered and washed twice with dichloromethane. The filtrate was washed with a saturated solution of sodium bicarbonate, dried over anhydrous sodium sulfate and evaporated to dryness to give a colorless oil. Crystallization from diethyl ether gave 11.2 g (89%) of (*RS,RS*)-**29**, mp 89-91°; nmr* (deuteriochloroform): δ 2.22 (s, 3H, CH_3CO), 3.45 (dt, 1H, C*H*-CH_2), 3.97 (d, 1H, J = 2.0 Hz, PhC*H*), 4.18 (dd, 1H, CH_AH_B), 4.46 (dd, 1H, CH_AH_B).

Anal. Calcd. for $C_{17}H_{17}NO_3$: C, 72.06; H, 6.09; N, 4.94. Found: C, 71.88; H, 6.07; N, 4.89.

(*RS,SR*)-2*H*-3,4-Dihydro-3-(α-acetoxybenzyl)-1,4-benzoxazine (**30**).

To a well stirred solution of 15.0 g (0.056 mole) of **29** in 300 ml of anhydrous DMF, 0.23 g (5.6 mmole) of 55% sodium hydride was added during 30 minutes. The temperature was slowly raised to 65° and maintained for 10 hours. The solution was then cooled to room temperature, poured into 1500 ml of ice-water and thoroughly extracted with diethyl ether. The extracts were washed with water, made anhydrous over anhydrous sodium sulfate and then concentrated to dryness *in vacuo*. The residual oil was chromatographed on a silica gel column using ethyl acetate:cyclohexane 3:1 as eluant and 11 g (70%) of (*RS,SR*)-**30** was obtained as a solid, mp 83-86°; ir (nujol): ν max 3400 cm^{-1}, 1742 cm^{-1} (C=O); nmr* (deuteriochloroform): δ 2.07 (s, 3H, CH_3CO), 3.08 (broad, 1H, NH), 3.73 (m, 1H, CHN), 4.24 (m, 2H, OCH_2), 5.74 (d, 1H, PhC*H*).

Anal. Clacd. for $C_{17}H_{17}NO_3$: C, 72.06; H, 6.05; N, 4.94. Found: C, 72.05; H, 6.01; N, 4.82.

(*RS,SR*)-2*H*-3,4-Dihydro-3-(α-hydroxybenzyl)-1,4-benzoxazine (**31**).

A solution of 11 g (0.039 mole) of (*RS,SR*)-**30** in 205 ml of 0.2*N* methanolic potassium hydroxide (0.041 mole) was kept at room temperature for 2 hours. The solvent was removed and the residual oil partitioned between water and diethyl ether. The aqueous layer was extracted twice with diethyl ether. The mixed extracts were washed with water, dried over anhydrous sodium sulfate and evaporated *in vacuo*. The syrup was dissolved in a little absolute ethanol and 20 ml of 14% ethanolic hydrochloric acid was added. After 1 hour at 10° the precipitate was filtered to give 9.2 g (85%) of **31** as the hydrochloride, mp 191-193° dec; nmr (deuteriochloroform): δ 2.91 (br, 1H, NH), 3.38 (dt, 1H, C*H*NH), 4.20 (d, 2H, OCH_2), 4.51 (d, 1H, PhC*H*OH).

Anal. Calcd. for $C_{15}H_{15}NO_2$·HCl: C, 64.86; H, 5.81; N, 5.04; Cl, 12.77. Found: C, 64.57; H, 6.01; N, 4.94; Cl, 12.39.

2*H*-3,4-Dihydro-3-(α-aminobenzyl)-1,4-benzoxazine (**1g**).

To a solution of 10 g (0.041 mole) of **31** in 200 ml of anhydrous benzene, 41 ml (0.055 ml) of thionyl chloride was slowly added at room temperature. After 3 hours the solvent was evaporated to dryness *in vacuo* and the crude oil (12.3 g) heated at 80° for 24 hours in autoclave with 400 ml of a 10% ammonia in ethanol. The solution was concentrated *in vacuo*, water was added and the aqueous solution was washed twice with ethyl acetate. It was then made basic with 8% sodium hydroxide and extracted with ethyl acetate. The oily residue obtained after evaporation of the solution to dryness was separated on a silica gel column (chloroform as eluant) to give a main product which, after evaporation of the solvent, was treated with 8% hydrochloric acid in ethanol to give 6.42 g (50%) of **1g** as a dihydrochloride, mp 225-228°; nmr* (DMSO-d_6): δ 4.06 (m, 3H, CH_2C*H*), 4.50 (d, 1H, PhCH), 8.24 (bs, 2H, NH_2^+), 9.22 (bs, 3H, NH_3^+).

Anal. Calcd. for $C_{15}H_{16}N_2O$·2HCl·½H_2O: C, 55.91; H, 5.94; N, 8.69; Cl, 22.35. Found: C, 56.24; H, 6.00; N, 8.55; Cl, 22.62.

The other product collected was 2*H*-3,4-dihydro-3-(α-ethoxybenzyl)-1,4-benzoxazine which weighed 1 g (10%) as the hydrochloride and melted at 158-160°; ms: m/z 269 (M^+), 222, 134 (100%).

Anal. Calcd. for $C_{17}H_{19}NO_2$·HCl: C, 66.76; H, 6.59; N, 4.58; Cl, 11.59. Found: C, 66.61; H, 6.62; N, 4.50; Cl, 11.58.

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REFERENCES AND NOTES

(1) C. Banzatti, A. Della Torre, P. Melloni*, D. Pieraccioli and P. Salvadori, *J. Heterocyclic Chem.*, **20** 139 (1983).

(2) P. Melloni, N. Mongelli, F. Lauria, A. Rossi and R. Tommasini, Carlo Erba SpA, German Offen., 2,658,806 (1977), *Chem. Abstr.*, **87**, 152227 (1977).

(3) For a review on 1,4-benzoxazines see M. Sainsbury, on Rodd's Chemistry of Carbon Compounds, II Ed, Vol IV, H. S. Coffey ed, Elsevier Scientific Publishing Co., Amsterdam, 1978, p 461.

(4) V. G. Tischenko and R. A. Minakova, *Khim. Geterosikl. Soedin*, **7**, 164 1971; *Chem. Abstr.*, **75**, 35900 (1971).

(5) Delépine, *Compt. Rend.*, **120**, 501 (1895).

(6) S. A. Matlin and P. G. Sammes, *J. Chem. Soc. Perkin Trans. I*, 2623 (1972).

(7) E. Lellmann and A. Donner, *Chem. Ber.*, **23**, 172 (1890).

(8) I. Murase, *Bull. Chem. Soc. Japan*, **32**, 827 (1959).

(9) *Ibidem.*, **33**, 59 (1960).

(10) E. Bayer and G. Schrenk, *Chem. Ber.*, **95**, 1184 (1960).

(11) E. Belgodere, R. Bossio, V. Parrin and R. Pepino, *J. Heterocyclic Chem.*, **14**, 997 (1977).

(12) In the course of publication a paper by D. R. Shridhar, C. V. Reddy Sastry, O. P. Bausal and P. Pulla Rao, *Synthesis*, **11**, 912 (1981) reported a one-step synthesis of some 3-aryl-2*H*-1,4-benzoxazines with potassium carbonate in refluxing acetone. Yields range between 34% and 64% (55% in case of 2*H*-3-phenyl-1,4-benzoxazine).

(13) J. Mathieu and J. Weill-Raynall, "Formation of C-C Bonds", Vol. I, G. Thieme Publishers, Stuttgart, 1973, p 450.

(14) G. W. Potter and A. M. Monro, *J. Heterocyclic Chem.*, **9**, 299 (1972).