137. Unusual Acid-Catalyzed Rearrangement of Two α,α'-Diimino-oximes

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Dedicated to Prof. *Albert Eschenmoser* on the occasion of his 60th birthday

(13.V.85)

2-[2-(Alkylimino)-2-phenylethylidene]pyrrolidines (vinamidines, **3–6**) were obtained either *via* activation of the corresponding vinologous amide **1** with *Meerwein* salt and subsequent treatment of the intermediate **2** with an amine, or more directly by acid-catalyzed condensation of the *Schiff* bases derived from acetophenone with 2-ethoxy-1-pyrroline. Nitrosation of these vinamidines led to α,α'-diimino-oximes. In two cases (**10**, **11**), these oximes underwent acid-catalyzed rearrangement with formation of a 5,6,7,8-tetrahydroimidazo[1,2-*a*]pyridine ring system (**12**, **13**). X-Ray analysis of one of these products (**13**) and also of one of the vinamidine salts (**6**) are presented.

1. Introduction. – In connection with a broader investigation on the hypoglycaemic activity of different vinamidine[1]) derivatives [2], we converted some of these compounds into α,α'-diimino-oximes by means of nitrosation. Having these structurally rather unusual oximes[2]) in hand, we were then interested in their behaviour under *Beckmann* conditions. In two cases, we found that in strongly acidic media at elevated temperature an unexpected rearrangement with formation of an annellated imidazole ring system took place. Here, we describe this reaction, together with two alternative ways of synthesis for the starting material.

2. Synthesis of Vinamidines. – The vinamidines were first prepared according to *Scheme 1*, starting from 2-pyrrolidinethione. Using the well-known *Eschenmoser* sulfur-extrusion sequence [3], the vinologous amide[3]) **1** was obtained. Treatment of **1** with $Et_3O^+BF_4^-$ led to the crystalline fluoroborate **2**, which, by reaction with amines, gave the vinamidines **3–6**. This procedure had, in principle, already been described for one special case in [3].

Mainly for ecological reasons, however, we were interested in an alternative process by way of which the phosphorus-containing reagents and also the fluoroborate could be avoided. We found that the same vinamidines could be prepared more directly by starting from the *Schiff* bases of acetophenone and the imino ether of 2-pyrrolidone. Surprisingly, in this case it turned out that acid catalysis gave more favourable results than base catalysis[4]). By using the methanesulfonic-acid salt of the *Schiff* base and performing the

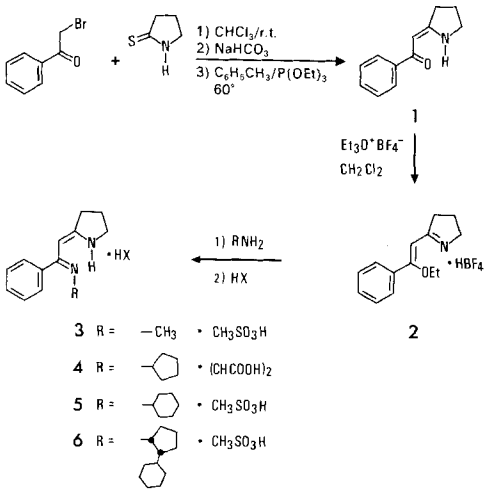
[1]) The term 'vinamidine' for a vinologous amidine was introduced by *Lloyd* and *McNab* in a review article on this class of compounds [1].

[2]) Only very few examples of α,α'-diimino-oximes are to be found in the literature. In most of the reported cases, one or both of the imines are part of an aromatic heterocycle.

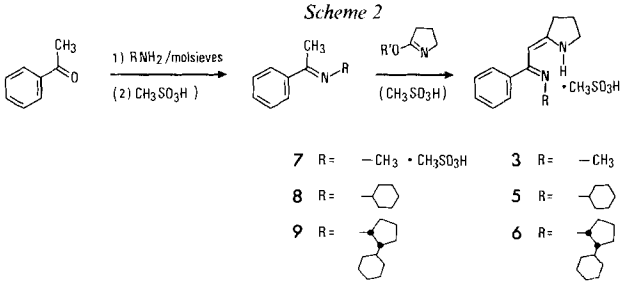
[3]) Preparation of **1** by a *Wittig* reaction was described by *Mitsutaka et al.* [4].

[4]) Exploratory experiments with DBU or LDA as base gave only traces of the desired products.

Scheme 1

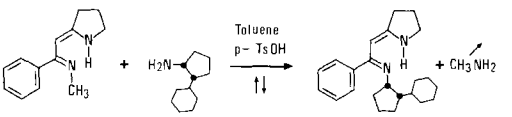


Scheme 2



reaction in the presence of an excess of the imino ether, a yield of 60% of the vinamidine was obtained for R = cyclohexyl *(Scheme 2)*. However, the yield proved to be susceptible to steric hindrance from the substituent on the N-atom of the *Schiff* base. With *cis*-2-cyclohexylcyclopentyl group as a substituent, the yield dropped to 28%. In this special case, it was preferable to prepare the *N*-methyl-vinamidine first. Methylamine could afterwards be exchanged for *cis*-2-cyclohexylcyclopentylamine[5]) in boiling toluene in high yield under catalysis with TsOH *(Scheme 3)*. All vinamidines were purified as their acid salts, especially as the well crystallizing fumarates or methanesulfonates.

Scheme 3



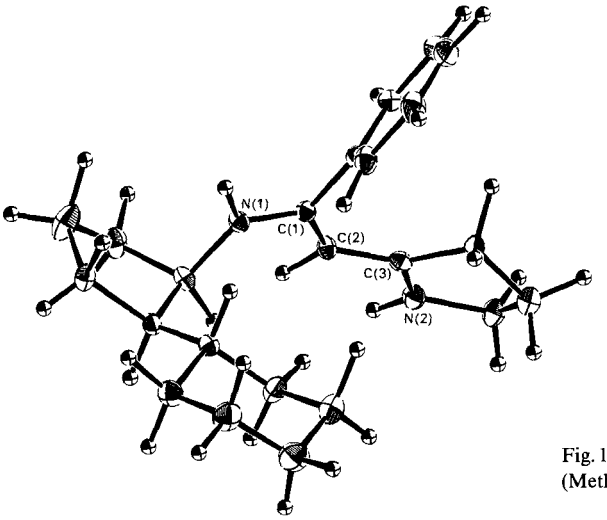
3. X-Ray Structure of 2-{2-[(*cis*-2-Cyclohexylcyclopentyl)imino]-2-phenylethylidene}pyrrolidine Methanesulfonate (6). – The crystal structure of **6** has been determined by single-crystal X-ray structure analysis *(Fig. 1* and *Table)*.

[5]) *cis*-2-Cyclohexylcyclopentylamine was prepared according to [5].

Table. *Bond Lengths of the Vinamidine System*

Bond	Length [Å][a])	Bond	Length [Å][a])
N(1)–C(1)	1.33	C(1)–C(2)	1.39
N(2)–C(3)	1.33	C(2)–C(3)	1.39

[a]) Standard deviation: 0.005–0.008 Å.



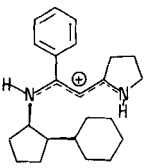
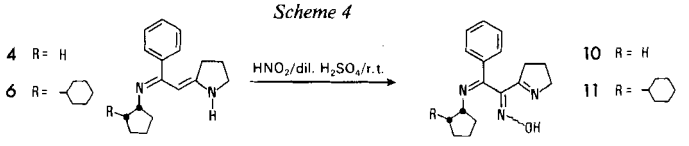


Fig. 1. *ORTEP drawing of* **6** (Methane sulfonate not shown)

The vinamidine chromophore shows a W-shaped conformation with a proton on both N-atoms[6]). The two N–C- and the two C–C-bond distances are equal, demonstrating that the charge is equally distributed over the π system. The aromatic ring is – obviously for steric reasons – not coplanar with the vinamidine-π-system.

4. Nitrosation of Vinamidines. – Nitrosation was easily achieved in aqueous acidic solution with $NaNO_2$ *(Scheme 4)*. The isolated product was an α,α'-diimino-oxime stemming from an initial *C*-nitrosation. No *N*-nitrosation product was found.

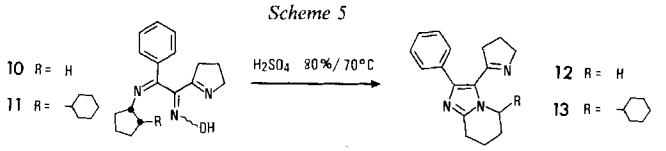
Scheme 4



5. Acid-Catalyzed Rearrangement of α,α'-Diimino-oximes 10 and 11. – When **11** was dissolved in 80% H_2SO_4 and the solution heated for 6 h to 70°, mainly one new product was formed (TLC). This new product could be isolated as a white crystalline powder. It turned out to be more lipophilic than the starting material and showed slightly basic properties. Micro-analysis and MS revealed that one molecule of H_2O had been eliminated during the reaction. H^1- and C^{13}-NMR spectra suggested the structure **13** *(Scheme 5)*. Other spectroscopic data were in agreement with this structure. Finally, the structure was confirmed by X-ray *(Fig. 2)*.

[6]) NMR and IR evidence suggests that the same conformation of the salt also exists in solution, but on deprotonation with base the U-shaped vinamidine, stabilized by an internal H-bond, is readily formed.

Scheme 5



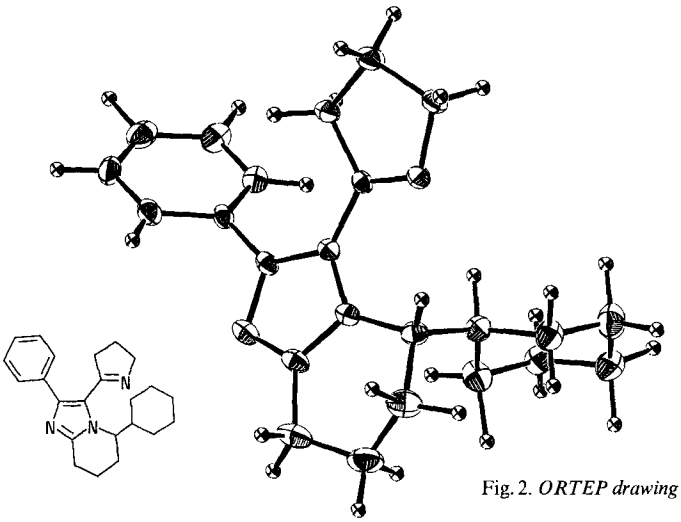
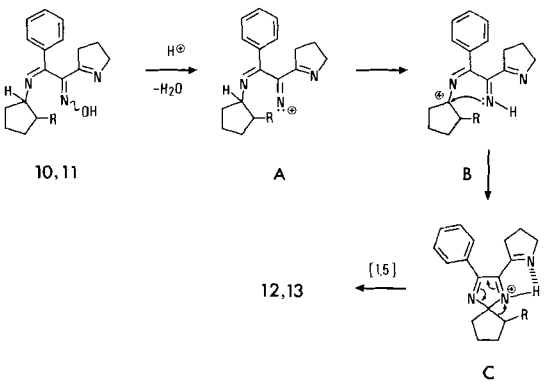


Fig. 2. *ORTEP drawing of* **13**

Single-crystal X-ray analysis reveals that the C=N bond of the pyrroline ring is only slightly turned against the plane of the imidazole ring with a torsion angle of 16° between the two rings. By contrast, a torsion angle of 50° was found between the imidazole and the phenyl rings. Again, as in **6**, steric reasons may be responsible for this distortion.

A possible mechanism for the reaction **11**→**13** is depicted in *Scheme 6*. After initial formation of the nitrenium cation **A** under the strongly acidic reaction conditions, a [1,5] H–shift to **B** followed by intramolecular ring closure between the imino-N-atom and the carbonium ion would lead to the spiro intermediate **C**. This intermediate could then rearrange *via* a [1,5] alkyl shift to the product. The observed regioselectivity of this

Scheme 6



reaction, with the newly formed tetrahydropyridine ring annellated *via* the imidazole N-atom adjacent to the pyrroline ring, cannot be explained by the influence of the additional cyclohexyl substituent in **11**, as the same selectivity is also observed when starting from **10**, in which no such substituent is present[7]). Probably the preferred direction of the [1,5] shift is best explained by the influence of the pyrroline ring. In the strongly acidic media, the pyrroline is protonated and renders the adjacent imino N-atom more electron-attracting.

To our knowledge, only one case of a somewhat similar rearrangement has been reported in the literature. *Veronese et al.* [6] found that 3-hydroxyiminopentane-2,4-dione, on heating with benzylamine in MeCN, gave 4-acetyl-5-methyl-2-phenylimidazole. It can be assumed that a similar reaction takes place, although no acid catalysis was needed in this case. We checked, therefore, whether the rearrangement of **11** to **13** could also be achieved without acid catalysis, but we found that prolonged boiling of a solution of **11** in MeCN did not lead to any conversion to **13**. The starting material was recovered unchanged. Only when **11** was treated under more drastic thermal conditions (heating of the melt to 220°), **13** could be isolated in low yield.

We thank Dr. *U. Renner* for support of this work, Dr. *T. Winkler* for interpretation of ^{1}H- and ^{13}C-NMR spectra, Mr. *S. Stutz* for skillful technical assistance and Dr. *J. Stanton* for valuable discussion.

Experimental Part

General. Starting materials were of *Fluka purum* or *Fluka puriss.* quality. Chromatographic separations were done on silica gel *60* (0.063–0.200; *Merck*, Darmstadt). Analytical samples were dried *in vacuo* and were free of significant impurities on TLC (*Merck*, Darmstadt, silica-gel plates with *F 254* indicator). Melting points were determined on a *Tottoli* melting point apparatus *(Büchi)* and are uncorrected. UV: *Cary 118;* IR: *Perkin-Elmer IR 157;* ^{1}H-NMR: *Bruker WM 250* or *Varian HA 100;* MS: *Finnigan MAT 212;* X-ray: see below.

1. Vinamidines *via* 2-(2-Pyrrolidinylidene)acetophenone (1) [4]. – 2-Pyrrolidinethione (101.2 g, 1.0 mol) was dissolved in 300 ml of $CHCl_3$. A soln. of 210 g (1.05 mol) of 2-bromoacetophenone in 400 ml of $CHCl_3$ was slowly added dropwise with ice cooling. A thick crystal slurry formed, which was stirred for 16 h at 22°. After cooling in an ice bath, the crystalline hydrobromide was filtered off and the filter residue washed with $CHCl_3$/hexane 1:3. To liberate the 2-[(1-pyrrolin-2-yl)thio]acetophenone, the hydrobromide was dissolved in about 1 l of ice water; the soln. was stirred with 100 ml of CH_2Cl_2 and sat. $NaHCO_3$ was added until the aq. phase permanently showed alkaline reaction. The org. phase was separated, and the aq. phase again extracted twice with CH_2Cl_2. Workup of the org. phase led to the crude 2-[(1-pyrrolin-2-yl)thio]acetophenone as a yellow oil. This was dried for 30 min at r.t. under high vacuum and then dissolved in a mixture of 1 l of toluene and 190 ml of $P(OEt)_3$. The mixture was heated under N_2 at 60° for 16 h. The dark soln. was concentrated and the remaining residue stirred at r.t. together with 350 ml of Et_2O. The resulting suspension was filtered, and the crystals were washed with Et_2O and subsequently recrystallized from acetone to give 123 g (66%) of **1**, m.p. 115–116°.

2-(2-Ethoxy-2-phenylethylidene)-1-pyrroline Tetrafluoroborate (**2**). A soln. of 62.7 g (0.33 mol) of $Et_3O^+BF_4^-$ in 120 ml of CH_2Cl_2[8]) was cooled in an ice bath. A second soln. of 56.2 g (0.3 mol) of **1** in 150 ml CH_2Cl_2[8]) was added dropwise during 0.5 h. After stirring for 3 h at 0° half of the solvent was distilled off on the rotovapor. Addition of 400 ml of AcOEt led to the crystallization of the product, which was filtered off and dried at 60° *in vacuo*. The crude fluoroborate **2** (73.2 g 65%; m.p. 122–123°) was directly used in the next step.

Preparation of Vinamidines from **2**. *General procedure:* Compound **2** was dissolved in an excess of the corresponding amine and the soln. heated under N_2 to 100° for 2 to 10 h. In the case of **3**, **2** was dissolved in a sat.

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[7]) In preliminary experiments with derivatives lacking a cyclic substituent on the imino-N-atom (*e.g.* isopropyl or isobutylimino) the same type of rearrangement was not observed. Instead, products stemming from a classical *Beckmann* rearrangement of the second type (*N*-substituted iminocyanides or their hydrolysis products, benzoylamides) could be identified.

[8]) CH_2Cl_2 was filtered through Alox (*Woelm* activity I) before use.

CH_3NH_2/MeOH soln. and the mixture kept at 22° overnight. The reactions were checked by TLC, and when completed the excess of amine was removed *in vacuo*. The residue was dissolved in CH_2Cl_2, extracted with 1N NaOH and 1N KOH. After evaporation, the remaining oil was concentrated several times with toluene in order to remove residual amine. Vinamidine salts were then prepared by dissolving the residue in i-PrOH and adding an equivalent amount of the corresponding acid dissolved in hot i-PrOH. The salts were recrystallized from EtOH or i-PrOH.

2-[2-(Methylimino)-2-phenylethylidene]pyrrolidine Methanesulfonate (**3**). Yield 85%; m.p. 146–147°. R_f ($CHCl_3$/MeOH/conc. NH_3 5:3:1) 0.73. IR (CH_2Cl_2, free base): 3260*w*, 1632*s*, 1610*m*, 1570*s*, 1495*m*, 1380*m*, 1340*m*, 1308*m*, 1138*m*. ^{1}H-NMR (250 MHz, (D_6)DMSO, free base): 1.72 (*m*, 2H); 2.50 (*t*, J = 8, 2H); 2.68, 2.70 (2*s*, 1:1, total 3H); 3.81 (*t*, J = 7.5, 2H); 4.68 (*s*, 1H); 7.34–7.51 (*m*, 5H); 9.77 (br. *s*, 1H). MS (free base): 200 (28, M^+), 199 (100), 171 (9), 157 (4). Anal. calc. for $C_{14}H_{20}N_2O_3S$ (296.39): C 56.74, H 6.80, N 9.45, S 10.82; found: C 56.70, H 6.90, N 9.62, S 10.85.

2-[2-(Cyclopentylimino)-2-phenylethylidene]pyrrolidine Fumarate (**4**). Yield 56%; m.p. 168–169°. R_f ($CHCl_3$/MeOH/conc. NH_3 40:10:1) 0.29. IR (CH_2Cl_2, free base): 3250–3100*w*, 1630*s*, 1610*m*, 1570*s*, 1495*m*, 1365*m*. ^{1}H-NMR (250 MHz, (D_6)DMSO, free base): 1.28–1.52 (*m*, 4H); 1.52–1.84 (*m*, 6H); 2.50 (*t*, J = 8, 2H); 3.58 (*m*, 1H); 3.81 (*t*, J = 8, 2H); 4.66 (*s*, 1H); 7.33–7.50 (*m*, 5H); 9.92 (*d*, J = 8, 1H). MS (free base): 254 (34, M^+), 253 (100), 225 (8), 185 (16), 170 (37). Anal. calc. for $C_{21}H_{26}N_2O_4$ (370.45): C 68.09, H 7.07, N 7.56; found: C 68.00, H 7.06, N 7.61.

2-[2-(Cyclohexylimino)-2-phenylethylidene]pyrrolidine Methanesulfonate (**5**). Yield 69%, m.p. 186–187°. R_f ($CHCl_3$/MeOH/conc. NH_3 40:10:1) 0.49. UV (MeOH): λ_{max} 334 (4.31). IR (CH_2Cl_2, free base): 1630*s*, 1612*m*, 1570*s*, 1490*m*, 1360*m*. ^{1}H-NMR (250 MHz, $CDCl_3$, free base): 1.08–1.40 (*m*, 6H); 1.62–1.87 (*m*, 6H); 2.56 (*t*, J = 8, 2H); 3.14 (*m*, 1H); 3.94 (*t*, J = 8, 2H); 4.68 (*s*, 1H); 7.30–7.42 (*m*, 5H); 9.84 (br., 1H). MS (free base): 268 (34, M^+), 267 (100), 225 (14), 211 (9), 185 (28), 170 (24). Anal. calc. for $C_{19}H_{28}N_2O_3S$ (364.50): C 62.61, H 7.74, N 7.68; found: C 62.6, H 7.7, N 7.8.

2-{2-[(cis-2-Cyclohexylcyclopentyl)imino]-2-phenylethylidene}pyrrolidine Methanesulfonate (**6**). Yield 65%; m.p. 181–182°. R_f ($CHCl_3$/MeoH/conc. NH_3 40:10:1) 0.59. UV ($CHCl_3$, free base): λ_{max} 327 (4.20). IR (CH_2Cl_2, free base): 1620*s*, 1600*m*, 1565*s*, 1480*m*. ^{1}H-NMR (100 MHz, $CDCl_3$): 0.66–1.92 (*m*, 22H); 2.32 (*s*, CH_3SO_3); 2.92–3.14 (*m*, 2H); 3.52–3.72 (*m*, 1H); 4.47 (*d*, J = 7, NH); 5.30, 5.62 (2*s*, total 1H, (*E*)/(*Z*)-isomers); 6.00–6.38 (*m*, 5H); 10.32 (br., 1H). ^{1}H-NMR (250 MHz, (D_6)DMSO, free base): 0.68–0.96 (*m*, 2H); 1.01–1.86 (*m*, 18H); 2.50 (*t*, J = 8, 2H); 3.61 (*m*, 1H); 3.83 (*t*, J = 7.5, 2H); 4.72 (*s*, 1H); 7.30–7.48 (*m*, 5H); 9.88 (*d*, 1H). MS (free base): 336 (94, M^+), 335 (100), 253 (64), 185 (89), 170 (72). Anal. calc. for $C_{24}H_{36}N_2O_3S$ (432.62): C 66.63, H 8.39, N 6.48, S 7.41; found: C 66.65, H 8.35, N 6.52, S 7.49.

Crystal Structure Analysis of **6**: Crystals were monoclinic, $P2_1/n$, a = 12.694 Å, b = 11.742 Å, c = 15.945 Å, β = 90.62°, Z = 4. On a *PICKER FACS-I* diffractometer 3724 independent reflections were measured, of which 3601 were considered observed ($I > 20(I)$). The structure was solved by direct methods using the MULTAN 78 program system [7]. All the H-atoms could be located in difference maps and included in the refinement with isotropic temperature factors. For all the other atoms anisotropic temperature factors were introduced. The refinement converged to a final value of R = 0.057.

2. Vinamidines Starting from *Schiff* Bases. – *Preparation of* Schiff *Bases.* N-*(α-Methylbenzylidene)-methylamine* (**7**)[9]). In a 2.5-l 3-necked flask equipped with a mechanical stirrer, containing 300 g of molecular sieves (3 Å, *Perlform, Merck*) were dissolved 240 g (2.0 mol) of acetophenone and 1.7 g of TsOH in 1.5 l of toluene. Methylamine gas (77.5 g; 2.5 mol) was then introduced through an immersed tube over a period of 2 h, during which the mixture was stirred and slightly cooled in an ice bath. After heating for 2 h to 55°, the slurry of the molecular sieves was filtered off through *Celite*, and the filtrate was concentrated under vacuum. By titration of an aliquot of this residue with 0.1N HCl, a content of 84.4% *Schiff* base was calculated. The crude base was then dissolved in 400 ml of CH_2Cl_2 and a soln. of 162.6 g (1.7 mol) of MsOH in 100 ml of CH_2Cl_2 was added under cooling. A crystal slurry formed. After addition of 1 l of AcOEt and further stirring for 0.5 h, the crystals were filtered off and dried under high vacuum at r.t. Yield 370 g (81%); m.p. 117–118°. The crude salt was used in the next step without further purification.

N-*(α-Methylbenzylidene)cyclohexylamine* (**8**)[9]). Methylphenylketone (12 g; 0.1 mol) and cyclohexylamine (12 g; 0,12 mol) were dissolved together with 0.1 g of TsOH in 200 ml of toluene. The soln. was refluxed for 15 h with the reaction water being removed by means of a water separator. After removal of the solvent the residue was

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[9]) Alternative procedures for the preparation of 7 and **8** are described in [8] and [9], respectively.

distilled under high vacuum: 12.2 g (61%) of **8** was obtained in the main fraction (b.p. 99–101°/0.001 Torr) and was directly used in the next step.

N-*(α-Methylbenzylidene)-[*cis-*(2-cyclohexylcyclopentyl)]amine* (**9**) was obtained analogously to **8**. Yield 68%; b.p. 140–150°/0.1 Torr. IR (CH_2Cl_2): 1630*m*, 1445*m*, 1370*w*, 1330*w*. ^{1}H-NMR (250 MHz, (D_6)DMSO): 0.85–2.00 (*m*, 18H); 2.20 (*s*, 3H); 4.09 (*m*, 1H); 7.39 (*m*, 3H); 7.79 (*m*, 2H). MS: 269 (6, M^+), 268 (5), 254 (44), 186 (18), 146 (23).

Vinamidines by Condensation of Schiff *Bases with 2-Ethoxy-1-pyrroline* [10]. – *General Procedure.* Either *Schiff*-basemethanesulfonate or free *Schiff* base (1 mol) with an equivalent amount of MsOH was heated under stirring together with 2 mol of 2-ethoxy-1-pyrroline at 100° for 2 h. Evolving EtOH was collected *via* an attached *Liebig* condenser. Excess of 2-ethoxy-1-pyrroline was afterwards distilled off at 70° under vacuum. The dark mixture was diluted with AcOEt and then cooled in an ice bath. Filtration of the precipitate and recrystallization from i-PrOH/Et_2O gave the corresponding vinamidine methanesulfonates. Yields **3**: 49%; **5**: 60%; **6**: 28% (for spectroscopic characterization of the products, see above).

Conversion of **3** *to* **6** *by Amine Exchange.* A soln. of 37.7 g (0.19 mol) of **3** (free base; obtained by extraction with toluene of an alkaline solution of the methane sulfonate), 32.5 g (0.20 mol) of (*cis*-2-cyclohexylcyclopentyl)amine [5], and 4.2 g (0.014 mol) of MsOH in 700 ml of toluene was heated in an oil bath. The outside temp. (125–135°) was controlled in such a way, that toluene (together with the generated $MeNH_2$) distilled off dropwise. From time to time, additional toluene was added. After 42 h, the orange mixture was cooled, extracted with 2N NaOH, evaporated, and the resulting crude base recrystallized from i-PrOH: 56.3 g (83%) **6** m.p. 119–120°. The methanesulfonate **6** was obtained by dissolving the base in AcOEt, adding an equivalent amount of MsOH and recrystallizing the product from CH_2Cl_2/AcOEt (for spectroscopic characterization of **6**, see above).

3. Nitrosation of 4 and 6. – *General Procedure.* Vinamidine methanesulfonate (30 mmol) was dissolved under cooling in an ice bath in 200 ml of H_2O and 40 ml of 1N H_2SO_4. A soln. of 2.5 g (36 mmol) of $NaNO_2$ in 50 ml of H_2O was added dropwise in 20 min. A voluminous precipitate formed. After further stirring for 10 min the suspension was neutralized with an excess of $NaHCO_3$ soln. and then extracted with AcOEt. The residue from the combined org. phases was recrystallized from AcOEt and acetone.

2-[2-(Cyclopentylimino)-1-(hydroxyimino)-2-phenyl]ethyl-1-pyrroline (**10**). Yield 66%; m.p. 201–202°. R_f (AcOEt) 0.58. IR (Nujol): 1630*m*, 1605*m*. ^{1}H-NMR (100 MHz, (D_6)DMSO): 1.47–2.05 (*m*, 10H); 2.88 (*t*, J = 8, 2H); 3.59 (*m*, 1H); 3.84 (*t*, J = 7.5, 2H); 7.22–7.41 (*m*, 3H); 7.51–7.70 (*m*, 2H); 12.70 (br., 1H). MS: 283 (6, M^+), 266 (62), 104 (100). Anal. calc. for $C_{17}H_{21}N_3O$ (283.38): C 72.06, H 7.47, N 14.83; found: C 71.77, H 7.46, N 14.86.

*2-[2-(*cis*-2-Cyclohexylcyclopentyl)imino-1-(hydroxyimino)-2-phenyl]-1-pyrroline* (**11**). Yield 67%; m.p. 183–186°. R_f (AcOEt) 0.82. IR (Nujol): 1645*m*, 1620*s*, 1455*s*, 1360*w*. ^{1}H-NMR (250 MHz, (D_6)DMSO): 0.57–1.94 (*m*, 20H); 2.70–2.99 (*m*, 2H); 3.56–3.67 (*m*, 1H); 3.67–4.06 (*m*, 2H); 7.30–7.44 (*m*, 3H); 7.48–7.60 (*m*, 2H); 12.06, 12.10 (2*s*, *ca.* 1:1, total, 1OH). MS: 365 (3, M^+), 348 (100), 304 (5). Anal. calc. for $C_{23}H_{31}N_3O$ (365.52): C 75.58, H 8.55, N 11.50; found: C 75.28, H 8.60, N 11.33.

4. Acid-Catalyzed Rearrangement of 10 and 11[10]. – *General Procedure.* The diimino-oxime (60 mmol) was dissolved in 50 ml of H_2SO_4 80% *w/w*. This soln. was stirred under N_2 at 70° for 6 h. After cooling, the dark mixture was poured under stirring into a mixture of crushed ice and CH_2Cl_2. The mixture was neutralized by addition of a sat. $NaHCO_3$ soln. Workup of the org. phase led to the crude product, which was chromatographed on a silica-gel column with AcOEt as the elucnt, and afterwards recrystallized from hexane.

2-Phenyl-3-(1-pyrrolin-2-yl)-5,6,7,8-tetrahydroimidazo[1,2-a]pyridine (**12**). Yield 64%; m.p. 100–101°. R_f (AcOEt) 0.16. IR (Nujol): 1630*m*, 1615*m*, 1420*m*, 1398*m*. ^{1}H-NMR (250 MHz, (D_6)DMSO): 1.67–1.80 (*q*, J = 7.5, 2H); 1.80–2.00 (*m*, 4H); 2.39 (*t*, J = 7, 2H); 2.82 (*t*, J = 6, 2H); 3.86 (*t*, J = 7.5, 2H); 4.13 (*t*, J = 6, 2H); 7.28–7.45 (*m*, 5H). ^{13}C-NMR ($CDCl_3$): 20.3 (*t*); 22.7 (*t*); 23.2 (*t*); 25.1 (*t*); 37.8 (*t*); 46.2 (*t*), 61.1 (*t*), 122.9 (*s*); 127.6 (*d*); 127.9 (*d*); 129.4 (*d*); 136.0 (*s*); 144.4 (*s*); 146.9 (*s*); 166.3 (*s*). MS: 265 (19, M^+), 264 (100). Anal. calc. for $C_{17}H_{19}N_3$ (265.36): C 76.95, H 7.22, N 15.84; found: C 76.81, H 7.30, N 16.14.

2-Phenyl-3-(1-pyrrolin-2-yl)-5-cyclohexyl-5,6,7,8-tetrahydroimidazo[1,2-a]pyridine (**13**). Yield 48%; m.p. 83–94°. R_f (AcOEt) 0.15. UV (MeOH): λ_{max} 278 (4.02). IR (CH_2Cl_2): 1620*m*, 1610*m*, 1510*w*, 1480*w*, 1440*m*, 1420*m*, 1390*w*. ^{1}H-NMR (250 MHz, (D_6)DMSO): 0.92–1.18 (*m*, 4H); 1.20–1.38 (*m*, 2H); 1.48–2.04 (*m*, 11H); 2.13–2.30

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[10]) Preliminary experiments for thermal rearrangement of **11** were performed as follows: *a*) 200 mg of **11** was dissolved in 5 ml of MeCN. The soln. was heated under reflux for 24 h. No reaction occurred. Starting material was recovered quantitatively; *b*) 200 mg of **11** was heated without solvent for 1 h to 220°. The resulting dark brown resin was then twice flash-chromatographed: 19 mg of **13** was isolated and identified by TLC and NMR.

(*q*, *J* = 8.5, 1H); 2.52–2.68 (*m*, 1H); 2.64–2.84 (*m*, 2H); 3.68–4.04 (*m*, 1H); 3.93–4.10 (*m*, 1H); 4.72–4.80 (*m*, 1H); 7.27–7.43 (*m*, 5H). ^{13}C-NMR ($CDCl_3$): 17.1 (*t*); 22.8 (*t*); 24.0 (*t*); 24.2 (*t*); 26.4 (*t*); 26.6 (*t*); 26.7 (*t*); 28.2 (*t*); 29.8 (*t*); 38.1 (*t*); 42.8 (*d*); 56.4 (*d*); 61.2 (*t*); 122.8 (*s*); 127.4 (*d*); 128.0 (*d*); 128.9 (*d*); 128.9 (*d*); 135.8 (*s*); 143.4 (*s*); 147.6 (*s*); 167.6 (*s*). MS: 347 (33, M^+), 346 (100), 264 (19), 225 (30). Anal. calc. for $C_{23}H_{29}N_3$ (347.51): C 79.49, H 8.41, N 12.09; found: C 79.71, H 8.46, N 12.18.

Crystal Structure Analysis of **13**. Crystals were monoclinic, $P2_1/n$, a = 10.316 Å, b = 8.967 Å. c = 21.262 Å, β = 91.11°, Z = 4. On a *Philips PW 1100* diffractometer 3881 independent reflections were measured, of which 3281 were considered observed ($I > 2(I)$). The structure was solved by direct methods using the MULTAN 78 program system [7]. All the H-atoms could be located in difference maps and included in the refinement with isotropic temperature factors. For all the other atoms anisotropic temperature factors were introduced. The refinement converged to a final value of R = 0.064.

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