NEW INTERMEDIATE FOR RAPID SYNTHESIS OF N-ISOPROPYL--2-AMINO-1-(4-IODOPHENYL)PROPANE (N-ISOPROPYL-4-IODO-AMPHETAMINE), LABELLED WITH RADIOACTIVE IODINE

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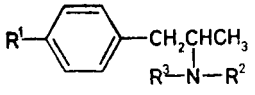
The triazene derivative of N-isopropyl-2-amino-1-phenylpropane *XIV*, synthesized in seven steps from 2-amino-1-phenylpropane (*II*), enables a rapid, simple and regiospecific preparation of N-isopropyl-2-amino-1-(4-iodophenyl)propane (N-isopropyl-4-iodoamphetamine; *I*), labelled with short-living isotopes of iodine, directly prior to application.

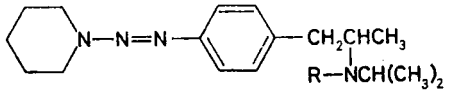
N-Isopropyl-2-amino-1-(4-iodophenyl)propane (N-isopropyl-4-iodoamphetamine; *I*), labelled with iodine radioisotopes (^{123}I, ^{125}I, ^{131}I), is recently used as a brain--imaging agent[1-5]. So far, its syntheses were based on direct iodination of a suitable intermediate or isotopic exchange in a derivative obtained by multistep synthesis from various starting compounds[1,6-10]. The lengthy and laborius procedures involved in such preparations make the use of short-living isotopes very limited. For this reason, we tried to find a stable intermediate, enabling rapid and regiospecific radioiodination even in biological and clinical laboratories, directly prior to application. Aromatic compounds can be easily iodinated *via* triazene derivatives[11,12]. Aryltriazenes are generally very stable compounds which can be stored almost indefinitely. On treatment with hydrogen iodide they decompose to give iodoaryl derivatives; the reaction is suitable for micropreparations and for work with highly radioactive material. The triazene derivative *XIV*, prepared as described below, proved to be very satisfactory. Its reaction with sodium iodide in acetone--trifluoracetic acid (20 min, room temperature) afforded the desired iodo derivative *I* in high yield. Compound *I*, labelled with ^{125}I, was obtained in 66% radiochemical yield in the same manner using [^{125}I] sodium iodide.

N-Isopropyl-2-amino-1-phenylpropane (*III*) was prepared by modified reductive amination[13]. The starting 2-amino-1-phenylpropane (*II*) reacted with acetone in the presence of sodium borohydride to give *III* in 95% yield. The further steps required protection of the free NH group in *III*. The N-acetyl derivative *IV*, obtained by acetylation of *III* with acetic anhydride in pyridine, was not suitable because the protecting group was not removed under the conditions used (refluxing with 10% ethanolic potassium hydroxide for 24 h or with ethanolic hydrazine hydrate for 8 h).

We used therefore the trifluoroacetyl group. The N-trifluoroacetyl derivative *VII*, prepared analogously to *IV*, was quantitatively deacetylated by refluxing with 10% ethanolic potassium hydroxide for 16 hours. The functionalization of the aromatic nucleus was tried first with the N-acetyl derivative *IV*, using the reaction with thallium(III) trifluoroacetate in trifluoroacetic acid (analogously to ref.[14]). The resulting organothallium intermediate *V* reacted with aqueous sodium iodide to give N-acetyl--N-isopropyl-2-amino-1-(4-iodophenyl)propane (*VI*). The *para*-position of the iodine atom follows from the symmetry of the spin system of the aromatic protons and carbon atoms in the corresponding NMR spectra. Thus, the thallation in this case proceeds with high regioselectivity in the position 4 of the aromatic nucleus. The analogous organothallium intermediate *VIII*, obtained by thallation of *VII*, was not isolated and directly treated with nitrosyl chloride (generated *in situ* from amyl nitrite and hydrochloric acid). Purification of the obtained 4-nitroso derivative *IX* by column chromatography and reduction with sodium borohydride in methanol in the presence of 10% palladium on charcoal gave the 4-amino derivative *X*. Since the yield of the nitroso derivative *IX* was low (31%), we tried to obtain the desired *X* by reduction of the corresponding nitro derivative. Direct nitration of N-trifluoroacetyl-N-isopropyl-2-amino-1-phenylpropane (*VII*) afforded a mixture of 2-nitro (*XII*; 29%) and 4-nitro (*XI*; 53%) derivative which was separated by column chromatography. Compound *XI* was then reduced with sodium borohydride in methanol in the presence of 10% palladium on charcoal to give the amine *X* in a high yield. This variant is more advantageous than that *via* the nitroso derivative *IX*. Diazotation of the amino derivative *X* at 0°C with nitrous acid followed by reaction with



I, $R^1 = I$; $R^2 = CH(CH_3)_2$; $R^3 = H$
II, $R^1 = R^2 = R^3 = H$
III, $R^1 = R^3 = H$; $R^2 = CH(CH_3)_2$
IV, $R^1 = H$; $R^2 = CH(CH_3)_2$; $R^3 = COCH_3$
V, $R^1 = Tl(OOCCF_3)_2$; $R^2 = CH(CH_3)_2$; $R^3 = COCH_3$
VI, $R^1 = I$; $R^2 = CH(CH_3)_2$; $R^3 = COCH_3$
VII, $R^1 = H$; $R^2 = CH(CH_3)_2$; $R^3 = COCF_3$
VIII, $R^1 = Tl(OOCCF_3)_2$; $R^2 = CH(CH_3)_2$; $R^3 = COCF_3$
IX, $R^1 = NO$; $R^2 = CH(CH_3)_2$; $R^3 = COCF_3$
X, $R^1 = NH_2$; $R^2 = CH(CH_3)_2$; $R^3 = COCF_3$
XI, $R^1 = NO_2$; $R^2 = CH(CH_3)_2$; $R^3 = COCF_3$
XII, $R^1 = o\text{-}NO_2$; $R^2 = CH(CH_3)_2$; $R^3 = COCF_3$



XIII, R = $COCF_3$
XIV, R = H

aqueous piperidine yielded the triazene *XIII* which was purified by column chromatography. The desired 1-(4-(2-(2-propylamino)propyl)benzeneazo)piperidine (*XIV*) was obtained by hydrolysis of *XIII* with 10% ethanolic potassium hydroxide (as for *VII*). Compound *XIV* was treated with sodium iodide in trifluoroacetic acid to afford N-isopropyl-2-amino-1-(4-iodophenyl)propane (*I*) in 88% yield. The reaction with radioactive iodide was performed in an analogous manner.

The rapidity, simplicity and regiospecificity of preparing N-isopropyl-2-amino-1-(4-iodophenyl)propane (*I*) from the triazene derivative *XIV* offers thus the attractive possibility of introducing a diagnostic kit for use in biological or clinical laboratories.

EXPERIMENTAL

Melting points were determined on a Kofler block and are uncorrected. ^{1}H and ^{13}C NMR spectra were measured on a Jeol FX-60 instrument (59·797 and 15·036 MHz, FT mode) in deuteriochloroform at 25°C with tetramethylsilane as internal standard. Mass spectra were taken on a Varian MAT 311 spectrometer (70 eV, ionisation current 1 mA, ion source temperature 200°C, direct inlet temperature 25—60°C). The ion composition (where given) was verified by high resolution measurements; error less than 5 ppm. Infrared spectra were taken in chloroform on a Perkin–Elmer 684 instrument. Thin-layer chromatography was performed on Silufol UV 254 plates (Kavalier, Votice), column chromatography on Silpearl silica gel (Kavalier, Votice). "Usual work-up of the reaction mixture" comprises washing the organic phase successively with water, 5% sodium carbonate solution, water, drying over sodium sulfate and concentration *in vacuo*.

N-Isopropyl-2-amino-1-phenylpropane (*III*)

Finely ground sodium borohydride (5·4 g) was added portionwise during 1 h to a stirred suspension of 2-amino-1-phenylpropane (amphetamine) sulfate (*II*, 15 g) in a mixture of methanol (193 ml) and acetone (86 ml). The reaction was slightly exothermic and the temperature was maintained at 25°C. After stirring at room temperature for 14 h, ground potassium carbonate (2·2 g) was added, the mixture was stirred for 15 min and concentrated *in vacuo* at 30°C. The residue was diluted with water (200 ml), extracted with ether (2 × 100 ml) and the combined ethereal extracts were worked up as usual. Evaporation of ether *in vacuo* afforded *III* (14·2 g; 95%) as a colourless oil. Mass spectrum, *m/z* (%, composition): 177 (M^+, 3); 162 (5); 134 (4); 120 (10); 91 (23); 86 (100, $C_5H_{12}N$); 44 (100); 36 (27). Hydrochloride, m.p. 151—153°C (methanol); reported[15] m.p. 153—154°C.

N-Acetyl-N-isopropyl-2-amino-1-phenylpropane (*IV*)

A mixture of N-isopropyl-2-amino-1-phenylpropane (*III*; 3 g), pyridine (6 ml), and acetic anhydride (6 ml) was heated to 60°C for 2 h on a water bath. After cooling, the mixture was diluted with water (50 ml) and extracted with ether (3 × 20 ml). The combined ethereal portions were combined and worked up in the usual manner, affording colourless oily *IV* (3·5 g; 94%), n_D^{20} 1·5119. ^{1}H NMR spectrum: 0·78 d, 3 H ($(CH_3)_2CH$, J = 6·7 Hz); 1·14 d, 3 H ($(CH_3)_2CH$, J = 6·7 Hz); 1·40 d, 3 H (CH_3CH, J = 6·1 Hz); 2·09 s, 3 H (CH_3CO); 2·67—3·30 m, 3 H (CH_2CH); 3·85 st, 1 H ($(CH_3)_2CH$, J = 6·1 Hz); 7·22 s, 5 H (C_6H_5). ^{13}C NMR spectrum:

18·1 q; 20·3 q; 21·0 q; 23·8 q; 40·4 t; 49·8 d; 52·4 d; 126·1 d; 128·3 d, 2 C; 129·5 d, 2 C; 140·6 s; 170·2 s. Mass spectrum, *m/z* (%, composition): 219 (M^+, 3); 162 (6); 128 (85, $C_7H_{14}NO$); 118 (10); 117 (11); 91 (32); 86 (100, C_4H_8NO); 45 (34). IR spectrum (cm^{-1}): 1 624 (C=O).

N-Acetyl-N-isopropyl-2-amino-1-(4-iodophenyl)propane (*VI*)

A solution of acetyl derivative *IV* (1 g) and thallium (*III*) trifluoroacetate (2·5 g) in trifluoroacetic acid (2·5 ml) in a sealed ampoule was set aside in the dark for 75 h at room temperature. A solution of sodium iodide (1 g) in water (1·5 ml) was then added and the mixture was stirred for 15 min. After addition of sodium thiosulfate (pentahydrate, 500 mg) in water (1 ml), the mixture was stirred for 10 min, neutralized with 2M-NaOH and extracted with ether (3 × 20 ml). The ethereal extracts were combined and worked up as usual, affording the iodo derivative *VI* as a yellowish oil (1·18 g; 75%), b.p. 156°C; n_D^{20} 1·4539. Mass spectrum *m/z* (%, composition): 345 (M^+, 3); 302 (3); 288 (5); 260 (4); 244 (25, C_9H_9I); 217 (10); 176 (7); 162 (10); 128 (100, $C_7H_{14}NO$); 118 (45); 117 (40); 91 (85); 86 (100).

N-Trifluoroacetyl-N-isopropyl-2-amino-1-phenylpropane (*VII*)

Trifluoroacetic anhydride (10 g) was added dropwise in the course of 15 min at room temperature to a stirred solution of N-isopropyl-2-amino-1-phenylpropane (*III*; 7 g) and 4-dimethylaminopyridine (5 mg) in dichloromethane (50 ml). After the exothermic reaction had subsided, the mixture was refluxed for 1 h, cooled, washed with 5% aqueous sodium carbonate (4 × 15 ml), dried over sodium sulfate and concentrated *in vacuo*. Yield 7·2 g (96%) of *VII*, b.p. 198°C; n_D^{20} 1·4730; crystallized on prolonged standing, m.p. 42–44°C. Mass spectrum, *m/z* (%, composition): 273 (M^+, 7); 182 (37, $C_7H_{11}NOF_3$); 149 (10); 140 (100, $C_4H_5NOF_3$); 91 (38); 86 (35); 44 (74); 28 (83). IR spectrum (cm^{-1}): 1 683 (C=O); 1 150–1 188 (CF_3). Hydrochloride m.p. 155–158°C (ether–ethanol).

N-Trifluoroacetyl-N-isopropyl-2-amino-1-(4-nitrosophenyl)propane (*IX*)

A solution of trifluoroacetyl derivative *VII* (3·27 g) and thallium(*III*) trifluoroacetate (10 ml) in a selaed ampoule was set aside in the dark for 75 h at room temperature. Trifluoroacetic acid was distilled off *in vacuo*, the residue mixed with dichloromethane (10 ml) and the mixture again concentrated *in vacuo* (repeated three times). The residue, devoid of trifluoroacetic acid, was dissolved in dichloromethane (50 ml), amyl nitrite (4 g) was added under stirring and the stirring was continued in the dark for 3 h. The mixture was stirred with conc. hydrochloric acid (2·5 ml) and acetic acid (5 ml) for 10 min and 2M-HCl (20 ml) was then added. After stirring for further 10 min, the mixture was filtered through glass wool, the organic phase was washed with water, dried over sodium sulfate and taken down. The obtained brown oil (2·5 g) was chromatographed on a column of silica gel (70 g) in benzene to give bright yellow crystals of the nitroso derivative *IX* (1·1 g; 31%), m.p. 75–77°C (benzene). ^1H NMR spectrum: 0·76 d, 3 H ($(CH_3)_2CH$, J = 6·7 Hz); 1·21 d, 3 H ($(CH_3)_2CH$, J = 6·7 Hz); 1·49 d, 3 H (CH_3, J = = 6·1 Hz); 2·72–3·85 m, 3 H (CH_2CH); 4·09 st, 1 H (J = 6·7 Hz); 7·41 d, 2 H (J = 7·9 Hz); 7·85 d, 2 H (J = 7·9 Hz). ^{13}C NMR spectrum: 18·2 q; 20·3 q; 20·9 q; 39·4 t; 49·4 dq (^4J(C, F) = = 3·9 Hz); 53·1 d; 121·3 d, 2 C; 123·8 s, 130·3 d, 2 C; 148·0 s; CF_3CO signals in the noise, not determined. Mass spectrum, *m/z* (%, composition): 302 (M + 1, 8), 182 (61, $C_7H_{11}F_3NO$), 147 (77, C_9H_9NO), 140 (100, $C_4H_5F_3NO$), 133 (23), 106 (65), 91 (23), 90 (24), 43 (85). IR spectrum (cm^{-1}): 1 684 (C=O), 1 602 (N=O), 1 150–1 188 (CF_3).

N-Trifluoroacetyl-N-isopropyl-2-amino-1-(4-aminophenyl)propane (*X*)

A) A solution of nitroso derivative *IX* (250 mg) in methanol (10 ml) was stirred with 10% Pd/C (25 mg) in an atmosphere of helium for 10 min. Sodium borohydride (120 mg) was added and the mixture was stirred at room temperature for 1 h. After filtration, the mixture was diluted with water (40 ml) and extracted with chloroform (3 × 25 ml). The combined chloroform extracts were worked up as usual, affording amine *X* as a yellow oil (220 mg; 93%). Mass spectrum, *m/z* (%, composition): 288 (M^+, 12); 182 (13, $C_7H_{11}F_3NO$); 140 (29 $C_4H_5F_3NO$); 133 (25); 106 (100, C_7H_8N); 79 (10, C_6H_7); 77 (11); 70 (11). IR spectrum (cm^{-1}): 1 150, 1 173 (CF_3), 1 682 (C=O), 1 621, 3 384 (NH_2).

B) Nitro derivative *XI* (900 mg) was reduced analogously as described for the reduction of *IX*, affording *X* as a yellow oil (760 mg; 93%).

Nitro Derivatives *XI* and *XII*

N-Trifluoroacetyl-N-isopropyl-2-amino-1-phenylpropane (*VII*; 1·5 g) was slowly added dropwise at −20°C to stirred nitric acid (*d* 1·52; 7·5 ml). The solution was then stirred at room temperature for 2 h and poured into ice-cold water (50 ml). The mixture was extracted with benzene (3 × × 30 ml), the benzene extracts were combined and worked up in the usual manner to give yellow oil (1·5 g) which was chromatographed on a silica gel column (30 g) in light petroleum–ether (19 : 1). Compound *XII* was eluted in the first, its isomer *XI* in the second fraction.

N-*Trifluoroacetyl*-N-*isopropyl*-2-*amino*-1-(2-*nitrophenyl*)*propane* (*XII*; 510 mg; 29%), m.p 71–72°C (light petroleum–ether). ^{1}H NMR spectrum: 0·47 d, 3 H ($(CH_3)_2CH$, J = 6·7 Hz); 1·19 d, 3 H ($(CH_3)_2CH$, J = 6·7 Hz); 1·52 d, 3 H (CH_3, J = 6·1 Hz); 3·16–4·24 m, 4 H; 7·19 to 7·67 m, 3 H; 7·90 dd, 1 H (J = 7·3 and 2·4 Hz). ^{13}C NMR spectrum: 18·8 q; 19·5 q; 20·9 q; 35·0 t; 49·2 dq (^4J(C, F) = 3·9 Hz); 51·8 d; 124·9 d; 128·0 d; 133·1 d; 133·6 d; 134·2 s; 142·1 s; CF_3CO signals in the noise, undetermined. Mass spectrum, *m/z* (%, composition): 318 (M^+, 3, $C_{14}H_{17}F_3N_2O_3$); 303 (2); 288 (6); 182 (65, $C_7H_{11}F_3NO$); 164 (10); 140 (100, $C_4H_5F_3NO$); 92 (25); 91 (23). IR spectrum (cm^{-1}): 1 150–1 190 (CF_3); 1 680 (CO); 1 349, 1 525 (NO_2).

N-*Trifluoroacetyl*-N-*isopropyl*-2-*amino*-1-(4-*nitrophenyl*)*propane* (*XI*, 920 mg, 53%); m.p. 65 to 68°C (light petroleum–ether). ^{1}H NMR spectrum: 0·75 d, 3 H ($(CH_3)_2CH$, J = 6·7 Hz); 1·21 d, 3 H ($(CH_3)_2CH$, J = 6·7 Hz); 1·49 d, 3 H (CH_3, J = 5·5 Hz); 3·11–3·66 m, 3 H; 4·10 st, 1 H ($(CH_3)_2CH$, J = 6·7 Hz); 7·32 and 8·18 AA'BB', 4 H ($J_{AB} + J_{AB'}$ = 7·9 Hz). ^{13}C NMR spectrum: 18·1 q; 20·3 q; 20·9 q; 39·0 t; 49·1 dq (^4J(C, F) = 3·9 Hz); 53·2 d; 123·8 d, 2 C; 126·0 s; 130·3 d, 2 C; 147·1 s; CF_3CO signals in the noise, undetermined. Mass spectrum, *m/z* (%, composition): 318 (M^+, 2); 288 (5); 260 (5); 182 (55, $C_7H_{11}F_3NO$); 164 (8); 163 (11); 140 (100, $C_4H_5F_3NO$); 106 (11); 91 (9); 90 (9); 70 (14). IR spectrum (cm^{-1}): 1 151–1 189 (CF_3), 1 682 (CO), 1 348, 1 522 (NO_2).

1-(4-(2-(2-Propyltrifluoroacetylamino)propyl)benzeneazo)piperidine (*XIII*)

To a stirred solution of *X* (600 mg) in ethanol (1 ml) was slowly added dropwise 1M-HCl (10 ml). Sodium nitrite (170 mg) in water (5 ml) was added dropwise with stirring at 0°C to −5°C. After 10 min, piperidine (920 mg) in water (7 ml) was added and the stirring was continued for 30 min. The mixture was poured into water (200 ml), adjusted to pH 10 with 5% sodium carbonate solution and extracted with chloroform (3 × 25 ml). The combined chloroform extracts were worked up as usual and the crude product was chromatographed on a column of silica gel (30 g) in light petroleum–ether (85 : 15). Yield 595 mg (75% of triazene *XIII*, m.p. 107–108°C (methanol). ^{1}H NMR spectrum: 0·82 d, 3 H ($(CH_3)_2CH$, J = 6·7 Hz); 1·19 d, 3 H ($(CH_3)_2CH$, J = 6·7 Hz);

1·45 d, 3 H (CH_3, J = 5·5 Hz); 2·72–3·51 m, 3 H; 1·70 m, 5 H; 3·78 m, 4 H; 4·09 st, 1 H (J = = 6·7 Hz); 7·11 and 7·38 AA'BB', 4 H ($J_{AB} + J_{AB'}$ = 7·9 Hz). ^{13}C NMR spectrum: 17·8 q; 20·3 q; 20·9 q; 24·4 t; 25·3 t, 2 C; 38·9 t; 48·2 t, 2 C; 49·0 dq (J(C, F) = 3·9 Hz); 53·9 d; 120·6 d, 2 C; 122·4 s; 129·9 d, 2 C; 136·9 s; $COCF_3$ signals in the noise, undetermined. Mass spectrum, m/z (%, composition): 384 (M^+, 14, $C_{19}H_{27}F_3N_4O$); 300 (40, $C_{14}H_{17}F_3N_3O$); 272 (29, $C_{14}H_{17}F_3NO$); 257 (8); 252 (9); 230 (15, $C_9H_9F_3N_4$); 222 (17); 203 (84, $C_{13}H_{17}NO$); 202 (29, $C_{12}H_{16}N_3$); 182 (54, $C_7H_{11}F_3NO$); 140 (100, $C_4H_5F_3NO$); 117 (54, C_9H_9); 91 (79, C_7H_7); 90 (62); 84 (75, $C_5H_{10}N$); 55 (33). IR spectrum (cm^{-1}): 1 104, 1 150, 1 182 (CF_3), 1 681 (C=O).

1-(4-(2-(2-Propylamino)propyl)benzeneazo)piperidine (*XIV*)

A solution of triazene *XIII* (525 mg) in 10% ethanolic potassium hydroxide (7 ml) was refluxed in the dark for 16 h. After cooling, the mixture was poured into water (50 ml) and extracted with ether (3 × 25 ml). The combined ethereal extracts were processed in the usual manner and taken down. The brown oily residue (500 mg) was chromatographed on a silica gel column (20 g) in ethyl acetate–methanol–conc. aqueous ammonia (17 : 2 : 1), affording the triazene *XIV* (290 mg; 73%), m.p. 178–180°C (decomposition) (ether). ^{1}H NMR spectrum: 0·96 d, 3 H (CH_3CH, J = 6·1 Hz); 1·03 d, 6 H ($(CH_3)_2CH$, J = 6·1 Hz); 1·69 br s, 5 H; 2·45–3·25 m, 4 H; 3·76 t, 4 H (J = 4·9 Hz); 7·11 and 7·37 AA'BB', 4 H ($J_{AB} + J_{AB'}$ = 8·6 Hz). ^{13}C NMR spectrum: 20·7 q; 22·8 q; 23·8 q; 24·4 t; 25·3 t, 2 C; 43·4 t; 45·4 d; 48·3 t, 2 C; 51·4 d; 120·5 d, 2 C; 129·8 d, 2 C; 137·0 s; 149·2 S. Mass spectrum, m/z (%, composition): 288 (M^+, 3); 230 (4); 203 (16); 175 (5); 98 (8); 91 (14); 90 (16); 86 (100, $C_5H_{12}N$); 84 (14, $C_5H_{10}N$); 70 (10); 56 (8); 55 (10).

N-Isopropyl-2-amino-1-(4-iodophenyl)propane (*I*)

A solution of triazene *XIV* (25 mg) in acetone (1 ml) was added dropwise to a stirred mixture of trifluoroacetic acid (1 ml) and sodium iodide (5·5 mg) at 0–5°C. After stirring at room temperature for 20 min, the mixture was diluted with water (25 ml), made alkaline with 2M-NaOH and extracted with ether (3 × 10 ml). The combined ethereal extracts were washed with 5% sodium thiosulfate and with water, dried over sodium sulfate and taken down to dryness, affording the iodo derivative *I* (23 mg; 80%) as a yellowish oil. Mass spectrum, m/z (%): 303 (M^+, 5); 288 (11); 245 (19); 217 (82); 128 (35); 117 (30); 91 (37); 90 (51); 86 (100); 70 (55). Hydrochloride: m.p. 155–157·5°C (ethanol–water); reported[7] m.p. 156–158°C.

N-Isopropyl-2-amino-1-(4-[^{125}I]iodophenyl)propane (*I*)

Trifluoroacetic acid (5 μl) and triazene *XIV* (5 mg; 11·6 μmol) in acetone (100 μl) were added to a cooled and stirred mixture of sodium iodide (1·83 mg; 12·1 μmol) and $Na^{125}I$ (0·57 MBq, without carrier; Amersham) in water (50 μl). After stirring at room temperature for 20 min, 1M sodium thiosulfate solution (10 μl) was added and the mixture was taken down to dryness. The residue was extracted with acetone (200 μl) and the extract chromatographed on a thin layer of silica gel (Silufol) in ethyl acetate–methanol–conc. aqueous ammonia (17 : 2 : 1). The iodo derivative *I* was eluted with methanol; activity 0·37 MBq (66% radiochemical yield).

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