PREPARATION AND PROPERTIES OF 2-(DIALKYLAMINOMETHYL)-CYCLOHEXYL AND 2-(DIALKYLAMINOMETHYL)PHENYL CARBANILATES

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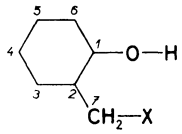
A series of 2-(dialkylaminomethyl)cyclohexyl and 2-(dialkylaminomethyl)phenyl esters of substituted carbanilic acid have been prepared and their identity verified by elemental analysis and evaluation of IR and ^{13}C NMR spectra. The spectral results have been used also for determination of isomerism of the starting 2-dialkylaminomethylcyclohexanols and final carbanilates. Local anaesthetic activity and acute toxicity have been tested with some of the substances.

In the context of studies of relations between structure and biological activity we synthetized, in the past few years, esters of carbanilic acid substituted with a basic group as compounds with high local anaesthetic activity[1]. It has been known for quite a long time that the local anaesthetic effect is accompanied very often by antiarrhythmic activity[2-6]. In order to extend our knowledge in this area, we focused our attention to preparation of structural analogues of trapencain (2-(1-pyrrolidinyl)-cyclohexyl 3-pentyloxycarbanilate) which is being introduced into practice as a cytoprotective agent and local anaesthetic.

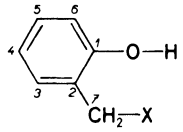
The starting 2-(dialkylaminomethyl)cyclohexanols were prepared by the Mannich reaction and subsequent reduction. Beside the usual complex hydrides, synhydride was also successfully used for the reduction. The 2-(dialkylaminomethyl)cyclohexanols obtained represent isomeric mixtures, which was proved by TLC using the *cis* and *trans* isomers of 2-(dimethylaminomethyl)cyclohexanol[7] as standard substances (Table VII). From the magnitude of spots it could be seen that the *cis* isomer was present in small amount in some cases (below 10%). The 2-(dialkylaminomethyl)cyclohexanols were separated on the preparative scale in the form of the corresponding 4-nitrobenzoates. In most cases it was possible to isolate the pure *trans* isomer, whereas a small amount of *cis* isomer was obtained in the case of 2--(morpholinomethyl)cyclohexanol.

According to refs[7-10] IR and ^1H NMR spectra are used for estimation of stereo-

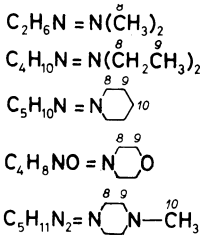
chemistry of 2-(dialkylaminomethyl)cyclohexanols. However, in the case of our compounds these spectra gave no unambiguous results. Evaluation of the ^{13}C NMR spectra has turned out to be the most suitable method for estimation of configuration of the isomers, the signals of the cyclohexane ring carbon atom carrying oxygen atom in the axial and in equatorial positions being sufficiently different in both the starting cyclohexanols (Table I) and their 4-nitrobenzoates.



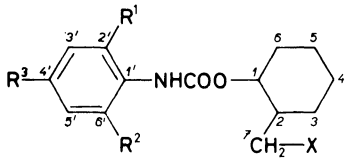
I, X = H
II, X = C_2H_6N
III, X = $C_4H_{10}N$
IV, X = $C_5H_{10}N$
V, X = C_4H_8NO
VI, X = $C_5H_{11}N_2$



VII, X = C_4H_8NO
VIII, X = $C_5H_{10}N$



The final carbanilates were prepared by the well-tried method[1] from the respective aryl isocyanate and 2-(dialkylaminomethyl)cyclohexanol. Either the pure isomers or their unseparated mixtures were used for the syntheses. The carbanilates were isolated either as solid bases or as salts with hydrochloric acid (Table II).



Compound	R^1	R^2	R^3	X
IX	$^{7'}CH_3$	$^{7'}CH_3$	H	$C_4H_{10}N$
X	$^{7'}CH_3$	$^{7'}CH_3$	$^{8'}CH_3$	$C_4H_{10}N$
XI	$^{7'}CH_3$	$^{7'}CH_3$	H	$C_5H_{10}N$
XII	$^{7'}CH_3$	$^{7'}CH_3$	CH_3	$C_5H_{10}N$
XIII	$^{7'}CH_3$	$^{7'}CH_3$	H	C_4H_8NO
XIV	$^{7'}CH_3$	$^{7'}CH_3$	$^{8'}CH_3$	C_4H_8NO
XV	OC_6H_{13}	H	H	C_4H_8NO
XVI	OC_7H_{15}	H	H	C_4H_8NO
XVII	$^{7'}CH_3$	$^{7'}CH_3$	H	$C_5H_{11}N_2$
XVIII	$^{7'}CH_3$	$^{7'}CH_3$	$^{8'}CH_3$	$C_5H_{11}N_2$
XIX	OC_4H_9	H	H	$C_5H_{11}N_2$
XX	OC_6H_{13}	H	H	$C_5H_{11}N_2$

TABLE I

^{13}C NMR spectra (δ, ppm) of N-substituted aminomethylcyclohexanols[a] *I*, *II*, *V*, *VI*

Compound	Isomer	C-1	C-2	C-3	C-4	C-5	C-6	C-7	C-8	C-9	C-10
I[b]	*cis*	70·70	36·40	29·40	24·70	21·50	32·60	16·80	—	—	—
II	*cis*	71·78	36·15	27·90	23·40	22·41	31·77	61·36	45·98	—	—
V	*cis*	69·52	35·08	26·38	22·22	21·70	31·32	60·31	53·81	66·02	—
VI	*cis*	71·47	36·13	27·50	22·87	22·87	32·03	60·30	55·16	53·73	45·94
I[c]	*trans*	76·40	40·30	33·70	25·70	25·20	35·50	18·60	—	—	—
II	*trans*	77·58	40·74	28·78	25·53	24·10	34·37	67·18	45·67	—	—
V	*trans*	77·32	39·50	28·72	25·47	24·04	34·24	66·14	54·06	66·73	—
VI	*trans*	77·58	40·02	28·91	25·60	24·17	34·44	65·88	55·16	53·73	45·94

[a] The numbering of carbon atoms follows the pattern shown in corresponding formulae; [b] ref.[11]; [c] ref.[12].

TABLE II

Characterization of carbanilates *IX*—*XXV*

Compound	Isomer[a] (Yield, %)	M.p., °C (solvent[a])	Formula (M.w.)	Calculated/Found		
				% C	% H	% N
IX[b]	*trans* (63)	170—173 (A)	$C_{20}H_{33}ClN_2O_2$ (369·0)	65·11 64·75	9·01 9·09	7·59 7·40
X[b]	*trans* (62)	183—186 (A)	$C_{21}H_{35}ClN_2O_2$ (383·0)	65·86 66·01	9·21 9·30	7·31 6·99
XI	*trans* (89)	95—96 (B)	$C_{21}H_{32}N_2O_2$ (344·5)	73·22 73·36	9·36 9·39	8·13 8·24
XI[b]		231—232 (C)	$C_{21}H_{33}ClN_2O_2$ (381·0)	66·21 66·36	8·73 8·79	7·35 7·45
XII	*trans* (86)	114—115 (D)	$C_{22}H_{34}N_2O_2$ (358·5)	73·70 73·59	9·56 9·63	7·81 7·72
XII[b]		233—234 (E)	$C_{22}H_{35}ClN_2O_2$ (395·0)	66·90 66·85	8·93 8·85	7·09 6·93
XIII	mixture[c] (82)	96—120 (D)	$C_{20}H_{30}N_2O_3$ (346·5)	69·33 69·56	8·73 8·85	8·09 7·90
XIII[b]		208—232 (A)	$C_{20}H_{31}ClN_2O_3$ (382·9)	62·73 62·32	8·16 8·46	7·31 7·20
XIV	mixture (72)	95—103 (B)	$C_{21}H_{32}N_2O_3$ (360·5)	69·97 70·36	8·95 9·25	7·77 7·61
XIV[b]		225—227 (F)	$C_{21}H_{33}ClN_2O_3$ (397·0)	63·54 63·83	8·38 8·11	7·06 6·72
XV[b]	mixture (70)	126—138 (A)	$C_{24}H_{39}ClN_2O_4$ (455·0)	63·35 63·20	8·64 8·39	6·16 6·01
XVI[b]	*cis* (61)	154—157 (A)	$C_{25}H_{41}ClN_2O_4$ (469·1)	64·02 64·36	8·81 9·01	5·97 6·13
XVII	*trans* (62)	135—137 (D)	$C_{21}H_{33}N_3O_2$ (359·5)	70·16 70·85	9·25 9·30	11·69 11·69
XVII[b,d]	*trans*	190 (G)	$C_{21}H_{37}Cl_2N_3O_3$ (450·5)	56·00 56·24	8·28 8·54	9·33 9·19
XVIII	*trans* (30)	47—50 (H)	$C_{22}H_{35}N_3O_2$ (373·5)	70·74 71·03	9·44 9·46	11·25 11·08
XIX[b,d]	*trans* (82)	187—191 (G)	$C_{23}H_{41}Cl_2N_3O_3$ (478·5)	57·73 58·09	8·64 8·39	8·78 8·79
XX[b,d]	*trans* (79)	161—163 (G)	$C_{25}H_{45}Cl_2N_3O_3$ (506·6)	59·28 58·41	8·95 8·52	8·30 8·24

TABLE II
(*Continued*)

Compound	Isomer (Yield, %)	M.p., °*R* (solvent[a])	Formula (M.w.)	Calculated/Found		
				% C	% H	% N
XXI[b]	—	168—169	$C_{20}H_{25}ClN_2O_3$	63·74	6·68	7·43
	(69)	(F)	(376·9)	63·57	7·02	7·48
XXII[b]	—	165—167	$C_{21}H_{27}ClN_2O_3$	64·52	6·96	7·16
	(56)	(A)	(390·9)	64·75	6·93	7·00
XXIII[b]	—	128—130	$C_{24}H_{33}ClN_2O_4$	64·20	7·41	6·24
	(48)	(I)	(449·0)	64·07	7·58	5·93
XXIV[b]	—	123—125	$C_{26}H_{37}ClN_2O_4$	65·46	7·82	5·87
	(30)	(I)	(477·0)	65·00	7·76	5·94
XXV[b]	—	118—120	$C_{21}H_{27}ClN_2O_2$	67·28	7·26	7·47
	(64)	(C)	(374·9)	67·65	7·46	7·28

[a] A acetone, B hexane, C ethanol, D heptane, E ethanol–ether, F aceton–ethanol, G acetonitrile, H petroleum ether, I ethyl acetate; [b] hydrochloride; [c] isomers separated by crystallization of carbanilates: *trans*, m.p. 102—104°C, *cis*, m.p. 128—130°C; [d] hydrate.

Beside the O-cyclohexyl carbanilates we also prepared some compounds with phenyl group (Table II). The starting 2-(morpholinomethyl)phenol and 2-(piperidinomethyl)phenol were prepared by aminomethylation and their identity was verified by evaluation of their ^1H and ^{13}C NMR spectra.

The identity of the carbanilates prepared was verified by means of elemental analysis and analysis of the IR and ^{13}C NMR spectra. In the IR spectra we identified, inter alia, the bands corresponding to valence vibrations of C=O, N—H, and C—O—C groups of carbanilates (Table III). In the ^{13}C NMR spectra we identified the signals of the individual carbon atoms of carbanilates (Tables IV and V). These spectra also served for estimation of stereochemistry of the substituents of cyclohexane ring and/or as a purity check of the individual isomers. In the case of compound *XIII* the spectrum revealed a relatively high amount of the *cis* isomer which could then be separated by crystallization of the final carbanilate.

Preliminary tests for acute toxicity and local anaesthetic activity were carried out with some of the carbanilates prepared. From the results given in Table VI it follows that all the substances tested show a local anaesthetic activity equal to or higher than that of the standards used (cocaine and procaine). Replacement of cyclohexyl by phenyl in the linking chain reduces both the activity and toxicity. No activity

TABLE III

Infrared spectra (ν, cm^{-1}) of carbanilates *IX*—*XXV*

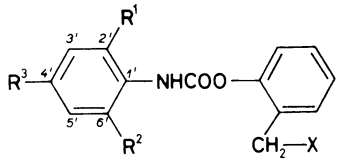
Compound	Technique[a]	N–H	C=O	C–O–C	H–N$^{(+)}$[b]
IX	A	3 422	1 717	1 210 1 215	—
X[c]	B	3 185 3 420	1 708	1 225	2 442
	C	3 175	1 703	1 220	2 552— —2 460
XI	B	3 430	1 719	1 222	—
	C	3 290	1 680	1 253	—
XI[c]	B	3 416	1 714	1 235	2 599
	C	3 133	1 707	1 232	2 597
XII	B	3 433	1 724	1 235	—
XII[c]	B	3 420	1 712	1 235	2 605
	C	3 136	1 707	1 223	2 599
XIII	B	3 427	1 716	1 213	—
	C	3 249	1 682	1 255	—
XIV	B	3 427	1 719	1 232	—
	C	3 232	1 685	1 249	—
XV[c]	B	3 428	1 726	1 222	2 400
	C	3 160	1 728	1 208	2 588
XVI[c]	B	3 428	1 726	1 220	2 200— —2 500
	C	3 336	1 730	1 208 1 220	2 436
XVII	B	3 420	1 702	1 225	—
XVII[c]	C	3 350	1 700	1 220	2 370
XVIII	B	3 420	1 700	1 220	—
XIX[c]	B	3 406	1 715	1 225	2 250
XX[c]	B	3 400	1 715	1 225	2 240
XXI[c]	B	3 172	1 754	1 220	2 592— —2 476
	C	3 420 3 180	1 748	1 210	2 448
XXII[c]	B	3 140	1 738	1 226	2 452
	C	3 416 3 184	1 746	1 210	2 448

TABLE III
(*Continued*)

Compound	Technique[a]	N–H	C=O	C–O–C	H–N$^{(+)b}$
XXIII[c]	B	3 248	1 748 1 720	1 262	2 676– –2 476
	C	3 424	1 756	1 252	2 240
XXIV[c]	B	3 424	1 754	1 252	2 932– –2 860
	C	3 252	1 750 1 724	1 246 1 212	2 560– –2 480
XXV[c]	C	3 152	1 748	1 220	2 636– –2 544

[a] A in dichlormethane, B in chloroform, C Nujol; [b] centre or upper and lower limits of the band; [c] hydrochloride.

differences were observed between the *cis* and *trans* isomers of the compounds investigated. As far as the substituents in aromatic ring are concerned, slightly more active and less toxic are the compounds with alkoxy group.



Compound	R^1	R^2	R^3	X
XXI	$^{7'}CH_3$	$^{7'}CH_3$	H	C_4H_8NO
XXII	$^{7'}CH_3$	$^{7'}CH_3$	$^{8'}CH_3$	C_4H_8NO
XXIII	OC_6H_{13}	H	H	C_4H_8NO
XXIV	OC_8H_{17}	H	H	C_4H_8NO
XXV	$^{7'}CH_3$	$^{7'}CH_3$	H	$C_5H_{10}N$

$OC_4H_9 = O-\overset{7'}{CH_2}-\overset{8'}{CH_2}-\overset{9'}{CH_2}-\overset{10'}{CH_3}$

$OC_6H_{13} = O-\overset{7'}{CH_2}-\overset{8'}{CH_2}-\overset{9'}{CH_2}-\overset{10'}{CH_2}-\overset{11'}{CH_2}-\overset{12'}{CH_3}$

$OC_7H_{15} = O-\overset{7'}{CH_2}-\overset{8'}{CH_2}-\overset{9'}{CH_2}-\overset{10'}{CH_2}-\overset{11'}{CH_2}-\overset{12'}{CH_2}-\overset{13'}{CH_3}$

$OC_8H_{17} = O-\overset{7'}{CH_2}-\overset{8'}{CH_2}-\overset{9'}{CH_2}-\overset{10'}{CH_2}-\overset{11'}{CH_2}-\overset{12'}{CH_2}-\overset{13'}{CH_2}-\overset{14'}{CH_3}$

TABLE IV

^{13}C NMR spectra (δ, ppm) of cyclohexyl part[a] of carbanilates *IX*–*XIV*, *XVI*–*XX*

Compound	Isomer	C-1	C-2	C-3	C-4	C-5	C-6	C-7	C-8	C-9	C-10
IX	*trans*[b]	76·99	38·79	30·79	24·82	23·91	31·84	55·49	49·08	8·58	—
X	*trans*[b]	76·99	38·67	30·83	24·98	23·93	31·82	55·52	49·12	8·54	—
XI	*trans*	76·41	40·28	29·89	24·82	24·43	32·10	61·72	55·36	25·99	24·43
XII	*trans*	76·17	40·31	29·89	24·92	24·51	32·12	61·60	55·23	26·03	24·33
XIII	*trans*[c]	76·02	39·76	29·63	24·82	24·30	31·97	61·33	54·32	67·05	—
XIV	*trans*[c]	75·89	39·76	29·63	24·82	24·30	31·97	61·33	54·32	67·05	—
XVII	*trans*	75·88	40·13	29·66	24·86	24·34	32·18	60·78	55·17	53·71	46·04
XVIII	*trans*[b]	75·88	40·25	29·66	24·86	24·39	32·18	60·79	55·17	53·65	45·98
XIX	*trans*[b]	74·18	37·32	29·95	23·98	23·46	31·12	60·02	50·25 48·44	49·61	42·94
XX	*trans*[b]	74·11	37·15	29·60	23·81	23·34	31·06	59·85	50·25 48·44	49·55	43·00
XIII	*cis*[c]	72·12	37·55	25·85	25·07	21·08	30·40	60·94	54·19	67·05	—
XIII	*cis*[d]	71·86	37·42	25·73	25·08	20·92	30·28	60·81	54·19	67·05	—
XIV	*cis*[c]	71·86	37·42	25·86	25·08	20·92	30·41	60·94	54·32	67·05	—
XVI	*cis*[b]	72·38	35·47	26·89	25·99	20·14	29·88	60·42	53·80 51·46	63·41	—

[a] The numbering of carbon atoms follows the pattern shown in corresponding formulae; [b] hydrochloride; [c] derived from the spectrum of the mixture of both isomers; [d] pure isomers.

TABLE V

^{13}C NMR spectra (δ, ppm) of aromatic part[a] of carbanilates *IX*—*XIV*, *XVI*—*XX*, *XXIII*—*XXIV*

Carbon	Compound												
	IX	*XI*	*XIII*	*XVII*	*X*	*XII*	*XIV*	*XVIII*	*XVI*	*XIX*	*XX*	*XXIII*	*XXIV*
C=O	153·9	154·6	154·9	154·4	154·0	154·5	154·8	154·6	152·8	152·7	152·8	150·8	150·8
C-1′	134·4	134·0	134·2	134·0	136·2	136·4	136·7	136·5	127·4	127·1	127·2	126·5	126·4
C-2′	135·8	135·9	135·9	135·9	135·4	135·6	135·7	135·6	147·2	147·5	147·6	150·1	150·1
C-3′	128·0	128·1	128·0	128·1	128·7	128·7	128·8	128·8	111·2	111·3	111·3	111·4	111·4
C-4′	126·8	127·1	126·9	127·0	131·6	131·3	131·4	131·3	123·3	123·4	123·4	123·2	123·2
C-5′	128·0	128·1	128·0	128·1	128·7	128·7	128·8	128·8	120·9	120·8	120·8	121·0	121·0
C-6′	135·8	135·9	135·9	135·9	135·4	135·6	135·7	135·6	118·4	118·7	118·8	120·3	120·3
C-7′	18·6	18·3	18·3	18·4	18·5	18·3	18·3	18·3	68·9	68·6	68·8	69·0	69·0
C-8′	—	—	—	—	20·9	20·9	20·9	20·9	29·0	31·1	29·0	29·1	29·2
C-9′	—	—	—	—	—	—	—	—	26·0	19·2	25·5	25·7	26·1
C-10′	—	—	—	—	—	—	—	—	29·0	13·9	31·4	31·5	29·4
C-11′	—	—	—	—	—	—	—	—	31·7	—	22·5	22·6	29·3
C-12	—	—	—	—	—	—	—	—	22·5	—	14·0	14·0	31·8
C-13′	—	—	—	—	—	—	—	—	14·0	—	—	—	22·7
C-14′	—	—	—	—	—	—	—	—	—	—	—	—	14·1

[a] The numbering of carbon atoms follows the pattern shown in corresponding formulae.

With compound *XIII* (2-(morpholinomethyl)cyclohexyl 2,6-dimethylcarbanilate) we also carried out orientation tests of antiarrythmic activity in strophantin-provoked arrythmias and of influence on heart rate. Whereas the dose of 4 mg per kg showed a positive effect, the double concentration already appeared as toxic.

Only evaluation of a larger series of carbanilates with various substituents will allow to make conclusions from pharmacological results.

EXPERIMENTAL

The IR spectra were measured with two-beam spectrophotometers Specord IR-75 and M-80 (Zeiss, Jena) in Nujol suspensions and in chloroform or dichloromethane solutions.

The ^{1}H NMR spectra were measured with a CW spectrometer Tesla BS-487 A with the working frequence of 80 MHz. The ^{13}C NMR spectra were measured with a FT NMR spectrometer Jeol FX-100 with the working frequence of 25·05 MHz, the compounds *XXI*—*XXV* on a Varian XL 300 apparatus. All the samples were measured as solutions in deuterochloroform with tetramethylsilane as the internal standard. The signals of individual carbon atoms were assigned with the help of literature data[11,12] for 2-methylcyclohexanol and according to the C–H splitting in the measurements by the off-resonance decoupling technique or with application of the DEPT experiment. The chemical shifts of carbon atoms of aromatic rings and alkoxy groups were compared with the calculated approximate values of chemical shift.

TABLE VI

Pharmacological properties of carbanilates *X*—*XVIII*, *XX*—*XXV*

Compound	Anaesthesia[a]		LD_{50} mg/kg
	surface[b]	infiltration[c]	
X	—	—	≦50
XI	—	—	<50
XII	—	—	50—100
XIII	—	18·5	50—200
XIV	25·0	4·0	300—600
XV	1·3	15·3	50—200
XVI	17·1	20·0	>600
XVII	5·0	14·2	<50
XVIII	5·0	11·1	50—100
XX	20·0	40·0	200—400
XXI	—	2·3	>600
XXII	—	1·0	300—500
XXIII	—	1·0	>600
XXIV	—	1·0	>600
XXV	—	2·0	400—500

[a] Relative activity; [b] cocain = 1·0; [c] procain = 1·0.

The orientation tests of acute toxicity were carried out with white mice according to Švec et al.[13], the efficiency index of surfacial and infiltration anaesthesia was estimated by the method by Vrba and Sekera[14]. The antiarrythmic activity and influence on the heart rate were evaluated according to refs[15,16].

2-(Dialkylaminomethyl)cyclohexanols

They were prepared by the Mannich reaction and subsequent reduction. The Mannich reaction was carried out in excess cyclohexanone with 36% aqueous solution of formaldehyde[8,9,17] or paraformaldehyde[18] and with the corresponding amine or ammonium chloride. The reduction of the 2-(dialkylaminomethyl)cyclohexanone hydrochloride formed was accomplished with sodium tetrahydridoborate in aqueous medium[19] or, after liberation of the base, with lithium tetrahydridoaluminate in tetrahydrofurane[8] or with sodium bis(2-methoxyethoxy)dihydridoaluminate in toluene solution according to a modified procedure[20] (the decomposition was carried out with 20% sodium hydroxide solution). The obtained mixtures of *cis* and *trans* isomers of 2-(dialkylaminomethyl)cyclohexanols were treated with 4-nitrobenzoyl chloride to give the hydrochlorides of 2-(dialkylaminomethyl)cyclohexyl 4-nitrobenzoates which were separated by crystallization from acetonitrile, ethanol, or acetone. The pure isomers (mostly *trans*) were obtained by hydrolysis with potassium hydroxide solution[8].

The purity of the cyclohexanols prepared was checked by TLC (Silufol, benzene–acetone–diethylamine 20 : 10 : 1) with detection in iodine vapours or by means of the Dragendorff reagent (the Munier modification[21]). Pure *cis* and *trans* isomers of 2-(dimethylaminomethyl)-cyclohexanol[7] were used as the standards (Table VII).

2-Morpholinomethylphenol and 2-Piperidinomethylphenol

Both the phenols were obtained by modifications of known procedures[22,23]. A solution of 0·5 mol amine in 50 ml ethanol was treated with 0·5 mol paraformaldehyde. After cooling to 25°C, a solution of 0·5 mol phenol in 50 ml ethanol was added. The mixture was left to stand at room temperature until it was clear, and then it was refluxed 2 h. Ethanol was evaporated and the respective phenol was distilled under reduced pressure or crystallized from a suitable solvent.

2-Morpholinomethylphenol (VII): m.p. 85–89°C (acetone). ^{1}H NMR spectrum: 6·52–7·17 m, 4 H (ArH); 3·58 s, 2 H (CH_2); 2·46 t, 4 H (CH_2–N, J = 4·5); 3·65 t, 4 H (CH_2–O, J = 4·5). ^{13}C NMR spectrum: 157·5 (C-1); 120·6 (C-2); 128·8 (C-3); 119·2 (C-4); 128·8 (C-5); 116·0 (C-6); 61·7 (CH_2); 52·7 (CH_2–N); 66·6 (CH_2–O). For $C_{11}H_{15}NO_2$ (193·1) calculated: 68·37% C, 7·82% H, 7·25% N; found: 68·50% C, 7·95% H, 7·09% N.

TABLE VII

TLC of isomeric N-substituted 2-aminomethylcyclohexanols

Compound:		*II*	*III*	*IV*	*V*
R_F	*cis*:	0·15	0·35	0·37	0·40
	trans:	0·44	0·51	0·64	0·56

2-Piperidinomethylphenol (VIII): b.p. 128–135°C/30 Pa (ref.[24] b.p. 126–130°C/36 Pa). ^{1}H NMR spectrum: 6·47–7·11 m, 4 H (ArH); 3·52 s, 2 H (CH_2); 2·37 m (centre), 4 H (CH_2N); 1·48 m (centre), 6 H (CH_2 in piperidine).

2-(Dialkylaminomethyl)cyclohexyl and 2-(Dialkylaminomethyl)phenyl Carbanilates

They were prepared by addition of the respective cyclohexanols or phenols to the corresponding substituted phenyl isocyanate. Equimolar amounts of the reactants were heated in anhydrous toluene 5 h. After cooling and evaporation of the solvent the obtained semi-solid or solid base of the corresponding carbanilate was purified by crystallization either as such or as the salt with hydrochloric acid (Table II).

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