Synthesis of Aminomethylazetidines Regioselective Reactions of Mesyloxymethylazetidinones with Nucleophiles II.

Éva Boros[a*], Ferenc Bertha[a], Gábor Czira[b], Antal Feller[c], József Fetter[a], Mária Kajtár-Peredy[d], Gyula Simig[c]

[a]Department of Organic Chemistry, Budapest University of Technology and Economics, H-1521 Budapest, Hungary
[b]Gedeon Richter Chemical Works Ltd, H-1475 Budapest 10, Hungary
[c]EGIS Pharmaceuticals Ltd., Chemical Research Division, H-1475 Budapest 10, Hungary
[d]Institute of Chemistry, Chemical Research Center, Hungarian Academy of Sciences, H-1525 Budapest, Hungary

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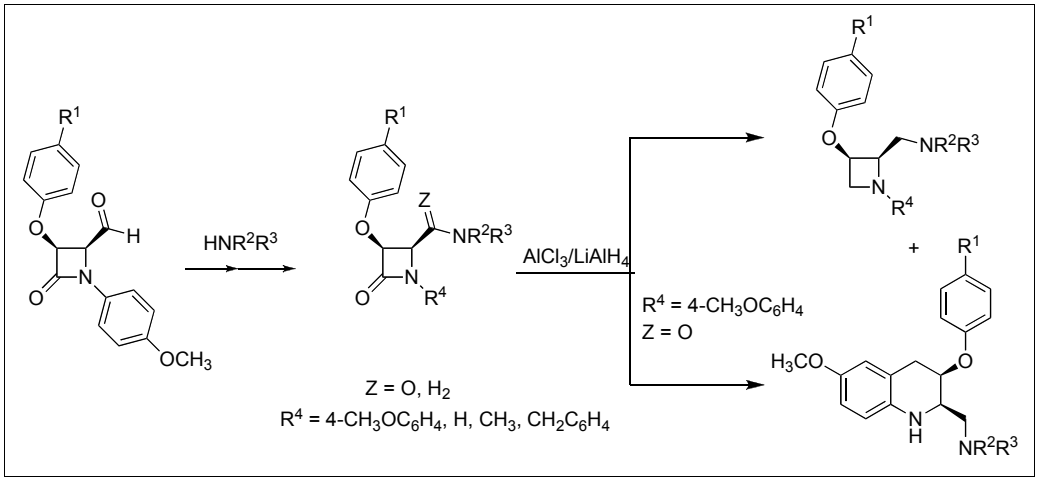

Two efficient methods have been developed for the synthesis of variously substituted 2-aminomethyl-azetidine derivatives **5** by regioselective nucleophilic substitution of 4-mesyloxymethylazetidin-2-ones **3** followed by reduction or by reduction of the appropriate 4-oxo-azetidine-2-carboxamides **7**. A novel ring transformation of 4-oxoazetidine-2-carboxamides **7** into tetrahydroquinolines **16** by reaction with lithium aluminium hydride / aluminium trichloride has been investigated.

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Introduction.

Several compounds containing two or more hetero-atoms in positions 1,4 or 1,5 to each other are well known antidepressants (Fluoxetine [1], Paroxetine [2], Reboxetine [3]). As the azetidine ring is a frequently occurring important constituent of drug molecules with similar effects on the central nerve system [4,5], investigation of azetidine derivatives containing heteroatoms in their side chains was expected to lead to promising drug candidates.

Here we report the successful syntheses of 2-(*N,N*-disubstituted aminomethyl)azetidines **5**[†] by reacting 4-mesyloxymethylazetidinones **3** with secondary amines, followed by [7] reduction of the resulting 4-(*N,N*-disubstituted aminomethyl)azetidin-2-ones **4** (see Scheme 1).

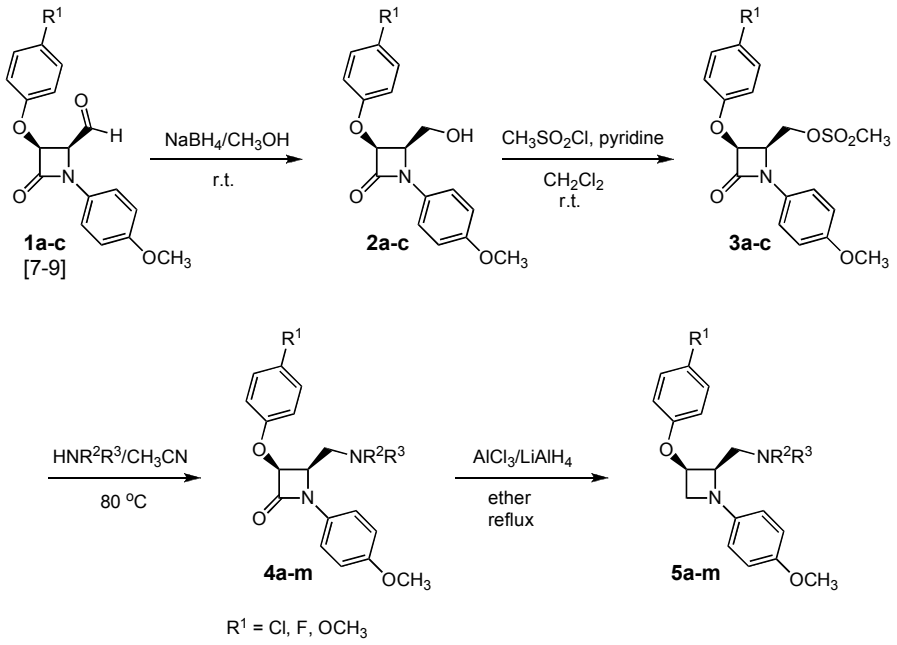
Attempts to prepare 1-unsubstituted analogues **11** of the compounds **5**, and their 1-alkyl derivatives (**12**, **13**), by removal of the 4-methoxyphenyl group met with failure (see below). Therefore an alternative method for the preparation of compounds **11**-**13** starting from the appropriate 4-oxoazetidine-2-carboxamides **7** was devised (see Scheme 2).

Results and Discussion.

3-Aryloxy-4-mesyloxymethylazetidin-2-ones **3** were synthesised from compounds **1a-c** *via* compounds **2a-c** (Scheme 2). The reaction of compounds **3** with secondary amines[‡] afforded the 4-aminomethyl-3-aryloxyazetidin-2-ones **4a-m**, whose reduction with lithium aluminium hydride/aluminium trichloride gave 2-aminomethyl-azetidine derivatives **5** in good yields (Table 1).

Since compounds **5** could not be converted into the *N*-unsubstituted analogues **11** by cerium ammonium nitrate, an alternative method for the synthesis of these compounds (**11**), and *N*-methyl (**12**) and *N*-benzyl (**13**) derivatives, from the oxoazetidinecarboxamides **7** as key intermediates was elaborated (see Scheme 2). The 1-(4-methoxyphenyl)-4-oxoazetidine-2-carboxyamides **7** smoothly underwent cerium ammonium nitrate induced *N*-(demethoxy-phenylation) to afford the desired compounds **8**. Alkylation of compounds **8** followed by reduction of the lactam and

Scheme 1



Synthesis of aminomethylazetidines **5** from azetidinecarbaldehydes **1** [7-9]

Table 1

Yields and melting points of compounds **4** and **5** synthesised by the method indicated in Scheme 1.

Compound	R^1	HNR^2R^3	Yield [%]	Mp [°C]
4a	Cl	piperidino	64	147-151[a]
4b	Cl	morpholino	50	147-148
4c	F	piperidino	81	142
4d	F	morpholino	84	124
4e	F	*N*-methylpiperazino	69	143
4f	F	*N*-benzylpiperazino	63	126
4g	CH_3O	pyrrolidino	38	133
4h	CH_3O	piperidino	66	147
4i	CH_3O	morpholino	56	167[b]
4j	CH_3O	thiomorpholino	88	178
4k	CH_3O	*N*-methylpiperazino	77	145
4l	CH_3O	benzylmethylamino	67	100
4m	CH_3O	hexamethylenimino	75	120
5a	Cl	piperidino	73	88-92[c]
5b	Cl	morpholino	55	132-134[d]
5c	F	piperidino	58	103-104
5d	F	morpholino	61	118
5e	F	*N*-methylpiperazino	43	103
5f	F	*N*-benzylpiperazino	62	135-136[e]
5g	CH_3O	pyrrolidino	27	63-64
5h	CH_3O	piperidino	43	80-81
5i	CH_3O	morpholino	74	99
5j	CH_3O	thiomorpholino	76	98
5k	CH_3O	*N*-methylpiperazino	79	95
5l	CH_3O	benzylmethylamino	76	oil
5m	CH_3O	hexamethylenimino	44	oil

Recrystallized from [a] acetonitrile, [b] toluene, [c] isopropyl alcohol, [d] methanol, [e] ethanol respectively.

amide carbonyl group gave the desired azetidines **12-13** in good yields. By reaction of compounds **8** with lithium aluminium hydride/aluminium trichloride – depending on the reaction time – along with the desired **11**, partly reduced intermediates **14** were also isolated, which could be reduced into **11** in a second reaction step. When allowing the reduction to go to completion, the yield of **11** decreases – presumably due to decomposition.

Scheme 2

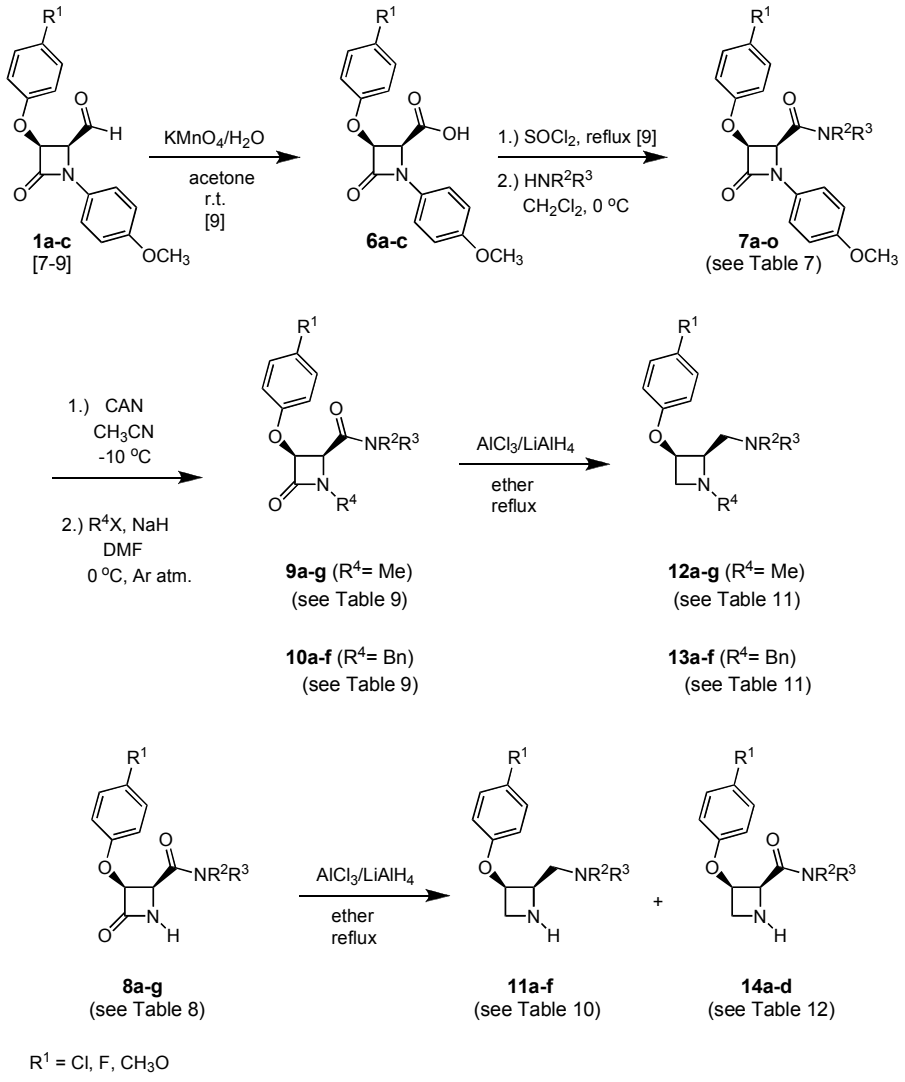


Table 2

Yields and melting points of compounds **11**-**14** obtained by the method shown in Scheme 2

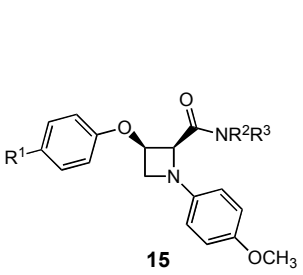
Compound	R^1	NR^2R^3	R^4	Yield [%]	Mp [°C]
11a	Cl	pyrrolidino	H	33	105
11b	Cl	piperidino	H	23+20% **14**	183
11c	Cl	hexamethylenimino	H	28+25% **14**	181[a]
11d	F	pyrrolidino	H	20	oil
11e	F	piperidino	H	25+26% **14**	110
11f	F	hexamethylenimino	H	28+31% **14**	193[a]
12a	Cl	pyrrolidino	methyl	70	184-186[a]
12b	Cl	piperidino	methyl	64	170-174[a]
12c	Cl	hexamethylenimino	methyl	68	140-145[a]
12d	F	pyrrolidino	methyl	80	180-184[a]
12e	F	piperidino	methyl	72	155-160[a]
12f	F	morpholino	methyl	88	172-177[a]

Table 2 (continued)

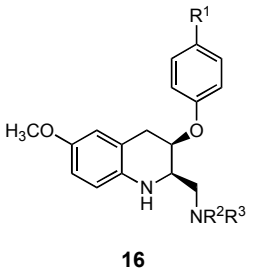
Compound	R^1	NR^2R^3	R^4	Yield [%]	Mp [°C]
12g	F	hexamethylenimino	methyl	68	150-153[a]
13a	Cl	pyrrolidino	benzyl	63	78
13b	Cl	piperidino	benzyl	65	oil
13c	Cl	hexamethylenimino	benzyl	63	oil
13d	F	pyrrolidinol	benzyl	60	70
13e	F	piperidino	benzyl	50	62
13f	F	hexamethylenimino	benzyl	57	79

[a] Recrystallized from $CH_3OH/(C_2H_5)_2O$.

In order to extend the latter method to the synthesis of compounds **5** as well, compounds **7** were reacted with lithium aluminium hydride/aluminium trichloride. Unfortunately, in a similar case of compounds **8**, this reaction afforded the reduced aminomethylazetidines **5** in low yields together with partly reduced intermediates **15** and unexpected ring transformation products **16** (Table 3).



15

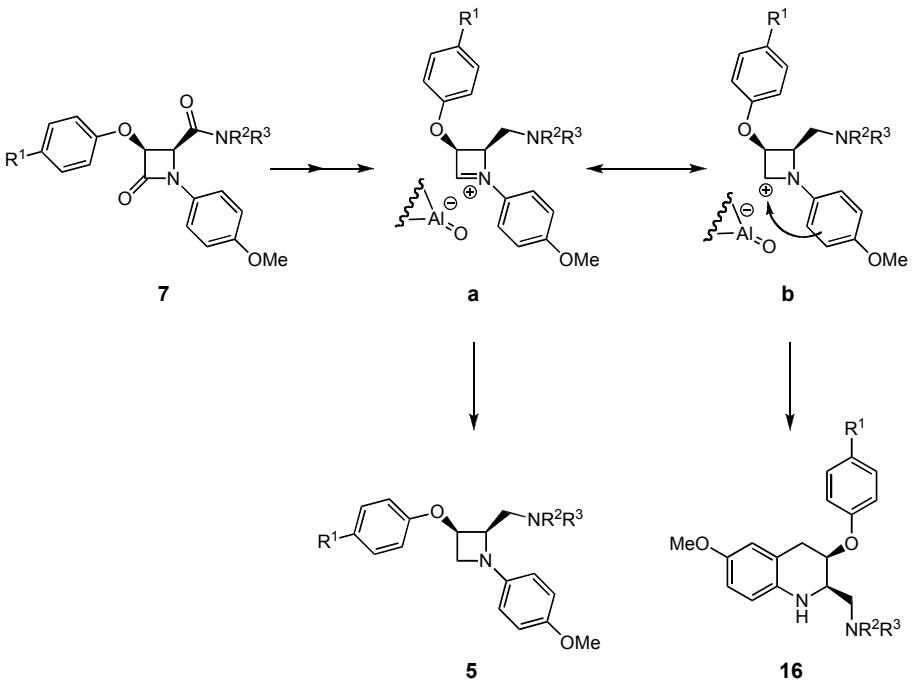


16

N-Arylazetidin-2-ones have previously been shown to undergo a Fries-type rearrangement: a Lewis acid catalysed cleavage of the N-C(O) bond followed by intramolecular acylation, resulting in the corresponding 2,3-dihydro-4(1*H*)-quinolinones [11-14], but no azetidinone-tetrahydroquinoline rearrangement has been reported yet. From the reaction mixtures of compounds **7** with lithium aluminium hydride/aluminium trichloride we have never isolated an intermediate dihydroquinolinone, and formation of tetrahydroquinolines has never been observed [11-14] on treatment of *N*-arylazetidin-2-ones with Lewis acids alone. Therefore it appears to be reasonable to assume that, in agreement with the mechanism suggested for the lithium aluminium hydride/aluminium trichloride reduction of azetidine-2-ones [6], the novel reductive *N*-arylazetidin-2-one – tetrahydroquinoline rearrangement takes place *via* the mesomeric cationic intermediate **a**→**b** as shown in Scheme 3.

This new ring transformation reaction constitutes a new method for the synthesis of chiral tetrahydroquinoline derivatives in a stereoselective manner.

Scheme 3



7 **a** **b**

5 **16**

Table 3

Products and yields in the reduction of oxoazetidinecarboxamides **7**.

Starting compound	R^1	NR^2R^3	Yield [%] (**15**)	(**16**)	(**5**)
7a	Cl	pyrrolidino	-	20	42
7b	Cl	morpholino	-	17	44
7f	Cl	diisopropylamino	12	43	11
7g	F	pyrrolidino	-	15	36
7j	F	diisopropylamino	14	39	10
7l	CH_3O	pyrrolidino	-	12	32
7m	CH_3O	dibenzylamino	-	33	37
7n	CH_3O	diethylamino	-	14	31
7o	CH_3O	diisopropylamino	18	35	3

Conclusions.

Thirty-three new aminomethylazetidinones were synthesised as potential effective drug candidates. Two synthetic methods have been developed for the preparation of these compounds. Thirteen 2-aminomethyl-3-aryloxy-1-(4-methoxyphenyl)azetidines have been synthesised by regioselective nucleophilic substitution of the corresponding 4-mesyloxymethylazetidinones and twenty analogous compounds containing a substitutent other than 4-methoxyphenyl at the ring nitrogen by reduction of the appropriate oxoazetidinecarboxylic amide. Ten chiral tetrahydroquinolines were synthesised by a novel ring transformation of *N*-arylazetidinones.

EXPERIMENTAL

Abbreviations: Mesyloxy: methylsulfonyloxy. *Techniques*: All reactions were monitored by thin layer chromatography (DC-Alufolien 60 F_{254}, Merck; visualized by UV_{254}, and/or UV_{366} irradiation and/or by dipping into phosphormolybdic acid soln., followed by heating), and allowed to go to completion. Separations of product mixtures by flash column chromatography were carried out using Kieselgel 60 G (Merck) as the adsorbent unless otherwise stated (pressure differences between the two ends of the columns 67-75 kPa). For preparative thin layer chromatography separations 20x20 cm glass plates coated with Kieselgel $PF_{254+366}$ (Merck; thickness of adsorbent layer 2.0 mm) were used (home-made ones, except when otherwise noted). The solvents are given in parentheses. The purity of the products was checked in combination with IR spectroscopy, by thin layer chromatography on DC-Alufolien 60 F_{254} (Merck); the individual compounds were detected by UV irradiation. Evaporations to dryness were carried out at reduced pressure. All new compounds described in the present paper were colourless crystals, unless otherwise stated. Melting point values were determined on a Kofler hot-stage melting point apparatus and are uncorrected. IR spectra were recorded on a Specord-75 or Specord M-80 spectrometer (Zeiss, Jena), measured as film (in the case of oils) or potassium bromide pellets (in the case of crystalline compounds), absorption bands are in cm^{-1}. NMR spectra were obtained with a Varian XL-400 (^1H: 400 MHz, ^{13}C: 100 MHz) spectrometer, chemical shifts (δ-values) are reported in ppm with respect to Me_4Si (δ= 0 ppm) as the internal standard, coupling constants (J) are given in Hz. Exact molecular mass determinations were made at 70 eV with a Finnigan-MAT 95 SQ hybride – tandem instrument using a heated direct inlet system and perfluorokerosene as the reference.

General Procedure for the Synthesis of *cis*-4-(Hydroxymethyl)-azetidin-2-ones **2a-c**.

To a solutions of 4-formyl β-lactams **1a-c** [7-9] (54.37 mmoles) in methanol (160 ml) was added sodium borohydride (65.25 mmoles) in small portions with vigorous stirring and external ice-cooling. The resulting mixture was stirred at room temperature until complete reaction. After evaporation of the solvent at reduced pressure, the residue was washed with water (200 ml) and extracted with dichloromethane (3×70 ml). The combined organic layers were dried on magnesium sulfate and evaporated to yield the corresponding compounds **2** that were recrystallized from ethyl acetate or diethyl ether. In the case of **2b** and **2c**, the products were filtered directly from the reaction mixture after cooling (Table 4).

General Procedure for the Synthesis of the 3-Aryloxy-1-(4-methoxyphenyl)-2-oxoazetidin-4-ylmethyl methanesulfonates **3a-c**.

Methanesulfonyl chloride (62.66 mmoles) was added dropwise to solutions of compounds **2** (52.22 mmoles) in pyridine (52 ml) with continuous stirring and external ice-cooling. The mixture was stirred at room temperature for 2 hours, then poured onto ice to obtain pure crystalline products **3** (Table 4).

General Procedure for the Synthesis of the Amino-methylazetidin-2-ones **4**.

To solutions of compounds **3** (0.625 mmoles) in acetonitrile or dimethyl formamide (1.6 -2 ml) was added 3.1 mmoles of the appropriate amine at room temperature. The reaction mixture was refluxed until complete reaction and evaporated *in vacuo*. The residue was washed with water and with 1 *M* sodium hydroxide solution. The crystalline product was filtered and purified by flash chromatography (dichloromethane:aceton = 10:0.5 or cyclohexane:ethyl acetate =3:1).

In the case of **4a-c, e, f, g, j** the crystalline products were filtered directly from the reaction mixture after cooling (Table 1 and Table 5).

General Procedure for the Synthesis of the Aminomethyl-azetidines **5**.

a.) To a solution of aluminium trichloride (15 mmoles) in anhydrous ether was added lithium aluminium hydride (15 mmoles). After refluxing for 50 minutes, 5 mmoles **4** was added, and the reaction mixture was refluxed until complete reaction (~4 hours). After cooling 20 ml ethyl acetate and 10 ml 10 *M* sodium hydroxide was added to the reaction mixture followed by 10 minutes stirring. The inorganic phase was then extracted with ethyl acetate (3×30 ml). The organic phase was dried on magnesium sulfate and evaporated *in vacuo*. The residue was purified by flash chromatography (dichloromethane:aceton = 10:0.1->10:0.5) (Table 6)

b.) To a solution of aluminium trichloride (120 mmoles) in anhydrous ether (590 ml) was added lithium aluminium hydride (120 mmoles) under argon at room temperature. After

1 hour reflux, 40 mmoles of the azetidinone compound **7** was added, and the reaction mixture was refluxed until complete reaction (3-5 hours). After addition of 1 *M* sodium hydroxide (270 ml) at 0 °C, the reaction mixture was stirred for 20 minutes. The white precipitate was filtered, and the separated inorganic layer was extracted with ether (3×100 ml) and with ethyl acetate (3×80 ml).

The combined ether phases were dried on magnesium sulfate and evaporated *in vacuo*. The residue was crystallised with ether to give partly reduced products **15**. The filtrate was purified by flash chromatography (dichloromethane:aceton = 7:0.1->7:1) to give products **5** and **16**.

The combined ethyl acetate phases were dried on magnesium sulfate and evaporated *in vacuo*. The residue was crystallised from diethyl ether to give products **15** (Tables 6, 13 and 14).

General Procedure for the Synthesis of Azetidinone Carboxyamides **7**.

To carboxylic acid **6** (50 mmoles) was added 120 ml thionyl chloride, and the reaction mixture was refluxed for 1 hour. Excess of the reagent was evaporated *in vacuo*. The acid chloride was dissolved in dichloromethane (100 ml) and added dropwise to a solution of the appropriate amine in dichloromethane (100 ml) with stirring and external ice cooling. After 30 minutes stirring, the reaction mixture was washed with 80 ml of water and 1 *M* hydrochloric acid. The organic phase was dried on magnesium sulfate and evaporated *in vacuo*. The residue was crystallised from diethyl ether (Table 7).

General Procedure for the Synthesis of *N*-Unsubstituted 4-oxoazetidinecarboxylic Amides **8**.

A solution of cerium ammonium nitrate (42.4 g) in water (300 ml) was added dropwise to a solution of the appropriate amide **7** (35 mmoles) in 240 ml of acetonitrile at -10 °C. The reaction mixture was stirred for 20 minutes then 300 ml of ethyl acetate was added. The separated inorganic phase was extracted with ethyl acetate (3×100 ml). The combined organic phases were washed with 10% sodium hydrogen sulfite (200 ml), water (200 ml) and concentrated sodium chloride (100 ml), dried on magnesium sulfate, and evaporated *in vacuo*. The residue was purified by flash chromatography (dichloromethane:aceton = 10:1→2:1).

In the case of morpholine derivative **8e**, the product crystallised directly from the reaction mixture after 5 minutes stirring. The filtrate was washed with concentrated sodium bicarbonate (50 ml), 10% sodium hydrogen sulfite (100 ml), 0.5 *M* sodium hydroxide (150 ml) and water (100 ml), then dried on magnesium sulfate and evaporated *in vacuo*. The residue was crystallised from ethyl acetate (Table 8).

General Procedure for the Synthesis of 1-Alkyl-4-oxoazetidine-carboxamides **9** and **10**.

To a solution of compound **8** (30 mmoles) in dry dimethyl formamide was added methyl iodide (90 mmoles) or benzyl bromide (90 mmoles) and 60% sodium hydride (33 mmoles) under argon at 0 °C. The reaction mixture was stirred at 0 °C for 1.5 hours (methyl iodide) or for 45 minutes (benzyl bromide), then poured onto water (1100 ml), and extracted with dichloromethane (4×100 ml). The combined organic layers were stirred with water (100 ml) giving an emulsion that was treated with charcoal and filtrated. The separated organic layer was dried on magnesium sulfate and evaporated *in vacuo*.

a.) In the case of methylation the residue was dissolved in ethyl acetate (150 ml), treated with charcoal and evaporated *in vacuo*. The resulting colourless crystals were washed with ether and recrystallised from ethyl acetate.

b.) In the case of benzylation, the residue was purified by flash chromatography (hexane:ethyl acetate = 3:1→1:1), and the product was crystallised from diethyl ether.

General Procedure for the Synthesis of Azetidines **11-12** (Hydrochloride Salts), **13** and **14**.

To a solution of aluminium trichloride (65 mmoles) in anhydrous ether (360 ml) was added lithium aluminium hydride (100 mmoles) under argon at 0 °C. After refluxing for 1 hour, 20 mmoles of the azetidinones **8-10** was added, and the reaction mixture was refluxed for 3-5 hours. After addition of 1 *M* sodium hydroxide (220 ml) at 0 °C, the reaction mixture was stirred for 20 minutes. The white precipitate was filtered, and the separated inorganic layer was extracted with diethyl ether (4×100 ml). The combined organic phase was washed with cc. sodium chloride (200 ml), dried on magnesium sulfate and evaporated *in vacuo*.

a.) In the case of compounds **11** the residue (the partly reduced product **14**) was crystallised from diethyl ether. The filtrate was flash chromatographed (dichloromethane:methanol = 10:0.1→10:2) to give pure products that were then transformed to their hydrochloride salt with etheric hydrochloric acid solution.

b.) In the case of compounds **12** the residue was dissolved in hexane, treated with charcoal and evaporated *in vacuo*. The resulting colourless oil was dissolved in methanol (10 ml). 2.1 eq. hydrochloric acid (5 *M* solution in diethyl ether) and 30 ml of ether was added to the solution to give crystalline product in good yields.

c.) In the case of compounds **13** the residue was purified by flash chromatography (hexane:diethyl ether = 10:1→10:2), and crystallised from hexane.

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REFERENCES AND NOTES

* Corresponding author: Tel.: 00 44 28 9033 5420; fax: 00 44 28 9066 5297; e-mail: eboros@mail.bme.hu.

† All chemical compounds discussed in the present paper are racemic and only one enantiomer is shown.

‡ Application of ammonia instead of secondary amines in the aminolysis step (step 3, Scheme 1), resulted in cleavage of the lactam ring even at room temperature [10]. A study into the reaction of mesyloxymethylazetidinones (**3**) with primary amines is in progress.

[1] B. B. Malloy and K. K. Schmiegel, DE 2500110; US 4314081 (1975, 1982 both to Lilly); *Chem. Abstr.*, **83**, 192809d (1975) for each patent..

[2] P. Melloni et al., DE 2901032; eidem; US 4229449 (1979, 1980 both to Farmitalia Carlo Erba). *Chem. Abstr.*, **91**, 211426k (1979) for each patent.

Table 4

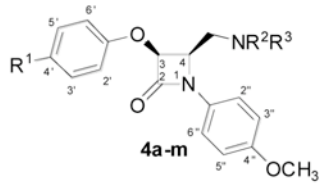
Yields, Melting Points, IR, NMR[a] and HRMS Data of Compounds **2** and **3**

Comp.	X	3-H	4-H	4-CH_2	2",6"-H	3",5"-H	4"-OMe	Y	Yield [%]	Mp [°C]	IR [cm^{-1}]	HRMS m/z (EI)
2a	Cl	5.33, d, $J_{3,4}$=5.1	4.47, ddd, $J_{4,CH2}$=3.6+4.8	4.11+4.15, 2dd, J_g=12.7	7.10, m	7.28, m		OH: 2.00, s	91	119-120[b]	3630, 1730, 1490, 1210, 770	$C_{17}H_{16}ClNO_4$ req.: 333.07679 found: 333.0771
2b	F	5.32, d, $J_{3,4}$=4.3	4.67, ddd, $J_{4,CH2}$=3.5+4.8	4.13+4.18, 2dd, J_g=12.5	7.02, m	7.13, m		OH: 2.06, dd, $J_{OH,CH2}$=5.5+7.5	81	103[c]	3620, 1745, 1490, 1220, 800	FB35
2c	MeO	5.29, d, $J_{3,4}$=5.1	4.44, ddd, $J_{4,CH2}$=3.6+4.7	4.11+4.16, 2dd, J_g=12.7	7.08, m	6.85, m	3.77, s	OH: 2.16, s	91	110	3630, 1730, 1490, 1360, 1210, 1000, 790	$C_{18}H_{19}NO_5$ req.: 329.12630 found: 329.1255
3a	Cl	5.40, d, $J_{3,4}$=5.0	4.73, ddd, $J_{4,CH2}$=5.3+5.4	4.61+4.66, 2dd, J_g=11.3	7.08, m	7.30, m		OSO_2Me: 2.90, s	88	139[b]	1750, 1500, 1350, 1220, 1155, 800	$C_{18}H_{18}ClNO_6S$ req.: 411.05434 found: 411.0541
3b	F	5.38, d, $J_{3,4}$=4.9	4.73, ddd, $J_{4,CH2}$=5.2+5.2	4.61+4.68, 2dd, J_g=11.1	7.09, m	7.03, m		OSO_2Me: 2.90, s	74	126[b]	1750, 1500, 1360, 1220, 1165, 920, 800	$C_{18}H_{18}FNO_6S$ req.: 395.08389 found: 395.0849
3c	MeO	5.36, d, $J_{3,4}$=4.7	4.71, ddd, $J_{4,CH2}$=5.2+5.2	4.60+4.67, 2dd, J_g=10.9	7.05, m	6.86, m	3.78, s	OSO_2Me: 2.88, s	99	132[d]	1750, 1500, 1350, 1210, 1165, 920, 800	$C_{19}H_{21}NO_7S$ req.: 407.13087 found: 407.10471

[a] Solvent: $CDCl_3$; 4-methoxyphenyl: 7.5 (m, 2",6"-H), 6.9 (m, 3",5"-H), 3.8 (s, OCH_3); [b] Recrystallized from CH_3OH, [c] CH_3OH/H_2O, [d] ethyl acetate

Table 5

NMR[a], IR and HRMS Data or Elemental Analysis of Compounds **4**

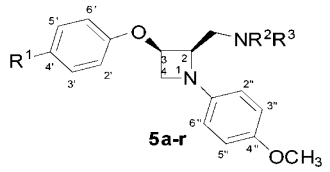


Comp.	R^1	3-H	4-H	4-CH_2	2",6"-H	3",5"-H	4"-OCH_3	NR^2R^3	IR [cm^{-1}]	Elemental analysis [%] or HRMS m/z (EI)
4a	Cl	5.27, d, $J_{3,4}$=5.0	4.44, ddd, $J_{4,CH2}$=4.6+6.6	2.75+2.89, 2dd, J_g=14.0	7.57, m	7.08, m		piperidino: 2.35-2.50+1.35-1.55, m	1741, 1500, 1390, 1210	$C_{22}H_{25}ClN_2O_3$ (400.89) req.: C: 65.91, H: 6.29, N: 6.99 found: C: 65.83, H: 6.31, N: 7.05
4b	Cl	5.30, d, $J_{3,4}$=5.0	4.46, ddd, $J_{4,CH2}$=4.7+6.5	2.82+2.86, 2dd, J_g=13.8	7.27, m	7.07, m		morpholino: 2.42-2.58+ 3.54-3.66, m	1735, 1500, 1100, 800	$C_{21}H_{23}ClN_2O_4$ (402.87) req.: C: 62.61, H: 5.75, N: 6.95; found: C: 62.47, H: 5.68, N: 6.74
4c	F	5.25, d, $J_{3,4}$=5.0	4.45, brm	2.76+2.85, 2brm	7.10, m	7.00, m		piperidino: 2.44+1.4-1.6, m	1745, 1500, 1380, 1210	$C_{22}H_{25}FN_2O_3$ req.: 384.18492 found: 384.1845
4d	F	5.27, d, $J_{3,4}$=5.0	4.48, brm	2.9, brm	7.10, m	6.99, m		morpholino: 3.65+2.57, m	1730, 1500, 1210, 800	$C_{21}H_{23}FN_2O_4$ req.: 386.16418 found: 386.1638
4e	F	5.26, d, $J_{3,4}$=5.1	4.44, ddd, $J_{4,CH2}$=4.4+6.7	2.83+2.90, 2dd, J_g=13.8	7.09, m	7.00, m		*N*-Me-piperazino: 2.25-2.65, m, 2.27, s	1735, 1500, 1390, 1210	$C_{22}H_{26}FN_3O_3$ req.: 399.19582 found: 399.1948
4f	F	5.25, d, $J_{3,4}$=5.0	4.43, ddd, $J_{4,CH2}$=4.3+6.6	2.82+2.90, 2dd, J_g=13.9	7.06, m	6.98, m		*N*-Bn-piperazino: 7.2-7.35+3.50+2.35-2.65, m	1745, 1500, 1390, 1210	$C_{28}H_{30}FN_3O_3$ req.: 475.22712 found: 475.2268
4g	CH_3O	5.25, d, $J_{3,4}$=5.1	4.46, dt, $J_{4,CH2}$=5.4	3.03, d	7.08, m	6.84, m	3.78, s	]pyrrolidino: 2.60+1.76, m	1750, 1500, 1210, 800	$C_{22}H_{26}N_2O_4$ req.: 382.18926 found: 382.1891
4h	CH_3O	5.23, d, $J_{3,4}$=5.1	4.43, ddd, $J_{4,CH2}$=4.7+6.2	2.75+2.85, 2dd, J_g=14.0	7.07, m	6.84, m	3.78, s	piperidino: 2.45+1.4-1.6, m	1750, 1500, 1390, 1220	$C_{23}H_{28}N_2O_4$ req.: 396.20491 found: 396.2056
4i	CH_3O	5.26, d, $J_{3,4}$=4.9	4.44, ddd, $J_{4,CH2}$=4.4+6.3	2.82+2.91, 2dd, J_g=13.9	7.06, m	6.85, m	3.79, s	morpholino: 3.62+2.53, m	1750, 1500, 1220, 1100	$C_{22}H_{26}FN_2O_5$ req.: 398.18417 found: 398.1850
4j	CH_3O	5.24, d, $J_{3,4}$=5.0	4.41, ddd, $J_{4,CH2}$=4.2+6.8	2.80+2.92, 2dd, J_g=14.0	7.05, m	6.85, m	3.78, s	tiomorpholino: 2.77+2.58, m	1755, 1500, 2220, 1010	$C_{22}H_{26}N_2O_4S$ req.: 414.16133 found: 414.1619
4k	CH_3O	5.24, d, $J_{3,4}$=5.0	4.43, ddd, $J_{4,CH2}$=4.5+6.5	2.82+2.92, 2dd, J_g=14.0	7.06, m	6.84, m	3.78, s	*N*-Me-piperazino: 2.57+2.38+2.27, m	1745, 1500, 1220, 800	$C_{23}H_{29}N_3O_4$ req.: 411.21581 found: 411.2161
4l	CH_3O	5.24, d, $J_{3,4}$=5.1	4.41, ddd, $J_{4,CH2}$=4.8+6.0	2.93+2.98, 2dd, J_g=14.0	7.07, m	6.84, m	3.78, s	*N*-Me-*N*-benzylamino: 2.28; 3.50+3.61+7.2-7.32, m	1755, 1500, 1220, 1100	$C_{26}H_{28}N_2O_4$ req.: 432.20491 found: 432.2053
4m	CH_3O	5.24, d, $J_{3,4}$=5.1	4.39, ddd, $J_{4,CH2}$=4.4+6.0	2.91+3.07, 2dd, J_g=14.2	7.07, m	6.85, m	3.78, s	hexamethilenimino: 2.70+1.60, m	1750, 1500, 1250, 1210, 1100, 800	$C_{24}H_{30}N_2O_4$ req.: 410.22056 found: 410.2208

[a] Solvent: $CDCl_3$; 4-methoxyphenyl: 7.5 (m, 2",6"-H), 6.9 (m, 3",5"-H), 3.8 (s, OCH_3)

Table 6

IR, NMR[a] and HRMS Data or Elemental Analysis of Compounds **5** Synthesised by Reduction of Compounds **4** or **7**



5a-r

Comp.	R^1	2-H	3-H	4-H	2-CH_2	2",6"-H	3",5"-H	4"-OCH_3	NR^2R^3	IR [cm^{-1}]	Elemental analysis [%] or HRMS m/z (EI)
5a	Cl	4.31, ddd, $J_{2,CH2}$=4.5+7.8	4.87, ddd, $J_{3,4}$=6.5+2.5 $J_{2,3}$=6.0	3.93+3.97, 2dd, J_g=8.5	2.70+3.05 2dd, J_g=13.5	7.2, m	6.8, m		piperidino: 1.35-1.70, m	1510, 1490, 1240, 1100, 810	$C_{22}H_{27}ClN_2O_2$ (386.92) req.: C: 68.29, H: 7.04, N: 7.24; found: C: 68.45, H: 6.93, N: 7.32
5b	Cl	4.34, ddd, $J_{2,CH2}$=4.5+7.7	4.92, brdd, $J_{3,4}$=6.5+2.5	3.92+3.96, 2dd, J_g=11	2.74+3.05 2dd, J_g=13.7	7.24, m	6.81, m		morpholino: 3.64-3.68, m	1510, 1490, 1220, 1100	$C_{21}H_{25}ClN_2O_3$ (388.88) req.: C: 64.85, H: 6.48, N: 7.20; found: C: 64.76, H: 6.67, N: 7.08
5c	F	4.34, brddd, $J_{2,CH2}$=4+8	4.88, ddd, $J_{3,4}$=6.0+2.5 $J_{2,3}$=6.0	3.87+3.97, 2dd, J_g=8.5	2.69+3.05 2dd, J_g=13.5	6.94, m	6.83, m		piperidino: 1.42-1.59, m	1490, 1210, 800	$C_{22}H_{27}FN_2O_2$ (370.46) req.: C: 71.33, H: 7.35, N: 7.56; found: C: 71.23, H: 7.18, N: 7.71
5d	F	4.33, brddd, $J_{2,CH2}$=4.5+8	4.91, ddd, $J_{3,4}$=6.5+2.5 $J_{2,3}$=6.5	3.91+4.00, 2dd, J_g=8.5	2.75+3.07 2dd, J_g=14.0	6.94, m	6.83, m		morpholino: 3.62-3.71, m	1500, 1220, 1100, 805	$C_{21}H_{25}FN_2O_3$ (372.43) req.: C: 67.72, H: 6.77, N: 7.52; found: C: 67.62, H: 6.75, N: 7.57
5e	F	4.32, brddd, $J_{2,CH2}$=4.5+7.5	4.89, ddd, $J_{3,4}$=6.5+2.5 $J_{2,3}$=6.5	3.89+4.00, 2dd, J_g=8.6	2.76+3.09 2dd, J_g=13.5	6.97, m	6.81, m		*N*-Me-piperazino: 2.41-2.63, m, 2.28, s	1500, 1210, 800	$C_{22}H_{28}FN_3O_2$ (385.47) req.: C: 68.55, H: 7.32, N: 10.90; found: C: 68.33, H: 7.30, N: 10.77
5f	F	4.32, brddd, $J_{2,CH2}$=4.5+7.5	4.88, ddd, $J_{3,4}$=6.5+2.5 $J_{2,3}$=6.5	3.88+3.98, 2dd, J_g=8.5	2.75+3.10 2dd, J_g=13.5	6.96, m	6.82, m		*N*-Bn-piperazino: 7.3, m, 3.51, s	1500, 1210, 800	$C_{28}H_{32}FN_3O_2$ (461.57) req.: C: 72.86, H: 6.99, N: 9.10; found: C: 72.84, H: 6.84, N: 8.98
5g	MeO	4.33, ddd, $J_{2,CH2}$=4.0+8.0	4.90, ddd, $J_{3,4}$=6.0+2.5 $J_{2,3}$=6.0	3.86+3.99, 2dd, J_g=8.7	2.90+3.28 2dd, J_g=13.5	6.81, m	6.81, m	3.75, s	pyrrolidino: 2.5-2.7+1.77-1.80, m	2990, 1490, 1200, 1020, 800	$C_{22}H_{28}N_2O_3$ (368.47) req.: C: 71.71, H: 7.66, N: 7.60; found: C: 71.58, H: 7.68, N: 7.55
5h	MeO	4.33, ddd, $J_{2,CH2}$=4.0+7.5	4.86, ddd, $J_{3,4}$=6.0+2.5 $J_{2,3}$=6.0	3.86+3.97, 2dd, J_g=8.6	2.72+3.08, 2dd, J_g=13.5	6.82, m	6.82, m	3.75, s	piperidino: 2.3-2.6+1.4-1.6, m	1500, 1210, 800	$C_{23}H_{30}N_2O_3$ (382.50) req.: C: 72.22, H: 7.91, N: 7.32; found: C: 71.97, H: 7.71, N: 7.25
5i	MeO	4.33, ddd, $J_{2,CH2}$=4.0+7.5	4.89, ddd, $J_{3,4}$=6.5+2.5 $J_{2,3}$=6.5	3.90+4.00, 2dd, J_g=8.5	2.77+3.10 2dd, J_g=13.5	6.80, m	6.80, m	3.76, s	morpholino: 3.66-3.70+2.4-2.65, m	1500, 1210, 1100, 800	$C_{22}H_{28}N_2O_4$ (384.47) req.: C: 68.73, H: 7.34, N: 7.29; found: C: 68.62, H: 7.30, N: 7.32
5j	MeO	4.30, ddd, $J_{2,CH2}$=4.5+7.5	4.88, ddd, $J_{3,4}$=6.5+2.6 $J_{2,3}$=6.5	3.88+4.00, 2dd, J_g=8.5	2.77+3.10 2dd, J_g=14.0	6.82, m	6.82, m	3.75, s	tiomorpholino: 2.6-2.9, m	1530, 1260, 1060, 830	$C_{22}H_{28}N_2O_3S$ (400.53) req.: C: 65.97, H: 7.05, S: 8.01; found: C: 66.10, H: 7.00, S: 7.80
5k	MeO	4.33, ddd, $J_{2,CH2}$=4.5+7.5	4.87, ddd, $J_{3,4}$=6.5+2.5 $J_{2,3}$=6.5	3.86+4.00, 2dd, J_g=8.5	2.79+3.12 2dd, J_g=13.5	6.81, m	6.81, m	3.75, s	*N*-Me-piperazino: 2.4-2.7, m, 2.29, s	1530, 1250	$C_{23}H_{31}N_3O_3$ (397.51) req.: C: 69.49, H: 7.86, N: 10.57; found: C: 69.19, H: 7.76, N: 10.40
5l	MeO	4.30, ddd, $J_{2,CH2}$=4.0+7.6	4.89, ddd, $J_{3,4}$=6.2+2.5 $J_{2,3}$=6.4	3.85+3.96, 2dd, J_g=8.6	2.83+3.28 2dd, J_g=13.5	6.81, m	6.81, m	3.75, s	*N*-Me-*N*-benzylamino: 2.29, s, 3.57=3.61, 2d, J_g=13.0, 7.22-7.35, m	1500, 1210, 1010, 800	$C_{26}H_{30}N_2O_3$ (418.53) req.: C: 74.61, H: 7.22, N: 6.69; found: C: 74.36, H: 7.16, N: 6.77

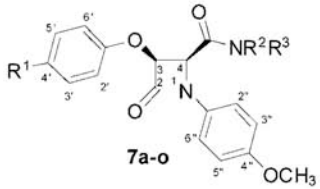
Table 6 (continued)

Comp.	R^1	2-H	3-H	4-H	2-CH_2	2",6"-H	3",5"-H	4"-OCH_3	NR^2R^3	IR [cm^{-1}]	Elemental analysis [%] or HRMS m/z (EI)
5m	MeO	4.28, ddd, $J_{2,CH2}$=4.0+7.7	4.88, ddd, $J_{3,4}$=6.5+2.5 $J_{2,3}$=6.5	3.86+3.97, 2dd, J_g=8.7	2.88+3.30 2dd, J_g=13.7	6.82, m	6.82, m	3.76, s	hexamethylenimino: 1.5-1.7, m	1510, 1210, 1030, 810	$C_{24}H_{32}N_2O_3$ (396.52) req.: C: 72.70, H: 8.13, N: 7.06; found: C: 72.54, H: 8.05, N: 6.99
5n	F	4.21, brddd, $J_{2,CH2}$=5.4+6.3	4.89, ddd, $J_{3,4}$=6.3+2.6 $J_{2,3}$=6.4	3.85+3.98, 2dd, J_g=8.7	2.93+3.23 2dd, J_g=14.7	6.98, m	6.77, m		diisopropylamino: 3.07+1.06+1.03	1505, 1240, 1205, 810, 750	$C_{23}H_{31}N_2O_2F$ req.: 386.2369 found: 386.2367
5o	F	4.34, ddd, $J_{2,CH2}$=3.9+8.4	4.92, ddd, $J_{3,4}$=6.3+2.5 $J_{2,3}$=6.4	3.87+3.97, 2dd, J_g=8.6	2.88+3.28, 2dd, J_g=13.2	6.97, m	6.81, m		pyrrolidino: 2.66+2.54+1.77, m	1500, 1230, 1190, 800	$C_{21}H_{25}N_2O_2F$ req.: 356.1900 found: 356.1907
5p	Cl	4.34, ddd, $J_{2,CH2}$=3.8+8.3	4.93, ddd, $J_{3,4}$=6.2+2.5 $J_{2,3}$=6.4	3.89+3.97, 2dd, J_g=8.7	2.87+3.27, 2dd, J_g=13.0	7.23, m	6.79, m		pyrrolidino: 2.66+2.53+1.77, m	1510, 1490, 1210, 800	$C_{21}H_{25}N_2O_2Cl$ req.: 372.1604 found: 372.1599
5q	MeO	4.28, ddd, $J_{2,CH2}$=4.1+7.6	4.90, ddd, $J_{3,4}$=6.3+2.5 $J_{2,3}$=6.3	3.85+3.96, 2dd, J_g=8.6	2.80+3.27 2dd, J_g=13.7	6.75-6.85, m	6.75-6.85, m	3.77, s	diethylamino: 3.21+1.07, m	1510, 1210, 1010, 800	$C_{22}H_{30}N_2O_9$ req.: 370.2256 found: 370.2257
5r	MeO	4.19, ddd, $J_{2,CH2}$=3.3+8.2	4.73, ddd, $J_{3,4}$=6.5+2.5 $J_{2,3}$=6.5	3.73+3.87, 2dd, J_g=8.6	2.89+3.40 2dd, J_g=14.0	6.82, m	6.71, m	3.77, s	dibenzylamino: 3.57=3.80, 2d, J_g=13.6, 7.20-7.42, m	1510, 1210, 1010, 800	$C_{32}H_{34}N_2O_3$ req.: 494.2569 found: 494.2569

[a] Solvent: $CDCl_3$; 4-methoxyphenyl : 6.8 (m, 2",6"-H), 6.6 (m, 3",5"-H), 3.77 (s, OCH_3)

Table 7

Yields, Melting Points, IR, NMR[a,c] and HRMS Data or Elemental Analysis of Compounds **7**



7a-o

Comp.	R^1	3-H	4-H	2",6"-H	3",5"-H	4"-OCH_3	NR^2R^3	Yield [%]	Mp [°C]	IR [cm^{-1}]	Elemental analysis [%] or HRMS m/z (EI)
7a	Cl	5.47, d, $J_{3,4}$=5.3	4.95, d	7.06, m	7.26, m		pyrrolidino: 3.25-3.65+1.8-2.05	92	159[d]	3050, 1770, 1730, 1680, 1520, 1450	$C_{21}H_{21}ClN_2O_4$ (400.86) req.: C: 62.92, H: 5.28, N: 6.99, Cl: 8.84; found: C: 62.79, H: 5.24, N: 6.92, Cl: 8.70
7b[b]	Cl	5.75, d, $J_{3,4}$=5.5	5.42, d	7.14, m	7.31, m		morpholino: 3.35-3.80, m	91	197[f]	1750, 1660, 1510, 1490, 1200	$C_{21}H_{21}N_2O_5Cl$ req.: 416.1139 found: 416.1143
7c	Cl	5.41, d, $J_{3,4}$=5.5	5.09, d	7.04-7.22, m	7.04-7.22, m		piperidino: 1.5-1.7+3.25-3.40+3.45-3.7, m	89	183[e]	3020, 1740, 1660, 1505, 1480, 1230	$C_{22}H_{23}ClN_2O_4$ (414.89) req.: C: 63.69, H: 5.59, N: 6.75, Cl: 8.55; found: C: 63.68, H: 5.63, N: 7.00, Cl: 8.51
7d	Cl	5.44, d, $J_{3,4}$=5.4	5.08, d	7.04, m	7.26, m		hexamethylenimino: 1.4-1.8+3.2-3.3+3.4-3.6, m	90	175[g]	3000, 1760, 1650, 1510, 1490, 1400	$C_{23}H_{25}ClN_2O_4$ (428.92) req.: C: 64.41, H: 5.87, N: 6.53, Cl: 8.27; found: C: 64.40, H: 5.63, N: 6.55, Cl: 8.31
7e	Cl	5.45 d, $J_{3,4}$=5.4	5.01, d	7.09, m	7.25, m		1,6-diMe-piperidino: 1.28+1.43, s, 4.90+ 3.86+1.45-1.90, m	78	215[d]	1780, 1640, 1510, 1490, 1210	$C_{24}H_{27}N_2O_4Cl$ req.: 442.1659 found: 442.1667

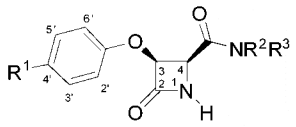
Table 7 (continued)

Comp.	R^1	3-H	4-H	2",6"-H	3",5"-H	4"-OCH_3	NR^2R^3	Yield [%]	Mp [°C]	IR [cm^{-1}]	Elemental analysis [%] or HRMS m/z (EI)
7f	Cl	5.45, d, $J_{3,4}$=5.5	4.98, d	7.10, m	7.25, m		diisopropylamino: 3.86+3.55+1.49+1.46 +1.29+1.23	86	238[d]	1790, 1650, 1510, 1490, 1240	$C_{23}H_{37}N_2O_4Cl$ req.: 430.1659 found: 430.1660
7g	F	5.45, d, $J_{3,4}$=5.4	4.95, d	7.08, m	6.99, m		pyrrolidino: 3.25-3.65+1.8-2.05	92	153[e]	3040, 1750, 1660, 1500, 1220, 1190	$C_{21}H_{21}FN_2O_4$ (384.41) req.: C: 65.62, H: 5.51, N: 7.29, F: 4.94; found: C: 65.38, H: 5.65, N: 7.37, F: 5.12
7h	F	5.40, d, $J_{3,4}$=5.5	5.10, d	6.93-7.10, m	6.93-7.10, m		piperidino: 1.5-1.7+3.25-3.50+3.50-3.70, m	69	145[e]	2935, 1745, 1652, 1504, 1406, 1251	$C_{22}H_{23}FN_2O_4$ (398.43) req.: C: 66.32, H: 5.82, N: 7.03, F: 4.77; found: C: 66.35, H: 5.90, N: 7.00, F: 4.60
7i	F	5.49 d, $J_{3,4}$=5.4	5.16, d	7.12, m	7.00, m		morpholino: 3.35-3.85, m	88	167	2930, 1765, 1505, 1380, 1240, 830	$C_{21}H_{21}N_2O_5F$ req.: 400.1434 found: 400.1433
7j	F	5.42 d, $J_{3,4}$=5.4	4.98, d	7.12, m	6.98, m		diisoprpylamino: 3.88+3.55+1.48+1.46 +1.30+1.24	94	257[d]	1785, 1650, 1510, 1250, 1205	$C_{23}H_{27}N_2O_4F$ req.: 414.1955 found: 414.1947
7k	F	5.40, d, $J_{3,4}$=5.5	5.07, d	6.90-7.10, m	6.90-7.10, m		hexamethylenimino: 1.4-1.8+3.21-3.32+3.45-3.66, m	90	152[e]	2995, 1750, 1650, 1500, 1450, 1390	$C_{23}H_{25}FN_2O_4$ (412.46) req.: C: 66.98, H: 6.11, N: 6.79, F: 4.61; found: C: 66.70, H: 6.10, N: 6.87, F: 4.50
7l	OCH_3	5.43, d, $J_{3,4}$=5.4	4.92, d	7.04, m	6.82, m	3.77, s	pyrrolidino: 3.25-3.6+1.6-2.0	78	135[f]	1740, 1660, 1505, 1230	$C_{22}H_{24}N_2O_5$ req.: 396.1685 found: 396.1685
7m	OCH_3	5.34, d, $J_{3,4}$=5.4	5.04, d	6.93, m	6.78, m	3.77, s	dibenzylamino: 3.84+5.63, 4.31+4.54, 7.25-7.5	78	145-146[f]	1780, 1690, 1510, 1400, 1230	$C_{32}H_{30}N_2O_5$ req.: 522.2155 found: 522.2146
7n	OCH_3	5.40, d, $J_{3,4}$=5.4	5.02, d	7.06, m	6.83, m	3.77, s	diethylamino: 3.78+3.38+3.24 +3.19+1.27+1.19	86	186[f]	1770, 1650, 1500, 1400, 1240, 1210	$C_{22}H_{26}N_2O_5$ req.: 398.1842 found: 398.1839
7o	OCH_3	5.40, d, $J_{3,4}$=5.4	4.96, d	7.09, m	6.83, m	3.76, s	diisopropylamino: 3.88+3.54+1.48+1.46 +1.29+1.24	78	187[g]	1775, 1650, 1510, 1230, 1210	$C_{24}H_{30}N_2O_5$ req.: 426.2155 found: 426.2157

[a]Solvent: $CDCl_3$, [b] $CDCl_3$+DMSO; [c]4-methoxyphenyl: 7.31, (m, 2",6"-H), 6.87 (m, 3",6"-H), 3.78, (s, OCH_3); [d] Recrystallized from dioxane, [e] ethyl acetate, [f] methanol, [g] ethanol

Table 8

Yields, Melting Points, IR, NMR[a] and HRMS Data or Elemental Analysis of Compounds **8**



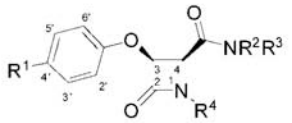
8a-g

Comp.	R^1	NH	2-H	3-H	2",3",5",6"-H	NR^2R^3	Yield [%]	Mp [°C]	IR [cm^{-1}]	Elemental analysis [%] or HRMS m/z (EI)
8a	Cl	8.84, br s	4.65, d, $J_{2,3}$=5.0	5.72, dd, $J_{3,NH}$=1.5	7.09-7.37, m	pyrrolidino: 1.59-1.81+3.00-3.10+3.28-3.45, m	77	207[b]	3520, 1780, 1630, 1490, 1225, 810	$C_{14}H_{15}ClN_2O_3$ (294.74) req.: C: 57.05, H: 5.13, N: 9.50, Cl: 12.03; found: C: 57.01, H: 5.07, N: 9.33, Cl: 12.10
8b	Cl	6.70, br s	4.69, d, $J_{2,3}$=5.2	5.44, dd, $J_{3,NH}$=1.4	7.06-7.25, m	piperidino: 1.50-1.75+3.20-3.40+3.60-3.75, m	60	126-128[c]	3290, 1770, 1620, 1480, 1220, 780	$C_{15}H_{17}ClN_2O_3$ (308.76) req.: C: 58.35, H: 5.55, N: 9.07, Cl: 11.48; found: C: 58.05, H: 5.74, N: 9.35, Cl: 11.33
8c	Cl	8.80, br s	4.78, d, $J_{2,3}$=5.1	5.71, dd, $J_{3,NH}$=1.5	7.08-7.37, m	hexamethylenimino: 1.30-1.70+3.11-3.23+3.36-3.57, m	76	209[b]	3290, 3000, 1770, 1620, 1480, 1220	$C_{16}H_{19}ClN_2O_3$ (322.79) req.: C: 59.94, H: 5.93, N: 8.68, Cl: 10.98; found: C: 59.59, H: 5.81, N: 8.72, Cl: 10.75
8d	F	7.80, br s	4.61, d, $J_{2,3}$=5.0	5.40, dd, $J_{3,NH}$=1.5	6.90-7.10, m	pyrrolidino: 1.8-2.0+3.20-3.30+3.35-3.50+3.52-3.60, m	46	169[c]	3280, 1770, 1620, 1500, 1180, 800	$C_{14}H_{15}FN_2O_3$ (278.28) req.: C: 60.43, H: 5.43, N: 10.07, F: 6.83; found: C: 60.29, H: 5.60, N: 10.02, F: 7.00
8e	F	6.70, br s	4.69, d, $J_{2,3}$=5.2	5.42, dd, $J_{3,NH}$=1.4	6.90-7.20, m	piperidino: 1.60-1.70+3.20-3.40+3.60-3.80, m	74	208[e]	3566, 3106, 2945, 1740, 1630, 1500	$C_{15}H_{17}FN_2O_3$ (292.31) req.: C: 61.63, H: 5.86, N: 9.58, F: 6.50; found: C: 61.48, H: 5.84, N: 9.44, F: 6.30
8f	F	8.80, brs	4.82, d, $J_{2,3}$=5.0	5.62, dd, $J_{3,NH}$=1.5	7.05-7.14, m	morpholine: 3.20-3.70, m	77	225-230[b]	3250, 1760, 1640, 1500, 1210, 1100	$C_{14}H_{15}N_2O_4F$ req.: 294.1016 found: 294.1018
8g	F	7.35, br s	4.70, d, $J_{2,3}$=5.0	5.41, dd, $J_{3,NH}$=1.6	6.90-7.10, m	hexamethylenimino: 1.45-1.95+3.20-3.30+3.40-3.60+3.70-3.80, m	71	205-206[e]	3300, 3020, 1790, 1640, 1520, 1225	$C_{16}H_{19}FN_2O_3$ (306.34) req.: C: 62.73, H: 6.25, N: 9.14, F: 6.20; found: C: 62.70, H: 6.21, N: 9.17, F: 6.12

[a] Solvent: $CDCl_3$; [b] Recrystallized from ethyl acetate, [c] acetonitrile, [d] ethanol, [e] methanol

Table 9

Yields, Melting Points, IR, NMR[a] Data and Elemental Analysis of Compounds **9** and **10**

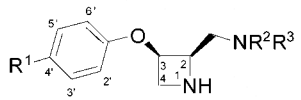


9a-g (R^4= CH_3)
10a-f (R^4= $CH_2C_6H_5$)

Comp.	R^1	2-H	3-H	2",3",5",6"-H	NR^2R^2	Yield [%]	Mp [°C]	IR [cm^{-1}]	Elemental analysis [%]
9a[b]	Cl	4.49, d, $J_{2,3}$=5.0	5.36, d	7.04+7.22, m	pyrrolidino: 1.8-2.0+3.12-3.23 +3.26-3.47+3.48-3.64, m	55	107[d]	1770, 1660, 1490, 1450, 1420, 1230	$C_{15}H_{17}ClN_2O_3$ (308.76) req.: C: 58.35, N: 9.07, Cl: 11.48; found: C: 58.58, N: 9.15, Cl: 11.51
9b[b]	Cl	4.86, d, $J_{2,3}$=5.0	5.69, d	7.10+7.38, m	piperidino: 1.25-1.70+ 3.15-3.60, m	68	174-175[d]	1770, 1660, 1490, 1480, 1420, 1240	$C_{16}H_{19}ClN_2O_3$ (322.79) req.: C: 59.54, N: 8.68, Cl: 10.98; found: C: 59.25, N: 8.62, Cl: 10.74
9c[b]	Cl	4.61, d, $J_{2,3}$=5.0	5.36, d	7.06+7.23, m	hexamethylenimino: 1.4-1.8+3.15-3.30+ 3.35-3.45+3.50+3.65, m	76	155-157[d]	2940, 1760, 1650, 1490, 1420, 1250	$C_{17}H_{21}ClN_2O_3$ (336.82) req.: C: 60.62, H: 6.28, N: 8.32, Cl: 10.53; found: C: 60.46, H: 6.22, N: 8.33, Cl: 10.58
9d[b]	F	4.49, d, $J_{2,3}$=5.0	5.34, d	6.90-7.10, m	pyrrolidino: 1.8-2.1+3.20-3.30+ 3.35-3.45+3.50-3.65, m	60	130[d]	1750, 1650, 1505, 1480, 1430, 1205	$C_{15}H_{17}FN_2O_3$ (292.31) req.: C: 61.63, N: 9.58, F: 6.50; found: C: 61.91, N: 9.59, F: 6.24
9e[b]	F	4.61, d, $J_{2,3}$=5.0	5.32, d	6.93-7.12, m	piperidino: 1.55-1.65+3.15- 3.30+3.60-3.65, m	75	158[d]	1760, 1660, 1500, 1420, 1205, 800	$C_{16}H_{19}FN_2O_3$ (306.34) req.: C: 62.73, N: 9.14, F: 6.20; found: C: 62.93, N: 9.14, F: 6.46
9f[b]	F	4.60, d, $J_{2,3}$=5.0	5.33, d	6.90-7.15, m	morpholino: 3.25-3.45+3.50-3.85, m	60	170[c]	1760, 1670, 1505, 1460, 1420, 1205	$C_{15}H_{17}FN_2O_4$ (308.31) req.: C: 58.44, N: 9.09, F: 6.16; found: C: 58.73, N: 9.13, F: 5.85
9g[b]	F	4.61, d, $J_{2,3}$=5.0	5.34, d	6.90-7.15, m	hexamethylenimino: 1.5-1.8+3.20-3.30+ 3.35-3.45+3.50-3.70, m	75	110[d]	1760, 1650, 1500, 1420, 1200, 800	$C_{17}H_{21}FN_2O_3$ (320.36) req.: C: 63.74, N: 8.74, F: 5.93; found: C: 64.00, N: 8.82, F: 5.73
10a[c]	Cl	4.31, d, $J_{2,3}$=5.0	5.33, d	7.04+7.23, m	pyrrolidino: 1.8-2.03.1-3.30+3.45-3.7, m	83	144	1770, 1650, 1490, 1460, 1410, 1250	$C_{21}H_{21}ClN_2O_3$ (384.86) req.: C: 65.54, H: 5.50, N: 7.28, Cl: 9.21; found: C: 65.48, H: 5.56, N: 7.24, Cl: 9.27
10b[c]	Cl	4.43, d, $J_{2,3}$=5.0	5.31, d	7.08+7.24, m	piperidino: 1.4-1.7+3.1-3.3+3.45-3.7, m	56	148	1780, 1640, 1490, 1450, 1400, 1260	$C_{22}H_{23}ClN_2O_3$ (398.89) req.: C: 66.24, H: 5.81, N: 7.02, Cl: 8.89; found: C: 66.02, H: 5.76, N: 6.87, Cl: 8.58
10c[c]	Cl	4.38, d, $J_{2,3}$=5.2	5.31, d	7.06+7.22, m	hexamethylenimino: 1.4-1.9+3.00-3.15+3.20- 3.55+3.65-3.80, m	60	136-138	1780, 1650, 1490, 1450, 1400, 1240	$C_{23}H_{25}ClN_2O_3$ (412.92) req.: C: 66.90, H: 6.10, N: 6.78, Cl: 8.59; found: C: 66.65, H: 6.02, N: 6.79, Cl: 8.69
10d[c]	F	4.31, d, $J_{2,3}$=5.0	5.31, d	6.9-7.1, m	pyrrolidino: 1.8-2.0+3.1-3.3+3.55-3.7, m	68	117	1750, 1620, 1485, 1430, 1390, 1320	$C_{21}H_{21}FN_2O_3$ (368.41) req.: C: 68.47, H: 5.75, N: 7.60, F: 5.16; found: C: 68.45, H: 5.75, N: 7.65, F: 5.27
10e[c]	F	4.45, d, $J_{2,3}$=5.2	5.28, d	6.9-7.2, m	piperidino: 1.4-1.7+3.1-3.2+3.55-3.7, m	72	118	1770, 1630, 1495, 1450, 1250, 1200	$C_{22}H_{23}FN_2O_3$ (382.43) req.: C: 69.09, H: 6.06, N: 7.33, F: 4.97; found: C: 69.25, H: 6.18, N: 7.30, F: 4.91
10f[c]	F	4.37, d, $J_{2,3}$=5.1	5.28, d	6.9-7.1, m	hexamethylenimino: 1.4-1.9+3.05-3.16+ 3.25-3.55+3.65-3.80, m	76	115	1770, 1630, 1500, 1450, 1200, 830	$C_{23}H_{25}FN_2O_3$ (396.46) req.: C: 69.68, H: 6.36, N: 7.07, F: 4.79; found: C: 69.38, H: 6.48, N: 7.10, F: 4.49

[a] solvent: $CDCl_3$; [b] *N*-CH_3: 3.02, s, [c] *N*-$CH_2C_6H_5$: 4.35+5.2 (dd, J_g=14.7-15, CH_2), 7.2-7.4 (m, C_6H_5); [d] Recrystallized from ethyl acetate, [e] ethyl acetate/diethylether

Table 10
IR, NMR[a] Data and Elemental Analysis of Compounds **11**



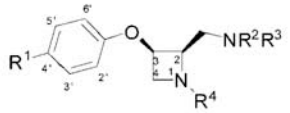
11a-f

Comp.	R^1	NH	2-H	3-H	4-H	2-CH_2	2",3",5",6"-H	NR^2R^3	IR [cm^{-1}]	Elemental analysis [%]
11a	Cl	8-11	5.60, m, $J_{2,3}$=6.5, $J_{2,CH2}$=10+2.3	5.30, ddd, $J_{3,4}$=4.5+6.5	4.06+4.55, dd, J_g=11.5	3.68+4.55, dd, J_g=14	6.88+7.28, m	pyrrolidino: 2.1+3.45-3.63, m	3540, 3100-2400, 1495, 1230	$C_{14}H_{19}ClN_2O$*2HCl (339.69) req.: C: 49.50, H: 6.23, N: 8.25, Cl: 31.31; found: C: 49.21, H: 6.44, N: 7.89, Cl: 30.97
11b	Cl	9.5-11.2	5.48, m, $J_{2,3}$=6.0, $J_{2,CH2}$=9	5.25, ddd, $J_{3,4}$=5.0+6.0	3.91+4.47, dd, J_g=11.5	3.57+4.14, dd, J_g=14.5	7.00+7.32, m	piperidino: 1.3-1.9+2.9-3.6, m	3550, 3100-2400, 1490, 1230	$C_{15}H_{21}ClN_2O$*2HCl (353.72) req.: C: 50.93, H: 6.55, N: 7.92, Cl: 30.07; found: C: 50.60, H: 6.60, N: 7.89, Cl: 29.84
11c	Cl	9.81	5.49, m, $J_{2,3}$=6.0, $J_{2,CH2}$=8.7+2.8	5.24, ddd, $J_{3,4}$=3.5+6.0	3.95+4.47, m	3.64+4.23, dd, J_g=14.5	6.93+7.30, m	hexamethylenimino: 1.5-2.0+3.15-3.60, m	3540, 3100-2500, 1495, 1230	$C_{16}H_{23}ClN_2O$*2HCl (367.75) req.: C: 52.26, H: 6.85, N: 7.62, Cl: 28.92; found: C: 51.97, H: 6.94, N: 7.69, Cl: 28.65
11d	F		5.54, m, $J_{2,3}$=6.5, $J_{2,CH2}$=9+2.5	5.32, ddd, $J_{3,4}$=4.5+6.5	4.06+4.55, dd, J_g=12	3.75+4.42, dd, J_g=14	6.93+7.03, m	pyrrolidino: 2.12+3.45-3.60, m	3500, 3050-2400, 1495, 1190	$C_{14}H_{19}FN_2O$*2HCl (323.24) req.: C: 52.02, H: 6.55, N: 8.67, Cl: 21.94; found: C: 51.75, H: 6.85, N: 8.60, Cl: 21.60
11e	F	6.3-7.9	5.36, ddd, $J_{2,3}$=6.5, $J_{2,CH2}$=9.6+3.2	5.21, ddd, $J_{3,4}$=4.8+6.5	4.02+4.45, ddd, J_g=11.2	3.26+3.95, dd, J_g=14.3	6.86+7.01, m	piperidino: 1.6+1.83+3.0-3.2, m	3500, 3100-2400, 1495, 1220	$C_{15}H_{21}FN_2O$*2HCl (337.26) req.: C: 53.42, H: 6.87, N: 8.31, Cl: 21.02; found: C: 53.45, H: 7.02, N: 8.45, Cl: 20.74
11f	F	9.66	5.40, m, $J_{2,3}$=6.5, $J_{2,CH2}$=2.8+8.8	5.18, ddd, $J_{3,4}$=3.7+6.3	3.90+4.43, ddd, J_g=11.4	3.68+4.11, dd, J_g=14.5	6.98+7.11, m	hexamethylenimino: 1.5-2.0+3.15-3.60, m	3500, 3100-2400, 1495, 1220	$C_{16}H_{23}FN_2O$*2HCl (351.29) req.: C: 54.71, H: 7.17, N: 7.97, Cl: 20.18; found: C: 54.40, H: 7.23, N: 8.04, Cl: 20.30

[a] Solvent: $DMSO_{d6}$+$CDCl_3$

Table 11

IR, NMR[a] Data and Elemental Analysis of Compounds **12** and **13**



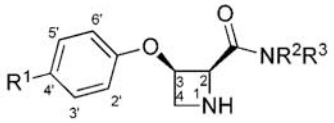
12a-g (R^4= CH_3)
13a-f (R^4= $CH_2C_6H_5$)

Comp.	R^1	2-H	3-H	4-H	2-CH_2	2",3",5",6"-H	NR^2R^3	IR [cm^{-1}]	Elemental analysis [%]
12a[b]	Cl	5.63, ddd, $J_{2,CH2}$=6.0+6.0, $J_{2,3}$=6.0	5.45, ddd, $J_{3,4}$=3.0+6.0	4.18+4.44, ddd, J_g=11.5	4.01+4.27, dd, J_g=14.5	7.00+7.28, m	pyrrolidino: 2.1+3.3-3.6, m	3100-2000, 1600, 1580, 1490, 1220	$C_{15}H_{21}ClN_2O$*2HCl (353.72) req.: C: 50.93, N: 7.92, Cl: 30.07; found: C: 50.71, N: 7.89, Cl: 29.89
12b[b]	Cl	5.41, br	5.28, br	4.0+4.3, br	3.8 br	7.02+7.41, m	piperidino: 1.4-1.9+3.4, m	3100-2000, 1600, 1580, 1480, 1220	$C_{16}H_{23}ClN_2O$*2HCl (367.75) req.: C: 52.26, N: 7.62, Cl: 28.92; found: C: 52.04, N: 7.64, Cl: 28.83
12c[b]	Cl	3.3-3.4, m, $J_{2,CH2}$=7.8, $J_{2,3}$=5.5	4.73, ddd, $J_{3,4}$=5.4+1.2	3.08+3.48, ddd, J_g=8.9	2.5-2.7+ 3.00, dd, J_g=13.3	6.75+7.19, m	hexamethylenimino: 1.57+2.5-2.7, m	3450, 3100-2400, 1500, 1480, 1240	$C_{17}H_{25}ClN_2O$*2HCl (381.77) req.: C: 53.48, H: 7.13, N: 7.34, Cl: 27.86; found: C: 53.24, H: 6.86, N: 7.50, Cl: 27.57
12d[b]	F	5.25, m, $J_{2,CH2}$=6.0,	5.25, m	4.04, m, 4.25, br,	3.87+4.04, dd, J_g=15	7.00+7.25, m	pyrrolidino: 1.95+3.1-3.7, m	3100-2000, 1500, 1220, 1180	$C_{15}H_{21}FN_2O$*2HCl (337.26) req.: C: 53.42, N: 8.31, Cl: 21.02, F: 5.63; found: C: 53.54, N: 8.42, Cl: 20.66, F: 5.43
12e[b]	F	5.62, br	5.33, br	3.85-4.5, m, 4.1, br,	3.85-4.5, m, 4.1, br,	7.0-7.15, m	piperidino: 1.4-2.0+3.1-3.7, m	3100-2200, 1500, 1220, 1180	$C_{16}H_{23}FN_2O$*2HCl (351.29) req.: C: 54.71, N: 7.97, Cl: 20.18, F: 5.41; found: C: 54.47, N: 7.94, Cl: 19.87, F: 4.95
12f[b]	F	5.41, m, $J_{2,3}$= 5.7	5.24, br, $J_{3,4}$=5.5+2.5	4.02+4.32, ddd, J_g=11.5	3.3-3.9, m	7.0+7.25, m	morpholino: 3.3-3.9, m	3100-2000, 1500, 1220, 1180	$C_{15}H_{21}FN_2O_2$*2HCl (353.26) req.: C: 51.00, N: 7.93, Cl: 20.07, F: 5.38; found: C: 50.90, N: 7.89, Cl: 19.77, F: 5.42
12g[b]	F	5.50, br	5.34, br, $J_{3,4}$=5.3	3.8-4.1, m, 4.36, dd, J_g=11.3	3.8-4.1, m	7.05+7.40, m	hexamethylenimino: 1.5-2.0+3.1-3.6, m	3100-2200, 1500, 1480, 1220, 1180	$C_{17}H_{25}FN_2O$*2HCl (365.32) req.: C: 55.89, N: 7.67, Cl: 19.41, F: 5.20; found: C: 55.75, N: 7.76, Cl: 19.83, F: 5.43
13a[c]	Cl	3.55-3.70, m, $J_{2,CH2}$=8.8, $J_{2,3}$=5.6	4.74, ddd, $J_{3,4}$=5.5+1.2	3.16+3.39, ddd, J_g=9.1	2.35-2.55, m, 3.04, dd, J_g=12.8	6.73+7.17, m	pyrrolidino: 1.7+2.35-2.55, m	3000-2700, 1600, 1580, 1490, 1240	$C_{21}H_{25}ClN_2O$ (356.90) req.: C: 70.67, H: 7.06, N: 7.85, Cl: 9.93; found: C: 70.73, H: 7.20, N: 7.79, Cl: 10.02
13b[c]	Cl	3.55-3.70, m, $J_{2,CH2}$=8.6, $J_{2,3}$=5.6	4.74, ddd, $J_{3,4}$=5.6+1.2	3.15+3.39, ddd, J_g=9.1	2.15-2.50, m, 2.89, dd, J_g=13.3	6.75+7.17, m	piperidino: 1.3-1.6+2.15-2.50, m	3000-2700, 1605, 1590, 1500, 1260	$C_{22}H_{27}ClN_2O$ (370.92) req.: C: 71.24, H: 7.34, : 7.55, Cl: 9.56; found: C: 71.40, H: 7.50, N: 7.46, Cl: 9.62
13c[c]	Cl	3.5-3.6, m, $J_{2,CH2}$=8.4+3.8, $J_{2,3}$=5.7	4.72, ddd, $J_{3,4}$=5.6+1.4	3.16+3.40, dd, J_g=9.1	2.39+3.03, dd, J_g=13.5	6.75+7.17, m	hexamethylenimino: 1.54+2.45-2.65, m	3100-2700, 1600, 1580, 1490, 1450	$C_{23}H_{29}ClN_2O$ (384.95) req.: C: 71.76, H: 7.59, N: 7.28, Cl: 9.21; found: C: 71.64, H: 7.55, N: 7.24, Cl: 9.30
13d[c]	F	3.55-3.70, m, $J_{2,CH2}$=8.8,	4.73, m, $J_{3,4}$=5.5+1.3	3.15+3.39, dd, J_g=9.1	2.35-2.55, m, 3.06, dd, J_g=12.8	6.71+6.95, m	pyrrolidino: 1.70-1.75+2.35-2.55, m	3000-2700, 1490, 1230, 1200	$C_{21}H_{25}FN_2O$ (340.44) req.: C: 74.09, H: 7.40, N: 8.23, F: 5.58; found: C: 74.02, H: 7.42, N: 8.19, F: 5.29
13e[c]	F	3.6-3.7, m, $J_{2,CH2}$=8.6+3.4,	4.7, m $J_{3,4}$=5.6	3.16, dd, 3.40, m, J_g=9.1	2.24+2.92, dd, J_g=13.3	6.70-6.95, m	piperidino: 1.3-1.6+2.15-2.50, m	2950, 2850-2700, 1500, 1250, 1210	$C_{22}H_{27}FN_2O$ (354.47) req.: C: 74.55, H: 7.68, N: 7.90, F: 5.36; found: C: 74.67, H: 7.77, N: 7.95, F: 5.10
13f[c]	F	3.5-3.6, m, $J_{2,CH2}$=8.4+3.8,	4.71, m, $J_{3,4}$=5.6	3.15, dd, 3.39, m, J_g=9.1	2.39+3.05, dd, J_g=13.5	6.73-6.95, m	hexamethylenimino: 1.54+2.50-2.70, m	2930, 2880-2700, 1600, 1580, 1450, 1360	$C_{23}H_{29}FN_2O$ (368.49) req.: C: 74.97, H: 7.93, N: 7.60, F: 5.16; found: C: 75.22, H: 8.03, N: 7.68, F: 4.88

[a] Solvent: $DMSO_{d6}$; [b] *N*-CH_3: ~2.96, s, [c] *N*-$CH_2C_6H_5$: 3.56+3.86 (dd, J_g=12.7, CH_2), 7.2-7.4 (m, C_6H_5)

Table 12

Yields, Meting Points, IR, NMR[a] Data and Elemental Analysis of Compounds **14**



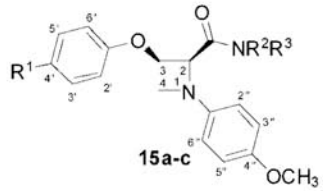
14a-d

Comp.	R^1	NH	2-H	3-H	4-H	2"3"5"6"-H	NR^2R^3	Yield [%]	Mp [°C]	IR [cm^{-1}]	Elemental Analysis [%]
14a	Cl	3.08, brs	4.70, d, $J_{2,3}$=7.2	5.18, ddd, $J_{3,4}$=5.5+5.5	3.61-3.85, m	6.64+7.21, m	piperidino: 1.50-1.75+3.20-3.25+3.61-3.85, m	20	100	3630, 3420, 3020, 1630, 1500, 1230	$C_{15}H_{19}ClN_2O_2$ (294.78) req.: C: 61.12, H: 6.50, N: 9.50, Cl: 12.03; found: C: 60.85, H: 6.64, N: 9.36, Cl: 12.00
14b	Cl	2.9, brs	4.67, d, $J_{2,3}$=7.1	5.17, q, J=7.1	3.10-3.85, m	6.63+7.20, m	hexamethylenimino: 1.4-1.9+3.10-3.85, m	25	111	3610, 2990, 1630, 1490, 1220, 1080	$C_{16}H_{21}ClN_2O_2$ (308.81) req.: C: 62.23, H: 6.85, N: 9.07, Cl: 11.48; found: C: 61.95, H: 6.86, N: 8.79, Cl: 11.07
14c	F	2.9, brs	4.66, d, $J_{2,3}$=7.2	5.15, dq, J=7.2	3.58-3.85, m	6.63-6.69+ 6.90-7.00, m	piperidino: 1.50-1.75+3.22-3.27+3.58-3.85, m	26	129	3600, 3000, 1640, 1500, 1190, 1000	$C_{15}H_{19}FN_2O_2$ (278.33) req.: C: 64.73, H: 6.88, N: 10.06, F: 6.83; found: C: 64.43, H: 6.90, N: 9.99, F: 6.58
14d	F	3.0-3.9, brs	4.67, d, $J_{2,3}$=7.1	5.12-5.20	3.0-3.9, m	6.62-6.68+ 6.91-6.99, m	hexamethylenimino: 1.4-1.09+3.0-3.9, m	31	115	2990, 1645, 1495, 1200, 1190, 805	$C_{16}H_{21}FN_2O_2$ (292.35) req.: C: 65.73, H: 7.24, N: 9.58, F: 6.50; found: C: 65.48, H: 7.24, N: 9.58, F: 6.15

[a] Solvent: $CDCl_3$

Table 13

Yields, Melting Points, IR, NMR[a,b] and HRMS Data of Compounds **15**



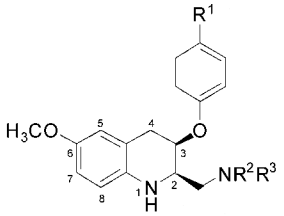
15a-c

Comp.	R^1	2-H	3-H	4-H	4"-OMe	2",3",5",6"-H	NR^2R^3	Mp [°C]	IR [cm^{-1}]	HRMS m/z (EI)
15a	Cl	4.75, d, $J_{2,3}$=6.8	5.07, ddd, $J_{3,4}$=5.5+2.3	3.94+4.00, dd, J_g=8.3		6.70+7.24, m	diisopropylamino: 3.86+3.45+1.54+ 1.50+1.24+1.11, m	175	3070-2900, 1670, 1500, 1210, 790	$C_{23}H_{29}N_2O_3Cl$ req.: 416.1867 found: 416.1871
15b	F	4.75, d, $J_{2,3}$=6.8	5.06, ddd, $J_{3,4}$=5.6+2.3	3.94+4.01, dd, J_g=8.3		6.72+6.97, m	diisopropylamino: 3.88+3.45+1.54+ 1.50+1.24+1.12, m	199-200	3050-2900, 1650, 1500, 1210, 800	$C_{23}H_{29}N_2O_3F$ req.: 400.2162 found: 400.2159
15c	F	4.74, d, $J_{2,3}$=6.7	5.05, ddd, $J_{3,4}$=5.5+2.3	3.92+4.02, dd, J_g=8.3	3.76, s	6.71+6.83, m	diisopropylamino: 3.86+3.45+1.56+ 1.51+1.24+1.13, m	154-156[c]	3100-2900, 1670, 1500, 1440, 1210	$C_{24}H_{32}N_2O_4$ req.: 412.2362 found: 412.2363

[a] Solvent: $CDCl_3$;[b] 4-methoxyphenyl: 6.45 (m, 3"5"-H), 6.80 (m, 2"6"-H), 3.75 (s, OCH_3); [c] Recrystallized from dioxane/diethylether

Table 14

Yields, Melting Points, IR, NMR[a,b] and HRMS Data of Compounds **16**



16a-j

Comp.	R^1	NH	2-H	2-CH_2	3-H	4-H	5,7,8-H	6-OCH_3	NR^2R^3	Mp [°C]	IR [cm^{-1}]	HRMS m/z (EI)
16a[b]	Cl	4.51, s	3.57, ddd, $J_{2,3}$=2.2, $J_{2,CH2}$=3.6+9.9	2.48+3.03, dd, J_g=11.8	4.61, ddd, $J_{3,4}$=3.9+4.3	2.95+3.07, dd, J_g=17.0	6.51+6.65+ 6.60, m	3.71, s	pyrrolidino: 2.62+2.49+ 1.78, m	108	3050-2900, 1510, 1490, 1250, 1020	$C_{21}H_{25}N_2O_2Cl$ req.: 372.1604 found: 372.1547
16b[b]	Cl	4.33, s	3.58, ddd, $J_{2,3}$=2.2, $J_{2,CH2}$=3.7+10.0	2.48+2.79, dd, J_g=12.1	4.58, ddd, $J_{3,4}$=3.3+4.2	2.97+3.07, dd, J_g=17.2	6.51+6.65+ 6.61, m	3.71, s	morpholino: 3.72+2.57+2.41, m	131	3030-2900, 1510, 1490, 1270, 1240, 1110, 1050	$C_{21}H_{25}N_2O_3Cl$ req.: 388.1554 found: 388.1553
16c[b]	Cl	4.25, s	3.42, ddd, $J_{2,3}$=2.3, $J_{2,CH2}$=8.4+5.5	2.69+2.72, dd, J_g=13.2	4.66, ddd, $J_{3,4}$=4.0+4.5	2.98+3.06, dd, J_g=17.0	6.52+6.64+ 6.56, m	3.70, s	diisopropylamino: 3.00+1.02+0.95, m	118	3480, 3050-2900, 1500, 1220, 800	$C_{23}H_{31}N_2O_2Cl$ req.: 402.2074 found: 402.2059
16d[c]	F	4.35, s	3.57, ddd, $J_{2,3}$=2.3, $J_{2,CH2}$=3.5+9.8	2.51+3.05, dd, J_g=11.8	4.56, ddd, $J_{3,4}$=3.8+4.3	2.94+3.04, dd, J_g=17.0	6.52+6.65+ 6.60, m	3.71, s	pyrrolidino: 2.63+2.50+ 1.80, m	90	3050-2900, 1500, 1250, 12020, 1020	$C_{21}H_{25}N_2O_2F$ req.: 356.1900 found: 356.1901
16e[c]	F	4.27, s	3.43, ddd, $J_{2,3}$=2.4, $J_{2,CH2}$=8.0+5.8	2.72+2.74, dd, J_g=13.2	4.61, ddd, $J_{3,4}$=4.0+4.5	2.98+3.04, dd, J_g=17.0	6.52+6.64+ 6.55, m	3.70, s	diisopropylamino: 3.00+1.02+0.96, m	90[e]	3450, 3020-2900, 1500, 1250	$C_{23}H_{31}N_2O_2F$ req.: 386.2369 found: 386.2363
16f[d]	OCH_3	4.51, s	3.54, ddd, $J_{2,3}$=2.2, $J_{2,CH2}$=3.3+10.0	2.49+3.08, dd, J_g=11.6	4.51, ddd, $J_{3,4}$=3.7+4.0	2.96+3.01, dd, J_g=17.0	6.52+ 6.64+ 6.59, m	3.71, s	pyrrolidino: 2.62+2.48+ 1.78, m	86	3500, 1490, 1250, 1200	$C_{22}H_{28}N_2O_3$ req.: 368.2099 found: 368.2102
16g[d]	OCH_3	4.60, s	3.42, dt, $J_{2,3}$=2.4, $J_{2,CH2}$=6.8	2.75, d,	4.58, ddd, $J_{3,4}$=4.2+4.5	2.99+3.02, dd, J_g=17.0	6.53+6.63+ 6.55, m	3.71, s	diisopropylamino: 3.01+1.02+ 0.97, m	85	3050-2950, 1505, 1250, 1020, 810	$C_4H_{34}N_2O_3$ req.: 398.2569 found: 398.2560
16h[d]	OCH_3	4.62, s	3.48, ddd, $J_{2,3}$=2.2, $J_{2,CH2}$=3.6+9.6	2.63+2.78, dd, J_g=12.4	4.54, ddd, $J_{3,4}$=4.0+4.1	2.96+3.02, dd, J_g=17.0	6.52+6.64+ 6.58, m	3.71, s	diethylamino: 2.61+2.49+ 1.00, m	87	3500, 3050-2900, 1500, 14890, 1210	$C_{22}H_{30}N_2O_3$ req.: 370.2256 found: 370.2257
16i[d]	OCH_3	~4, s	3.75, ddd, $J_{2,3}$=2.4, $J_{2,CH2}$=4.3+9.0	2.77+2.86, dd, J_g=12.7	4.53, ddd, $J_{3,4}$=4.8+4.5	2.89+2.93, dd, J_g=17.0	6.46+6.60+ 6.47, m	3.69, s	dibenzylamino: 3.51+3.72+ 7.15-7.3, m	oil	3200-2900, 1500, 1220, 1010, 800	$C_{32}H_{34}N_2O_3$ req.: 494.2569 found: 494.2570
16j[d]	OCH_3	4.25, s	3.48, ddd, $J_{2,3}$=2.5, $J_{2,CH2}$=8.8+4.5	2.93+3.00, dd, J_g=11.8	4.57, ddd, $J_{3,4}$=4.4+4.5	2.94+2.99, dd, J_g=17.0	6.52+6.64+ 6.59, m	3.71, s	benzylamino: 3.81+7.2-7.35, m	78-79	3200-2900, 1490, 1210, 1010, 800	$C_{25}H_{28}N_2O_3$ req.: 404.2099 found: 404.2101

[a] Solvent: $CDCl_3$; [b] 4-chlorophenoxy: 6.88+7.22, m, [c] 4-fluorophenoxy: 6.90+6.95, m, [d] 4-methoxyphenoxy: 6.81+6.87, m, 3.76, s (OCH_3); [e] Recrystallized from hexane

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