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SYNTHESIS OF NONRACEMIC 9-(1-METHOXYCARBONYLETHYL)-1,2,3,4-TETRAHYDROCARBAZOLE*

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A new approach has been proposed to the synthesis of indole derivatives containing a chiral substituent at the nitrogen atom, comprizing Fischer indolization of phenylhydrazines with a chiral substituent at the α-nitrogen atom. The initial hydrazines were obtained by the alkylation (Mitsunobu reaction applying optically active esters of lactic acid) of anilines containing an electron-accepting substituent at the amino group. Subsequent removal of the activating acceptor grouping was realized by nitrosation of the chiral secondary aniline followed by reduction of the corresponding N-nitroso compound.

Keywords: N-aryl-2,2,2-trichloroethylcarbamates, nonracemic 9-(1-methoxycarbonylethyl)-1,2,3,4-tetrahydrocarbazole, N-trifluoroacetyl-, N-benzenesulfonyl, N-tosylanilines, chiral N-alkyl-N-phenylhydrazine, (*S*)-lactic acid ethyl ester, Mitsunobu alkylation, desulfonylation, Fischer indolization, removal of activating groups.

A whole series of indole derivatives, containing if only one asymmetric carbon atom, are of interest in medicine and biochemistry. Most of the stereoselective methods of synthesizing chiral indole derivatives are based on the use of natural tryptophan. A possible alternative approach to different chiral derivatives of indole in our view might be based on the use of N-alkylanilines containing a chiral substituent at the nitrogen atom. Examples of the synthesis of indole derivatives containing a chiral substituent at the nitrogen atom are extremely rare. For example, such compounds of the indole series may be obtained by the transformation of 1-alkyl-3-nitropyridinium salts under the action of acetonimines of chiral primary amines [1], however this reaction enables the preparation of indole derivatives containing alkyl (mostly methyl) groups in position 2 of the indole ring. A second approach is based on the direct introduction of a chiral substituent at the indole nitrogen atom by alkylation with optically active alcohols under the conditions of the Mitsunobu reaction [2,3], but this is only possible in the presence of an acceptor group in positions 2 and 3 of the indole ring which provides an increase in the NH acidity of such compounds compared with unsubstituted indole.

Our investigations in recent years have been linked to the search for a universal approach to the synthesis of indole derivatives containing a chiral substituent at the nitrogen atom. N-Alkylanilines are widely used as starting compounds for obtaining N-alkylindoles. The conversion of N-alkylanilines into the corresponding indole derivatives may be effected by various methods [4,5]. Chiral N-alkylanilines may therefore be used as universal synthetic precursors of indole derivatives containing a chiral substituent at the nitrogen atom.

* Dedicated to the remarkable heterocyclist A. F. Pozharskii on the occasion of his 65th birthday.

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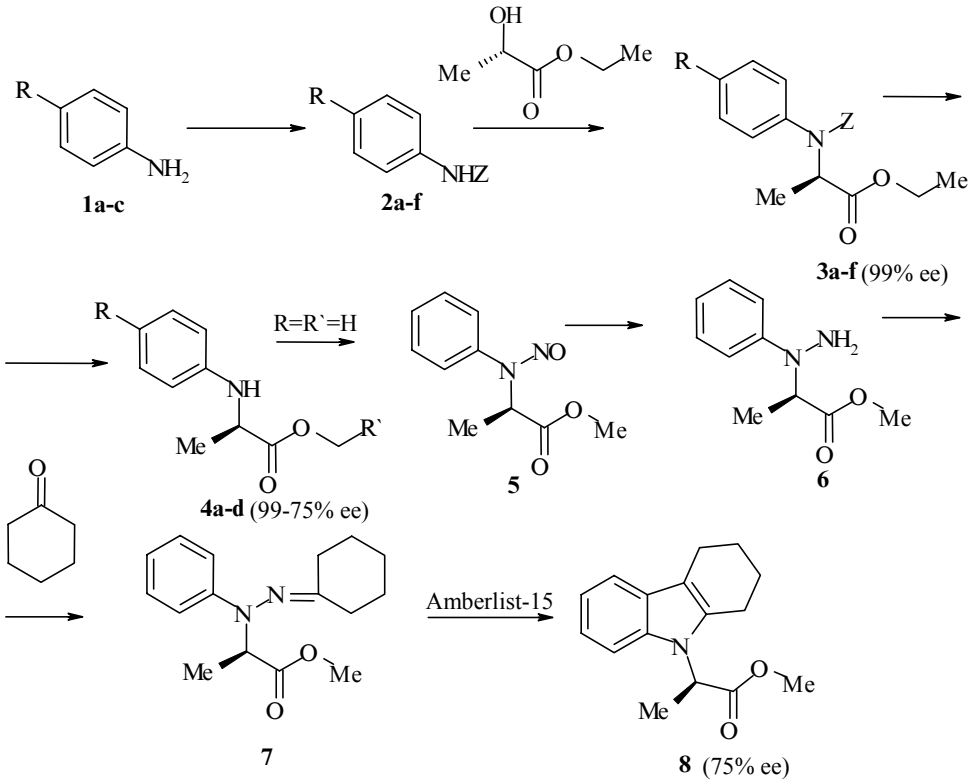
Recently we proposed a method of synthesis of racemic derivatives of 2-(1-indolyl)propionic acid derivatives based on Fischer cyclization of the corresponding arylalkylhydrazones [6]. From these investigations we have developed a modified variant of this method enabling nonracemic derivatives of indole to be obtained.



1 a R = H, **b** R = NO_2, **c** R = MeO; **2**, **3 a-c** R = H, **d**, **e** R = NO_2, **f** R = OMe; **a** Z = $COCF_3$; **b** Z = SO_2Ph; **c** Z = $CO_2CH_2CCl_3$; **d** Z = $COCF_3$; **e**, **f** Z = Ts; **4 a** R = H, R' = Me; **b** R = R' = H; **c** R = NO_2, R' = Me; **d** R = OMe, R' = H

According to the above-mentioned scheme hydrazones of chiral N-alkyl-N-arylhydrazines may serve as precursors of indole derivatives containing a chiral substituent at the nitrogen atom. The corresponding hydrazines, in their turn, may be obtained from chiral N-alkylanilines by nitrosation and subsequent reduction. Chiral N-alkylanilines therefore serve as starting materials in the synthesis of indoles with chiral substituents at the nitrogen atom using the Fischer method.

Contemporary approaches to the synthesis of nonracemic N-alkylanilines with a chiral substituent at the nitrogen atom are linked with the asymmetric hydrogenation of imines using chiral catalysts [7], or with the asymmetric addition of organometallic reagents to imines catalyzed by chiral catalysts [8,9]. In spite of the broad possibilities of these catalytic methods they are rarely able to give optically active compounds with high enantiomeric purity.

One of the most convenient methods of synthesizing optically active amines applicable to contemporary synthetic practice is based on the alkylation of a substrate containing a labile hydrogen atom using the stereospecific Mitsunobu reaction with alcohols with the participation of the oxidation–reduction system triphenylphosphine–azodicarboxylic acid ester. The Mitsunobu reaction has one essential limitation, *viz*. the substrate being used must possess enhanced acidity ($pK_a > 15$). Certain modifications of the Mitsunobu reaction have been developed recently enabling substrates with higher values of pK_a to be introduced into the process of alkylation with alcohols. The following systems have been proposed for use: azodicarboxylic acid dipiperidide–tributylphosphine [10], cyanomethylenetributylphosphorane [11], and azodicarboxylic acid N,N,N',N'-tetramethylamide [12].

The NH-acidity of anilines is insufficient for their possible alkylation under the conditions of the Mitsunobu reaction. We therefore used anilines containing trifluoroacetyl, 2,2,2-trichloroethoxycarbonyl, benzenesulfonyl, and tosyl acceptor activating groups at the nitrogen atom. Cases are known of alkylation under Mitsunobu conditions of sulfonamides, trifluoroacetylanilines [10], and 2,2,2-trichloroethoxycarbamates [13]. Trifluoroacetanilides **2a,d** and 2,2,2-trichloroethyl N-phenylcarbamate **2c** were obtained by the direct acylation of the corresponding anilines in yields greater than 90%. N-Arylsulfonylanilides **2b,e,f** were synthesized by the interaction of the corresponding sulfonyl chlorides with the initial anilines. Tosylation was carried out by two methods: 1) in THF using equimolar amount of triethylamine at room temperature, and 2) in pyridine in the presence of 5% (molar) 4-(N,N-dimethylamino)pyridine with heating. On using the first method N-tosylanilines **2b,f** were obtained, sulfonamide **2e** was not detected under these conditions, only the disubstututed product, N,N-bis(*p*-toluenesulfonyl)-4-nitroaniline was isolated. The use of the second method led to the preparation of anilide **2e** in 73% yield.

All the obtained anilides were used as substrates in the Mitsunobu reaction with commercially available (*S*)-hydroxypropionic (lactic) acid ethyl ester. We investigated the use of various oxidation–reduction systems for these substrates in the Mitsunobu reaction. These were diisopropyl ester of azodicarboxylic acid–triphenylphosphine (**A**), dipiperidide of azodicarboxylic acid–tributylphosphine (**B**), and cyanomethylene-tributylphosphorane (**9**) (**C**).

The conditions for alkylating different anilides **2a-f** and the yields of the alkylation products are given in Table 1. According to the data in the Table the yields of alkylation products **3a-e** from substrates **2a-f** using system **B** exceeded the yields of alkylation products insignificantly than when using the oxidation–reduction system **A**. In addition it may be concluded that activation of anilines by an arenesulfonyl group is more efficient by virtue of the greater NH acidity of arenesulfonylanilides. On going from anilides with activating group $Z = CF_3CO$ and $Z = Cl_3CCH_2CO_2$ (compounds **3a,c**) to benzenesulfonylanilide $Z = PhSO_2$ (compound **3b**) the yields were increased from 30-60 to 68-80%. Evidence that the degree of NH acidity is the deciding factor giving success in alkylation is provided by the fact that introduction of a nitro group into the aromatic ring increases the yield of alkylation products significantly (to 87%, compound **3e**), while the introduction of an electron-donating methoxy group leads to its reduction (to 77%, compound **3f**).

On using system **C** all the substrates participated in the Mitsunobu reaction in high yield, however the difficult availability and instability of phosphorane **9** hindered its use to a significant extent. The maximum yield of alkylation products was achieved using equimolar amounts of all reactants. Increase in the amount of trifluoroacetanilide and oxidation–reduction system used to 1.2- and 1.5-fold in relation to the alcohol did not lead to an increase in the yield of alkylation product **3a** and only hindered its chromatographic isolation extremely, due to the presence of the large quantity of unreacted reactants in the reaction mixture. A study of the effect of the nature of the solvent (benzene, THF, and DMF) and the reaction time on the Mitsunobu alkylation process showed (Table 1) that THF was the most effective solvent for system **A** keeping the reaction mixture at

TABLE 1. Yields of Alkylation Products with (*S*)-Lactic Acid Ethyl Ester **3** under Conditions of the Mitsunobu Reaction

Reaction product	Substrate	Yield of reaction products, %								
		A			**B**			**C**		
		THF	C_6H_6	DMF	THF	C_6H_6		THF	C_6H_6	
3a	**2a**	47	31	—	38	52	—	34	61	—
3d	**2d**	51	37	—	32	57	—	31	70	—
3c	**2c**	11	—	—	27	42	—	56	83	—
3b	**2b**	68	54	12	60	78	—	54	80	—
3e	**2e**	77	58	18	74	81	—	75	87	—
3f	**2f**	65	59	6	60	69	—	64	77	—

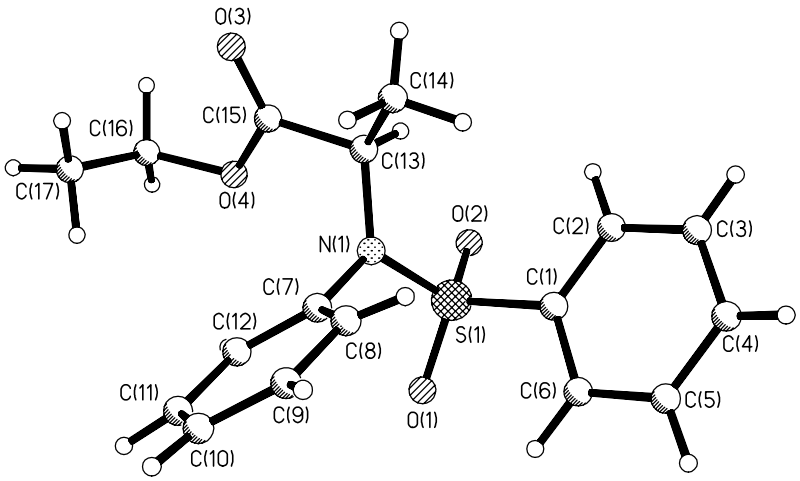


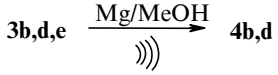
Fig. 1. Spatial model of the compound **3b** molecule.

room temperature for 24 h (yield of compound **3d** was 77%). Boiling for 24 h in benzene was optimal for systems **B** and **C** (yields of compound **3d** were 81 and 87% respectively). Considering all the factors mentioned above a procedure is given in Experimental using the most convenient system **A**.

It is known that the Mitsunobu reaction is accompanied by complete inversion of the configuration of the initial alcohol on forming the alkylation product [3]. Since we used an alcohol of the (*S*)-configuration as alkylating agent the obtained derivatives of 2-aminopropionic acid must possess the (*R*)-configuration. To confirm the (*R*)-configuration of the obtained alkylation products **3a-e** X-ray structural investigation was carried out on compound **3b**, which completely confirmed the expected configuration. An overall view of the compound **3b** molecule is given in Fig. 1.

The following stage of our work was connected with a study of the possible removal of the activating groups. Conversion of trifluoroacetanilides to the corresponding anilines is readily effected by various means such as KOH/EtOH or K_2CO_3/MeOH–H_2O, or $NaBH_4$/EtOH [14,15]. Conversion of 2,2,2-trichloroethyl arylcarbamates into N-alkylanilines also occurs under mild conditions, using the system Zn/NaH_2PO_4–THF [13].

As is known benzene- and toluenesulfonyl groups are fairly difficult to remove from a nitrogen atom and this usually requires extremely forcing conditions, such as the use of Na–liquid ammonia, Na–naphthalene system, or concentrated H_2SO_4, and the yields do not usually exceed 60% [16]. The use of such conditions is usually inappropriate for 2-aminopropionic acid derivatives due to the presence of groups capable of reduction. Most of all, such conditions may lead to racemization of the products of alkylation with chiral alcohols. The removal of sulfonyl groups by the action of magnesium in methanol under ultrasonic irradiation is also known [17]. This method enabled us to obtain methyl esters of (*R*)-2-(N-phenyl)aminopropionic acid **4** from the corresponding N-arylsulfonamides **3** in high yield.



Removal of the sulfonyl group by the action of magnesium in methanol under ultrasonic irradiation proved to be unsuitable for substrate **3e** containing a nitro group. The reaction led to the formation of mixture of unidentified compounds. Attempts were undertaken to remove the tosyl group using trimethyliodosilane [18], however initial sulfonylaniline was isolated exclusively from the reaction mixture. Consequently the sole means of obtaining compound **4c** was mild hydrolysis of substrate **3d** in the system K_2CO_3/MeOH–H_2O.

The formation of methyl esters under desulfonation conditions is in agreement with the report on accompanying transesterification under the action of magnesium and ultrasonic irradiation [17].

When analyzing aniline **4b** obtained in this way by HPLC on a chiral support it was discovered that it contained admixture of the (*S*)-isomer (25%), which indicates partial racemization of the Mitsunobu reaction product during removal of the activating group. In turn, a special ^{1}H NMR spectroscopic investigation of the diastereomers of N-phenylalanine methyl ester **4b** with (*S*)-1,1-binaphthol (ratio 1:1) clearly indicates the presence of two singlets for the signals for the (*R*)- and (*S*)-isomer OCH_3 group protons at 3.14 ppm in a ratio of 4:1.

All the esters of 2-(N-aryl)aminopropionic acid obtained by us revealed optical activity.

The further sequence of conversions from the optically active alkylanilines **4** to indoles containing a chiral substituent at the nitrogen atom was worked out using methyl ester of (*R*)-2-(N-phenyl)aminopropionic acid (**4b**) as example, and comprised synthesis of (*R*)-2-(N-nitroso-N-phenyl)aminopropionic acid methyl ester (**5**), its subsequent reduction to the corresponding hydrazine **6**, the preparation of its hydrazone **7** with cyclohexanone, and cyclization to the desired 9-(1-methoxycarbonylethyl)-1,2,3,4-tetrahydrocarbazole (**8**). The nitrosation of aniline **4b** with ethyl nitrite led to nitrosoamine **5** in quantitative yield. According to the data of ^{1}H NMR spectra compound **5** exists as mixture of geometric isomers. For the reduction of nitrosoamine **5** to the corresponding hydrazine **6** we used the zinc–hydrochloric acid–methanol system at -78°C [6], the application of which led to practically no side reaction of N–N bond fission. Due to instability hydrazine **6** obtained by the reduction was converted without further purification into hydrazone **7**, which also without isolation and purification was cyclized into tetrahydrocarbazole **8**. Indolization of cyclohexanone hydrazone **7** proceeds extremely readily and the formation of significant quantities of the indole derivative **8** is observed even on stirring hydrazine **6** with cyclohexanone in the presence of catalytic amounts of *p*-toluenesulfonic acid.

TABLE 2. Bond Angles (ω) in Structure **3b**

Angle	ω, deg.	Angle	ω, deg.	Angle	ω, deg.
O(2)–S(1)–O(1)	120.8(1)	C(2)–C(1)–S(1)	119.9(2)	C(10)–C(9)–C(8)	120.0(2)
O(2)–S(1)–N(1)	106.8(1)	C(6)–C(1)–S(1)	119.0(2)	C(11)–C(10)–C(9)	119.9(2)
O(1)–S(1)–N(1)	106.5(1)	C(3)–C(2)–C(1)	119.3(2)	C(10)–C(11)–C(12)	120.6(2)
O(2)–S(1)–C(1)	107.7(1)	C(2)–C(3)–C(4)	120.3(2)	C(7)–C(12)–C(11)	119.5(2)
O(1)–S(1)–C(1)	107.3(1)	C(5)–C(4)–C(3)	120.2(2)	N(1)–C(13)–C(14)	114.7(2)
N(1)–S(1)–C(1)	107.1(1)	C(4)–C(5)–C(6)	120.3(2)	N(1)–C(13)–C(15)	111.4(2)
C(15)–O(4)–C(16)	116.5(2)	C(5)–C(6)–C(1)	118.9(2)	C(14)–C(13)–C(15)	110.2(2)
C(7)–N(1)–C(13)	120.0(2)	C(12)–C(7)–C(8)	120.4(2)	O(3)–C(15)–O(4)	124.1(2)
C(7)–N(1)–S(1)	118.0(1)	C(12)–C(7)–N(1)	118.3(2)	O(3)–C(15)–C(13)	123.1(2)
C(13)–N(1)–S(1)	120.6(2)	C(8)–C(7)–N(1)	121.3(2)	O(4)–C(15)–C(13)	112.7(2)
C(2)–C(1)–C(6)	121.1(2)	C(7)–C(8)–C(9)	119.5(2)	O(4)–C(16)–C(17)	111.8(2)

TABLE 3. Bond Lengths (*d*) in Structure **3b**

Bond	*d*, Å	Bond	*d*, Å	Bond	*d*, Å
S(1)–O(2)	1.437(2)	N(1)–C(13)	1.473(3)	C(7)–C(8)	1.394(3)
S(1)–O(1)	1.437(2)	C(1)–C(2)	1.397(3)	C(8)–C(9)	1.400(3)
S(1)–N(1)	1.638(2)	C(1)–C(6)	1.398(3)	C(9)–C(10)	1.394(3)
S(1)–C(1)	1.765(2)	C(2)–C(3)	1.384(4)	C(10)–C(11)	1.379(4)
O(3)–C(15)	1.205(3)	C(3)–C(4)	1.400(3)	C(11)–C(12)	1.396(3)
O(4)–C(15)	1.331(3)	C(4)–C(5)	1.389(4)	C(13)–C(14)	1.515(4)
O(4)–C(16)	1.464(3)	C(5)–C(6)	1.396(3)	C(13)–C(15)	1.533(3)
N(1)–C(7)	1.447(3)	C(7)–C(12)	1.388(3)	C(16)–C(17)	1.506(4)

TABLE 4. Coordinates of Atoms ($\times 10^4$) and Their Isotropic Equivalent (for H isotropic) Thermal Parameters (U) in Structure **3b**

Atom	x	y	z	U
S(1)	2202(1)	5042(1)	1581(1)	19(1)
O(1)	3086(2)	6696(3)	2233(1)	24(1)
O(2)	1093(2)	5570(3)	565(1)	25(1)
O(3)	-1403(2)	2152(3)	2634(2)	31(1)
O(4)	-550(1)	5460(3)	2689(1)	25(1)
N(1)	1615(2)	3856(3)	2443(2)	19(1)
C(1)	3159(2)	3107(4)	1216(2)	19(1)
C(2)	2542(2)	1567(5)	379(2)	25(1)
C(3)	3299(2)	8(5)	134(2)	28(1)
C(4)	4669(2)	-11(5)	710(2)	26(1)
C(5)	5278(2)	1545(4)	1530(2)	24(1)
C(6)	4526(2)	3117(4)	1795(2)	23(1)
C(7)	2464(2)	3682(4)	3631(2)	19(1)
C(8)	3300(2)	1917(4)	4039(2)	21(1)
C(9)	4102(2)	1804(4)	5196(2)	24(1)
C(10)	4057(2)	3446(4)	5932(2)	23(1)
C(11)	3242(2)	5201(5)	5514(2)	23(1)
C(12)	2437(2)	5333(4)	4361(2)	24(1)
C(13)	388(2)	2589(4)	1989(2)	23(1)
C(14)	576(2)	167(5)	2120(2)	25(1)
C(15)	-611(2)	3344(4)	2489(2)	20(1)
C(16)	-1442(2)	6313(5)	3202(2)	30(1)
C(17)	-1025(3)	5655(5)	4430(2)	33(1)
H(2)	1590(30)	1580(50)	-10(20)	28(7)
H(3)	2870(30)	-1000(60)	-420(30)	29(8)
H(4)	5110(30)	-1110(50)	540(30)	26(7)
H(5)	6220(30)	1620(50)	1880(20)	22(6)
H(6)	4960(20)	4240(40)	2400(20)	11(6)
H(8)	3420(30)	860(50)	3600(20)	18(6)
H(9)	4600(30)	560(50)	5470(20)	23(7)
H(10)	4530(30)	3260(50)	6710(20)	22(7)
H(11)	3250(30)	6520(50)	6010(20)	24(7)
H(12)	1950(20)	6560(40)	4046(19)	17(5)
H(13)	-21(19)	3010(40)	1210(18)	10(4)
H(141)	980(30)	-130(60)	2940(20)	28(7)
H(142)	1220(40)	-170(90)	1730(30)	68(12)
H(143)	-200(30)	-590(50)	1690(20)	18(7)
H(161)	-2360(30)	5570(60)	2780(30)	33(8)
H(162)	-1410(30)	7690(70)	3010(30)	38(9)
H(171)	-50(40)	6090(60)	4820(30)	44(9)
H(172)	-1560(30)	6700(70)	4750(30)	43(9)
H(173)	-1220(30)	4070(60)	4550(30)	32(8)

Determination of the enantiomeric composition of indole **8** by HPLC using a chiral mobile phase showed the presence of both (*S*)- and (*R*)-enantiomers in the ratio 1:3.97 (~75% ee).

The results obtained by us therefore permit the suggestion that partial racemization occurs only at the desulfonation step. The ratio of enantiomers remains the same in all the remaining steps of the conversion of hydrazine to indole.

EXPERIMENTAL

The IR spectra were obtained on a UR 20 instrument for nujol suspensions or pure compounds. Chromato-mass spectral investigations of reaction mixtures and isolated compounds was carried out using a Carlo Erba/Kratos Fractovap Series 4200 gas-liquid chromatograph, Hewlett Packard Ultra 1 column (25 m × 0.2 mm, thickness of stationary phase 0.33 μm), carrier gas was helium (1 ml/min), stream divider 1:10, evaporator temperature 280°C, temperature gradient from 150 to 280°C (5°C/min), ITD 700 (Finnigan MAT) mass spectral detector, ionization by electron impact, 70 eV, mass range *m/z* 45-400. The ^{1}H and ^{13}C NMR spectra were obtained on a Bruker AMX 400 (400 and 100 MHz respectively) spectrometer in DMSO-d_6, if no other solvent is indicated, internal standard was TMS. Specific rotation was measured on a Jasco DIP 360 polarimeter (589 nm). Melting points were measured in open capillaries, values given are not corrected. A check on the course of reactions and the purity of isolated compounds was effected by TLC on Silufol UV 254 plates and by gas chromatography with the mass spectral detector.

X-Ray Structural Investigations. In molecule **3b** the dihedral angle between the planes of the benzene rings C(1)–C(2)–C(3)–C(4)–C(5)–C(6) and C(7)–C(8)–C(9)–C(10)–C(11)–C(12) was 138.3°. The remaining geometric parameters in the investigated molecule have the usual values [19]. The colorless crystals of compound **3b** were monoclinic, at -163°C: a = 10.962(4), b = 6.191(2), c = 12.699(5) Å; β = 112.23(1)°; V = 798(1) Å^3; d_{calc} = 1.388 g/cm^3; Z = 2; space group $P2(1)$. Unit cell parameters and intensities of 4308 independent reflections were measured on a SMART 1000 CCD diffractometer (λMoKα = 0.71073 Å, graphite monochromator, ω-scanning with 0.3° step, exposure time 10 sec. The structure was solved by the direct method, revealing all the non-hydrogen atoms, and refined by a full-matrix least-squares method in anisotropic approach for the non-hydrogen atoms. Hydrogen atoms were revealed objectively with Fourier difference syntheses and refined isotropically. The final values of the divergence factors were R_1 = 0.05 for 3910 reflections with $I > 2\sigma$ and R_w = 0.131 for 4308 reflections. All calculations were carried out with the programs SAINT [20] and SHELXTL-97 [21] (PC version). Bond angles and bond lengths for compound **3b** are given in Tables 2 and 3.

Trifluoroacetanilide (2a) [22], 4-Nitrotrifluoroacetanilide (2d) were obtained by the methods described [23]. Melting points and spectral characteristics agreed with literature data.

N-Benzenesulfonylaniline (2b). Triethylamine (11.11 g, 110 mmol) was added dropwise to solution of aniline (10.22 g, 110 mmol) in THF (150 ml). The mixture was stirred for 15 min in an ice bath, then benzenesulfonyl chloride (19.38 g, 110 mmol) was added dropwise, and the mixture stirred for 6 h at room temperature. The reaction mixture was poured into ice–water (120 ml), the resulting oil was extracted with chloroform (3 × 100 ml), the organic layer was washed with 5% hydrochloric acid solution (200 ml), with water (3 × 100 ml), and dried with anhydrous sodium sulfate. After removing volatile components in vacuum and storing in a desiccator over P_2O_5, the residue was recrystallized from benzene–hexane. White crystals (22.1 g, 86%) were obtained; mp 105°C (benzene). According to [24] mp 103°C. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 7.19 (2H, dt, *J* = 7.0, *J* = 2.0, Ar); 7.25-7.35 (3H, m); 7.42 (2H, tt, *J* = 7.0, *J* = 2.0, Ar); 7.53 (1H, tt, *J* = 7.0, *J* = 2.0, Ar); 7.70 (2H, dt, *J* = 7.0, *J* = 2.0, Ar); 11.10 (1H, br s, NH).

N-(4-Toluenesulfonyl)-4-methoxyaniline (2f) was obtained analogously. Yield 96%; mp 110-112°C (benzene–hexane). According to [25] mp 110-112°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.32 (3H, s, CH_3); 3.31 (3H, s, CH_3O); 7.09 (2H, d, *J* = 8.7, Ar); 7.39 (2H, d, *J* = 8.1, Ar); 7.76 (2H, d, *J* = 8.1, Ar); 8.13, 7.09 (2H, d, *J* = 8.7, Ar); 9.40 (1H, br. s, NH).

N,N-Bis(4-toluenesulfonyl)-4-nitroaniline. Yield 80%; mp 224-226°C (ethanol). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.46 (6H, s, CH_3); 7.32 (2H, d, *J* = 8.8); 7.51 (4H, d, *J* = 8.1); 7.71 (4H, d, *J* = 8.1); 8.30 (2H, d, *J* = 8.8).

N-(4-Toluenesulfonyl)-4-nitroaniline (2e). *p*-Nitroaniline (6.9 g, 50 mmol) was dissolved in pyridine (30 ml), then 4-(N,N-dimethylamino)pyridine (0.3 g, 2.5 mmol) and *p*-toluenesulfonyl chloride (9.53 g, 50 mmol) were added. The mixture was stirred at room temperature for 15 min, then 5 h at 90-100°C. The

reaction mixture was poured into mixture of concentrated HCl (40 ml) with ice, the precipitated solid was filtered off, washed on the filter with ice-water, air-dried, and recrystallized from ethanol. A bright yellow crystalline substance (10.5 g, 73%) was obtained; mp 189-190°C (ethanol). According to [26], mp 189-190°C. IR spectrum, ν, cm^{-1}: 3340 (NH), 1170, 1350 (SO_2), 1320, 1520 (NO_2). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.33 (3H, s, CH_3); 7.30 (2H, d, *J* = 9.0); 7.39 (2H, d, *J* = 8.1); 7.76 (2H, d, *J* = 8.1); 8.13 (2H, d, *J* = 9.0); 11.24 (1H, s, NH).

2,2,2-Trichloroethyl N-Phenylcarbamate (2c) was obtained according to the method of [27]. The melting point and spectral characteristics agreed with the literature data.

Cyanomethyltributylphosphonium Chloride [11], Cyanomethylenetributylphosphorane [11], and Azodicarboxylic Acid Dipiperidinediamide were obtained according to the methods described [28]. The melting points and spectral characteristics agreed with the literature data.

N-Acyl-N-arylalanine Ethyl Esters (General Procedure). A. Solution of diisopropyl ester of azodicarboxylic acid (2.61 g, 13 mmol) in freshly distilled THF (5 ml) was added dropwise to mixture of triphenylphosphine (3.36 g, 13 mmol), substrate (13 mmol) and (*S*)-lactic acid ethyl ester (13 mmol) in THF (50 ml) with ice and water cooling and stirring. The reaction mixture was left at room temperature for 24 h, after which the solvent was removed under reduced pressure. The residue was chromatographed on a column of silica gel in the solvent system ethyl acetate–petroleum ether, 1:5.

B. Mixture of tributylphosphine (1.5 mmol) and azodicarboxylic acid dipiperidide (1.5 mmol) was added with stirring in an atmosphere of argon to solution of (*S*)-lactic acid ethyl ester (1 mmol) and substrate (1.5 mmol) in dry benzene (3 ml). The reaction mixture was maintained at 100°C for 24 h, the solvent was removed under reduced pressure, and the residue chromatographed on a column of silica gel in the solvent system ethyl acetate–petroleum ether, 1:5.

C. Cyanomethylenetributylphosphorane (0.36 g, 1.5 mmol) was added with stirring in an atmosphere of argon to solution of (*S*)-lactic acid ethyl ester (1 mmol) and substrate (1.5 mmol) in dry benzene (10 ml). The reaction mixture was maintained at 100°C for 24 h, the solvent was removed under reduced pressure, and the residue chromatographed on a column of silica gel in the solvent system ethyl acetate–petroleum ether, 1:5.

(*R*)-2-(N-Phenyl-N-trifluoroacetyl)aminopropionic Acid Ethyl Ester (3a). Yield 61% (C) of a viscous oil. IR spectrum, ν, cm^{-1}: 1730 (C=O). Mass spectrum, *m/z* (*I*, %): 193 (13) $[M\text{-}COCF_3]^+$, 120 (100), 77 (10). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.16 (3H, t, *J* = 7.1, $CH_2\underline{CH_3}$); 1.37 (3H, d, *J* = 7.1, $CH\underline{CH_3}$); 4.03 (1H, q, *J* = 7.1, $\underline{CH}CH_3$); 4.09 (2H, q, *J* = 7.1, $CH_3\underline{CH_2}$); 6.52-6.60 (3H, m, Ar); 7.08 (2H, t, *J* = 7.8, Ar). ^{13}C NMR spectrum, δ, ppm: 15.01 (CH_3CH_2); 18.88 (CH_3CH); 52.25 (CH); 61.21 (CH_2CH_3); 113.7 (2C, CH); 116.07 (CF_3, q, *J* = 289); 117.81 (C, CH); 129.85 (2C, CH); 148.06 (C); 159.30 ($COCF_3$, q, *J* = 38); 175.15 (C=O). Found, %: C 53.41; H 5.18; N 4.46. $C_{13}H_{14}F_3NO_3$. Calculated, %: C 53.98; H 4.88; N 4.84. $[\alpha]_D^{23}$ 2.5 ($CHCl_3$, c 0.03).

(*R*)-2-(N-Benzenesulfonyl-N-phenyl)aminopropionic Acid Ethyl Ester (3b). Yield 80% (C), mp 55°C (ethanol). IR spectrum, ν, cm^{-1}: 1140, 1340 (SO_2), 1730 (C=O). Mass spectrum, *m/z* (*I*, %): 333 (5) $[M]^+$, 260 (70) $[M\text{-}PhSO_2]^+$, 119 (100). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 1.20 (3H, t, *J* = 7.0, $\underline{CH_3}CH_2$); 1.28 (3H, d, *J* = 7.0, CH_3); 4.10 (2H, q, *J* = 7.0, $CH_3\underline{CH_2}$); 5.09 (1H, q, *J* = 7.0, CH); 7.19 (2H, dt, *J* = 7.0, *J* = 2.0); 7.25-7.35 (3H, m); 7.42 (2H, tt, *J* = 7.0, *J* = 2.0); 7.53 (1H, tt, *J* = 7.0, *J* = 2.0); 7.70 (2H, dt, *J* = 7.0, *J* = 2.0). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 16.03 (CH_3CH_2); 19.27 (CH_3); 59.34 (CH); 63.68 (CH_2); 130.13 (2C, CH); 130.81 (2C, CH); 131.21 (2C, CH); 134.24 (2C, CH); 134.80 (CH); 134.90 (CH); 138.07 (C); 142.45 (C); 173.68 (C=O). Found, %: C 61.31; H 6.00; N 4.08. $C_{17}H_{19}NO_4S$. Calculated, %: C 61.23; H 5.76; N 4.20. $[\alpha]^{21}{}_D$ –15.2 (CH_3OH, c 1.2).

(*R*)-2-(N-Phenyl-N-2,2,2-trichloroethoxycarbonyl)aminopropionic Acid Ethyl Ester (3c). Yield 83% (C), viscous liquid. Mass spectrum, *m/z* (*I*, %): 298 (16), 296 (43), 294 (44) $[M\text{-}CO_2Et]^+$, 192 (7), 133 (33), 131 (35), 120 (95), 119 (99), 104 (81), 95 (35), 77 (100), 61 (24), 51 (45), 44 (26). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.21 (3H, *J* = 7.0, $\underline{CH_3}CH_2$); 1.33 (3H, m); 4.15 (2H, q, *J* = 7.0, $CH_3\underline{CH_2}$); 4.69 (1H, q, *J* = 7.0,

CH); 4.77-4.89 (2H, m, CH_2CCl_3); 7.31-7.37 (3H, m, Ar); 7.39-7.46 (2H, m, Ar). ^{13}C NMR spectrum, δ, ppm: 14.51 (CH_3CH_2) 16.06 (CH_3); 58.12 (CH_2); 61.43 (CHN); 75.12 (CH_2CCl_3); 96.23 (CCl_3); 128.16 (CH); 128.88 (2C, CH); 129.39 (2C, CH); 140.09 (C); 153.48 ($CO_2CH_2CCl_3$); 171.45 (C=O). Found, %: C 45.82; H 4.43; N 3.86. $C_{14}H_{16}Cl_3NO_4$. Calculated, %: C 45.61; H 4.37; N 3.80. $[\alpha]_D^{22}$ 2.1 ($CHCl_3$, c 0.09).

(*R*)-2-(N-4-Nitrophenyl-N-trifluoroacetyl)aminopropionic Acid Ethyl Ester (3d). Yield 70% (C), viscous liquid. Mass spectrum, *m/z* (*I*, %): 334 (17) $[M]^+$, 289 (13), 260 (43) $[M\text{-}CO_2Et]^+$, 234 (43), 217 (59), 204 (11), 171 (14), 165 (28), 122 (27), 101 (53), 73 (100). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.88 (3H, t, *J* = 7.0, $\underline{CH_3}CH_2$); 2.25 (3H, d, *J* = 7.0, CH_3); 4.85 (2H, q, *J* = 7.0, $CH_3\underline{CH_2}$); 5.80 (1H, q, *J* = 7.0, CH); 7.47 (2H, d, *J* = 9.0); 8.77 (2H, d, *J* = 9.0). ^{13}C NMR spectrum, δ, ppm: 14.90 (CH_3CH_2); 17.53 (CH_3CH); 62.24 (CH); 73.56 (CH_2CH_3); 116.51 (CF_3, q, *J* = 287); 121.05 (2C, CH); 125.87 (2C, CH); 144.69 ($COCF_3$, q, *J* = 36); 144.83 (C); 150.39 (C); 170.16 (C=O). Found, %: C 46.81; H 3.94; N 8.40. $C_{13}H_{13}F_3N_2O_5$. Calculated, %: C 46.71; H 3.92; N 8.38. $[\alpha]_D^{22}$ 1.7 ($CHCl_3$, c 0.5).

(*R*)-2-(N-4-Methoxyphenyl-N-4-toluenesulfonyl)aminopropionic Acid Ethyl Ester (3f). Yield 77% (C); mp 69°C (ethanol–hexane). IR spectrum, ν, cm^{-1}: 1160, 1340 (SO_2), 1605 (Ar), 1750 (C=O). Mass spectrum, *m/z* (*I*, %): 377 (2) $[M\text{-}H]^+$, 304 (10), 187 (45), 174 (42), 149 (65), 128 (85), 105 (95), 101 (100), 91 (100). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.10-1.20 (6H, m); 2.09 (3H, s, CH_3); 3.74 (3H, s, OCH_3); 4.03 (2H, q, *J* = 7.0, $CH_3\underline{CH_2}$); 4.99 (1H, q, *J* = 7.0, CH); 6.88 (2H, d, *J* = 7.0); 6.99 (2H, d, *J* = 7.0); 7.37 (2H, d, *J* = 7.0); 7.55 (2H, d, *J* = 7.0). ^{13}C NMR spectrum, δ, ppm: 13.83 (CH_3CH_2); 16.72 (CH_3); 20.99 (CH_3Tos); 55.26 (CH_3O); 56.78 (CH); 60.88 (CH_3CH_2); 114.08 (2C); 127.33 (2C); 127.79, 129.45 (2C); 132.80 (2C); 137.20, 143.23, 159.25, 170.97 (C=O). Found, %: C 60.39; H 6.26. $C_{19}H_{23}NO_5S$. Calculated, %: C 60.46; H 6.14. $[\alpha]_D^{21}$ 13.0 ($CHCl_3$, c 4.6).

(*R*)-2-(N-4-Nitrophenyl-N-4-toluenesulfonyl)aminopropionic Acid Ethyl Ester (3e). Yield 87% (C); mp 81°C (ethyl acetate–hexane). IR spectrum, ν, cm^{-1}: 1320, 1520, 1168, 1350 (SO_2), 1750 (C=O). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.15 (3H, t, *J* = 7.2, $\underline{CH_3}CH_2$); 1.23 (3H, d, *J* = 7.2, $\underline{CH_3}CH$); 2.40 (3H, s, CH_3Tos); 4.08 (2H, t, *J* = 7.2, $CH_3\underline{CH_2}$); 5.07 (1H, q, *J* = 7.2, $CH_3\underline{CH}$); 7.40 (2H, d, *J* = 7.8); 7.44 (2H, d, *J* = 9.0); 7.61 (2H, d, *J* = 8.1); 8.24 (2H, d, *J* = 9.3). ^{13}C NMR spectrum, δ, ppm: 13.82 (CH_3CH_2); 16.78 (CH_3); 21.02 (CH_3Tos); 57.36 (CH); 61.22 (CH_3CH_2); 124.31 (2C); 127.37 (2C); 129.77 (2C); 131.82 (2C); 136.44, 142.44, 143.94, 146.86, 170.79 (C=O). Found, %: C 55.05; H 5.06; N 6.99. $C_{18}H_{20}N_2O_6S$. Calculated, %: C 55.09; H 5.14; N 7.14. $[\alpha]_D^{21}$ 20.5 ($CHCl_3$, c 4.6).

(*R*)-N-Phenylalanine Ethyl Ester Hydrochloride (4a). Zinc dust (4 g, 62 mmol) and then aqueous 1 M NaH_2PO_4 solution (8 ml, dropwise) were added to solution of 2,2,2-trichloroethyl N-phenylcarbamate (**3c**) (1.47 g, 4 mmol) in THF (40 ml) with cooling to -10°C and vigorous stirring in an atmosphere of argon. The reaction mixture was stirred vigorously for 6-8 h at 15°C in an argon atmosphere. The completeness of the reaction was checked by TLC (silica gel, ethyl acetate–petroleum ether, 1:3). The excess of zinc was filtered off, the solid was washed with THF (20 ml), the filtrate evaporated in vacuum, and the residue dissolved in diethyl ether (50 ml). The solution was washed with 0.2 M aqueous citric acid solution (50 ml), with 1 M aqueous $NaHCO_3$ solution (50 ml), and with saturated sodium chloride solution (30 ml), and dried over anhydrous Na_2SO_4. After removing the solvent in vacuum a white crystalline powder (0.65 g, 84%) was obtained having mp 175-176°C (ethanol). IR spectrum, ν, cm^{-1}: 1730 (C=O). Mass spectrum, *m/z*, (*I*, %): 193 (15) $[M]^+$, 120 (100) $[M\text{-}CO_2Et]^+$, 77 (12). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.15 (3H, t, *J* = 7.0, $\underline{CH_3}CH_2$); 1.37 (3H, d, *J* = 7.2, CH_3); 4.06 (2H, q, *J* = 7.0, $CH_3\underline{CH_2}$); 4.17 (1H, q, *J* = 7.2, CH); 6.81 (3H, m, Ph); 7.19 (2H, t, *J* = 8.1, Ph); 8.09 (3H, br. s, NH_3^+). ^{13}C NMR spectrum, δ, ppm: 14.43 (CH_3CH_2); 18.22 (CH_3CH); 52.58 (CH); 60.78 (CH_2CH_3); 114.33 (2C, CH); 118.28 (CH); 129.29 (2C, CH); 148.12 (C); 174.65 (C=O). Found, %: C 57.61; H 7.18; N 6.36. $C_{11}H_{16}ClNO_2$. Calculated, %: C 57.52; H 7.02; N 6.10. $[\alpha]_D^{22}$ 5.9 ($CHCl_3$, c 0.09).

(*R*)-2-(N-4-Nitrophenyl)aminopropionic Acid Ethyl Ester (4c). Sodium borohydride (0.3 g, 7.2 mmol) was added with vigorous stirring in an atmosphere of argon with cooling to 5°C to solution of compound **3d** (0.3 g, 9 mmol) in absolute ethanol (10 ml). The reaction mixture was stirred vigorously for 4 h at

room temperature in the argon atmosphere. The completeness of the reaction was checked by TLC (silica gel, ethyl acetate–petroleum ether, 1:3). The reaction mixture was poured into water and ice, and 5 M HCl solution was added dropwise to pH ~4. The mixture was extracted with methylene chloride (2 × 100 ml). The organic extract was dried with anhydrous Na_2SO_4. After removing volatile components in vacuum and storing in a desiccator over P_2O_5 the residue was recrystallized. Yield 85%, mp 147°C (ethanol). IR spectrum, ν, cm^{-1}: 1605 (Ar), 1750 (C=O). Mass spectrum, m/z (I, %): 238 (9) $[M]^+$, 165 (100) $[M\text{-}CO_2Et]^+$, 149 (5), 119 (38). ^1H NMR spectrum, δ, ppm (*J*, Hz): 1.15 (3H, t, *J* = 7.0, $\underline{CH_3}CH_2$); 1.23 (3H, d, *J* = 7.0, CH_3); 4.07 (2H, q, *J* = 7.0, $CH_3\underline{CH_2}$); 5.06 (1H, q, *J* = 7.0, CH); 7.44 (2H, d, *J* = 9.0); 8.24 (2H, d, *J* = 9.0); 8.87 (NH). $[\alpha]_D^{21}$ 3.7 ($CHCl_3$, c 0.1).

Removal of N-(4-Toluenesulfonyl) Activating Group (General Procedure). Magnesium dust (4.80 g, 200 mmol) was added to solution of substrate (10 mmol) in absolute methanol (50 ml). The reaction mixture was placed in an ultrasound bath and subjected to ultrasonic irradiation for 30 min. Magnesium residue was filtered off, and magnesium washed with methanol (50 ml). The solution was concentrated in vacuum, poured into saturated ammonium chloride solution, the mixture was extracted with ether, the extract was washed with saturated ammonium carbonate solution (30 ml), and with saturated sodium chloride solution (50 ml), then dried over anhydrous Na_2SO_4. The solvent was removed at reduced pressure, the residue was dissolved in a small quantity of methanol, and an excess of a saturated solution of hydrogen chloride in ether was added. The solvent was removed in vacuum, and the residue recrystallized from methanol–ether. The solid precipitated on cooling was filtered off, and dried in vacuum over alkali and phosphorus pentoxide.

(*R*)-N-Phenylalanine Methyl Ester Hydrochloride (4b). Yield 64.2%, mp 135-137°C. IR spectrum, ν, cm^{-1}: 750 (Ph), 1740 (C=O), 2200-2600 (NH_2^+). Mass spectrum, m/z (I, %): 179 (45) $[M]^+$, 148 (46), 120 (100), 91 (40), 76 (45). ^1H NMR spectrum, δ, ppm (*J*, Hz): 1.38 (3H, d, *J* = 7.0); 3.57 (3H, s, CH_3O); 4.21 (1H, q, *J* = 7.0, CH); 6.80 (2H, d, *J* = 7.0); 7.00 (NH); 7.10-7.25 (3H, m). $[\alpha]_D^{21}$ -1.0 (CH_3OH, c 0.48).

(*R*)-N-(4-Methoxyphenyl)alanine Methyl Ester Hydrochloride (4d). Yield 86%, mp 129-130°C. IR spectrum, ν, cm^{-1}: 750 (Ph), 1740 (C=O), 2200-2600 (NH_2^+). Mass spectrum, m/z (I, %): 209 (61) $[M]^+$, 150 (100), 134 (63), 123 (11), 119 (34), 108 (43), 92 (31), 77 (34), 63 (19). ^1H NMR spectrum (D_2O), δ, ppm (*J*, Hz): 1.24 (3H, d, *J* = 7.2, $\underline{CH_3}CH$); 3.54 (3H, s, CH_3O); 3.56 (3H, s, $\underline{CH_3}O_2C$); 4.21 (1H, q, *J* = 7.0, $CH_3\underline{CH}$); 6.83 (2H, d, *J* = 8.7); 7.10 (2H, d, *J* = 8.7). ^{13}C NMR spectrum, δ, ppm: 15.79 (CH_3CH); 51.76 (CH); 54.99 (CH_3O_2C); 55.22 (CH_3O); 114.47 (2C, CH); 119.64 (2C, CH); 140.14 (C); 155.43 (C); 171.42 (C=O). Found, %: C 55.61; H 7.14; N 5.56. $C_{12}H_{18}ClNO_3$. Calculated, %: C 55.49; H 6.99; N 5.39. $[\alpha]_D^{21}$ -1.0 (CH_3OH, c 5.82).

(*R*)-N-Nitroso-N-phenylalanine Methyl Ester (5). Cold aqueous solution (50 ml) of potassium hydroxide (0.29 g, 5.2 mmol) was added in one portion with cooling and vigorous stirring to solution of compound **4b** (1.12 g, 5.2 mmol) in water (20 ml). Amine was extracted with ether (3 × 50 ml), the extract washed with water, with saturated sodium chloride solution, and dried with anhydrous Na_2SO_4. The solvent was removed at reduced pressure, the residue (1 g) was dissolved in anhydrous THF (10 ml), and a 14% solution (4.5 ml) of ethyl nitrite (~7.2 mmol) in alcohol was added in portions with stirring and cooling. The reaction mixture was stored in the dark for 12 h at room temperature. Volatile components were removed in vacuum at a bath temperature of 40°C, and a yellow oily liquid (1.08 g, 99%) was obtained. The compound was used in further conversions without additional purification. IR spectrum, ν, cm^{-1}: 1730 (C=O), 1430 (N=O). ^1H NMR spectrum, δ, ppm (*J*, Hz): 1.41 (3H, d, *J* = 7.1, CH_3); 3.63 (3H, s, CH_3O); 5.15 (1H, q, *J* = 7.1, CH); 7.31-7.60 (5H, m, Ph). Mass spectrum, *m/z*, (*I*, %): 208 (7) $[M]^+$, 178 (23) $[M\text{-}N{=}O]^+$, 120 (100), 104 (38), 91 (7), 77 (32).

(*R*)-2-(1-Phenylhydrazino)propionic Acid Methyl Ester (6). Concentrated HCl (6 ml, 72 mmol) was added to solution of nitrosoamine **5** (9 mmol) in absolute methanol (100 ml) cooled to -80°C and in atmosphere of argon. Zinc dust (4.68 g) was added in portions with vigorous stirring to the solution. The reaction mixture was stirred vigorously for 6-8 h at -80 to -70°C in atmosphere of argon. The completeness of the reduction was checked by TLC (silica gel, ethyl acetate–petroleum ether, 1:3, visualizing with an alcoholic solution of ferric

chloride). The excess of zinc was filtered off, the solid was washed with methanol (20 ml), the filtrate evaporated in vacuum at room temperature to a volume of ~20 ml, poured into water and ice (100 ml), and made alkaline by adding of 24% aqueous ammonia solution (20 ml) (pH ~12). The mixture was extracted with methylene chloride (4 × 50 ml), the extract washed with saturated sodium chloride solution (30 ml), and dried over anhydrous Na_2SO_4. After removing the solvent in vacuum a yellowish brown oily substance (1.65 g, 95%) was obtained, which was used to prepare hydrazones without further purification. Mass spectrum, *m/z* (*I*, %): 194 (25) $[M]^+$, 135 (100) $[M\text{-}CO_2Me]^+$, 118 (26), 104 (20), 91 (18), 77 (45).

(*R*)-1-(1-Methoxycarbonylethyl)-2,3,4,5-tetrahydrocarbazole (8). Cyclohexanone (0.39 g, 4 mmol) and a catalytic amount of *p*-toluenesulfonic acid were added to solution of compound **6** (0.78 g, 4 mmol) in benzene (10 ml), and the mixture boiled for 8 h with a Dean and Stark stillhead. The formation of hydrazone **7** was confirmed by chromato-mass spectrometry {*m/z* (*I*, %): 274 (5) $[M]^+$, 215 (100) $[M\text{-}CO_2Me]^+$, 118 (50), 104 (15), 96 (80), 77 (63), 69 (18), 55 (30)}. Benzene was removed under reduced pressure, the residue dissolved in toluene (40 ml), Amberlist 15 (2 g) was added, and the mixture stirred vigorously for 3 h at 90-100°C. The resin was filtered off, washed with ethyl acetate (60 ml), the filtrate was evaporated in vacuum, and the residue chromatographed on a column of silica gel, mobile phase hexane–ethyl acetate with concentration gradient up to 5 vol. % of the latter. A viscous liquid (0.63 g, 61%) was obtained. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.59 (3H, d, *J* = 7.2, $C\underline{H}_3CH$); 1.73-1.92 (4H, m); 2.54-2.74 (4H, m); 3.64 (3H, s, CH_3O); 5.40 (1H, q, *J* = 7.2, $CH_3C\underline{H}$); 6.98 (1H, t, *J* = 7.4); 7.02 (1H, t, *J* = 7.1); 7.22 (1H, d, *J* = 8.1); 7.38 (1H, d, *J* = 7.1). Mass spectrum, *m/z* (*I*, %): 257 (35) $[M]^+$, 198 (100) $[M\text{-}CO_2Me]^+$, 170 (30), 156 (5), 143 (3), 128 (4), 115 (4), 98 (3), 77 (3). Found, %: C 74.73; H 7.50; N 5.35. $C_{16}H_{19}NO_2$. Calculated, %: C 74.68; H 7.44; N 5.44. $[\alpha]_D^{21}$ 4.2 ($CHCl_3$, c 0.04).

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