Removal of the Pyrrolidine Substituent by Dehydrogenation of 4-Pyrrolidin-2-yl-3,4-dihydro- and 1,2,3,4-tetrahydroisoquinolines

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Pyrrolidin-2-yl-groups located at C-4 of 3,4-dihydro- or 1,2,3,4-tetrahydroisoquinolines, respectively, are lost in the course of dehydrogenation of these isoquinoline derivatives. However, acyclically substituted isoquinolines, hydrogenated in ring B, 2-benzyl-4-(1-dimethylaminoethyl)-1,2,3,4-tetrahydroisoquinoline, *e.g.*, show loss of the amine group only by benzylic cleavage, affording 4-ethylisoquinoline. Scope and limitation of this reaction are determined using specifically substituted isoquinolines.

Abspaltung des Pyrrolidinylrestes bei der Dehydrierung von 4-Pyrrolidin-2-yl-3,4-dihydro- und 1,2,3,4-tetrahydroisochinolinen

C-4-Pyrrolidin-2-yl-3,4-dihydro- oder 1,2,3,4-tetrahydroisochinoline verlieren bei der Pd-katalysierten Dehydrierung diese Substituenten, während offenkettig substituierte ringhydrierte Isochinoline, z.B. 2-Benzyl-4-(1-dimethylaminoethyl)-1,2,3,4-tetrahydroisochinolin nur die Aminfunktion unter Benzylspaltung zu 4-Ethylisochinolin abspalten. Die Grenzen dieser Reaktion werden anhand der Dehydrierung speziell substituierter Isochinolin-Derivate abgesteckt.

In the context of the removal of a *N*-methylpyrrolidine group by dehydrogenation from C-4 of the 3,4-dihydroisoquinoline skeleton in the course of the synthesis of the papaveraceae alkaloid macrostomine (**1**)[1)] we have reported on the dehydrogenation of simple 3,4-dihydro- and 1,2,3,4-tetrahydroisoquinolines with pyrroline- and pyrrolidine increments at C-4: besides analogous losses we observed the expected dehydrogenation reaction (Scheme 3 in lit.[2)]) and rearrangements (Scheme 4 in lit.[2)])[2)].

Here we describe experiments performed in order to get some insight into scope and limitation of this abnormality.

Results of Dehydrogenation Experiments

These experiments were performed under standard conditions: 10 % Pd/C, tetraline, 190° - 210°C, N_2, 1 - 2 h. Whilst the 1-methyl-4-(2,5-dihydro-*N*-methylpyrrol-2-yl)-3,4-dihydroisoquinoline **2** is nicely aromatized in the pyrroline- as well as in the dihydroisoquinoline-moiety (Scheme 5 in Lit.[2)]), the 3,4-dihydro-5*H*-pyrrole group and the 3,4,5,6-tetrahydropyridine increment at C-4 of the (aromatic) isoquinolines **3** and **4**, respectively, remain unchanged.

This holds true also for the pertinent *sec* amines **5** and **6**, and also the corresponding *N*-methylated pyrrolidine- and piperidine-derivatives **7** and **8** are not dehydrogenated. In all theses cases the heterocyclic ring at C-4 of the isoquinoline systems is not split off. As already observed by *Seebach*[3)] in his synthesis of macrostomine (**1**), the loss of the pyrrolidine increment is prevented by *N*-formylation: cpds. **9** and **10** are dehydrogenated in the isoquinoline ring only, affording **9a** and **10a**. - From these experiments we can conclude that

a) the non-bonding electron pair at the N-atom of the attached ring is a prerequisite for this cleavage. Here only the tetrahydroisoquinoline system is dehydrogenated.

b) the loss of the fully hydrogenated *N*-heterocycle is synchronous with the dehydrogenation of the 3,4-dihydro- or 1,2,3,4-tetrahydroisoquinoline nucleus.

In order to check point b) we have prepared cpd. **11** with two substituents at C-4. Here, the 3,4-dihydroisoquinoline system as well as the *N*-methylpyrrolidine group should survive the dehydrogenation conditions, because we expected aromatization not to occur. This assumption, however, turned out to be wrong: there was loss of the pyrrolidine increment in **11** (for the fate of this group cf. lit.[2)]), and the 3,4-dihydroisoquinoline system was aromatized affording the 1,4-dimethylisoquinoline **12**. Curiously enough this reaction took place even without Pd as a catalyst by thermal cleavage only. So it seemed reasonable to assume that gain of aromatization energy is the driving force for this cleavage, but this assumption is disputable because dehydrogenation of 6,7-dimethoxy-1-methyl-4-(*N*-methylpyrrolidin-2-yl)-3,4-dihydroisoquinoline (**13**) under standard conditions affords *inter alia* 6,7-dimethoxy-1-methyl-*3,4-dihydro*isoquinoline (**14**)[2)]. Our speculation that subsequent hydrogenation of the isoquinoline system to the pertinent 3,4-dihydro-derivative due to dehydrogenation of tetraline[4)] had occured, was discarded because a pertinent experiment with isoquinoline itself led to dimerization only (not shown).

A *N*-methylpyrrole ring at C-4 does not interfere with dehydrogenation of the 1,2,3,4-tetrahydro- or the 3,4-dihydroisoquinoline system (cf. **15**, **16**).

Up to now we have described dehydrogenation of molecules having the amine function as part of a ring system bound to C-4 of the isoquinoline by its C-2. Therefore, we dehydrogenated analogous open chain compounds.

+) Dedicated to Prof. Dr.h.c. *A. Brossi*, NIH, USA, on the occasion of his 70th birthday.

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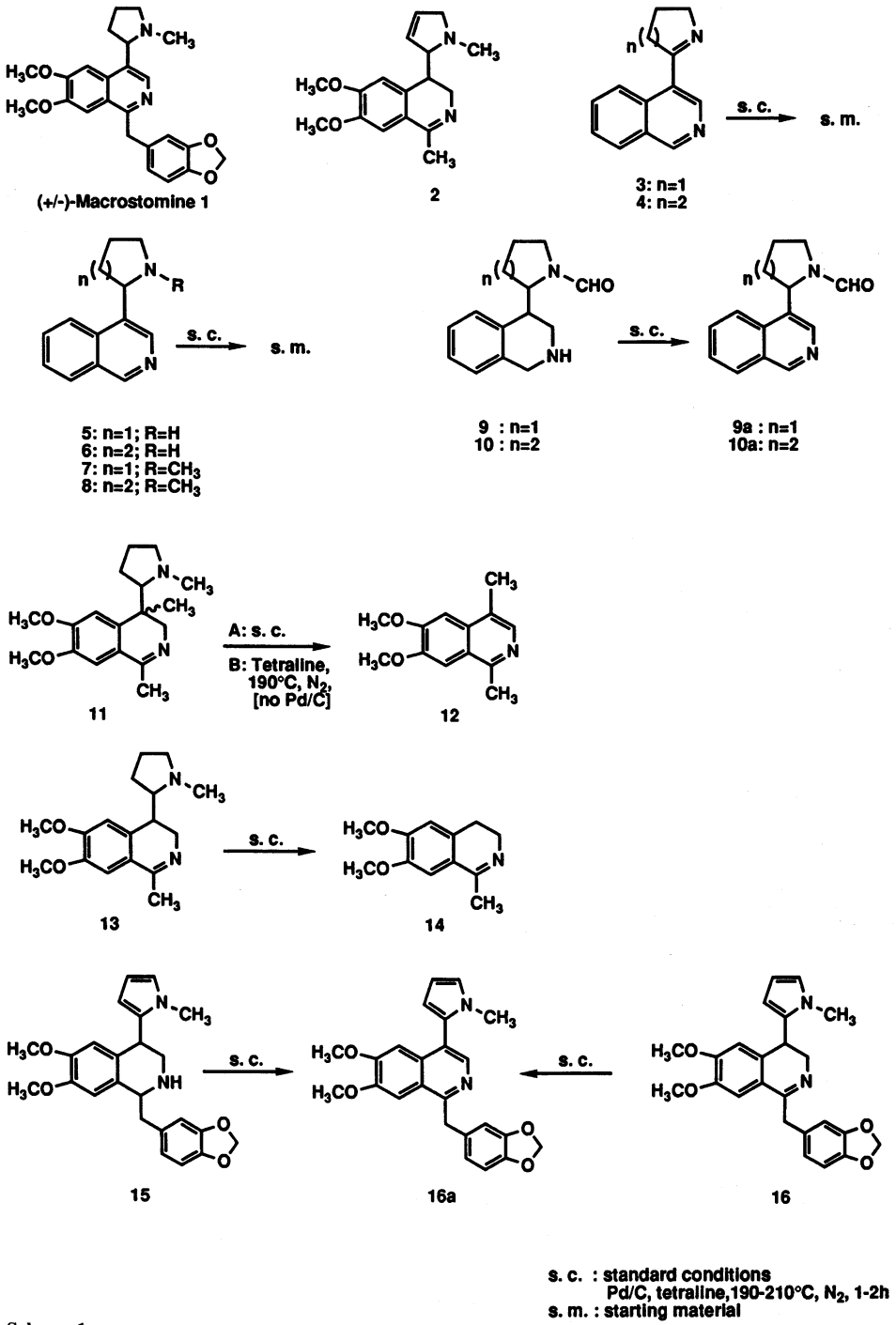
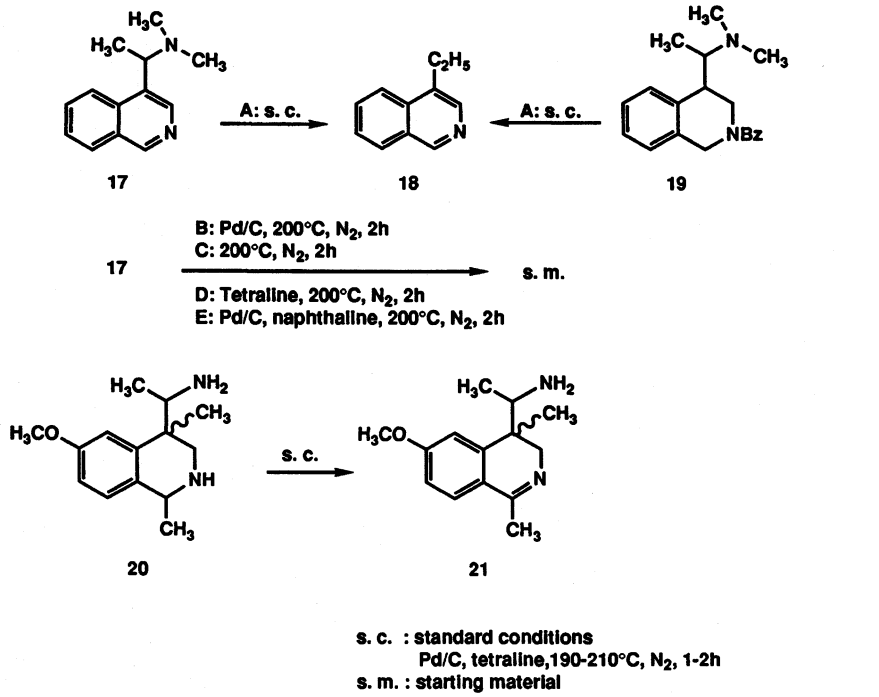


Scheme 1

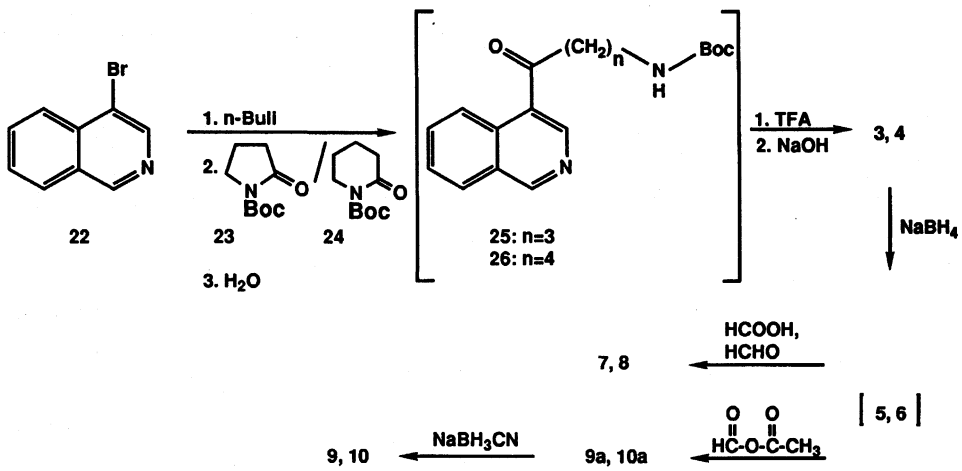
4-(1-Dimethylaminoethyl)isoquinoline (**17**) shows benzylamine cleavage (tetraline as a hydrogen source) affording 4-ethylisoquinoline (**18**)[5]. Cpd. **18** also arose from the *N*-benzylated tetrahydroisoquinoline **19**. Because *Seebach et al.*[3] have found that *N*-benzylated tetrahydroisoquinolines are debenzylated hydrogenolytically during dehydrogenation, there are no objections against the reaction of **19**.

If we omit one component of the standard conditions (Scheme 2, cpd. **17**, experiments B-E), no benzylamine cleavage occurs, indicating that this cleavage is a hydrogenolytic one. - Contrary to the 4-pyrrolidinyl-substituted 1,4-dimethyl-3,4-dihydroisoquinoline **11** the open-chain substituted tetrahydroisoquinoline **20** (mixture of diastereomers) is dehydrogenated to the 3,4-dihydroisoquinoline **21** which is stable under standard conditions. Here no thermal cleavage occured (cf. cpd. **11**).

We hypothesize from these experiments that the title reaction is restricted to cyclic amines with N in the 2-position, substituting C-4 of the 3,4-dihydro- or 1,2,3,4-tetrahydroisoquinoline. Probably - but consider the thermal degradation in the case of cpd. **11** - the hydrogenolytic cleavage depends on a more or less flat orientation of the said com-



Scheme 2



Scheme 3

pounds at the surface of the catalyst, facilitated by the somewhat restricted conformational mobility of the amine being part of a ring, and is triggered by the gain of resonance energy during aromatization of the hydrogenated ring B of the isoquinoline system. Up to now we have no chance to check this speculation.

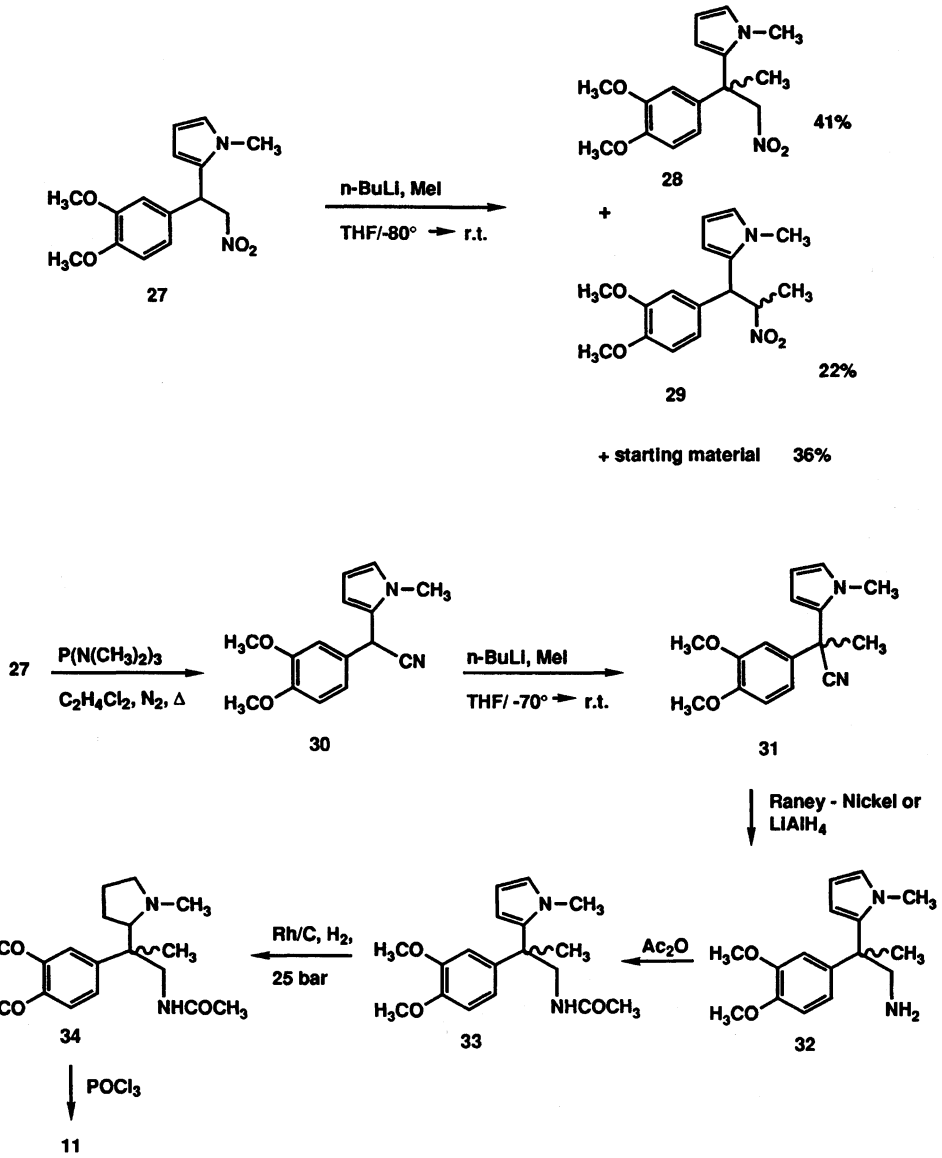
Synthesis of test compounds

a) *Ring substituents*

The isoquinoline derivatives substituted at C-4 by a *N*-formyl- or *N*-CH_3-pyridine- or piperidine-ring were prepared according to Scheme 3:

4-Bromoisoquinoline (**22**)[5] was deprotonated to its anion which reacted with *N*-Boc-pyrrolidin-2-one (**23**)[6] or *N*-Boc-piperidin-2-one (**24**)[7] affording the urethanes **25** and **26**, respectively. Deprotection and subsequent intramolecular condensation led to the imines **3** and **4** which were reduced to the pertinent *sec* amines **5** and **6**. *Eschweiler-Clarke* methylation yielded the *N*-methylpyrrolidine-/*N*-methylpiperidine-substituted isoquinolines **7** and **8**, whilst *N*-formylation to **9a**, **10a** with subsequent reduction afforded the *N*-formylated tetrahydroisoquinolines **9** and **10**.

For the synthesis of the twofold substituted 3,4-dihydroisoquinoline **11** we first followed *Seebach's* concept of alkylation of twofold deprotonated 2-phenyl-1-nitroethanes[8], but in addition to C-2, C-1 of the nitroethane **27**



Scheme 4

was methylated, probably due to the two substituents at the benzylic position (Scheme 4). Besides starting material **27** we obtained the methyl derivatives **28** and **29**. So we went on with the nitril **30** which was nicely methylated in α-position, yielding nitril **31**. Further steps (Scheme 4) are routine.

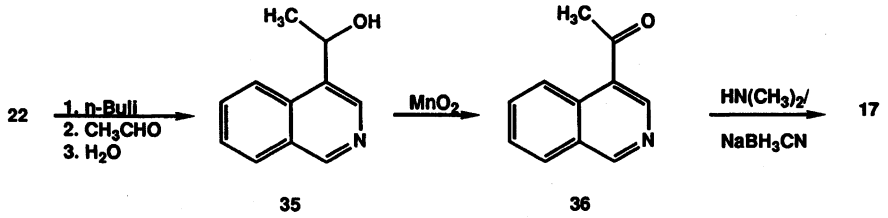
b) *Open chain substituents*

Reaction of the isoquinoline-C-4-anion, obtained from 4-bromoisoquinoline (**22**) (*vide supra*) with acetaldehyde produced the *sec* carbinol **35**[9] which was dehydrogenated to the ketone **36**[9]. Reductive amination with dimethylamine afforded the *tert.* amine **17** (Scheme 5).

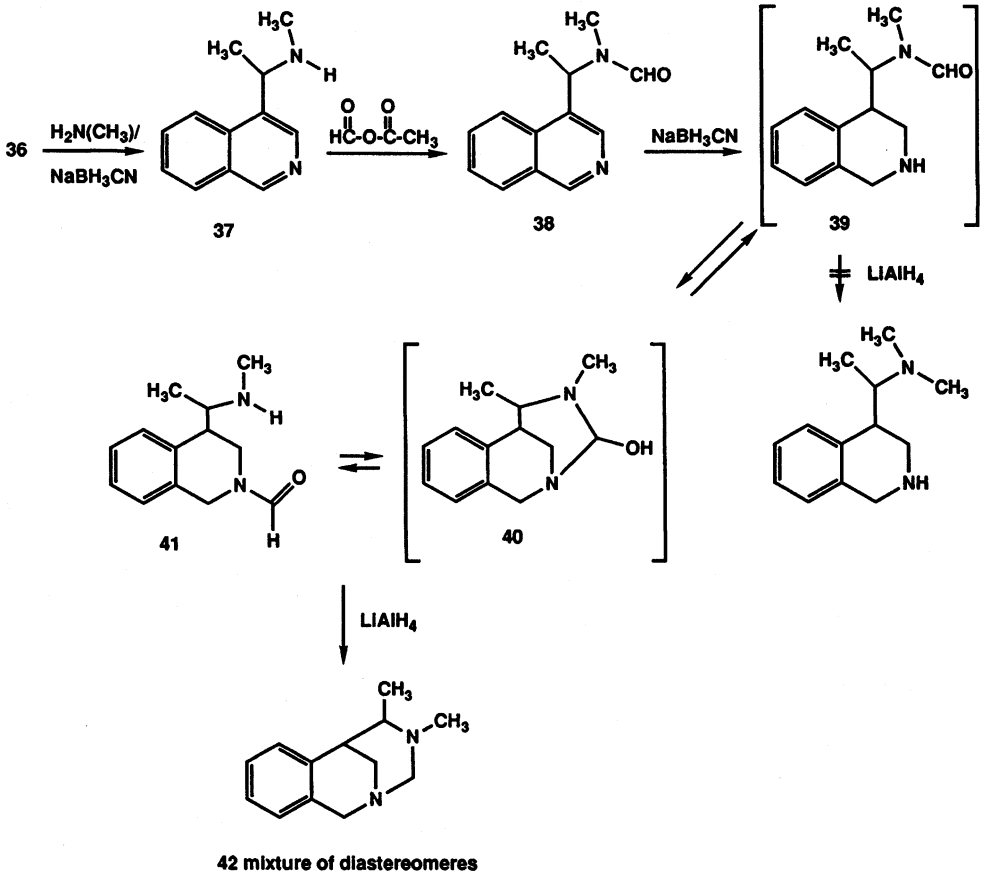
Ketone **36** when treated analogously with methylamine yielded the *sec.* amine **37** which was *N*-formylated (**38**) and reduced in the isoquinoline part.

Here a mixture of **39** and **41** (main isomer) was obtained, due to a shift of the *N*-formyl group (Scheme 6). This was indicated by the MS-fragments CH_3-CH=$\overset{+}{N}CH_3$(CHO) (m/z = 86 of **39**) and CH_3-CH=$\overset{+}{N}H(CH_3)$ (m/z = 58 of **41**) with high rel. intensities, whilst $M^{+\cdot}$ at m/z = 218 indicated that reduction of the isoquinoline increment had occured. Loss of 58 mu (C_2H_4NO) from **39** is unlikely and was excluded by HR-MS (C_3H_8N calcd. 58.06567; C_2H_4NO calcd. 58.02929; found 58.06571). Reduction of this mixture with $LiAlH_4$ led to a mixture of diastereomers with $M^{+\cdot}$ at m/z = 202 instead of m/z = 204. Probably the benzo[*f*]-1,3-diazabicyclo[3.3.1]nonan **42** had been formed. This requires loss of water from the α-hydroxyamino group of **40** yielding an iminium ion and subsequent reduction.

As we could not avoid this formyl-migration, we have benzylated cpd. **38** at the isoquinoline-*N* (**43**) and reduced the isoquinolinium ion to the 1,2,3,4-tetrahydro-derivative **44**. No problems arose with this compound when we reduced the *N*-formyl increment to the *tert* amine side chain, but



Scheme 5

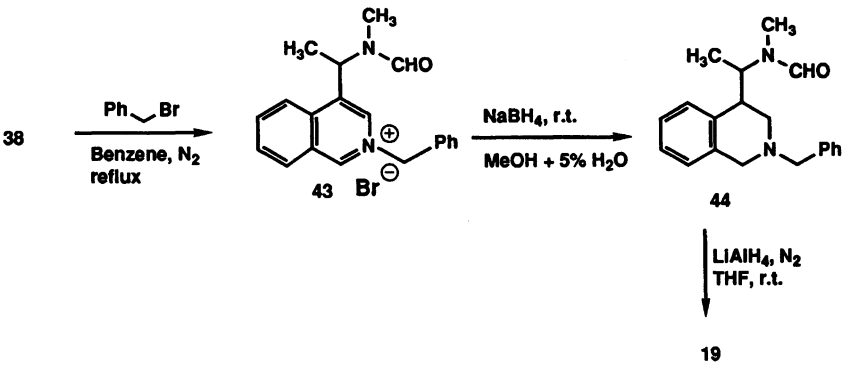


Scheme 6

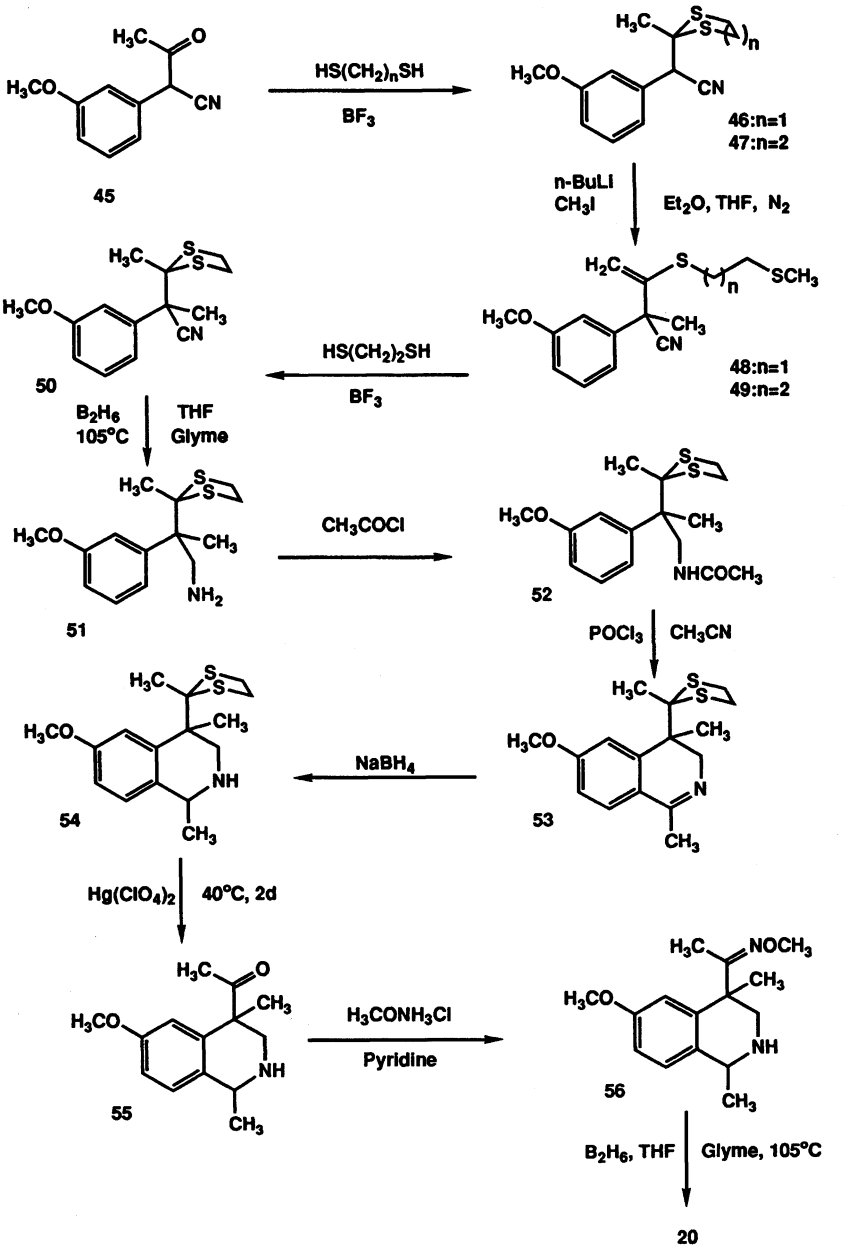
all our efforts to cleave the *N*-benzyl moiety hydrogenolytically failed (*Hartung*[10], *Grewe*[11], *Cava*[12], *Yagi*[13], *Amat*[14),15], *Seebach*[3]). So we used the *N*-benzylated tetrahydroisoquinoline **19** directly for the dehydrogenation experiment (*vide supra*).

4-(1-Aminoethyl)-6-methoxy-1,4-dimethyl-1,2,3,4-tetrahydroisoquinoline (**20**) was synthesized starting from ketone **45**[16]) (Scheme 8) which was converted into the 1,3-dithiolane **46** and the 1,3-dithiane **47**, respectively. Methylation occured in α-position of the nitril, but in addition a SCH_3-group arose, resulting from base-catalyzed β-elimination after *S*-methylation (**48**, **49**). This ring cleavage was reversed for **48** by treating it with 1,2-dimercaptoethane/BF_3, yielding **50**. Reduction of the nitril **50** afforded the *prim* amine **51** which was acetylated (**52**). *Bischler-Napieralski* reaction at room temp. produced the 3,4-dihydroisoquinoline **53** which was reduced as usual (**54**). The dithiolane ring was removed by $Hg(ClO_4)_2$[17]. The resulting ketone **55** could not be transformed to a *N*-dimethylaminoethyl increment under various conditions (cf. preparation of **17** for comparison). So we prepared the *prim* amine *via* the *O*-methyloxime **56** which was reduced by diborane.

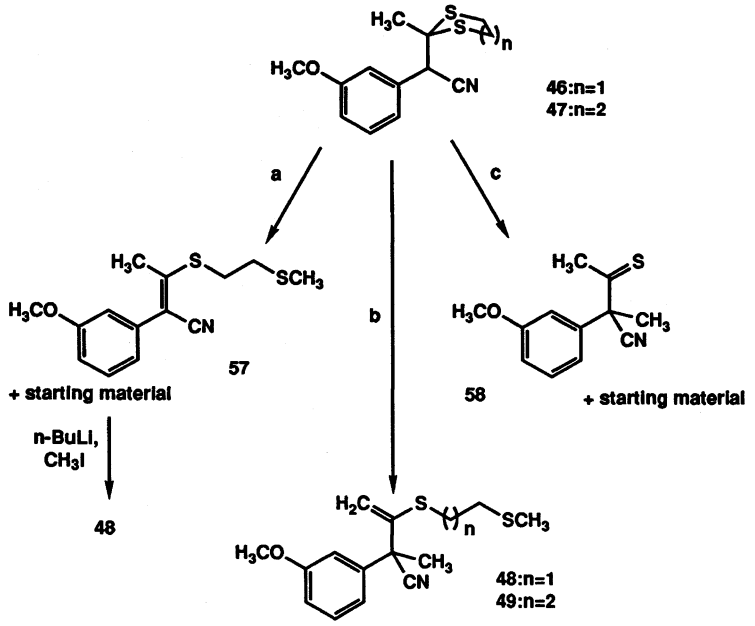
In order to avoid ring cleavage of the dithiolan/dithian system in **46** and **47**, respectively, these molecules were treated with H_3CI under the conditions shown in Scheme 9, but these efforts failed: large scale experiments yielded the α,β-unsaturated nitril **57**. Further methylation afforded the *C*-α-methylated nitrils **48** and **49** which were directly obtained when using smaller quantities of **46** or **47**. An equimolar concentration of H_3CI at room temp. led to the thioketone **58** by an unknown mechanism[18]).



Scheme 7



Scheme 8



run	CH_3I	46/47	solvent	time	temp.
a	2.1 mole-eq.	50g	THF/Et_2O/ HMPT	10h	-30°C
b	2.1 mole-eq.	<10g	THF/Et_2O/ TMEDA	2h	-30°C
c	1 mole-eq.	<10g	THF/Et_2O	12h	+25°C

Scheme 9

Experimental Part

General remarks: lit.[2].- UV-spectra: MeOH, if not stated otherwise.- ^{1}H-NMR-spectra: 90 MHz, in $CDCl_3$, if not stated otherwise.- Temp. in °C.- Drying over Na_2SO_4.- Column chromatography (cc): SiO_2.

A. Preparation of the compounds

4-(Pyrrolin-2-yliden)-isoquinoline (**3**)

To 17 ml (27.2 mmole) of n-BuLi (15% in hexane) in 50 ml of dry Et_2O/THF (1:1) were added under N_2 5.6 g (27.0 mmole) of 4-bromoisoquinoline (**22**) in 30 ml of dry THF and 5 g (27.0 mmole) of *N*-(tert-butoxycarbonyl)-pyrrolidin-2-one (**23**) in 10 ml of dry THF drop by drop at -90° with stirring. Stirring was continued for 1 h at -90° and for 2 h at -75°. At this temp. the mixture was quenched by dropwise addition of 20 ml of 2N HCl. After removal of the cooling bath the mixture was allowed to warm to room temp. and extracted with Et_2O. The extracts were washed with 10% aqueous $NaHCO_3$, dried, and evaporated to give a brownish oil (94%) of **25** (not purified). After direct treatment with 10 ml of trifluoroacetic acid at 0° and stirring for 2 h at room temp. 50 ml of water were added and the mixture was made alkaline by careful addition of 5% NaOH. Work-up gave a brownish oil. Chromatography (cyclohexane:ethyl acetate = 1:1) and recrystallization from petrolether gave 210 mg (4%) analytically pure **3**, colourless needles, mp. 68°.- $C_{13}H_{12}N_2$ (196.2) Calcd. C 79.6 H 6.16 N 14.3 Found C 79.3 H 6.14 N 14.1.- UV: λ max (log ε) = 221 (4.35); 284 (3.45); 321 nm (3.45).- IR (KBr): $\tilde{\nu}$ = 2970 cm^{-1} (CH).- ^{1}H-NMR: δ (ppm) = 2.05-2.15 (m; 2H, CH_2), 3.10-3.20 (m; 2H, CH_2), 4.20-4.30 (m; 2H, CH_2), 7.60-8.00 (m; 3H aromat.), 8.75 (s; 1H aromat.), 9.20-9.25 (m; 2H aromat.).- MS: m/z = 196 (98%, $M^{+\cdot}$), 195 (100, M - H)$^+$.

4-(Piperidein-2-yliden)-isoquinoline (**4**)

Following the procedure for **3**, 5.4 g (27 mmole) *N*-(tert-butoxycarbonyl)-piperidin-2-one (**24**) gave 350 mg (6%) **4** as a light amber oil.- $C_{14}H_{14}N_2$ (210.3).- UV: λ max (log ε) = 217 (4.43); 273 (3.48); 322 nm (3.48).- IR (film): $\tilde{\nu}$ = 2940 cm^{-1} (CH).- ^{1}H-NMR: δ (ppm) = 1.60-2.00 (m; 4H, CH_2), 2.50-2.65 (m; 2H, CH_2), 3.85-4.10 (m; 2H, CH_2), 7.50-8.35 (m; 4H aromat.), 8.60 (s; 1H aromat.), 9.25 (s; 1H aromat.).- MS: m/z = 210 (68%, $M^{+\cdot}$), 209 (100, M - H)$^+$.

4-(N-Methyl-pyrrolidin-2-yl)-isoquinoline (**7**)

To a solution of 100 mg (0.51 mmole) of **3** in 2 ml of dry MeOH were added 38 mg (1.0 mmole) of $NaBH_4$ under N_2 at 0° in portions. After stirring for 3 h at 0° 5 ml of water were added and the mixture was made alkaline and extracted with Et_2O. The extracts were washed with brine, dried, and evaporated to give a brownish oil (**5**). Without purification raw **5** was refluxed in 5 ml of 35% aqueous formaldehyde and 3 ml of formic acid for 20 h. After addition of 2 ml of 2N HCl the mixture was concentrated *in vacuo*, made alkaline by 5% NaOH and extracted with Et_2O. The extracts were washed with brine, dried, and evaporated: brownish oil (94%). Chromatography (MeOH:ethyl acetate = 1:1) gave 53 mg (49%) **7** as an amber oil.- $C_{14}H_{16}N_2$ (212.3).- UV: λ max (log ε) = 218 (4.58); 272 (3.88); 310 (3.78); 323 nm (3.88).- IR (film): $\tilde{\nu}$ = 2960 cm^{-1} (CH).- ^{1}H-NMR (250 MHz): δ (ppm) = 1.84-2.09 (m; 3H, CH), 2.27 (s; 3H, N-CH_3), 2.32-2.46 (m; 2H, CH), 3.31-3.37 (m; 1H, CH), 3.67-3.73 (m; 1H, CH), 7.56-7.73 (m; 2H aromat.), 8.06 (d; J = 8.4 Hz, 1H aromat.), 8.33 (d; J = 8.4 Hz, 1H aromat.), 8.64 (s; 1H aromat.), 9.16 (s; 1H aromat.).- MS: m/z = 212 (17%, $M^{+\cdot}$), 84 (100, $C_5H_{10}N$)$^+$.

4-(N-Methyl-piperidin-2-yl)-isoquinoline (**8**)

Following the procedure for **7**, 100 mg (0.48 mmole) of **4** gave a brownish oil (**6**) which afforded 56 mg (52%) **8** as a light amber oil.- $C_{15}H_{18}N_2$ (226.3).- UV: λ max (log ε) = 220 (4.60); 272 (3.71); 310 (3.61); 323 nm (3.72).- IR (film): $\tilde{\nu}$ = 2940 cm^{-1} (CH).- ^{1}H-NMR (250 MHz): δ (ppm) = 1.41-1.62 (m; 1H, CH), 1.67-1.99 (m; 4H, CH), 2.02 (s; 3H, N-CH_3), 2.12-2.29 (m; 2H, CH), 3.10-3.43 (m; 2H, CH), 7.56-7.73 (m; 2H aromat.), 7.97 (d; J = 8.2 Hz, 1H aromat.), 8.64 (d; J = 8.2 Hz, 1H aromat.), 8.73 (s; 1H aromat.), 9.14 (s; 1H aromat.).- MS: m/z = 226 (16%, $M^{+\cdot}$), 98 (100, $C_6H_{12}N)^+$.

4-(N-Formyl-pyrrolidin-2-yl)-isoquinoline (**9a**)

To 100 mg (0.51 mmole) of **3** in 2 ml of dry MeOH were added in portions 38 mg (1.0 mmole) of $NaBH_4$ under N_2 at 0°. After stirring for 3 h at 0° 5 ml of water were added, the mixture was made alkaline and extracted with Et_2O. The extracts were washed with brine, dried, and evaporated: brownish oil (**5**). Without purification raw **5** was treated with 3 ml of acetic-formic anhydrid at 0° for 2 h. After addition of 5 ml of ice water the mixture was made alkaline by 5% NaOH and extracted with CH_2Cl_2. The extracts were washed with brine, dried, and evaporated to give a dark oil. Chromatography (MeOH:ethyl acetate = 8:2) gave 76 mg (66%) of **9a** as a pale brown oil.- $C_{14}H_{14}N_2O$ (226.3).- UV: λ max (log ε) = 217 (4.35); 260 (3.52); 308 (3.26); 322 nm (3.35).- IR (film): $\tilde{\nu}$ = 2960 (CH); 1665 cm^{-1} (N-CHO).- ^{1}H-NMR (250 MHz): δ (ppm) = 1.91-2.20 (m; 3H, CH), 2.46-2.61 (m; 1H, CH), 3.76-3.93 (m; 2H, CH), 5.59-5.87 (m; 1H, CH), 7.60-8.07 (m; 4H aromat.), 8.25-8.50 (m; 2H, 1H aromat., CHO), 9.16-9.26 (m; 1H aromat.).- MS: m/z = 226 (47%, $M^{+\cdot}$), 197 (100, M - CHO)$^+$.

4-(N-Formyl-piperidin-2-yl)-isoquinoline (**10a**)

Following the procedure for **9a**, 100 mg (0.48 mmole) of **4** gave a brownish oil (**6**) which led to 55 mg (48%) **10a** as a light amber oil.- $C_{15}H_{16}N_2O$ (240.3).- UV: λ max (log ε) = 218 (4.48); 272 (3.43); 308 (3.34); 321 nm (3.44).- IR (film): $\tilde{\nu}$ = 2960 (CH); 1665 cm^{-1} (N-CHO).- ^{1}H-NMR (250 MHz): δ (ppm) = 1.50-2.40 (m; 6H, CH), 3.21-3.58 (m; 1.5H, CH), 4.31-4.43 (m; 0.5H, CH), 5.02-5.08 (m; 0.5H, CH), 6.27-6.29 (m; 0.5H, CH), 7.59-8.23 (m; 5H, 4H aromat., CHO), 8.56-8.60 (2s; 1H aromat.), 9.18-9.25 (2s; 1H aromat.).- MS: m/z = 240 (63%, $M^{+\cdot}$), 211 (100, M - CHO)$^+$.

4-(N-Formyl-pyrrolidin-2-yl)-1,2,3,4-tetrahydroisoquinoline (**9**)

A paste of 50 mg (0.22 mmole) of **9a** and 25 mg (0.4 mmole) of $NaBH_3CN$ was suspended and stirred in 2.5 ml of a mixture of CH_2Cl_2:HOAc = 10:1 for 24 h under N_2 at room temp. Water was added, the mixture was made alkaline, and extracted with CH_2Cl_2. The extracts were washed with brine, dried, and evaporated to give a brownish oil. Chromatography (MeOH:ethyl acetate = 8:2) gave 21 mg (41%) of **9** as a pale brown oil.- $C_{14}H_{18}N_2O$ (230.3).- UV: λ max (log ε) = 205 (4.18), 259 nm (2.69).- IR (film): $\tilde{\nu}$ = 3300 (NH); 2960 (CH); 1665 cm^{-1} (N-CHO).- ^{1}H-NMR (250 MHz): δ (ppm) = 1.39-2.28 (m; 5H, CH), 2.61-2.80 (m; 1H, CH), 2.88-3.19 (m; 2H, CH), 3.22-3.84 (m; 2H, CH), 4.05 (s; 1H, NH), 4.22-4.36 (m; 1H, CH), 4.50-5.10 (m; 1H, CH), 6.83-7.40 (m; 4H aromat.), 8.19-8.35 (m; 1H, CHO).- MS: m/z = 230 (3%, $M^{+\cdot}$), 70 (100, $C_4H_8N)^+$.

4-(N-Formyl-piperidin-2-yl)-1,2,3,4-tetrahydroisoquinoline (**10**)

Following the procedure for **9**, 28 mg (0.12 mmole) of **10a** gave 8 mg (27%) **10** as a brown oil.- $C_{15}H_{20}N_2O$ (244.3).- UV: λ max (log ε) = 202 (4.20), 260 nm (2.71).- IR (film): $\tilde{\nu}$ = 3300 (NH); 2960 (CH); 1665 cm^{-1} (N-CHO).- MS: m/z = 244 (9%, $M^{+\cdot}$), 84 (100, $C_5H_{10}N)^+$.

6,7-Dimethoxy-1,4-dimethyl-4-(N-methylpyrrolidin-2-yl-)-3,4-dihydroisoquinoline (**11**)

100 mg (0.31 mmole) acetamide **34** in 1 ml of absol. acetonitril were refluxed with 0.11 ml $POCl_3$ for 3 h under N_2. After cooling $POCl_3$ and acetonitril were distilled off *in vacuo*, the residue was dissolved in 8 ml of ice water, alkalized by 10 % NaOH and extracted with CH_2Cl_2. The org. phase was dried and evaporated: reddish mixture of diastereomers which was purified and separated by cc ($CHCl_3$:EtOH:conc. NH_3 = 85:14:1): 67 mg (72%), oil.- $C_{18}H_{26}N_2O_2$ (302.2).- IR (film): $\tilde{\nu}$ = 2963 (CH); 2786 (N-CH_3); 1630 cm^{-1} (C=N).- ^{1}H-NMR: δ (ppm) = 1.0 (s; 3H, CH_3); 1.3-1.6 (m; 4H, NCHC<u>H</u>$_2$C<u>H</u>$_2$); 2.05-4.05 (m; 5H, 2 x CH_2, CH); 2.15 (s; 3H, =C-CH_3); 2.2 (s; 3H, N-CH_3); 3.75 and 3.8 (2 x s; 6H, OCH_3); 6.75 (s; 1H, arom.); 6.85 (s; 1H, aromat.).- MS (70 eV): m/z = 219 (3.5%, MH - $C_5H_{10}N)^{+\cdot}$, 218 (2.5, M - $C_5H_{10}N)^+$, (100, $C_5H_{10})^+$.- MS-FD: m/z = 303 (100%, MH)$^+$.

4-(1-N,N-Dimethylaminoethyl)-isoquinoline (**17**)

To a solution of 65 ml dimethylamine (5.6 M in absol. EtOH) were added 75 ml of dry EtOH, 25 ml of 5N gaseous HCl in dry EtOH, 10.11 g (59 mmole) of 4-acetylisoquinoline (**36**)[9], 3.05 g (48.5 mmole) $NaBH_3CN$, and 10 g molecular sieve (3 Å). The mixture was stirred for 72 h at room temp. and acidified by HCl (pH < 2). After evaporation of excess EtOH the residue was suspended in water, alkalized with solid KOH (pH > 10), and brine was added. The solution was extracted with Et_2O (3 x 100 ml) and the extracts were washed with 10% $NaHCO_3$, dried, and evaporated to give a brown oil. Chromatography (MeOH:ethyl acetate = 1:9) and subsequent Kugelrohr distillation gave 4.8 g (41%) **17** as a colourless oil. **17**-monopicrate: needles, mp. 198°.- $C_{19}H_{19}N_5O_7$ (429.4) Calcd. C 53.2 H 4.46 N 16.3 Found C 53.3 H 4.65 N 16.0.- UV: λ max (log ε) = 218 (4.53); 272 (3.55); 3.09 (3.44); 322 nm (3.54).- IR (film): $\tilde{\nu}$ = 2980 cm^{-1} (CH).- ^{1}H-NMR (base): δ (ppm) = 1.50 (d; J = 6.9 Hz, 3H, CH-C<u>H</u>$_3$), 2.30 (s; 6H, N-CH_3), 3.90 (q; J = 6.9 Hz, 1H, C<u>H</u>-CH_3), 7.50-8.10 (m; 3H aromat.), 8.50 (s; 1H aromat.), 8.60 (s; 1H aromat.), 9.20 (s; 1H aromat.).- MS: m/z = 200 (20%, $M^{+\cdot}$), 185 (100, M - $CH_3)^+$.

2-Benzyl-4-(1-N,N-dimethylaminoethyl)-1,2,3,4-tetrahydroisoquinoline (**19**)

Under N_2 0.10 g (0.2 mmole) **44** in 5 ml of absol. THF were slowly added to 0.10 g $LiAlH_4$ in 10 ml of absol. THF at 0°. After stirring for 15 min at 0° and for 12 h at room temp., 10 ml of THF:water = 1:1 were dropped into the suspension with cooling, keeping the temp. at 0°. After stirring for 5 min the mixture was extracted 3 x with 5 ml of Et_2O each. The org. phase was washed with brine and water, dried, and evaporated: dark brown oil, purified by cc (ethyl acetate:MeOH = 1:1): 31 mg (34%) yellow oil.- UV: λ max (log ε) = 207 nm (4.62).- IR (film): $\tilde{\nu}$ = 2931 (CH), 2965 cm^{-1} (CH).- ^{1}H-NMR (250 MHz): δ (ppm) = 0.81 (d; J = 5.4 Hz, 3H, CH-C<u>H</u>$_3$), 2.18 (s; 6H, N(CH_3)$_2$), 2.37 (dd; J_1 = 2.6 Hz, J_2 = 7.7 Hz, 1H, N-C<u>H</u>$_2$-CH), 2.64-2.72 (m; 1H, CH-C<u>H</u>-CH_3), 2.88-3.06 (m; 1H, C<u>H</u>-CH-CH_3), 3.32 (d; 1H, J_1 = 2.6 Hz, J_2 = 7.7 Hz, N-C<u>H</u>$_2$-CH), 3.37 (AB-system; J = 14.7 Hz, 1H, Ar-C<u>H</u>$_2$-N), 3.66 (s, 2H, CH_2-Ph), 3.85 (AB-system; J = 14.7 Hz, 1H, Ar-C<u>H</u>$_2$-N), 6.91-7.01 (m; 1H aromat.), 7.07-7.21 (m; 3H aromat.), 7.28-7.42 (m; 5H aromat.).- MS (70 eV): m/z = 294 (0.5%, $M^{+\cdot}$), 250 (0.5, M - $NMe_2)^+$, 222 (0.5, M - $CHMeNMe_2)^+$, 91 (10, $C_7H_7)^+$, 72 (100, $CHMeNMe_2)^+$.

4-(1-Aminoethyl)-6-methoxy-1,4-dimethyl-1,2,3,4-tetrahydroisoquinoline (**20**)

0.050 g (0.19 mmole) **56** were dissolved in 1 ml of absol. THF/1,2-dimethoxyethane 1:1, mixed with 1 ml of BH_3-THF-complex, and stirred for 15 min at room temp., for 1 h at 65°, and for 5 h at 105°. After addition

of 2 ml of EtOH and 1 ml of water at 0°, alkalization by dil. NH_3, extraction with Et_2O, and drying, the solvents were distilled off *in vacuo* (Kugelrohr, 0.02 torr, 50°). Amine **20** is purified by prep. tlc (CH_2Cl_2:acetone:MeOH = 6:3:1): 35 mg (78%) colourless oil, which could not be further purified.- UV: λ max (log ε) = 203 (4.24), 250 (3.20), 278 nm (2.75).- IR (film): $\tilde{\nu}$ = 3332 (NH), 2925 cm^{-1} (CH).- ^{1}H-NMR: δ (ppm) = 1.40 (d; J = 8.2 Hz, 3H, CH-C<u>H</u>$_3$), 1.51 (d; J = 6.4 Hz, 3H, CH-C<u>H</u>$_3$), 1.90 (s; 3H, CH_3), 2.25 (s; 3H, NH, NH_2, exchangeable), 3.02 (AB-system, J = 9.3 Hz, 1H, <u>H</u>CH), 3.18 (AB-system, J = 9.3 Hz, 1H, HC<u>H</u>), 3.75 (q; J = 8.2 Hz, 1H, C<u>H</u>CH$_3$), 3.88 (s; 3H, OCH_3), 4.10 (q; J = 6.4 Hz, 1H, C<u>H</u>CH$_3$), 6.68-7.40 (m; 3H aromat.).- MS (70 eV): m/z = 234 (1.7%, $M^{+\cdot}$), 233 (6, M - H)$^+$, 219 (20, M - CH_3)$^+$, 218 (87, 233 - CH_3)$^{+\cdot}$, 205 (8, RDA), 190 (33, M - H_3CCHNH_2)$^+$.

2-(3,4-Dimethoxyphenyl)-2-(N-methylpyrrol-2-yl)-1-nitropropane (**28**) *and 1-(3,4-Dimethoxyphenyl)-1-(N-methylpyrrol-2-yl)-2-nitropropane* (**29**)

The solution of 10.9 mg (0.38 mmole) 2-(3,4-dimethoxyphenyl)-2-(*N*-methylpyrrol-2-yl)-1-nitroethane (**27**)[2] in 5 ml of absol. THF and 0.70 ml DMPU was cooled to -80°. Then 1.20 ml n-BuLi (15% in hexane) were added, resulting in a red-brown solution. After stirring for 30 min at -80° 0.60 ml CH_3I were added drop by drop, then the cooling device was removed. After 3 h, when the mixture has reached room temp., it was stored at +4°C for 24 h, then it was cooled to -50°, and 8-10 drops of glacial acetic acid were added. After addition of 2 ml of water and 30 ml of Et_2O, the mixture was allowed to warm up to room temp. Then the org. phase was washed with a satd. solution of $NaHCO_3$ and with water, dried, and the solvents were evaporated. Purification by cc (CH_2Cl_2): 98 mg of a mixture: 36% **27**; 41% **28**; 22% **29**.- ^{1}H-NMR: δ (ppm) = 1.69 (d; 0.6H CHC<u>H</u>$_3$, **29**), 1.91 (s; 1.23H, CCH_3, **28**), 3.10 (s; 0.41H, NCH_3), 3.35 (s; 0.36H, NCH_3), 3.45 (s; 0.22H, NCH_3); 3.70-3.91 (m; 6H, OCH_3); 4.12-5.25 (m; 2.34H, CHC<u>H</u>$_2$ and CCH_2), 6.03-6.92 (m; 6H aromat.).

2-(3,4-Dimethoxyphenyl)-2-(N-methylpyrrol-2-yl)-acetonitril (**30**)

To the solution of 2.9 g (10.0 mmole) **27**[2] in 10 ml of absol. 1,2-dichloroethane were added 4.60 ml (25.0 mmole) tris-(dimethylamino)phosphine within 5 min under N_2. The solution was slowly warmed to 50° and then refluxed for 20 min under N_2. After cooling 20 ml of water were added and the aqueous phase was extracted 2 x with 25 ml of CH_2Cl_2 each. The org. phase was washed with water (2 x) and satd. NaCl solution, dried, and evaporated at 40°: yellow oil, purification by cc (CH_2Cl_2): 1.0 g **30** (40%).- $C_{16}H_{16}N_2O_2$ (256.1).- IR (film): $\tilde{\nu}$ = 2938 (CH); 2838 (N-CH_3); 2242 (CN); 1595 cm^{-1}.- ^{1}H-NMR: δ (ppm) = 3.4 (s; 3H, NCH_3), 3.8 (s; 3H, OCH_3), 3.85 (s; 3H, OCH_3), 5.15 (s; 1H, CHCN), 6.0-6.9 (m; 6H aromat.).- MS (70 eV): m/z = 256 (98%, $M^{+\cdot}$), 241 (28, M - CH_3)$^+$, 230 (20, M - CN)$^+$, 225 (100, M - OCH_3)$^+$.

2-(3,4-Dimethoxyphenyl)-2-(N-methylpyrrol-2-yl)-propionitril (**31**)

Under N_2 8 ml of absol. THF and absol. Et_2O each were cooled to -70° in a three-necked flask with stirrer and thermometer. Then 2.70 ml n-BuLi (15% in hexane) were added slowly under N_2 followed by dropwise addition of 0.512 g (2.0 mmole) of nitril **30** in 5.3 ml of absol. THF. After removing of the cooling bath the mixture was allowed to warm up to -30° under stirring. At this temp. 0.9 g of CH_3I in 20 ml of absol. Et_2O were added in one portion (during this addition the temp. may rise to -10°). The mixture was stirred at room temp. for 20 h under N_2, then cooled to -70° again, and 5 ml of EtOH and 5 ml of satd. NH_4Cl solution were added. The cooling device was removed and the mixture was stirred until NH_4Cl was dissolved. The brownish solution was mixed with 5 ml of satd. NaCl solution and extracted 3 x with 5 ml of Et_2O each. The org. phase was washed with water, dried, evaporated, and purified by cc (CH_2Cl_2): 412 mg **31** (76%), colourless crystals, m.p. 85-87° (hexane:EtOH = 9:1).- $C_{16}H_{18}N_2O_2$ (270.1) Calcd. C 71.0 H 6.66 N 10.3 Found C 71.0 H 6.80 N 10.1.- IR (film): $\tilde{\nu}$ = 2938 (CH); 2838 (N-CH_3); 2234 (CN); 1593 cm^{-1} (C=C).- ^{1}H-NMR: δ (ppm) = 1.95 (s; 3H, CH_3); 3.25 (s; 3H, NCH_3); 3.75 and 3.82 (2 x s; 6H, OCH_3); 6.0-6.82 (m; 6H aromat.).- MS (70 eV): m/z = 270 (32%, $M^{+\cdot}$), 255 (100, M - CH_3)$^+$.

2-(3,4-Dimethoxyphenyl)-2-(N-methylpyrrol-2-yl)-propylamine (**32**)

Method **A**: 20 g *Raney*-Ni were activated and suspended in a solution of 3.1 g (11.5 mmole) nitril **31** in 20 ml of absol. EtOH and 3 ml of EtOH, satd. with NH_3 gas. This mixture was stirred for 7 d under H_2 of 14 bar. Stirring was continued with 10 g activated *Raney*-Ni for 5 d. After filtration and evaporation the residue was dissolved in Et_2O and the solution was washed with brine. The aqueous phase was thorougly extracted with Et_2O, the ether phase was dried and evaporated. Purification by cc (CH_2Cl_2:MeOH = 9:1): 2.67 g **32** (85%), yellowish oil.- $C_{16}H_{22}N_2O_2$ (274.2).- MS (70 eV): m/z = 274 (1.4%, $M^{+\cdot}$), 244 (100, M - CH_2NH_2)$^+$.

Method **B**: 300 mg (1.11 mmole) **31** were dried over night at room temp., 0.01 Torr, dissolved in 5 ml of absol. THF, and added slowly to a suspension of 160 mg $LiAlH_4$ in 3 ml of absol. Et_2O under N_2, using a syringe and a diaphragma. Then the mixture was heated to reflux for 5 h under N_2, cooled to 0° and quenched by careful addition of a THF/ice mixture. After 15 min $Al(OH)_3$ was separated, the aqueous phase was extracted 2 x with Et_2O, the combined org. phase was dried and evaporated: yellowish oil; for purification see above: 270 mg (90%) **32**, which was directly acetylated to **33**.

N-Acetyl-2-(3,4-dimethoxyphenyl)-2-(N-methylpyrrol-2-yl)-propylamine (**33**)

Under N_2 1.20 g (4.44 mmole) **32** were dissolved in 20 ml of acetic acid anhydride under cooling, then slowly warmed to 50° and stirred at this temp. for 2 h.- After cooling to 0°, hydrolysis, addition of NaOH to pH 8-9, separate extractions with Et_2O and CH_2Cl_2, the org. phase was dried and evaporated. Purification by cc (ethyl acetate): 1.19 g (85%), m.p. 95-97° (EtOH).- $C_{18}H_{24}N_2O_3$ (316.2) Calcd. C 68.3 H 7.7 N 8.9 Found C 67.9 H 8.1 N 7.6, deviations in elem. analysis are due to EtOH (^{1}H-NMR).- IR (film): $\tilde{\nu}$ = 3370 (NH); 2963 (CH); 1655 cm^{-1} (CO).- ^{1}H-NMR: δ (ppm) = 1.5 (s; 3H, CH_3); 1.8 (s; 3H, $COCH_3$); 2.95 (s; 3H, NCH_3); 3.6 and 3.7 (2 x s; 6H, OCH_3); 5.0-5.4 (br. m; 1H, NH); 5.95-6.7 (m; 6H aromat.).- MS (70 eV): m/z = 257 (6%, M - CH_3CONH_2)$^+$, 244 (100, M - $CH_2NHCOCH_3$)$^+$.

N-Acetyl-2-(3,4-dimethoxyphenyl)-2-(N-methylpyrrolidin-2-yl)-propylamine (**34**)

The solution of 2.20 g (6.96 mmole) **33** in 18 ml of absol. acetic acid was stirred vigorously with 700 mg Rh/C under H_2 (25 bar) for 5 d.- After cooling the solution was neutralized with 10% NaOH, alkalized with $NaHCO_3$, and filtrated. The catalyst was washed with CH_2Cl_2 and the aqueous phase was extracted with CH_2Cl_2. The org. layer was dried and evaporated. Purification by cc (CH_2Cl_2:MeOH = 4:1): brownish oil, crystallizing from diisopropyl ether:acetone = 10:1: colourless crystals, 1.47 g (66%), m.p. 84-88°.- $C_{18}H_{28}N_2O_3$ (320.2) Calcd. C 67.4 H 8.75 N 8.5 Found C 66.7 H 8.19 N 9.1.- IR (film): $\tilde{\nu}$ = 3372 (NH); 2963 (CH); 2786 (NCH_3); 1660 cm^{-1} (CO).- ^{1}H-NMR: δ (ppm) = 1.3 (s; 3H, CH_3); 1.6-1.9 (m; 2H, CH_2); 1.95 (s; 3H, $COCH_3$); 2.15 (s; 3H, NCH_3); 2.35-4.3 (m; 7H, 3 x CH_2, CH); 3.95 (s; 6H, OCH_3); 6.9-7.1 (m; 3H aromat.), 7.5-7.8 (m; 1H, NH).- MS (70 eV): m/z = 320 (0.12%, $M^{+\cdot}$), 248 (0.06, M - $CH_2NHCOCH_3$)$^+$, 84 (100, $C_5H_{10}N$)$^+$.- MS-FD: m/z = 321 (100%, MH)$^+$.

4-(1-N-Methylaminoethyl)-isoquinoline (**37**)

Following the procedure for **17**, 9 ml of 8 M methylamine in absol. EtOH, 16 ml of EtOH, 5.6 ml of 5 N HCl in EtOH, 2 g of **36**[9], 0.5 g (7.9

mmole) of $NaBH_3CN$ and 2 g molecular sieve (3 Å) gave 1.04 g (48%) **37** as a colourless oil.- $C_{12}H_{14}N_2$ (186.3).- UV: λ max (log ε) = 218 (4.43); 272 (3.56); 309 (3.44); 322 nm (3.55).- IR (film): $\tilde{\nu}$ = 3300 (NH); 2980 cm^{-1} (CH).- ^{1}H-NMR: δ (ppm) = 1.50-1.55 (d; J = 6.9 Hz, 3H, CH-C<u>H</u>$_3$), 1.80 (s; 1H, NH), 2.40 (s; 3H, NCH_3), 4.30-4.55 (q; J = 6.9 Hz, 1H, C<u>H</u>-CH_3), 7.25-8.40 (m; 4H aromat.), 8.70 (s; 1H aromat.), 9.20 (s; 1H aromat.).- MS: m/z = 186 (8%, $M^{+\cdot}$), 171 (100, M - CH_3)$^+$.

4-(1-N-Formyl-N-methylaminoethyl)-isoquinoline (**38**)

355 mg (1.9 mmole) of **37** were treated with 5 ml of acetic-formic anhydride at 0° for 15 min. After addition of 10 ml of ice water the mixture was made alkaline by 5 % NaOH and extracted with Et_2O. The extracts were washed with brine, dried, and evaporated. Kugelrohr distillation gave 385 mg (95%) **38** as a colourless oil.- **38**-monopicrate: needles, m.p. 194°.- $C_{19}H_{17}N_5O_8$ (443.4) Calcd. C 51.4 H 3.86 N 15.8 Found C 50.8 H 3.86 N 15.6.- UV: λ max (log ε) = 220 (4.41); 271 (3.78); 307 (3.60); 320 nm (3.73).- IR (film): $\tilde{\nu}$ = 2990 (CH); 1665 cm^{-1} (N-CHO).- ^{1}H-NMR (250 MHz) (base): δ (ppm) = 1.71-1.86 (2d; J = 6.9 Hz, 3H, CH-C<u>H</u>$_3$), 2.53-2.68 (2s; 3H, NCH_3), 5.46-5.49 (q; J = 6.9 Hz, 0.2H, C<u>H</u>-CH_3), 6.37-6.45 (q; J = 6.9 Hz, 0.8H, C<u>H</u>-CH_3), 7.62-8.12 (m; 5H, 4H aromat., CHO), 8.57-8.59 (2s; 1H aromat.), 9.24-9.26 (2s; 1H aromat.).- MS: m/z = 214 (100%, $M^{+\cdot}$).

2-Formyl-4-(1-N-methylaminoethyl)-1,2,3,4-tetrahydroisoquinoline (**41**)

A paste of 250 mg (1.2 mmole) **38** and 125 mg (2 mmole) of $NaBH_3CN$ was suspended and stirred in 11 ml of CH_2Cl_2:HOAc = 10:1 for 24 h under N_2 at room temp. Water was added, the mixture was made alkaline and extracted with CH_2Cl_2. The extracts were washed with brine, dried, and evaporated to give a yellowish oil. Chromatography (MeOH:CH_2Cl_2 = 3:7) gave 165 mg (62%) **41** as a pale yellow oil.- $C_{13}H_{18}N_2O$ (218.3).- UV: λ max (log ε) = 205 (3.95), 260 (2.45).- IR (film): $\tilde{\nu}$ = 3300 (NH); 2970 (CH); 1665 cm^{-1} (N-CHO).- ^{1}H-NMR (250 MHz): δ (ppm) = 0.97-1.27 (m; 3H, CH), 1.73 (s; 1H, NH), 2.38-2.43 (m; 2H, CH), 2.58-3.55 (m; 4H, CH), 4.04-5.00 (m; 3H, CH), 7.03-7.31 (m; 4H aromat.), 8.14-8.30 (m; 1H, CHO).- MS: m/z = 218 (2%, $M^{+\cdot}$), 58 (100, C_3H_8N)$^+$.

3,4-Dimethyl-benzo[f]-1,3-diaza-bicyclo[3.3.1]nonane (**42**)

110 mg (0.5 mmole) of **41** in 2 ml of dry Et_2O were added dropwise to 95 mg (2.5 mmole) of $LiAlH_4$ in 3 ml of Et_2O. The mixture was refluxed for 2 h. Excess $LiAlH_4$ was destroyed by careful addition of MeOH under cooling. After addition of 3 ml of ice water the mixture was extracted with Et_2O (3 x 10 ml) and the extracts were washed with 10% $NaHCO_3$, dried, and evaporated to give a brown oil. Chromatography (MeOH:CH_2Cl_2 = 2:8) gave 48 mg (47%) of **42** as an amber oil.- $C_{13}H_{18}N_2$ (202.3).- IR (film): $\tilde{\nu}$ = 2970 cm^{-1} (CH).- ^{1}H-NMR: δ (ppm) = 1.15-1.25 (m; 3H, CH), 2.05 (s; 3H, NCH_3), 2.25-2.30 (m; 1H, CH), 2.40-2.50 (m; 1H, CH), 2.65-2.85 (m; 1H, CH), 2.90-3.05 (m; 1H, CH), 3.20-3.60 (m; 2H, CH), 3.75-3.90 (m; 1H, CH), 4.05-4.50 (m; 1H, CH), 7.00-7.35 (m; 4H aromat.).- MS: m/z = 202 (7%, $M^{+\cdot}$), 145 (100, M - C_3H_7N)$^+$.

2-Benzyl-4-[1-(N-formyl-N-methylamino)-ethyl]isoquinolinium bromide (**43**)

Under N_2 1.50 g (8.79 mmole, 300%) benzylbromide were added dropwise at 0° during 2 h to 0.63 g (2.93 mmole) formylamide **38**, dissolved in 5 ml of absol. benzene. The mixture was stirred for 2 h at room temp. and refluxed for 10 h. A brown oil precipitated. About 2.5 ml of benzene were distilled off *in vacuo*, then the mixture was cooled to 0° and stirred for 10 h after addition of 10 ml of Et_2O: the amorphous redish precipitate was collected under N_2 on a glas frit and washed with cold Et_2O: 1.03 g (91%) pink crystals, melting range 60-70°C.- IR (film): $\tilde{\nu}$ = 2981 (CH); 1655 cm^{-1} (CHO).- ^{1}H-NMR: δ (ppm) = 1.25 (d; J = 6.9 Hz, 3H, CHC<u>H</u>$_3$), 2.13 (s; 1.2H, rotamere, NCH_3), 2.20 (s; 1.8H, rotamere, NCH_3), 4.32 (s; 2H, CH_2Ph), 5.95 (q; J = 6.9 Hz, 1H, C<u>H</u>CH_3), 6.90-7.22 (m; 5H aromat.), 7.52-8.34 (m; 6H aromat.), 9.56 (s; 1H, CHO).- MS (70 eV): m/z = 214 (14%; educt, **38**), 199 (4, M - CH_3)$^+$, 185 (12, M - CHO)$^+$, 170/172 (3, $C_6H_5CH_2Br$, thermal decomposition in the inlet system), 156 (12, M - NCH_3CHO)$^+$, 91 (100, C_7H_7)$^+$.

2-Benzyl-4-[1-(N-formyl-N-methylamino)-ethyl]-1,2,3,4-tetrahydroisoquinoline (**44**)

To 0.40 g (1.04 mmole) **43**, dissolved in 20 ml of absol. MeOH, were added 0.50 g $NaBH_4$ at 0°. After addition of 1 ml of water the reaction mixture was stirred for 15 min at 0° and 16 h at room temp.- After acidification by 10 ml of 2 N HCl, MeOH was evaporated *in vacuo*. After addition of 10 ml of water and alkalization by dil. NaOH at 0° **44** was extracted by Et_2O. The org. phase was washed with brine and water, dried, and evaporated *in vacuo* at 40°: yellow oil. Purification by cc (CH_2Cl_2:-toluene:ethyl acetate = 8:1:2): 0.16 g (52%).- IR (film): $\tilde{\nu}$ = 2927, 2855 (CH), 1669 cm^{-1} (CHO).- ^{1}H-NMR: δ (ppm) = 1.27 (d; J = 6.0 Hz, 3H, CH-C<u>H</u>$_3$), 2.24-2.57 (m; 2H, CH_2), 2.78 (s; 3H, NCH_3), 2.91-3.12 (m; 1H, CH-C<u>H</u>-CH_3), 3.31 (AB-system, J = 5.4 Hz, 1H, CH_2), 3.48 (s, 2H, CH_2Ph), 3.64 (AB-system, J = 5.4 Hz, 1H, CH_2), 3.96-4.21 (m, 1H, CH_2-C<u>H</u>-CH), 6.77-7.48 (m, 9H aromat.), 8.00 (s, 1H, CHO).- MS (70 eV): m/z = 308 (0.5%, $M^{+\cdot}$), 305 (1.5, M - 3H)$^+$, 217 (50, M - C_7H_7)$^+$, 91 (100, C_7H_7)$^+$.

2-(3-Methoxyphenyl)-2-(2-methyldithiolan-2-yl)acetonitril (**46**) and *2-(3-Methoxyphenyl)-2-(2-methyldithian-2-yl)acetonitril* (**47**)

1.0 g (5.0 mmole) nitril **45**[16] were dissolved in 7 ml of boiling CH_2Cl_2 by vigorous stirring. 1.50 ml of ethane-1,2-dithiole or propane-1,3-dithiole for **47**, respectively, and then 1.00 ml of $BF_3 \cdot Et_2O$ were added drop by drop at room temp. The reaction mixture was stirred for 24 h at 20°, mixed with 10 ml of ice water, slightly alkalized by 5 % NaOH and extracted with CH_2Cl_2 (3 x 5 ml). The org. phase was washed with brine, with water, dried, and evaporated: yellowish-greenish oil which was purified by two-fold Kugelrohr distillation (150-180°, 0.02 torr).

46: 1.17 g (88%) colourless oil.- IR (film): $\tilde{\nu}$ = 2964 (CH), 2836 (CH), 2242 cm^{-1} (CN).- ^{1}H-NMR: δ (ppm) = 1.76 (s; 3H, CH_3), 3.26-3.30 (m; 4H, SCH_2CH_2S), 3.77 (s; 3H, OCH_3), 4.17 (s; 1H, CH-CN), 6.75-7.45 (m, 4H aromat.).- MS (70 eV): m/z = 224 (0.3%, M - HCN)$^{+\cdot}$, 146 (1.5, M - $C_4H_7S_2$)$^+$, 119 (100, $C_4H_7S_2$)$^+$.

47: 1.21 g (87%) colourless oil.- ^{1}H-NMR: δ (ppm) = 1.59 (s; 3H, CH_3), 1.74-2.21 (m; 2H, $SCH_2C\underline{H}_2CH_2S$), 2.72-3.03 (m; 4H, $SC\underline{H}_2CH_2C\underline{H}_2S$), 3.79 (s; 3H, OCH_3), 4.44 (s; 1H, CH-CN), 6.80-7.45 (m; 4H aromat.).

2-(3-Methoxyphenyl)-3-(1,4-dithiapentyl)-but-3-enyl-2-cyanide (**48**) and *2-(3-Methoxyphenyl)-3-(1,5-dithiahexyl)-but-3-enyl-2-cyanide* (**49**)

30 ml of THF and Et_2O each and 3 ml of freshly distilled TMEDA were cooled to -70°. Then 10 ml of n-BuLi (15% in hexane) were slowly added under N_2 followed by very slow addition of 2.00 g (7.55 mmole) **46** (for **48**) or 2.11 g (7.55 mmole) **47** (for **49**) in 20 ml of absol. THF. A tough red-brown precipitate was formed. The mixture was allowed to warm up to -30°, then 3.38 g CH_3I in 20 ml of Et_2O were added in one portion, allowing temp. raise to -10°. After 12 h stirring at room temp. the mixture was cooled to -70°, 10 ml of satd. NH_4Cl solution and 10 ml of EtOH were added, and the mixture was stirred at room temp. until precipitated NH_4Cl was dissolved. After addition of 5 ml of brine the mixture was extracted 3 x with 5 ml Et_2O each. Washing with water, drying, and evaporation afforded yellow oils which were purified by cc (CH_2Cl_2:cyclohexane = 2:1).

48: 1.44 g (65%) colourless oil.- IR (film): $\tilde{\nu}$ = 2920 (CH), 2836 (CH), 2240 (CN), 1601 cm^{-1} (H_2C=CH).- ^{1}H-NMR: δ (ppm) = 1.94 (s; 3H, CH_3), 2.10 (s; 3H, CH_3), 2.48-3.03 (m; 4H, SCH_2CH_2S), 3.79 (s; 3H, OCH_3), 5.20 (AB-system, J = 3.0 Hz, 1H, HCH), 5.77 (AB-system, J = 3.0 Hz, 1H, HCH), 6.72-7.37 (m, 4H aromat.).- MS (70 eV): m/z = 293 (2.5%, $M^{+\cdot}$), 266 (1, M - HCN)$^{+\cdot}$, 246 (1.5, M - SCH_3)$^+$, 218 (3, M - C_3H_7S)$^+$, 75 (100, C_3H_7S)$^+$.

49: 1.58 g (68%) colourless oil.- ^{1}H-NMR: δ (ppm) = 1.95 (s; 3H, CH_3), 2.07 (s; 3H, CH_3), 2.36-3.00 (m; 2H, $SCH_2CH_2CH_2S$), 2.53 (t; J = 7.5 Hz, 2H, $CH_2CH_2CH_2$), 2.82 (t; J = 7.5 Hz, 2H, $SCH_2CH_2CH_2S$), 3.80 (s; 3H, OCH_3), 5.21 (AB-system, J = 2.4 Hz, 1H, HCH), 5.78 (AB-system, J = 2.4 Hz, 1H, HCH), 6.82-7.51 (m, 4H aromat.).

2-(3-Methoxyphenyl)-2-(2-methyldithiolan-2-yl)-propionitril (**50**)

To 0.10 g (0.34 mmole) **48** or 0.11 g (0.34 mmole) **49**, respectively, in 10 ml of absol. CH_2Cl_2 were added under N_2 0.035 g ethane-1,2-dithiole and 0.1 g $BF_3 \cdot 2\ Et_2O$ at 0°. After stirring for 18 h at room temp. and addition of 5 ml of ice water, the mixture was alkalized with 2N NaOH and extracted with Et_2O. The org. phase was washed (2 x 5 ml of water), dried, and evaporated: brown oil which was purified by cc (CH_2Cl_2:cyclohexane = 4:1): 0.065 g (72%) colourless crystals, m.p. 60-62° (MeOH).- $C_{14}H_{17}NOS_2$ (279.4) Calcd. C 60.2 H 6.13 N 5.0 Found C 60.4 H 6.11 N 4.8.- IR (KBr): $\tilde{\nu}$ = 3005 (CH), 2936 (CH), 2236 cm^{-1} (CN).- ^{1}H-NMR: δ (ppm) = 1.80 (s; 3H, CH_3), 2.10 (s; 3H, CH_3), 3.11-3.40 (m; 4H, SCH_2CH_2S), 3.80 (s; 3H, OCH_3), 6.72-7.00 (m; 1H aromat.), 7.21-7.39 (m; 3H aromat.).- MS (70 eV): m/z = 279 (0.1%, $M^{+\cdot}$), 161 (1.3), 146 (1.0), 119 (100, $C_4H_7S_2$)$^+$.

2-(3-Methoxyphenyl)-2-(2-methyldithiolan-2-yl)-propylamine (**51**)

1.00 g (3.58 mmole) **50** in 25 ml of absol. THF:1,2-dimethoxyethane = 1:1 were cooled to 0°. Then 7.2 ml THF-BH_3 complex (1 molar in THF) were added carefully by a syringe and the mixture was stirred at 0° for 15 min at room temp., 1 h at 65°, and 10 h at 105° (tlc control).- For work-up the mixture was cooled to 0°, 5 ml of cold EtOH were added slowly, NH_3 rendered the mixture sligthly alkaline, and **51** was extracted with Et_2O. Drying and evaporation yielded a brownish oil; purification by cc (ethyl acetate:EtOH = 4:1): 0.133 g brown oil.- IR (film): $\tilde{\nu}$ = 3367 (NH), 2920 cm^{-1} (CH).- ^{1}H-NMR: δ (ppm) = 1.67 (m; 8H, 2 x CH_3 and CH_2NH_2), 2.87-3.23 (m; 6H, SCH_2CH_2S, CH_2NH_2), 3.73 (s; 3H, OCH_3), 6.65-7.37 (m; 4H aromat.).- MS (70 eV): m/z = 283 (2.5%, $M^{+\cdot}$), 254 (10, M - CH_2NH)$^+$, 293 (10, M - $C_4H_7S_2$)$^+$, 119 (100, $C_4H_7S_2$)$^+$.

N-Acetyl-2-(3-methoxyphenyl)-2-(2-methyldithiolan-2-yl)propylamine (**52**)

0.20 g (0.71 mmole) **51** in 5 ml of absol. CH_2Cl_2 were mixed with 0.55 g acetyl chloride at 0° under N_2 and stirred at 0° and at room temp. for 1 h each. The red mixture was cooled to 0°, neutralized by N NaOH and extracted with Et_2O (3 x 5 ml). The org. phase was washed with satd. $NaHCO_3$ solution, with water, dried, and evaporated: yellow oil, purification by cc (ethyl acetate:MeOH = 3:2): 0.19 g (82%).- IR (film): $\tilde{\nu}$ = 3314 (NH), 3081 (NH), 2973 (CH), 2925 (CH), 1655 cm^{-1} (CO).- ^{1}H-NMR: δ (ppm) = 1.63 (s; 3H, CH_3), 1.70 (s; 3H, CH_3), 1.83 (s; 3H, CH_3), 2.97-3.40 (m; 4H, SCH_2CH_2S), 3.82 (s; 3H, OCH_3), 4.20 (d; J = 6 Hz, 2H, CH_2NH), 5.60 (t; J = 6 Hz, 1H, CH_2NH), 6.75-7.40 (m; 4H aromat.).- MS (70 eV): m/z = 325 (0.5%, $M^{+\cdot}$), 254 (1, M - $CH_2NHCOCH_3$)$^+$, 119 (100, $C_4H_7S_2$)$^+$.

6-Methoxy-1,4-dimethyl-4-(2-methyldithiolan-2-yl)-3,4-dihydroisoquinoline (**53**)

In a throrougly dried flask 0.44 g (1.34 mmole) **52** in 10 ml of absol. acetonitril were cooled to 0° under N_2 and slowly mixed with 1.5 ml of freshly distilled $POCl_3$ in 2 ml of absol. acetonitril, followed by stirring for 24 h at room temp. Then about 6 ml of acetonitril were distilled off at the oil pump. After addition of 6 ml of acetone, the dark brown solution was neutralized by addition of NaOH, then alkalized by $NaHCO_3$-solution. The separated crystals were washed with cold CH_2Cl_2 and discarded (inorganic material). The filtrate was extracted with Et_2O (3 x 5 ml), the ether layer was combined with the CH_2Cl_2-washing, dried and evaporated: dark brown oil which was directly reduced to the tetrahydroisoquinoline **54**.

53: 0.35 g (85%).- UV: λ max (log ε) = 202 (4.23), 248 (3.50), 276 nm (3.68).- IR (film): $\tilde{\nu}$ = 2923, 2836 (CH), 1640 cm^{-1}.- ^{1}H-NMR: δ (ppm) = 1.58 (s; 3H, CH_3), 1.67 (s; 3H, CH_3), 2.26 (s; 3H, CH_3), 2.95-3.38 (m; 4H, SCH_2CH_2S), 3.37 (AB-system, J = 15 Hz, 1H, HCH), 3.80 (s; 3H, OCH_3), 4.26 (AB-system, J = 15 Hz, 1H, HCH), 6.78 (dd; J_1 = 9 Hz, J_2 = 2.4 Hz, 1H, 7-H), 7.20 (d; J = 2.4 Hz, 1H, 5-H), 7.41 (d; J = 9 Hz, 1H, 8-H).- MS (70 eV): m/z = 307 (0.2%, $M^{+\cdot}$), 305 (1.5, M - 2H)$^{+\cdot}$, 189 (40, M+H - $C_4H_7S_2$)$^{+\cdot}$, 119 (100, $C_4H_7S_2$)$^+$.

6-Methoxy-1,4-dimethyl-4-(2-methyldithiolan-2-yl)-1,2,3,4-tetrahydroisoquinoline (**54**)

0.34 g (1.09 mmole) crude dihydroisoquinoline **53** in 10 ml of absol. MeOH were cooled to 0°, mixed with 0.30 g $NaBH_4$ in portions, and stirred for 4 h at 0°. The excess of $NaBH_4$ was destroyed by about 5 ml of 2N HCl, MeOH was distilled off at 20° and the aqueous phase was neutralized by $NaHCO_3$. Extraction with Et_2O and cc (ethyl acetate:EtOH = 3:2) afforded 0.30 g (88%) of a colourless oil.- IR (film): $\tilde{\nu}$ = 3330 (NH), 2967, 2925, 2834 cm^{-1} (CH).- ^{1}H-NMR: δ (ppm) = 1.45 (d; J = 6.9 Hz, 3H, $CHCH_3$), 1.48 (s; 3H, CH_3), 1.86 (s; 3H, CH_3), 2.13 (s; 1H, NH, exchangeable), 2.87 (AB-system, J = 11.7 Hz, 1H, HCH), 3.04-3.30 (m; 4H, SCH_2CH_2S), 3.47 (AB-system, J = 11.7 Hz, 1H, HCH), 3.79 (s; 3H, OCH_3), 4.07 (q; J = 6.9 Hz, 1H, $CHCH_3$), 6.67-7.44 (m; 3H aromat.).- MS (70 eV): m/z = 309 (1.5%, $M^{+\cdot}$), 294 (1.4, M - CH_3)$^+$, 191 (40, M+H - $C_4H_7S_2$)$^{+\cdot}$, 119 (100, $C_4H_7S_2$)$^+$.

4-Acetyl-6-methoxy-1,4-dimethyl-1,2,3,4-tetrahydroisoquinoline (**55**)

To 0.34 g (1.1 mmole) **54** in 10 ml of freshly distilled $CHCl_3$ and 12 ml of MeOH were added 0.49 g $Hg(ClO_4)_2 \cdot 2\ H_2O$ in 8 ml of MeOH drop by drop, affording a white precipitate. The suspension was stirred under N_2 for 1 h at room temp. and for 48 h at 40°. After filtration and washing of the solid with $CHCl_3$ and MeOH, the solvents were evaporated at 20°. The remaining brown oil was dissolved in 2N HCl of 0°, stirred for 1 h, neutralized by $NaHCO_3$, and the base was extracted by Et_2O. Usual purification (CH_2Cl_2:acetone:MeOH = 6:3:1) afforded 0.12 g (47%) colourless oil.- IR (film): $\tilde{\nu}$ = 3336 (NH), 2965, 2929, 2834 (CH), 1702 cm^{-1} (CO).- ^{1}H-NMR: δ (ppm) = 1.36 (s; 3H, CH_3), 1.40 (d; J = 6.3 Hz, 3H, $CHCH_3$), 2.08 (s; 3H, CH_3), 2.26 (s; 1H, NH, exchangeable), 2.83 (AB-system, J = 11.7 Hz, 1H, HCH), 3.54 (AB-system, J = 11.7 Hz, 1H, HCH), 3.75 (s; 3H, OCH_3), 4.07 (q; J = 6.3 Hz, 1H, $CHCH_3$), 6.65-7.21 (m; 3H aromat.).- MS (70 eV): m/z = 233 (33%, $M^{+\cdot}$), 218 (100, M - CH_3)$^+$, 190 (30, M - $COCH_3$)$^+$, 189 (50, M - $COCH_3$-H)$^{+\cdot}$, 43 (20, $COCH_3$)$^+$.

4-(1-Methoxyiminoethyl)-6-methoxy-1,4-dimethyl-1,2,3,4-tetrahydroisoquinoline (**56**)

The mixture of 0.10 g (0.83 mmole) **55** and 0.12 g (2.4 mmole) *O*-methyl-hydroxylammonium chloride in 10 ml of pyridine was heated to reflux under N_2 for 2 h. Pyridine was removed at the oil pump at 60°, the residue was dissolved in 3 ml of 2N HCl and extracted with Et_2O. The aqueous phase was alkalized by dil. NaOH and extracted with ether. Purification by cc (CH_2Cl_2:acetone:MeOH = 6:3:1): 0.082 g (76%) colourless oil.- IR (film): $\tilde{\nu}$ = 3336 (NH), 2932 (CH), 1611 cm^{-1} (C=N).- ^{1}H-NMR: δ (ppm) = 1.39 (s; 3H, CH_3), 1.43 (d; J = 6.3 Hz, 3H, $CHCH_3$), 1.73 (s; 3H, CH_3), 1.94 (s; 1H, NH), 2.79 (AB-system, J = 11.7 Hz, 1H, HCH), 3.40 (AB-system, J = 11.7 Hz, 1H, HCH), 3.76 (s; 3H, $NOCH_3$), 3.90 (s; 3H,

OCH_3), 4.12 (q; J = 6.3 Hz, 1H, C<u>H</u>CH_3), 6.65-7.50 (m; 3H aromat.).- MS (70 eV): m/z = 262 (0.6%, $M^{+\cdot}$), 259 (10, M - 3H)$^+$, 247 (60, M - CH_3)$^+$, 231 (75, M - OCH_3)$^+$, 190 (100, M - $H_3CCNOCH_3$)$^+$.

There is no indication for diastereomers.

2-(3-Methoxyphenyl)-3-(2,5-dithiapentyl)-crotononitril (**57**)

750 ml of absol. THF and 750 ml of absol. Et_2O were cooled to -70° in a three necked flask and mixed with 250 ml cooled n-BuLi (15% in hexane) under N_2. With vigorous stirring 50.0 g (0.19 mole) nitril **46** in 100 ml of absol. THF were added drop by drop keeping the temp. at -70°. Then the cooling device was removed and the mixture was allowed to reach -30°. At this temp. 84.5 g CH_3I (0.60 mole) in 200 ml of absol. Et_2O were added in one portion and the mixture was stirred at room temp. for 2 h. After cooling to -70° 250 ml of cooled EtOH and 250 ml of satd. NH_4Cl solution were added.- After reaching 0° water was added slowly until precipitated NH_4Cl had dissolved. After mixing with 100 ml of brine, extraction with Et_2O, and purification of crude brown **57** by cc (CH_2Cl_2:cyclohexane = 2:1), 17.4 g (33%) colourless oil were obtained. IR (film): $\tilde{\nu}$ = 2919 (CH); 2836 (CH); 2203 (CN); 1599 cm^{-1} (C=C).- ^{1}H-NMR (*E/Z*-mixture): δ (ppm) = 2.05 (s; 2H, CH_3), 2.15 (s; 1H, CH_3), 2.20 (s; 1H, CH_3), 2.51 (s; 2H, CH_3), 2.52-3.32 (m; 4H, SCH_2CH_2S), 3.74 (s; 3H, OCH_3), 6.73-7.52 (m; 4H aromat.).- MS (70 eV): m/z = 279 (16%, $M^{+\cdot}$), 219 (18, M - C_2H_4S)$^+$, 204 (19, M - $C_2H_4SCH_3$)$^+$, 75 (100, $C_2H_4SCH_3$)$^+$.

Preparation of **48** from **57** follows the preparation of **48** from **46**: **57**: 2.00 g (7.2 mmole).- **48**: 1.60 g, 72%.

2-(3-Methoxyphenyl)-2-thioacetyl-propionitril (**58**)

To the solution of 0.850 g (3.20 mmole) **46** in 10 ml of absol. THF:Et_2O = 1:1 were added under N_2 1.95 ml of n-BuLi (15% in hexane) and 5 ml of Et_2O at -70°. The cooling bath was removed, the mixture was stirred for 15 min at room temp., 0.454 g CH_3I in 5 ml of Et_2O were added drop by drop, and the mixture was stirred at room temp. for 10 h. After addition of 10 ml of satd. NH_4Cl solution at 0° the mixture was stirred for 15 min and extracted with Et_2O. Usual work-up yielded a yellow oil which was purified by cc (CH_2Cl_2:cyclohexane = 2:1): 0.37 g (53%) colourless oil.- IR (film): $\tilde{\nu}$ = 3002 (CH); 2202 (CN); 1600 cm^{-1} (CS).- ^{1}H-NMR: δ (ppm) = 2.31 (s; 3H, CH_3); 2.50 (s; 3H, CH_3); 3.74 (s; 3H, OCH_3); 6.70-7.47 (m; 4H aromat.).- MS (70 eV): m/z = 219 (50%, $M^{+\cdot}$); 204 (100, M - CH_3)$^+$; 189 (50, 204 - CH_3)$^{+\cdot}$; 171 (30).

B. Dehydrogenation experiments

Standard conditions

The tetraline quantity necessary for the respective compound was freed from O_2 by bubling N_2 into it at 100° for 15 min.- After cooling to room temp. the compound to be tested and Pd/C (10%) were added. After heating for 1-2 h under reflux tetraline was distilled off in a Kugelrohr apparatus. The pertinent product was purified by cc.

4-(N-Formyl-pyrrolidin-2-yl)-isoquinoline (**9a**)

15 mg **9**, 1 ml of tetraline, 5 mg Pd/C, 1 h. Cc: MeOH:ethyl acetate = 8:2.- Data see above.

4-(N-Formyl-piperidin-2-yl)-isoquinoline (**10a**)

15 mg **10**, 1 ml of tetraline, 5 mg Pd/C, 1 h. (Cc: cf. **9a**).- Data see above.

6,7-Dimethoxy-1,4-dimethylisoquinoline (**12**)

run **A**: 5.0 mg **11**, 1 ml of tetraline, 5.0 mg Pd/C, 1 h.- Cc: $CHCl_3$:EtOH:conc. NH_3 = 85:14:1.- 4.1 mg brownish oil.- MS (70 eV): m/z = 217 (100%, $M^{+\cdot}$), 202 (16, M - CH_3)$^+$.- UV (qual.): max = 201; 238; 280; 326 nm.

run **B**: same conditions as for run **A**, but no Pd/C: 4.0 mg **12**.

6,7-Dimethoxy-1-methyl-3,4-dihydroisoquinoline (**14**): Lit.[2].

6,7-Dimethoxy-1-(3,4-methylendioxybenzyl)-4-(N-methylpyrrol-2-yl)-isoquinoline (**16a**)

200 mg **15** or 200 mg **16**, respectively, 6 ml of tetraline, 50 mg Pd/C, 2 h.- Solvents were evaporated: brownish oil. Cc: ethyl acetate, distillation (Kugelrohr, 0.05 mm Hg, 250°): 150 mg yellow crystals (72%).- m.p. 69-71°.- **16a**-picrate: m.p. 172-173° (dec.).- **16a**-picrate: $C_{30}H_{25}N_5O_{11}$ (631.5) Calcd. C 57.0 H 3.99 N 11.1 Found C 56.9 H 4.09 N 10.9.- UV: λ max (log ε) = 216 (4.49), 287 nm (4.08).- IR (KBr): $\tilde{\nu}$ = 2795 cm^{-1} (NCH_3).- MS (70 eV): m/z = 402 (79%, $M^{+\cdot}$), 401 (100), 386 (7), 385 (14), 298 (14), 282 (23), 268 (94), 186 (20).- ^{1}H-NMR: δ (ppm) = 3.38 (s; 3H, NCH_3); 3.87 (s; 3H, OCH_3); 3.95 (s; 3H, OCH_3); 4.36 (s; 2H, OCH_2O); 5.87 (s; 2H, $PhCH_2$), 6.45-7.06 (m; 8H aromat.), 8.1 (s; 1H, 3-H).

4-Ethylisoquinoline (**18**)[5]

36 mg **17** or 45 mg **19**, respectively, 1 ml of tetraline, 30 mg Pd/C or 45 mg, respectively, 1 h.- Cc: ethyl acetate.- $C_{11}H_{11}N$ (157.2).- IR (film): $\tilde{\nu}$ = 2950 cm^{-1} (CH).- ^{1}H-NMR (250 MHz): δ (ppm) = 1.39 (t; J = 7.54 Hz, 3H, CH_2-C<u>H</u>$_3$), 3.07 (q; J = 7.54 Hz, 2H, C<u>H</u>$_2$-CH_3), 7.57-8.03 (m; 4H aromat.), 8.40 (s; 1H aromat.), 9.13 (s; 1H aromat.).- MS: m/z = 157 (73%, $M^{+\cdot}$), 142 (100, M - CH_3)$^+$.- UV: λ max (log ε) = 217 (4.33); 271 (3.27); 308 (3.15); 322 nm (3.25).

4-(1-Aminoethyl)-6-methoxy-1,4-dimethyl-3,4-dihydroisoquinoline (**21**)

31 mg **20**, 1 ml of tetraline, 13 mg Pd/C, 1 h.- UV (MeOH, 0.1HCl): λ max (log ε) = 202 (4.15); 258 (3.70); 315 nm (3.75).- MS (70 eV): m/z = 232 (1.1%; $M^{+\cdot}$), 188 (3; M - H_3CCHNH_2)$^+$, 187 (8; M - H_3CCHNH_2 - H)$^{+\cdot}$, 44 (24; H_3CCHNH_2)$^+$.

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