Model Studies of the Reduction of 3-Phenyl-6*H*-1,2-oxazines, Chemo- and Stereoselectivity: Synthesis of Amino Alcohols, Amino Acids, and Related Compounds

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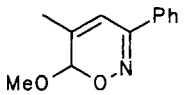
Received March 3, 1992

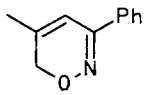
Key Words: 1,2-Oxazines / Hydrogenation, catalytic / Amino alcohols / γ-Amino acids / Pyrroles / γ-Lactams

While palladium-catalyzed hydrogenation of 3-phenyl-6*H*-1,2-oxazine **1** produces primary amine **5** in a nitrogen-transposition reaction, the reductions of the related 1,2-oxazines **2**, **10**, and the 1,2-oxazin-6-one **3** afford the expected amino alcohols **4**, **11**, and the γ-amino acid **6**, respectively, with low diastereoselectivites. In the presence of acetic acid **3** is reductively converted into γ-keto carboxylic acid **9** and **1** into the γ-lactam derivative **12** probably by a ring contraction to a nitrone intermediate. Raney nickel as the catalyst is able to transform 1,2-oxazine **7** bearing an exo-methylene unit into 3,4-dihydro-2*H*-pyrrole **13**. The reaction of 6*H*-1,2-oxazine **1** with aluminium amalgam produces pyrrole **14** in moderate yield. Treatment of **1** with sodium in 2-propanol brings about its transformation into pyrrolidine derivative **15** together with pyrrole **14** and amino alcohol **4** as minor products. The chemoselectivity and stereoselectivity of these reductions are discussed including mechanistic proposals for the multistep processes involved.

Reductive ring cleavage of the N–O bond in isoxazole derivatives belongs to the well established methods for stereoselective synthesis of 1,3-difunctional compounds such as β-hydroxy ketones, β-hydroxy oximes, or β-amino alcohols[2–6]. In contrast, the corresponding homologous heterocycles – 1,2-oxazines – have found only rather limited applications although they should open routes to useful 1,4-difunctional building blocks. Due to Kresze's efforts[7] the reductive cleavage of 3,6-dihydro-2*H*-1,2-oxazines has been studied in some detail[8], but only a few reports deal with reductive transformations of 5,6-dihydro-4*H*-1,2-oxazines[8–11], and to the best of our knowledge only one example for reductive cleavage of a 6*H*-1,2-oxazine has been published[12]. In this paper we describe model experiments dealing with the reduction of easily available 3-phenyl-6*H*-1,2-oxazine **1**[13,14], compounds **2**[15] and **3**, which can be prepared from **1**, and of other related 1,2-oxazines under various conditions.



1



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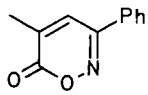
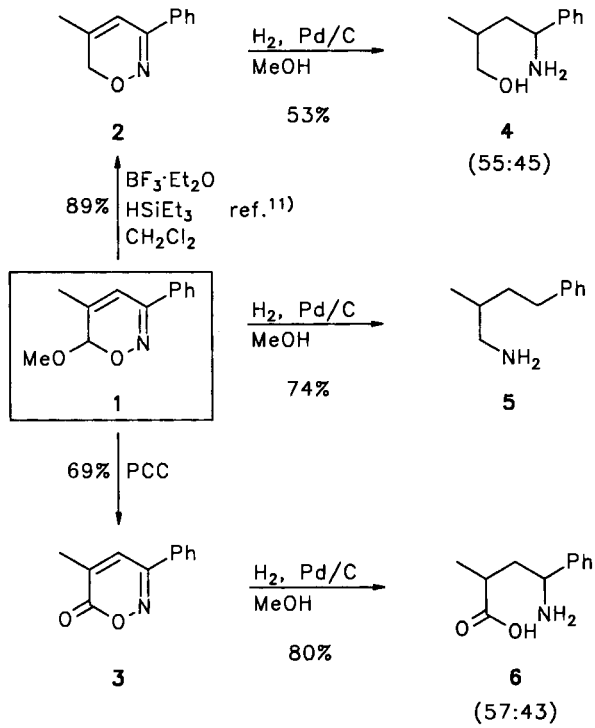


3

Results

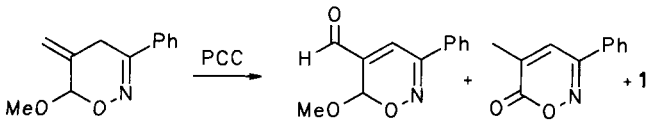
When 6*H*-1,2-oxazine **1** is treated with hydrogen for 24 h in the presence of a palladium catalyst the primary amine **5** is isolated in good yield. A similar nitrogen transposition has been found for the corresponding 5,6-dihydro-6-(trimethylsiloxy)-4*H*-1,2-oxazine[11], and therefore a reduction of the C-4–C-5 double bond in **1** is probably the first step of the transformation **1** → **5** (for the detailed mechanism see refs.[11,16] and Scheme 1).



When the acetal moiety at C-6 of **1** is removed either by reduction giving 1,2-oxazine **2**[15] or by oxidation providing 6*H*-1,2-oxazin-6-one **3**, catalytic hydrogenations of these compounds take the expected course. From **2** amino alcohol **4** is obtained and 1,2-oxazinone **3** is converted into the γ-aminobutanoic acid (GABA) derivative **6**. In contrast to transformation **1** → **5**, the benzylic C–N bond is not cleaved in these examples. In both reactions the stereoselectivity is disappointingly low providing mixtures of diastereomers close to 1:1. These results are taken as evidence that

after reduction of the CC double bond, the N–O bond is reductively cleaved first, and then the resulting imine function is converted into the amine group. The opposite sequence should cause much higher diastereoselectivities due to the cyclic fixation during reduction of the C=N bond[17].

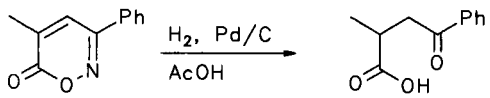
6*H*-1,2-Oxazin-6-one **3**[18] can smoothly be prepared by oxidation of **1** with pyridinium chlorochromate (PCC)[19]. On the other hand, when 1,2-oxazine **7**, which is formed as an intermediate during the synthesis of **1**[13], is treated with this oxidizing agent, a mixture of the aldehyde **8** and 6*H*-1,2-oxazin-6-one **3** together with 1,2-oxazine **1** are isolated. The aldehyde **8** probably arises by oxidation of **7** to give primarily a 5-hydroxymethyl-substituted 6*H*-1,2-oxazine. 1,2-Oxazin-6-one **3** should be formed via compound **1** which is generated by acid-catalyzed rearrangement **7** → **1**[13].



7 **8** **3**

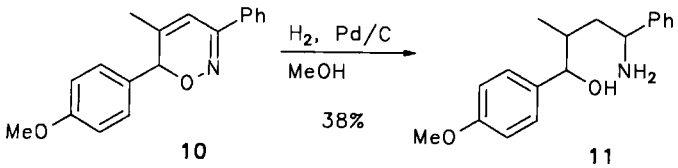
23% 19% 12%

If the catalytic reduction of 6*H*-1,2-oxazin-6-one **3** is performed in acetic acid instead of methanol as the solvent, the γ-keto carboxylic acid **9** is obtained. Apparently, the intermediate imine is trapped by the solvent to give an acylal-type intermediate which is not reducible and provides **9** after aqueous workup. This experiment therefore supports our hypothesis concerning the sequence of reduction steps in the transformation **3** → **6**.



3 59% **9**

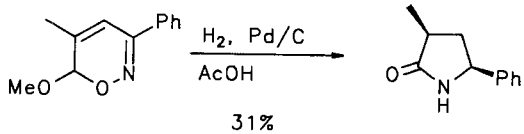
The reduction of 6-arylated 1,2-oxazine **10**[15] proceeds under standard conditions as expected and gives γ-amino alcohol **11**. Although no assignment for the four diastereomers is possible, it is evident that in this example the primary reduction of the CC double bond also occurs with very modest stereoselectivity (70:30 at best).



10 38% **11**

(50:20:15:15)

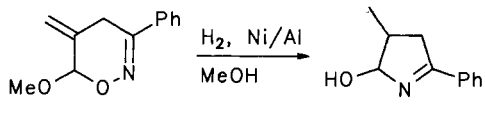
The reduction of 6*H*-1,2-oxazine **1** in acetic acid takes an entirely different course and provides γ-lactam **12** in modest yield but diastereomerically almost pure. Similar reactions of 6*H*-1,2-oxazines have been observed in the presence of Lewis acids and weak nucleophiles[20]. The crucial step in these transformations may be an acid-catalyzed ring contraction producing a nitrone[21] which is reduced in this example to form an *N*-hydroxypyrrolidine intermediate (see Scheme 1). Acid-induced 1,2-elimination of water gives a 4,5-dihydro-2-methoxy-3*H*-pyrrole (intramolecular redox process) and aqueous workup affords the isolated γ-lactam **12**[22]. The high stereoselectivity of this transformation is surprising; the ^{1}H-NMR data and mechanistic plausibility make the *cis*-configuration for the major diastereomer very likely.



1 31% **12**

(*cis* : *trans* = 93:7)

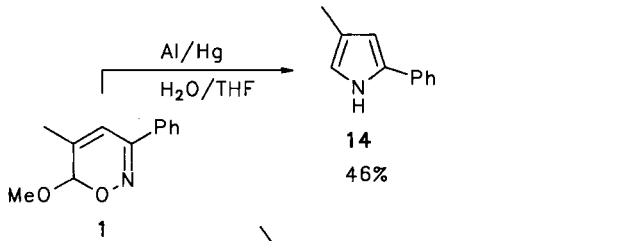
6*H*-1,2-Oxazine **1** cannot be reduced with Raney nickel as the catalyst at room temperature[23], but its isomer **7** is transformed into 3,4-dihydro-2*H*-pyrrole derivative **13** in good yield. The exo-methylene unit of **7** is apparently more reactive than the trisubstituted conjugated CC double bond of **1**. In **7** Raney nickel causes double bond reduction and cleavage of the N–O bond; the intermediate γ-imino aldehyde cyclizes to the tautomeric form **13**. This compound is surprisingly stable towards hydrolysis and elimination. Examples for the synthesis of this type of heterocycles, which are intermediates in the Paal-Knorr synthesis of pyrroles, have been reported only recently[24].



7 64% **13**

(85:15)

Two reduction methods involving electron transfer have also been examined[25]. The reaction of 6*H*-1,2-oxazine **1** with aluminium amalgam[10] produces pyrrole derivative **14**[26]. Thus, an additional possibility to transform 1,2-oxazine derivatives into pyrroles under mild conditions has been

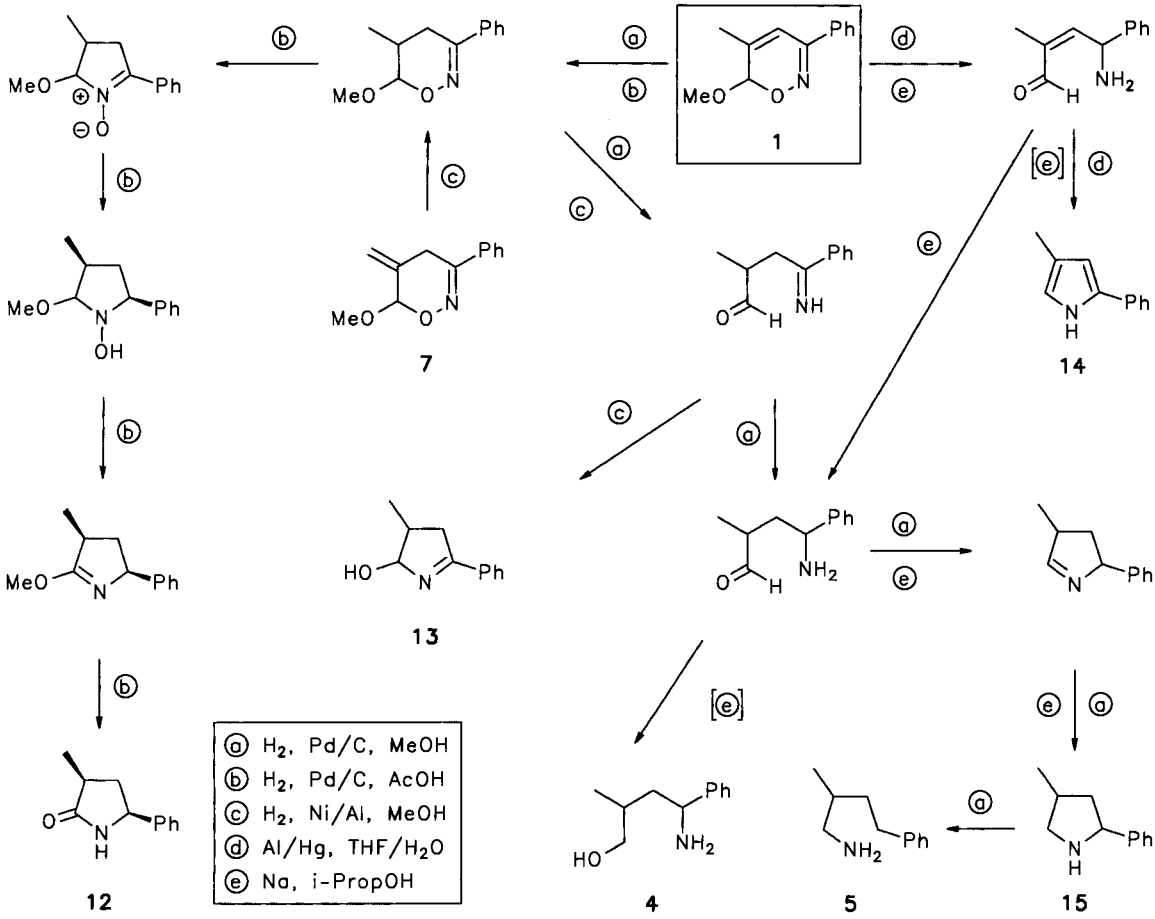


14 46%

1

15 47% (1:1) **4** 7% (1:1) 2%

Scheme 1



found[27]. Probably, the reducing agent cleaves the N–O bond and reduces the imino function to give an unsaturated γ-amino aldehyde which cyclizes to pyrrole **14**. Its formation via **13** seems to be less likely.

The reduction of 1,2-oxazine **1** with sodium in 2-propanol[28] provides pyrrolidine derivative **15** as the major product (*cis*:*trans* ≈ 1:1). Minor components are amino alcohol **4** and pyrrole **14**. Pyrrolidine **15** is probably not formed via pyrrole **14**, since these heterocycles are relatively inert towards sodium as reducing agent[29]. Therefore, a pathway with the γ-amino aldehyde as intermediate seems to be more likely, which mainly provides **15** and as a side product amino alcohol **4** (Scheme 1).

Discussion

The results presented here demonstrate that 6*H*-1,2-oxazine derivatives can be reduced to give rather different products, depending on the reaction conditions and the functionality of the 6*H*-1,2-oxazine. In most examples the diastereoselectivities are low since the stereogenic centers are created by reductions of acyclic intermediates. An exception is γ-lactam **12** which is isolated with high diastereomeric purity. For compound **1** Scheme 1 summarizes our results and suggests mechanistic pathways for these multistep reactions. The sequences as depicted for reduction conditions a-e are probable according to literature reports, although singular steps may be interchangeable.

Financial support of this work by the *Deutsche Forschungsgemeinschaft*, the *Fonds der Chemischen Industrie*, and the *Vereinigung von Freunden der Technischen Hochschule zu Darmstadt* is thankfully appreciated.

Experimental

For general information see ref.[15] The preparation of the 1,2-oxazines required as starting materials is described in refs.[13,15]

5-Methyl-3-phenyl-6H-1,2-oxazin-6-one (**3**): A solution of 1,2-oxazine **1** (0.203 g, 1.00 mmol) in dichloromethane (20 ml) was heated to reflux with pyridinium chlorochromate (0.216 g, 1.00 mmol) for 60 h. The resulting mixture was filtrated through a pad of Al_2O_3 (neutral, activity III, *tert*-butyl methyl ether), the solvents were evaporated, and the crude product was recrystallized (diethyl ether/dichloromethane, 2:1) to provide 0.129 g (69%) of **3** as colorless crystals, m.p. 133–134°C (ref.[18] 135–136°C). – ^{1}H NMR ($CDCl_3$): δ = 7.85–7.40 (m, 5H, Ph), 7.27 (q, *J* = 1.5 Hz, 1H, 4-H), 2.30 (d, *J* = 1.5 Hz, 3H, Me). – IR (KBr): $\tilde{\nu}$ = 3090–3010 cm^{-1} (=C–H), 2980–2800 (C–H), 1730 (C=O), 1640 (C=C), 1540 (C=N).

$C_{11}H_9NO_2$ (187.2) Calcd. C 70.58 H 4.85 N 7.48
Found C 70.52 H 4.72 N 7.48

Oxidation of 1,2-Oxazine **7** *with Pyridinium Chlorochromate:* A solution of **7** (0.609 g, 3.00 mmol) and pyridinium chlorochromate

(0.648 g, 3.00 mmol) in dichloromethane (60 ml) was stirred for 55 h at room temp. The solvent was evaporated and the residue filtrated through a pad of Al_2O_3 (neutral, activity III, dichloromethane). The crude product mixture was separated by radial chromatography (pentane/ethyl acetate, 9:1) to give three fractions.

1st fraction: 0.075 g (12%) of 1,2-oxazine **1**.

2nd fraction: 0.167 g (26%) of impure aldehyde **8**.

3rd fraction: 0.105 g (19%) of 1,2-oxazinone **3**.

Crude aldehyde **8** was recrystallized (*tert*-butyl methyl ether) to afford 0.148 g (23%) of pure **8** as colorless needles, m.p. 97–98°C. – ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 9.86 (s, 1H, CHO), 7.8–7.7, 7.5–7.3 (2 m, 2H, 3H, Ph), 7.19 (s, 1H, 4-H), 5.94 (s, 1H, 6-H), 3.58 (s, 3H, OMe). – ^{13}C NMR ($CDCl_3$): δ = 189.9 (d, CHO), 154.3 (s, C-3), 133.6, 132.7, 130.6, 129.0, 126.0, 125.4 (2 s, 4 d, C-5, Ph, C-4), 91.8 (d, C-6), 56.5 (q, OMe). – IR (CCl_4): $\tilde{\nu}$ = 3120–2990 cm^{-1} (C–H, =C–H), 2930, 2830 (CHO), 1690 (C=O), 1640 (C=C, weak), 1575 (C=N, weak).

$C_{12}H_{11}NO_3$ (217.2) Calcd. C 66.35 H 5.10 N 6.45
Found C 66.51 H 5.11 N 6.28

General Procedure for the Catalytic Hydrogenation of 1,2-Oxazines: Dry methanol (5 ml/1 mmol of 1,2-oxazine) and Pd (10%)/C (0.100 g/1 mmol of 1,2-oxazine) in a 25-ml flask were saturated with hydrogen for 1 h at room temp. Then, the corresponding 1,2-oxazine and – if required – an additive were added, and the mixture was stirred under hydrogen at normal pressure for 24 h at room temp. The suspension was filtered through a sintered glass plug which contained a pad of Celite eluting with diethyl ether. The filtrate was concentrated in vacuo and the crude product purified by column chromatography on Al_2O_3 (neutral, activity III) or by kugelrohr distillation. For the individual experiments see Table 1.

Table 1. Catalytic hydrogenations of 1,2-oxazines **1**, **2**, **3**, and **10**

1,2-Oxazine	g (mmol)	Additive	Product	Yield g (%)	Ratio of Diastereomers
1	0.406 (2.00)	-	**5**	0.240 (74)	-
2	0.346 (2.00)	-	**4**	0.188 (53)	55:45
3	0.220 (1.18)	-	**6**	0.182 (80)	57:43
3	0.748 (4.00)	a)	**9**	0.450 (59)	-
10	0.327 (1.17)	-	**11**	0.126 (38)	50:20:15:15
1	0.609 (3.00)	b)	**12**	0.161 (31)	95:5

a) Reaction performed in 20 ml of acetic acid. – b) Reaction performed in 15 ml of acetic acid.

Analytical and spectroscopic data of the reduction products **5**, **4**, **6**, **9**, **11**, **12**:

2-Methyl-4-phenylbutylamine (**5**): B.p. 105°C/0.2 Torr, colorless oil (ref.[11], b.p. 150°C/0.02 Torr). – ^{1}H- and ^{13}C-NMR data are identical with those reported earlier[11].

4-Amino-2-methyl-4-phenyl-1-butanol (**4**): B.p. 140–150°C/0.04 Torr, pale yellow oil. – ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.38–7.18 (m, 5H, Ph), 4.05 (dd, *J* = 6.5/7 Hz, 0.57H, 4-H), 3.87 (dd, *J* = 4/9 Hz, 0.43H, 4-H), 3.52, 3.47, 3.41, 3.36 (4 dd, all signals J_{AB} = 11, *J* = 4/4.5/6/8 Hz, 2H, 1-H), 3.32–3.21 (m, 3H, NH_2, OH), 1.91–1.53 (m, 3H, 2-, 3-H), 0.93, 0.88 (2 d, both *J* = 6.5 Hz, 1.29H, 1.71H, Me). – ^{13}C NMR ($CDCl_3$): δ = 147.5*, 146.0, 128.7*, 128.6, 127.3*, 127.0, 125.8, 125.6* (2 s, 6 d, Ph), 68.4*, 67.8 (2 t, C-1), 56.4*, 53.1 (2 d, C-4), 45.9*, 44.1 (2 t, C-3), 36.1*, 32.9 (2 d, C-2), 18.4*, 17.1 (2 q, Me); *minor diastereomer. – IR (film): $\tilde{\nu}$ = 3580–3010 cm^{-1} (N–H, O–H, =C–H), 3000–2800 (C–H).

$C_{11}H_{17}NO$ (179.3) Calcd. C 73.70 H 9.56 N 7.81
Found C 73.43 H 9.64 N 8.02

4-Amino-2-methyl-4-phenylbutanoic Acid (**6**): M.p. 149–151°C (dec.), colorless crystals after recrystallization (water/ethanol, 2:1). – ^{1}H NMR (D_2O, 300 MHz): δ = 7.52–7.35 (m, 5H, Ph), 4.32 (dd, *J* = 6.5/8 Hz, 0.57H, 4-H), 4.24 (dd, *J* = 5/10.5 Hz, 0.43H, 4-H), 2.39–1.81 (m, 3H, 2-, 3-H), 1.11 (d, *J* = 6 Hz, 1.7H, Me), 1.07 (d, *J* = 7 Hz, 1.3H, Me). – ^{13}C NMR (D_2O), major isomer: δ = 187.4 (s, CO_2), 139.9, 131.5–130.1 (s, d, Ph), 56.7 (d, C-4), 42.1 (d, C-2), 41.2 (t, C-3), 19.8 (q, Me); minor isomer: δ = 187.2 (s, CO_2), 139.7, 131.5–130.1 (s, d, Ph), 57.1 (d, C-4), 42.5 (d, C-2), 41.5 (t, C-3), 21.1 (q, Me). – IR (KBr): $\tilde{\nu}$ = 3680–3150 cm^{-1} (O–H, N–H), 3130–2780 (=C–H, C–H), 1630 [C=O (broad)]. – MS (EI, 70 eV): *m/z* (%) = 194 (38) [M^+ + 1], 193 (33) [M^+], 192 (11), 177 (24), 176 (59), 175 (100) [$M^+ - H_2O$], 174 (12), 149 (12) [$M^+ - CO_2$], 106 (19), 78 (11).

A correct elemental analysis was obtained from the acetate of **6** prepared by reaction of **6** with acetic acid followed by evaporation of the solvent.

$C_{13}H_{19}NO_4$ (253.3) Calcd. C 61.64 H 7.56 N 5.53
Found C 61.78 H 7.17 N 5.71

2-Methyl-4-oxo-4-phenylbutanoic Acid (**9**): M.p. 130–133°C, colorless crystals after recrystallization (chloroform). – ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.96, 7.80–7.31 (m_c, m, 2H, 4H, Ph, CO_2H), AB of ABX system (δ_A = 3.47, δ_B = 3.04, J_{BX} = 5, J_{AX} = 7, J_{AB} = 18 Hz, 2H, 3-H), 3.13 (m_c, 1H, 2-H), 1.31 (d, *J* = 8 Hz, 3H, Me). – ^{13}C NMR ($CDCl_3$): δ = 198.0 (s, C-4), 181.5 (s, C-1), 136.5, 133.3, 128.6, 128.1 (s, 3 d, Ph), 41.8 (t, C-3), 34.8 (d, C-2), 17.1 (q, Me). – IR (KBr): $\tilde{\nu}$ = 3600–2600 cm^{-1} (O–H, C–H), 1705, 1675 (C=O).

$C_{11}H_{12}O_3$ (192.2) Calcd. C 68.74 H 6.29
Found C 69.07 H 6.15

4-Amino-1-(4-methoxyphenyl)-2-methyl-4-phenyl-1-butanol (**11**): Colorless oil after radial chromatography (*tert*-butyl methyl ether/2-propanol, 9:1). – ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.44–7.18, 6.95–6.77 (2 m, 7H, 2H, Ph, C_6H_4), 4.59 (d, *J* = 5 Hz, 0.2H, 1-H), 4.56 (d, *J* = 4 Hz, 0.5H, 1-H), 4.41 (d, *J* = 6 Hz, 0.15H, 1-H), 4.25 (d, *J* = 8 Hz, 0.15H, 1-H), 4.44–4.29, 4.17–3.82 (2 m, 0.15H, 0.85H, 4-H), 3.78, 3.77, 3.76 (3 s, 1.5H, 0.9H, 0.6H, OMe), 2.85 (broad s, 3H, NH_2, OH), 2.40–1.20 (m, 3H, 2-, 3-H), 0.92, 0.87, 0.86, 0.67 (4 d, all *J* = 6.5 Hz, 1.5H, 0.6H, 0.45H, 0.45H, 2-Me). – ^{13}C NMR ($CDCl_3$): δ = 158.7, 158.4*, 147.5, 147.0, 146.5*, 146.2, 136.6, 136.5, 136.1*, 135.6 (10 s, *ipso*-C), 128.6–125.7 (d, Ph), 113.5, 113.4, 113.3* (3 d, C_6H_4), 79.2, 77.1, 76.8*, 76.2 (4 d, C-1), 63.1, 56.0, 55.3, 55.2, 54.3, 52.8 (2 d and 4 q, OMe, C-4), 45.2, 43.5*, 42.3, 41.6 (4 t, C-3), 40.4, 38.3*, 37.7 (3 d, C-2), 18.5, 17.1*, 15.7, 13.2 (4 q, 2-Me); * major isomer. – IR (CCl_4): $\tilde{\nu}$ = 3660–3100 cm^{-1} (O–H, N–H), 3025, 3010 (=C–H), 2990–2780 (C–H).

$C_{18}H_{23}NO_2$ (285.4) Calcd. C 75.57 H 8.12 N 4.91
Found C 75.32 H 7.94 N 4.89

3-Methyl-5-phenyl-2-pyrrolidinone (**12**): M.p. 118.5–122°C (*trans*:*cis* = 7:93), colorless crystals after recrystallization (*tert*-butyl methyl ether); ref.[22]: separated isomers without assignment: m.p. 113 and 127°C. – ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.46–7.25 (m, 5H, Ph), 6.34, 6.16 (2 broad s, 0.07H, 0.93H, NH), 4.73 (dd, *J* = 5.5/7 Hz, 0.07H, 5-H), 4.65 (dd, *J* = 6.5/9 Hz, 0.93H, 5-H), 2.78–2.50 (m, 2H, 4-H), 2.23 (m_c, 0.07H, 3-H), 1.60 (m_c, 0.93H, 3-H), 1.24 (d, *J* = 7 Hz, 3H, Me). – ^{13}C NMR ($CDCl_3$): δ = 180.7 (s, C-2), 142.3, 128.8, 128.6*, 127.8, 127.6*, 125.8, 125.5* (s, 6 d, Ph),

56.4, 55.6* (2 d, C-5), 40.9, 39.4* (2 t, C-4), 37.1, 34.8* (2 d, C-3), 15.9*, 15.8 (2 q, Me); * minor isomer. – IR (KBr): $\tilde{\nu}$ = 3200 cm^{-1} (N–H), 3100–3000 (=C–H), 3000–2880 (C–H), 1680 (C=O).

Reductions Employing Raney Nickel: Procedure and workup analogous to the general procedure; however, Raney nickel was employed instead of palladium on carbon.

3,4-Dihydro-2-hydroxy-3-methyl-5-phenyl-2H-pyrrole (**13**): 1,2-Oxazine **7** (0.609 g, 3.00 mmol) and Raney nickel (0.300 g) in 20 ml of methanol afforded after 24 h at room temp. 0.413 g of crude product which was dissolved in chloroform, and the solution was filtered through cotton. After evaporation of the solvent the residue (pale yellow solid, m.p. 95–105°C) was recrystallzed from *tert*-butyl methyl ether to provide 0.334 g (64%) of **13** as colorless crystals, m.p. 106–109.5°C. Ratio of diastereomers in the crude and the purified compound: 85:15. – ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.9–7.7, 7.6–7.4 (2 m, 2H, 3H, Ph), 6.5 (broad s, 1H, OH), 5.77 (broad d, *J* = 6 Hz, 0.15H, 2-H), 5.44 (broad d, *J* = 5.5 Hz, 0.85H, 2-H), 3.35 (ddd, *J* = 1/9/19 Hz, 0.85H, 4-H), 3.07 (ddd, *J* = 1/8/19 Hz, 0.15H, 4-H), 2.78 (ddd, *J* = 1/4/19 Hz, 0.15H, 4-H), 2.71–2.59 (m, 0.15H, 3-H), 2.52 (ddd, *J* = 1/7/19 Hz, 0.85H, 4-H), 2.35 (m_c, 0.85H, 3-H), 1.25 (d, *J* = 7 Hz, 2.55H, Me), 1.12 (d, *J* = 7 Hz, 0.45H, Me). – ^{13}C NMR ($CDCl_3$), major isomer: δ = 173.7 (s, C-5), 133.7, 131.2, 128.9, 128.0 (s, 3 d, Ph), 101.6 (d, C-2), 42.3 (t, C-4), 39.5 (d, C-3), 17.7 (q, Me); minor isomer: δ = 174.1 (s, C-5), 133.8, 130.3, 128.8, 127.5 (s, 3 d, Ph), 95.4 (d, C-2), 42.3 (t, C-4), 35.5 (d, C-3), 13.7 (q, Me). – IR (KBr): $\tilde{\nu}$ = 3180 cm^{-1} (O–H), 3100–3020 (=C–H), 2980–2700 (C–H), 1685 (C=N). – MS (EI, 70 eV): *m/z* (%) = 175 (35) [M^+], 174 (19) [M^+ – 1], 160 (15), 159 (23), 158 (9) [M^+ – OH], 157 (11), 156 (12), 144 (14), 133 (14), 132 (10), 131 (16), 130 (16), 118 (25), 117 (71) [$PhCNCH_2^+$], 115 (14), 106 (30), 105 (14), 104 (100) [$PhCNH^+$], 103 (8) [$PhCN^+$], 91 (31), 77 (47) [Ph^+], 72 (36) [M^+ – PhCN], 51 (24) [$C_4H_3^+$], 41 (21), 39 (17) [$C_3H_3^+$], 32 (26).

$C_{11}H_{13}NO$ (175.2) Calcd. C 75.40 H 7.48 N 7.99
Found C 75.52 H 7.55 N 7.98

4-Methyl-2-phenylpyrrole (**14**): Aluminium amalgam foil was prepared according to ref.[10] (for details see ref.[11]). To a solution of 1,2-oxazine **1** (0.812 g, 4.00 mmol) in 50 ml of tetrahydrofuran/water (10:1) were given at 0°C four pieces of foil (2 × 2 cm). After 3 h another four pieces, and after further 3 h again four pieces of foil were added. This procedure was repeated the two following days until **1** was consumed (TLC control). The reaction took 3 d at 0°C. Tetrahydrofuran (150 ml) was added and the mixture stirred for 15 min at room temp. Filtration through a sintered glass plug, which contained a pad of Celite, drying ($MgSO_4$), and evaporation in vacuo afforded the crude product. Two sublimations (80°C/0.5 Torr) gave 0.289 g (46%) of **14** as colorless crystals, m.p. 146–148°C (ref.[26] 150°C).

Reduction of 1,2-Oxazine **1** *Employing Sodium in 2-Propanol:* To a solution of **1** (1.22 g, 6.00 mmol) in tetrahydrofuran/2-propanol (20 ml/15 ml) were added at 0°C sodium pieces (total amount: 1.80 g, 78.0 g atom). Then the mixture was stirred for 8 h at room temp., excess of sodium was removed by filtration, and 30 ml of ice-cold 3 N KOH was added. The aqueous phase was extracted with ethyl acetate (3 × 30 ml), and the combined organic phases were dried (Na_2SO_4) and concentrated in vacuo to afford 0.56 g of a crude product mixture. Kugelrohr distillation provided 0.398 g (41%) of *4-methyl-2-phenylpyrrolidine* (**15**) (b.p. 55°C/0.01 Torr, ratio of diastereomers = 1:1, colorless oil) and 0.146 g (15%) of a mixture of amino alcohol **4**, compound **15**, and pyrrole **14** (b.p. 100°C/0.01 Torr, ratio = 48:36:16).

15: ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.36–7.18 (m, 5H, Ph), 4.21 (t, *J* = 7.5 Hz, 0.5H, 2-H), 4.17 (dd, *J* = 6/10 Hz, 0.5H, 2-H), 3.33, 3.18, 2.70, 2.54 (4 dd, *J* = 7/10, 8/10, 7/10, 7.5/10 Hz, 0.5H each, 5-H), 2.31, 1.94–1.70, 1.50–1.15 (m_c, 2 m, 3H, 3-H, 4-H), 2.19 (s, 1H, NH), 1.08, 1.05 (2 d, *J* = 7 Hz, 1.5H each, Me). – ^{13}C NMR ($CDCl_3$): δ = 145.2, 144.9, 128.2, 126.6, 126.3 (2 s, 3 d, Ph), 63.1, 61.6 (2 d, C-2), 55.2, 54.2 (2 t, C-5), 43.8, 42.5 (2 t, C-3), 34.6, 33.2 (2 d, C-4), 19.2, 19.1 (2 q, Me). – IR (film): $\tilde{\nu}$ = 3550–3120 cm^{-1} (N–H), 3060, 3030 (=C–H), 3000–2750 (C–H), 1595 (Ph).

$C_{11}H_{15}N$ (161.3) Calcd. C 81.94 H 9.38 N 8.68
Found C 81.19 H 9.44 N 8.29

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[106/92]

CAS Registry Numbers

1: 117341-61-4 / **2**: 117341-66-9 / **3**: 113549-23-8 / **4** (isomer 1): 142483-96-3 / **4** (isomer 2): 142483-97-4 / **5**: 65476-99-5 / **6** (isomer 1): 142483-98-5 / **6** (isomer 2): 142483-99-6 / **7**: 117341-58-9 / **8**: 142484-00-2 / **9**: 1771-65-9 / **10**: 128500-49-2 / **11** (isomer 1): 142484-01-3 / **11** (isomer 2): 142561-59-9 / **11** (isomer 3): 142561-60-2 / **11** (isomer 4): 142561-61-3 / **12** (*cis*): 76403-49-1 / **12** (*trans*): 76403-50-4 / **13** (*cis*): 142484-02-4 / **13** (*trans*): 142484-03-5 / **14**: 20055-04-3 / **15** (*cis*): 142484-04-6 / **15** (*trans*): 142484-05-7