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TETRAHEDRON

Synthesis of Benzyl Substituted Tetrahydropyridines and 1,2,3,4-Tetrahydroisoquinolines via Acid Catalyzed Cyclization of γ,δ-Unsaturated *N*-Formyl-*N*-styryl Amines

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Abstract: Acid-catalyzed cyclization of *N*-(3-methylbut-3-enyl)-*N*-styrylformamides **1-3** in the presence of 9-BBN triflate gave access to 2-benzyl-1-formyl-4-methyl-1,2,5,6-tetrahydropyridines **4a-6a** and minor amounts of the isomeric 1,2,3,6-tetrahydropyridines **4b-6b**. Triflic acid catalyzed cyclization of *N*-2-(arylethyl)-*N*-styrylformamides **7**, **8** gave the corresponding 1-benzyl-2-formyl-1,2,3,4-tetrahydroisoquinolines **9** and **10**.

1,2,3,4-Tetrahydroisoquinolines and tetrahydropyridines are found in nature as alkaloids of a large number of plant species. The most important class of the former compounds is that of the 1-benzyl-1,2,3,4-tetrahydroisoquinolines which exhibit a wide range of physiological activities.[1] Moreover, they act as precursors for many other groups of alkaloids such as morphinans, bisbenzylisoquinolines, aporphines, and protoberberines. Examples of naturally occurring 1-benzyl-1,2,3,4-tetrahydroisoquinolines are laudanosine (up to 0.1% in opium) and reticuline, a precursor for morphine alkaloids.

The most stable compounds in the series of tetrahydropyridines are the 1,2,5,6-tetrahydropyridines. Alkaloids with this parent structure are guvacine (1,2,5,6-tetrahydropyridine-3-carboxylic acid) and its 1-methyl derivative arecaidine which are found in the nuts of *Areca catechu*.[2] Synthetically prepared 1-methyl-4-phenyl-1,2,5,6-tetrahydropyridine is a potent neurotoxic substance which causes chronic Parkinsonism in humans when used intraveneously.[3] The less stable 2,3,4,5-tetrahydropyridines also occur in nature with the alkaloid coniceine (6-propyl-2,3,4,5-tetrahydropyridine) from *Conium maculatum* as most striking example.[4] Tetrahydropyridines are important starting materials for the synthesis of benzomorphans,[5] compounds with an analgesic activity similar to that of the morphinans.

Recently, we showed that substituted *N*-[2-(cyclohex-1-enyl)ethyl]-*N*-styrylformamides can be easily converted into the corresponding 1-benzyl-2-formyloctahydroisoquinolines in the presence of a Lewis or Brønsted acid.[6] These cyclizations probably proceed *via* the *N*-formyliminium ion which is formed after addition of a proton or a Lewis acidic cation to the β carbon atom of the enamide double bond. To gain more insight into the scope and limitations of the acid catalyzed cyclization of γ,δ-unsaturated *N*-formyl-*N*-styryl amines we investigated other similar enamides in the synthesis of tetrahydropyridines and 1,2,3,4-tetrahydroisoquinolines. Here we wish to report on the results of these cyclization reactions.

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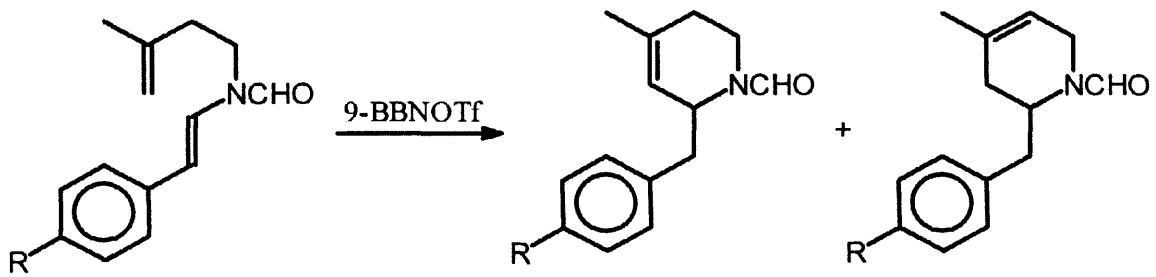
RESULTS AND DISCUSSION

Synthesis of tetrahydropyridines

We started our investigations with the cyclization of *N*-(3-methylbut-3-enyl)-*N*-styrylformamide (**1**), prepared by Wittig-alkenylation of 3-methylbut-3-enyldiformamide.[7] Initially, the cyclization was performed in the presence of one equivalent of $Cp_2Ti(CF_3SO_3)_2$ in a boiling mixture of toluene and THF at 93°C. The major product was isolated by column chromatography in 40% yield. Analysis of this product by MS and ^{1}H NMR showed that it was an isomeric mixture of tetrahydropyridines. With one equivalent of 9-borabicyclo[3.3.1]non-9-yl triflate (9-BBN triflate) the cyclization could be performed at temperatures of 50-70°C and the cyclic product was isolated in the same yield. At lower temperatures it was not possible to obtain a complete conversion of **1**. The cyclization of **1** requires a higher temperature than necessary for the corresponding *N*-[2-(cyclohex-1-enyl)ethyl] derivative since the methyl substituted double bond is less electron-rich than the trisubstituted cyclohexenyl double bond.

The cyclization product obtained from **1** was investigated in more detail. A TLC-pure product was analyzed by gas chromatography and showed two peaks (ratio 85:15) with only a small difference in retention time. In the mass spectrum of both compounds the base peak had *m/z* 124, which is characteristic for the loss of a benzyl group from a tetrahydropyridine skeleton. The combined data suggest the formation of two isomeric tetrahydropyridines. This was confirmed by the ^{1}H-NMR spectrum from which we concluded that the major isomer is the 1,2,5,6-tetrahydropyridine. Two rotamers were visible due to restricted rotation in the *N*-formyl bond in approximately 60:40 ratio in $CDCl_3$ at room temperature. The minor isomer showed the signals of the methyl group at about δ 1.72 partly overlapping the signals of the methyl group of the major isomer. From this we assume that the minor isomer also has the methyl group on a double bond and is 2-benzyl-1-formyl-4-methyl-1,2,3,6-tetrahydropyridine. The cyclization of **1** is depicted in Scheme 1.



1, R = H
2, R = OMe
3, R = Cl

4a
5a
6a

4b R = H
5b R = OMe
6b R = Cl

Scheme 1. Formation of two isomeric tetrahydropyridines in the cyclization of the enamides **1-3**

The cyclization was also performed with two *N*-(3-methylbut-3-enyl)-*N*-styrylformamides with a methoxy or chloro substituent at the *para* position of the phenyl ring.[7] From the *p*-methoxy substituted enamide **2** two isomeric 1-formyl-2-(*p*-methoxybenzyl)-4-methyltetrahydropyridines (**5a** and **5b**, Scheme 1) were obtained. The *p*-chloro compound **3** gave two isomeric *p*-chlorobenzyltetrahydropyridines (**6a** and **6b**, Scheme 1). In both cases the 1,2,5,6-tetrahydropyridine derivative was the major constituent. The results with *N*-3-methylbut-3-enyl substituted enamides are summarized in Table 1. The chloro substituted enamide shows the greatest preference for the major isomer. This trend was also observed in the cyclization of the chloro substituted *N*-[2-(cyclohex-1-enyl)ethyl]-*N*-styrylformamides.[6]

We also investigated the cyclization of *N*-but-3-enyl-*N*-styrylformamide[8] with an unsubstituted double bond. The reaction was performed in the presence of various strong Lewis and Brønsted acids[6] under drastic conditions but these attempts resulted only in the formation of a complex mixture of products. Analysis of the mixtures by ^{1}H NMR gave no indication for the formation of a cyclic product. Apparently, the unsubstituted double bond is not reactive enough for cyclization with the *N*-formyliminium ion.

Table 1. Cyclization of *N*-(3-Methylbut-3-enyl)-*N*-styrylformamides.

Enamide	Substituent	Product	Yield (%)[1]	Isomer ratio[2]
1	H	**4a + 4b**	40	85:15
2	*p*-OMe	**5a + 5b**	60	75:25
3	*p*-Cl	**6a + 6b**	44	90:10

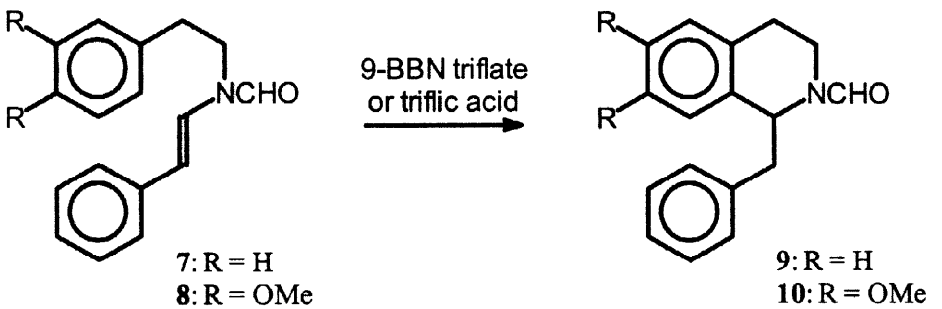
(1) The isolated yield is given. The products were isolated by column chromatography.
(2) Determined by GC. The major isomer is the 1,2,5,6-tetrahydropyridine.

Synthesis of 1,2,3,4-tetrahydroisoquinolines

To investigate cyclizations which involve the reaction of an aromatic nucleus we focused our attention on the preparation of 2-formyl-1,2,3,4-tetrahydroisoquinolines. From these compounds various other isoquinoline derivatives can be prepared.[9] The synthesis of 2-formyl-1,2,3,4-tetrahydroisoquinolines *via* *N*-formyliminium ions has been reported earlier.[10] The *N*-formyliminium ions were generated *in situ* from a formamide and an aldehyde in an acidic medium. The method was succesful with unreactive arene nucleophiles where the widely used Pictet-Spengler condensation fails to give satisfactory results.

We prepared two enamides for the cyclization experiments, *N*-2-phenylethyl-*N*-styrylformamide (**7**) and the dimethoxy activated compound *N*-[2-(3,4-dimethoxyphenyl)ethyl]-*N*-styrylformamide (**8**). Both enamides were prepared by formylation of the imine *in situ* formed from the corresponding arylethylamine and phenylacetaldehyde.[8] The cyclization of **7** (Scheme 2) was first studied in the presence of one equivalent of 9-BBN triflate in toluene at 50°C, but under these conditions no conversion of the enamide was observed. When the temperature was raised to 110°C a complete conversion of **7** was observed after 16 h. With one equivalent of trifluoromethanesulfonic acid (triflic acid) a complete conversion could be reached after 7 h at 50°C and tetrahydroisoquinoline **9** was isolated in 35% yield.

As expected, enamide **8** proved to be much more active in the cyclization reaction than **7**. A complete conversion was observed after 10 minutes in toluene at 50°C in the presence of 0.5 equivalent of 9-BBN triflate or triflic acid and 1-benzyl-2-formyl-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline (**10**, Scheme 2) was obtained in about 70% yield. Complete conversion of **8** was also reached after 20 h at 50°C using only 10 mol% of triflic acid and the isolated yield of **10** was the same as found with larger amounts of triflic acid.



7: R = H
8: R = OMe

9: R = H
10: R = OMe

Scheme 2. Synthesis of tetrahydroisoquinolines from *N*-arylethyl enamides

In conclusion, we have shown that γ,δ-unsaturated *N*-styrylformamides are convenient starting compounds for the synthesis of tetrahydropyridines and tetrahydroisoquinolines. The 9-BBN triflate catalyzed cyclization of *N*-(3-methylbut-3-enyl)-*N*-styrylformamides gave access to 2-benzyl-1-formyl-4-methyltetrahydropyridines. The triflic acid catalyzed cyclization of the suitable enamides gave the desired 1-benzyl-2-formyl-1,2,3,4-tetrahydroisoquinolines, even with the unreactive enamide **7** as starting compound. We previously showed that a wide variety of substituted *N*-styrylformamides is available by Wittig-alkenylation of diformamides, so a wide range of substituted 1-benzyl-2-formyl-1,2,3,4-tetrahydroisoquinolines is in principle accessible by this enamide cyclization method.

EXPERIMENTAL

^{1}H- and ^{13}C-NMR spectra were recorded with a Varian VXR-400S spectrometer with $CDCl_3$ as solvent and tetramethylsilane as internal reference. Mass spectra were determined using a VG 70-SE spectrometer (electron ionisation 70 eV). Infrared spectra were recorded using a Beckman IR-4210 spectrophotometer or a Perkin Elmer Spectrum 1000 spectrophotometer. Gas chromatography was performed with a Packard 427 gas chromatograph with a CP Sil5 GB (10 m x 0.53 mm) column. Samples for GC-MS were chromatographed with a CP Sil5 GB (25 x 0.25 mm) column and analyzed with a V70-SE spectrometer. Column chromatography was performed over silica (Merck kieselgel 60, particle size 63-200 μm) and Thin Layer Chromatography (TLC) on deactivated silica (0.25 mm, Merck F_{254}).

9-BBN Triflate (0.5 M solution in hexanes) was purchased from Aldrich and triflic acid was purchased from Acros. $Cp_2Ti(CF_3SO_3)_2$ was prepared *in situ* by reaction of the chloride with silver triflate.[11] The synthesis of *N*-but-3-enyl-*N*-styrylformamide[8] and the *N*-(3-methylbut-3-enyl)-*N*-styrylformamides **1-3**[7] have been reported elsewhere.

Cyclization of *N*-(3-methylbut-3-enyl)-*N*-styrylformamides. General procedure.

A solution of 9-BBN triflate in hexanes (1 M, one equivalent) was added to a solution of the enamide in toluene. The reaction mixture was heated to 50-70°C and stirred until TLC (eluent CH_2Cl_2/MeOH 95:5) showed a complete conversion of the enamide. The solution was washed with a saturated solution of $NaHCO_3$. The aqueous layer was extracted with toluene and the combined organic layers were washed with water and a saturated solution of NaCl. After drying (Na_2SO_4) the solvent was evaporated under reduced pressure. The crude product was purified by column chromatography over silica gel using a mixture of dichloromethane and methanol (96:4) as eluent.

2-Benzyl-1-formyl-4-methyl-1,2,5,6-tetrahydropyridine (4a) and its isomer (4b)

2-Benzyl-1-formyl-4-methyl-1,2,5,6-tetrahydropyridine (**4a**) and its isomer (**4b**) were obtained from *N*-(3-methylbut-3-enyl)-*N*-styrylformamide (**1**) according to the general procedure. Enamide **1** (0.62 g, 2.88 mmol) yielded 0.25 g (1.16 mmol, 40%) of **4a** and **4b** as an oil.
MS: values for **4a** (85%): 215 (M^+, 1), 124 (100), 96 (37), 91 (17), 81 (10), 65 (10). — HRMS: *m/z* 215.1321; calcd. for $C_{14}H_{17}NO$: 215.1310. — ^{1}H NMR (**4a**): rotamer ratio 60:40, value for the minor rotamer in parentheses: δ 1.73 (1.68) [d, 3 H, CH_3, J = 1.2 Hz], 1.90 (2.16) (m_c, 2 H, CH_2), 3.02 and 2.80 (ddd and m_c, 3 H, CH_2N and benzylic proton), 3.46 (dd) and (3.98) (m_c) [1 H, benzylic proton, J = 5.8 and 12.8 Hz], 4.44 (dd) and (4.78) (m_c) [1 H, CHN, J = 6.4 and 13.1 Hz], 5.44 (5.27) [m_c, 1 H, C=CH, J = 1.2 and 2.4 Hz], 7.20 (m_c, 5 H, ArH), 7.56 (8.02) (s, 1 H, CHO). — ^{13}C NMR (both rotamers of **4a**): δ 161.32, 161.22, 137.98, 134.29, 132.57, 129.64, 129.30, 128.98, 128.70, 128.25, 126.82, 126.40, 121.14, 120.80, 56.50, 50.29, 41.34, 40.44, 39.84, 33.39, 30.24, 29.31, 23.26. — IR: ν (neat)/cm^{-1}: 1660 (C=O).

1-Formyl-2-(*p*-methoxybenzyl)-4-methyl-1,2,5,6-tetrahydropyridine (5a) and its isomer (5b)

1-Formyl-2-(*p*-methoxybenzyl)-4-methyl-1,2,5,6-tetrahydropyridine (**5a**) and its isomer (**5b**) were obtained from *N*-(*p*-methoxystyryl)-*N*-(3-methylbut-3-enyl)formamide (**2**) according to the general procedure. Enamide **2** (0.50 g, 2.04 mmol) yielded 0.30 g (1.22 mmol, 60%) of **5a** and **5b** as an oil which solidified on standing.
M.p. 95-98°C. — MS: values for **5a** (75%): 245 (M^+, 3), 124 (100), 96 (28). HRMS: *m/z* 245.1407; calcd. for $C_{15}H_{19}NO_2$: 245.1416. — ^{1}H NMR (**5a**): rotamer ratio 60:40; value for the minor rotamer in parentheses: δ 1.73 (1.68) [d, 3 H, CH_3, J = 1.2 Hz], 1.88 (2.16) (m_c, 2 H, CH_2), 3.02 (ddd) and (2.76) (dd) (3 H, CH_2N and one benzylic proton), 3.46 (dd) and (3.92) (m_c) [1 H, one benzylic proton, J = 6.0 and 13.0 Hz], 3.78 (s, 3 H, OCH_3), 4.43 (dd) and (4.76) (m_c) [1 H, CHN, J = 6.3 and 13.3 Hz], 5.44 (m_c) and (5.27) (m_c) [1 H, C=CH, J = 1.5 and 2.5 Hz], 6.92 (6.98) [dd, 4 H, ArH, J = 2.7 and 8.9 Hz], 7.56 (8.06) (s, 1 H, CHO). — ^{13}C NMR (both rotamers of **5a**): δ 161.40, 161.23, 158.48, 158.24, 134.19, 132.49, 130.56, 130.41, 130.28, 129.94, 129.59, 121.18, 120.90, 114.11, 113.68, 56.69, 55.20, 50.42, 40.94, 40.43, 38.89, 33.39, 30.23, 29.33, 23.27. — IR: ν (neat)/cm^{-1}: 1668 (C=O).

2-(*p*-Chlorobenzyl)-1-formyl-4-methyl-1,2,5,6-tetrahydropyridine (6a) and its isomer (6b)

2-(*p*-Clorobenzyl)-1-formyl-4-methyl-1,2,5,6-tetrahydropyridine (**6a**) and its isomer (**6b**) were obtained from *N*-(*p*-chlorostyryl)-*N*-(3-methylbut-3-enyl)formamide (**3**) according to the general procedure. Enamide **3** (0.50 g, 2.01 mmol) yielded 0.22 g (0.88 mmol, 44%) of **6a** and **6b** as an oil which solidified on standing.

M.p. 66-71°C. — MS: values for **6a** (90%): 124 (100), 96 (41), 81 (11). — ^{1}H NMR (**6a**): rotamer ratio 60:40, value for the minor rotamer in parentheses: δ 1.69 (1.74) [d, 3 H, CH_3, J = 1.5 Hz], 2.16 (1.88) (m_c, 2 H, CH_2), 2.80 (m_c) and 3.02 (ddd) (3 H, CH_2N and one benzylic proton), 3.47 (dd) and (3.95) (m_c) [1 H, one benzylic proton, J = 5.5 and 13.1 Hz], (4.44) (dd) and 4.78 (m_c) [1 H, CHN, J = 6.1 and 13.1 Hz], (5.25) (m_c) and 5.43 (m_c) [1 H, C=CH, J = 1.4 and 2.6 Hz], 7.15 [m_c, 4 H, ArH, J = 8.5 Hz], 8.05 (7.60) (s, 1 H, CHO). — ^{13}C NMR (both rotamers of **6a**): δ 161.28, 136.06, 134.68, 133.04, 132.74, 132.29, 130.94, 130.64, 128.85, 128.40, 120.78, 120.43, 56.28, 50.13, 40.69, 40.44, 39.13, 33.45, 30.19, 29.26, 23.29. — IR: ν (neat)/cm^{-1}: 1662 (C=O).

N-2-Phenylethyl-*N*-styrylformamide (7)

Compound **7** was prepared according to a procedure described in Ref. 8. 2-Phenylethylamine (1.67 g, 13.79 mmol) yielded 1.734 g (6.91 mmol, 50%) of **7** as an oil which solidified on standing.
M.p. 56-58°C. — MS: 251 (M^+, 100), 160 (69), 147 (76), 132 (89), 105 (60), 91 (58), 77 (62). — HRMS: *m/z* 251.1312; calcd. for $C_{17}H_{17}NO$: 251.1310. — ^{1}H NMR: rotamer ratio : 60:40, value for the minor rotamer in parentheses: δ 2.96 [m_c, 2 H, CH_2CH_2N, J = 7.6 and 8.2 Hz (major rotamer), J = 6.7 Hz (minor rotamer), 3.90 [m_c, 2 H, CH_2N, J = 7.6 and 8.2 Hz] and (3.79) [t, 2 H, CH_2N, J = 6.7 Hz], 6.08 (6.20) [d, 1 H, N-*CH*=CH, J = 14.3 Hz], 7.01 (7.74) [d, 1 H, N-CH=*CH*, J = 14.7 Hz], 7.22 (m_c, 10 H, ArH), 8.38 (7.78) (s, 1 H, CHO). — ^{13}C NMR: both rotamers: δ 162.28, 161.16, 138.26, 137.72, 136.19, 135.95, 128.89, 128.79, 128.63, 127.43, 127.04, 126.91, 126.78, 126.70, 125.82, 125.50, 122.89, 112.52, 111.34, 47.69, 42.65, 33.80, 32.85. — IR: ν (neat)/cm^{-1}: 1644 (C=C) and 1691 (C=O).

N-[2-(3,4-Dimethoxyphenyl)ethyl]-*N*-styrylformamide (8)

Compound **8** was prepared according to a procedure described in Ref. 8. 2.50 g (13.79 mmol) of 2-(3,4-dimethoxyphenyl)ethylamine yielded 1.865 g (6.00 mmol, 44%) of **8** as an oil which solidified on standing.
M.p. 57-59°C. — MS: 311 (M^+, 25), 164 (100), 151 (52), 105 (25), 91 (39), 77 (29). — HRMS: *m/z* 311.1536; calcd. for $C_{19}H_{21}NO_3$: 311.1521. — ^{1}H NMR: rotamer ratio: 60:40, value for the minor rotamer in parentheses: δ 2.90 (m_c, 2 H, CH_2CH_2N), 3.83 (m_c, 2 H, CH_2N), 3.84 (3.85) (s, 3 H, OCH_3), 3.84 (3.88) (s, 3 H, OCH_3), 6.09 (6.20) [d, 1 H, N-*CH*=CH, J = 14.4 Hz], 6.67 [ddd, 1 H, ArH, J = 2.3, 7.8 and 10.7 Hz], 6.80 (m_c, 2 H, ArH), 7.01 (7.76) [d, 1 H, N-CH=*CH*, J = 14.4 Hz], 7.31 (m_c, 5 H, ArH), 8.39 (7.77) (s, 1 H, CHO). — ^{13}C NMR: both rotamers: δ 162.32, 161.23, 149.24, 149.08, 148.11, 147.88, 136.22, 135.96, 130.79, 130.25, 128.81, 128.77, 127.47, 126.91, 126.80, 125.79, 125.49, 122.87, 120.97, 120.76, 112.48, 112.13, 111.46, 111.46, 111.39, 55.94, 47.82, 42.70, 33.31, 32.46. — IR: ν (neat)/cm^{-1}: 1644 (C=C) and 1689 (C=O).

1-Benzyl-2-formyl-1,2,3,4-tetrahydroisoquinoline (9)

N-2-Phenylethyl-*N*-styrylformamide (**7**, 0.512 g, 2.04 mmol) was dissolved in 50 ml of toluene and 0.18 ml (0.306 g, 2.04 mmol) of triflic acid was added. The mixture was heated at 50°C in a thermostatted flask. The reaction was monitored by TLC and a complete conversion of **7** was observed after 7 h. The mixture was washed with a saturated solution of $NaHCO_3$ (50 ml) and the aqueous layer was extracted with toluene (25 ml). The combined organic layers were washed with a saturated solution of NaCl (75 ml) and dried (Na_2SO_4). The solvent was

removed under reduced pressure and the residue was purified by column chromatography (CH_2Cl_2/MeOH 97:3). This gave 0.180 g (0.72 mmol, 35%) of **9** as an oil.

MS: 251 (M^+, 0.5), 160 (100), 132 (55), 117 (28), 105 (20), 91 (25), 77 (16). — ^{1}H NMR: rotamer ratio: 60:40, value for the minor rotamer in parentheses: δ 2.67-3.32 (m, 5 H, CH_2CH_2N, benzylic protons, one proton of CH_2N), (3.54) (ddd) and 4.48 (ddd) [1 H, one proton of CH_2N, J = 2.6, 6.0 and 13.1 Hz], 4.65 (dd) and 5.64 (t) [1 H, CHN, J = 4.2 and 10.1 Hz (major rotamer), J = 6.4 Hz (minor rotamer)], 7.20 (m_c, 9 H, ArH), 7.55 (8.10) (s, 1 H, CHO). — ^{13}C NMR: both rotamers: δ 161.38, 161.34, 137.28, 135.73, 135.35, 134.02, 133.34, 129.69, 129.33, 128.90, 128.85, 128.22, 127.49, 127.32, 127.11, 126.94, 126.87, 126.63, 126.46, 126.40, 59.41, 52.44, 43.42, 41.94, 40.75, 34.10, 29.50, 28.04. — IR: ν (neat)/cm^{-1}: 1671 (C=O).

1-Benzyl-2-formyl-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline (10)

N-[2-(3,4-Dimethoxyphenyl)ethyl]-*N*-styrylformamide (**8**, 0.188 g, 0.605 mmol) was dissolved in 10 ml of toluene and triflic acid (0.045 g, 0.302 mmol) in 10 ml of CH_2Cl_2 was added. The mixture was heated for 10 min in a thermostatted flask at 50°C. After removal of the CH_2Cl_2 under reduced pressure the organic layer was washed with a saturated solution of $NaHCO_3$ (10 ml). The aqueous layer was extracted with toluene (2 x 10 ml) and the combined organic layers were washed with a saturated solution of NaCl (20 ml) and dried (Na_2SO_4). The solvent was removed under reduced pressure to give crude **10** as a solid. The product was recrystallized from diethyl ether which yielded 0.127 g (0.408 mmol, 67%) of pure **10**.

M.p. 124-126°C. — MS: 220 (M^+-benzyl, 100), 192 (29), 176 (19), 148 (10), 91 (15). — ^{1}H NMR: rotamer ratio: 60:40, value for the minor rotamer in parentheses: δ 2.60-3.48 (m, 5 H, CH_2CH_2N, $ArCH_2$, one proton of CH_2N), (3.58) (ddd) and 4.50 (ddd) (1 H, one proton of CH_2N), 3.83 (3.63) (s, 3 H, OCH_3), 3.87 (3.85) (s, 3 H, OCH_3), 4.60 (dd) and 5.53 (t) (1 H, CHN), 6.55 (s, 1 H, ArH), 6.63 (6.24) (s, 1 H, ArH), 7.25 (m_c, 5 H, ArH), 7.65 (8.13) (s, 1 H, CHO). — ^{13}C NMR: both rotamers: δ 161.30, 161.24, 148.35, 147.92, 147.61, 147.29, 137.60, 137.34, 129.93, 129.43, 128.84, 128.33, 127.43, 127.09, 126.64, 126.11, 125.20, 111.69, 111.28, 110.41, 109.90, 59.05, 56.06, 55.94, 55.85, 55.67, 43.52, 42.07, 40.77, 34.19, 29.12, 27.68. — IR: ν (neat)/cm^{-1}: 1669 (C=O).

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