model included anisotropic non-hydrogen atoms and fixed isotropic hydrogens. The final crystallographic residual was 0.049 and additional crystallographic information can be found in Tables II–IV.[12]

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Notes

Optically Active Tetrahydro-α-phenyl-6,7-dimethoxyisoquinoline-1-methanols from (1-Phenylethyl)ureas. Absolute Configuration of (−)- and (+)-Isomers of the Erythro Series

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Introduction

1,2,3,4-Tetrahydro-α-phenylisoquinoline-1-methanols (1-(α-hydroxybenzyl)-1,2,3,4-tetrahydroisoquinolines, TIQM) are less known than their 1-benzyl analogues, which represent an important group of the isoquinoline alkaloids.[1–3] TIQM occur as optically active alkaloids in plants,[4,5] and the (±)-erythro isomers prepared by synthesis have shown interesting pharmacological properties.[6] This suggested that a general strategy for a practical synthesis of optically active TIQM could be designed and the absolute configurations of the optical isomers could be determined.

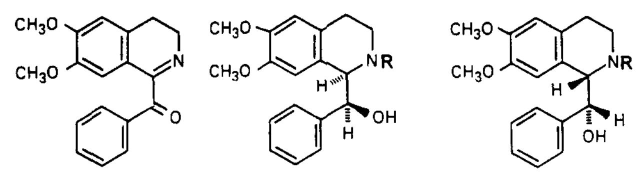
The resolution of the erythro isomer ((±)-**2**) and the threo isomer ((±)-**3**) could be accomplished by reaction of each of the racemic amines with an optically active 1-phenylethyl isocyanate to give the diastereomeric (1-phenylethyl)ureas (**4** and **5**, respectively), followed by separation and subsequent hydrolysis.

This method applied before to prepare optically active tetrahydroisoquinolines[7] is now extended to a synthesis of optically active amino alcohols. Catalytic deoxygenation of the optically active alcohol to the deoxy congener of known absolute configuration, together with assignments of erythro and threo stereochemistry established by ^{1}H NMR spectroscopy, seem to offer a method for determination of absolute configuration. The results of this investigation, which show (−)-**2** to have the 1*R*,α*S* configuration and (+)-**2** the 1*S*,α*R* configuration are reported here.

Results and Discussion

A convenient starting material for the synthesis of optically active TIQM is the known 1-benzoyl-3,4-dihydro-6,7-dimethoxyisoquinoline (**1**).[8–11] Reduction of **1** with sodium borohydride in methanol at room temperature afforded a 77:23 mixture of erythro alcohol (±)-**2** and threo isomer (±)-**3**, which were separated by crystallization followed by flash chromatography. A high degree of stereospecificity in the reduction of 1-benzoyl-3,4-dihydroisoquinolines with sodium borohydride in methanol, leading predominantly to erythro isomers, has frequently been observed.[11–14]

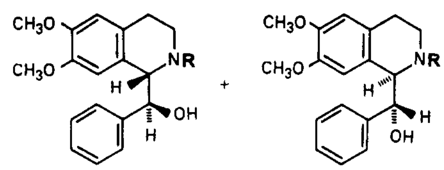
Chart I



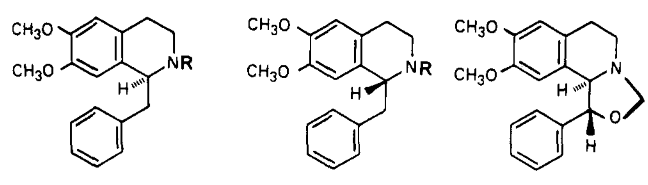
1

(−)-2, R=H
(−)-4a, R=CONHCH(CH_3)C_6H_5
(+)-6, R=CH_3

(+)-2, R=H
(−)-4b, R=CONHCH(CH_3)C_6H_5
(−)-6, R=CH_3



(±)-3, R=H
(±)-5, R=CONHCH(CH_3)C_6H_5
(±)-7, R=CH_3



(+)-8a, R=CONHCH(CH_3)C_6H_5
(−)-9, R=H

(−)-8b, R=CONHCH(CH_3)C_6H_5
(+)-9, R=H

(±)-10

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The relative stereochemistry of 1,2-amino alcohols can be assigned on the basis of ^{1}H NMR spectral data. It has been shown by many examples that the vicinal coupling constant between C(1) and C(α) protons in the erythro isomers is smaller (J = 3–5 Hz) than that in the threo series (J = 7–9 Hz).[11,13-15] In our case the major product (±)-**2** (mp 139–140 °C), which moved slower on TLC ($CHCl_3$/CH_3OH/NH_4OH = 90:9:1), was assigned the erythro configuration, because of its coupling constant J = 4.8 Hz. Its diastereomer (±)-**3** (mp 145–147 °C) with a coupling constant J = 7.7 Hz thus has the threo configuration. Reaction of (±)-**2** with (*R*)-(+)-1-phenylethyl isocyanate afforded a mixture of ureas **4a,b**, which were separated by crystallization, followed by flash chromatography on silica gel (hexane/ethyl acetate = 3:2). The threo isomer (±)-**3** similarly gave urea **5** as a mixture of diastereomers, which, however, resisted separation by crystallization or chromatography on alumina and silica gel plates with commonly used solvents.

Conversion of ureas **4a,b** into optically active (−)-**2** and (+)-**2**, respectively, was accomplished in refluxing butanol in the presence of a catalytic amount of sodium butoxide in 80% yield. On the basis of their specific rotations, both optically active amines seem to be identical with materials prepared by enantiospecific synthesis from (*S*)- and (*R*)-*N*-(*O*-acetylmandeloyl)homoveratrylamide, respectively.[16]

Reductive N-methylation of (−)-**2** and (+)-**2** with formaldehyde in the presence of Raney nickel catalyst afforded the *N*-methyl bases (+)-**6** and (−)-**6**, respectively. Changes in the sign of specific rotation when going from a *N*-nor- to *N*-methyl-base has often been observed in this group of compounds.[17] Our assignment of the erythro configuration for **2** and **6** is supported by the apparent identity of our material with that prepared differently.[11,18] Similarly, *N*-methylamine (±)-**7** prepared from (±)-**3** by reductive N-methylation seems to be identical with material obtained by Kano et al. in a stereoselective synthesis.[19] It is noteworthy that in the reductive methylation of (±)-**3**, compound **10** was obtained as the major product. Its oxazolidine structure was deduced from the molecular composition, $C_{19}H_{21}NO_3$, and spectral data. The ^{1}H NMR spectrum integrated for seven aromatic protons and $J_{1'\alpha}$ = 8 Hz indicated a trans stereochemistry between C(1) and C(α) protons. There is no OH stretching band in the IR spectrum. Formation of cyclic ethers in the reductive N-methylation of amino alcohols with formaldehyde in this series of compounds has been reported.[13,20] Assignment of the absolute configuration at C(1) of (−)-**2** was achieved by catalytic deoxygenation over Pd/C catalyst in acetic acid/perchloric acid[21] to (1*S*)-1-benzyl-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline ((−)-**9**). Both optical isomers of **9** were obtained from (±)-**9** by reaction with (*R*)-(+)-1-phenylethyl isocyanate and separation of ureas **8a,b** by crystallization followed by flash chromatography on a silica gel with hexane/ethyl acetate (4:1), followed by alcoholysis. They also seem identical with materials reported elsewhere and obtained by classical resolution.[22]

The 1*R* configuration for amine (+)-**9** (derived from (−)-**9**·HCl) was deduced from its CD spectrum, which showed negative Cotton effect at 281 nm, opposite to that of (−)-norreticuline of known absolute configuration.[2] This information together with the erythro configuration established for **2** and **6** by ^{1}H NMR spectroscopy allowed assignment of the 1*R*,α*S* configuration for (−)-**2** and the 1*S*,α*R* configuration to (+)-**2**. The synthesis of the optical isomers of **6** reported here, together with a synthesis of the optical isomers of **7** reported by Kano et al.,[23] makes it possible to prepare all four optically active amino alcohols from ketone **1**.

Conclusions

Resolution of secondary amines into optical isomers by separation of optically active urea derivatives has the advantage over conventional methods (chemical resolution, enzymic resolution, etc.) of affording both of the isomers in pure form. The yield of optically pure amines in the alcoholysis reaction of pure ureas is high, making both optical isomers available at the same time. The success of the urea derivitization separation method depends entirely on the successful separation of diastereomeric ureas, which, as shown here, was not accomplished with the threo isomer **5**.

Experimental Section

All melting points are uncorrected. ^{1}H NMR spectra ($CDCl_3$) were recorded at 300 MHz. Chemical ionization mass spectral data were obtained with NH_3 as ionizing gas. Flash chromatography was performed on Merck silica gel 60, 60A. TLC was carried out on Analtech silica gel GHLF uniplates. CD spectra were recorded in ethanol at room temperature on a JASCO Model J-500A recording spectropolarimeter.

(±)-*erythro*- and (±)-*threo*-1,2,3,4-Tetrahydro-6,7-dimethoxy-α-phenyl-1-isoquinolinemethanols ((±)-2 and (±)-3). Benzoyl derivative **1**[8-11] (The oily derivative **1** was identical in terms of TLC and spectral data with a sample of crystalline **1** (mp 79–81 °C) provided by Dr. G. Lenz) (3.86 g, 13 mmol) was reduced with $NaBH_4$ (0.98 g, 26 mmol) in methanol (60 mL) containing water (1 mL) for 2 h at room temperature. Methanol was then removed under reduced pressure, and products were isolated by the standard extraction procedure with ethyl ether. The crystalline solid (3.42 g) was recrystallized twice from 95% ethanol to give pure erythro isomer (±)-**2** (1.12 g). Flash chromatography [SiO_2, 1:40; $CHCl_3$–CH_3OH (19:1)] afforded additional 0.76 g of isomer (±)-**2** and 0.56 g of isomer (±)-**3**. The total yield of this reaction was 63%, and the ratio of (±)-erythro to (±)-threo isomers was 77:23.

(±)-**2**: mp 139–140 °C; ^{1}H NMR δ 3.64 (s, 3 H, 7-OCH_3), 3.83 (s, 3 H, 6-OCH_3), 4.32 (d, J = 4.8 Hz, 1 H, 1-H), 5.00 (d, J = 4.8 Hz, 1 H, α-H), 6.44, 6.53 (2 s, 1 H each, 8-H, 5-H); CIMS m/z 300 (M^+ + 1, 100), 282 (M − OH, 20), 192 (100). Anal. Calcd for $C_{18}H_{21}NO_3$: C, 72.22; H, 7.07; N, 4.68. Found: C, 72.28; H, 7.09; N, 4.65.

(±)-**3**: mp 145–147 °C; ^{1}H NMR δ 3.37 (s, 3 H, 7-OCH_3), 3.83 (s, 3 H, 6-OCH_3), 3.89 (d, J = 7.8 Hz, 1 H, 1-H), 4.65 (d, J = 7.6 Hz, 1 H, α-H), 5.67 (s, 1 H, 8-H), 6.55 (s, 1 H, 5-H); CIMS m/z 300 (M^+ + 1, 100), 282 (M − OH, 15), 192 (80). Anal. Calcd for $C_{18}H_{21}NO_3$: C, 72.22; H, 7.07; N, 4.68. Found: C, 72.32; H, 7.07; N, 4.65.

(1*R*,α*S*)-1,2,3,4-Tetrahydro-6,7-dimethoxy-α-phenyl-2-[((*R*)-1-phenylethyl)carbamoyl]-1-isoquinolinemethanol (4a)

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and Its (1*S*,α*R*)-Diastereoisomer (4b). To an ice-cold solution of (±)-**2a** (2.99 g, 10 mmol) in chloroform (30 mL) was added (*R*)-(+)-1-phenylethyl isocyanate (1.62 g, 11 mmol) under argon. The mixture was stirred at room temperature for 1 h and then evaporated, and the residue was partitioned between ethyl ether and water. The organic phase was separated and washed with 5% HCl and then worked up in a standard way to give 4.7 g of a foam, which was crystallized from ethyl acetate. Fractional crystallization afforded 1.38 g (30%) of **4a** and 0.57 g of **4b**. Flash chromatography (SiO_2, 1:50, hexane–EtOAc, 6:1, 5:1, 4:1, 3:1) supplied an additional amount (0.47 g) of **4b** (total yield: 23%) and 1.46 g (33%) of a mixture of the diastereomers.

4a: mp 211–212 °C; $[\alpha]^{27}_D$ −31.2° (*c* 1.2, $CHCl_3$); ^1H NMR δ 3.84 (s, 6 H, 6-OCH_3, 7-OCH_3), 5.02–5.16 (m, 3 H, 1-H, α-H, PhC*H*CH_3), 5.50 (s, 1 H, H-8); CIMS *m/z* 447 (M^+ + 1, 25), 429 (M − OH, 20), 192 (100). Anal. Calcd for $C_{27}H_{30}N_2O_4$: C, 72.62; H, 6.77; N, 6.27. Found: C, 72.63; H, 6.82; N, 6.28.

4b: mp 181–182 °C; $[\alpha]_D$ −34.1° (*c* 0.9, $CHCl_3$); ^1H NMR δ 3.85 (s, 6 H, 6-OCH_3, 7-OCH_3), 5.00–5.14 (m, 3 H, 1 H, α-H, PhC*H*CH_3), 5.48 (s, 1 H, 8-H); CIMS *m/z* 447 (M^+ + 1, 10), 429 (M − OH, 15), 192 (100). Anal. Calcd for $C_{27}H_{30}N_2O_4$: C, 72.62; H, 6.77; N, 6.27. Found: C, 72.72; H, 6.82; N, 6.25.

(1*S*,α*S*)- and (1*R*,α*R*)-1,2,3,4-Tetrahydro-6,7-dimethoxy-α-phenyl-2-[((*R*)-1-phenylethyl)carbamoyl]-1-isoquinolinemethanol (5). Diastereoisomers **5** were obtained from (±)-**3** according to the above procedure as a foam and could not be separated by either crystallization or chromatography. Yield 80%. Anal. Calcd for $C_{27}H_{30}N_2O_4 \cdot {}^1/_2H_2O$: C, 71.19; H, 6.85; N, 6.15. Found: C, 71.16; H, 6.63; N, 5.83.

(−)-(1*R*,α*S*)-1,2,3,4-Tetrahydro-6,7-dimethoxy-α-phenyl-1-isoquinolinemethanol ((−)-2). A solution of **4a** (0.446 g, 1 mmol) in *n*-butanol (10 mL) containing 1.0 M sodium butoxide (0.5 mL) was refluxed for 5 h under argon. The solvent was then removed in vacuo, and the residue was partitioned between water and ethyl ether. The organic phase was extracted with 2 N HCl; the acidic aqueous layer was basified with 10% NaOH, reextracted with ethyl ether, and worked up in the usual way. The crystalline residue (0.24 g, 80%) was recrystallized from ethyl ether: mp 125–126 °C; $[\alpha]^{27}_D$ −59.3° (*c* 1, $CHCl_3$). ^1H NMR and MS spectra are identical with those of the racemic (±)-**2**.

(+)-(1*S*,α*R*)-1,2,3,4-Tetrahydro-6,7-dimethoxy-α-phenyl-1-isoquinolinemethanol ((+)-2). Isomer (+)-**2** was obtained from **4b** in a similar manner as (−)-**2**, with 80% yield: mp 123–124 °C; $[\alpha]^{27}_D$ + 59.0° (*c* 1, $CHCl_3$). ^1H NMR and MS spectra are identical with those of (±)-**2** and (−)-**2**.

(+)-(1*R*,α*S*)-1,2,3,4-Tetrahydro-6,7-dimethoxy-2-methyl-α-phenyl-1-isoquinolinemethanol ((+)-6). A mixture of (−)-**2** (0.1 g, 0.3 mmol) 37% aqueous formaldehyde (0.13 mL) and Raney nickel catalyst (ca. 41 mg) in methanol (10 mL) was hydrogenated under 40 psi at room temperature for 12 h. The catalyst was filtered off and washed with methanol, and then the solvent was evaporated in vacuo. The residue was dissolved in ethyl ether and extracted with 5% HCl, and the acidic aqueous phase was basified with 10% NaOH and reextracted with ether. The residue that was left after the standard workup (0.07 g, 67%) cyrstallized from ethyl ether: mp 108–110 °C; $[\alpha]^{27}_D$ +15.5° (*c* 1, $CHCl_3$); ^1H NMR δ 2.68 (s, 3 H, N-CH_3), 3.30 (s, 3 H, 7-OCH_3) 3.78 (d, *J* = 3.2 Hz, 1 H, 1-H), 3.82 (s, 3 H, 6-OCH_3), 5.14 (d, *J* = 3.2 Hz, 1 H, α-H), 5.59 (s, 1 H, 8-H); CIMS *m/z* 314 (M^+ + 1, 100). Anal. Calcd for $C_{19}H_{23}NO_3$: C, 72.82; H, 7.40; N, 4.47. Found: C, 72.75; H, 7.44; N, 4.42.

(−)-(1*S*,α*R*)-1,2,3,4-Tetrahydro-6,7-dimethoxy-2-methyl-α-phenyl-1-isoquinolinemethanol ((−)-6). Compound (−)-**6** was prepared from (+)-**2** according to the same procedure as compound (+)-**6** with 95% of yield: mp 108–109 °C; $[\alpha]^{27}_D$ −16.4° (*c* 1, $CHCl_3$). ^1H NMR and MS spectra were identical with those of (+)-**6**. Anal. Calcd for $C_{19}H_{23}NO_3$: C, 72.82; H, 7.40; N, 4.47. Found: C, 72.78; H, 7.43; N, 4.46.

Racemic *erythro*- and *threo*-1,2,3,4-Tetrahydro-6,7-dimethoxy-2-methyl-α-phenyl-1-isoquinolinemethanol ((±)-6 and (±)-7). Racemic *N*-methylamino alcohols (±)-**6** and (±)-**7** were prepared from (±)-**2** and (±)-**3**, respectively, according to the same procedure used to prepare enantiomer (+)-**6** from (−)-**2**.

(±)-**6**: yield 86%; mp 126–128 °C (lit.[10] mp 119–121 °C); ^1H NMR and MS spectral data were identical with those of (+)-**6** and (−)-**6**. Anal. Calcd for $C_{19}H_{23}NO_3$: C, 72.82; H, 7.40; N, 4.47. Found: C, 72.65; H, 7.49; N, 4.44.

During the N-methylation of compound (±)-**3** two products (±)-**7** and **10** were formed. They were separated by flash chromatography (SiO_2, 1:30; benzene–ethyl ether 9:1).

Compound 10: yield 67%; mp 129.5–132 °C; ^1H NMR δ 3.61 (s, 3 H, 7-OCH_3), 3.86 (s, 3 H, 6-OCH_3), 4.07 (d, *J* = 8 Hz, 1 H, 1-H), 4.61 (d, *J* = 8 Hz, 1 H, α-H), 4.83 (d, *J* = 6 Hz, 1 H, *H*-CH), 5.11 (d, *J* = 6 Hz, 1 H, *H′*-CH), 5.89 (s, 1 H, 8-H); CIMS *m/z* 312 (M^+ + 1, 100), 206 (55). Anal. Calcd for $C_{19}H_{21}NO_3$: C, 73.29; H, 6.80; N, 4.50. Found: C, 73.22; H, 6.80; N, 4.71.

(±)-**7**: yield 10%; mp 154–156 °C (lit.[19] mp 155–157 °C); ^1H NMR δ 2.66 (s, 3 H, N-CH_3), 3.24 (s, 3 H, 7-OCH_3), 3.40 (d, *J* = 9.2 Hz, 1 H, 1-H), 3.82 (s, 3 H, 6-OCH_3), 4.40 (d, *J* = 9.2 Hz, 1 H, α-H), 5.32 (s, 1 H, 8-H); CIMS *m/z* 314 (M^+ + 1, 100). Anal. Calcd for $C_{19}H_{23}NO_3$: C, 73.29; H, 6.80; N, 4.50. Found: C, 73.22; H, 6.80; N, 4.71.

Catalytic Deoxygenation of (−)-2. Alcohol (−)-**2** (100 mg, 0.3 mmol) in acetic acid (1.5 mL) containing perchloric acid (0.15 mL) and 10% Pd–C catalyst (20 mg) was hydrogenated at 70 °C for 12 h. Another aliquot of catalyst (20 mg) was added, and the mixture was hydrogenated for an additional 24 h. After cooling to room temperature, methylene chloride (10 mL) was added, and the slurry was filtered through a pad of Celite-545; 10% NaOH was then added until the pH was ca. 10, and the organic layer was separated and evaporated. The residue was taken up into ethyl ether and then H extracted with 5% HCl; the aqueous phase basified with 10% NaOH, extracted with ethyl ether, and worked up as usual. The resulting oil (0.075 g, 79%) was treated with 3.5% HCl in methanol and left for crystallization. Crystalline needles of (+)-**9**·HCl were obtained (0.055 g): mp 184–186 °C; $[\alpha]^{27}_D$ +24.9° (*c* 1.2, CH_3OH). ^1H NMR and MS spectral data are identical with those of (+)-**9**·HCl prepared from tetrahydroisoquinoline (±)-**9** (see below).

(1*S*)- and (1*R*)-1,2,3,4-Tetrahydro-1-benzoyl-6,7-dimethoxy-2-[((*R*)-1-phenylethyl)carbamoyl]isoquinoline (8a,b). A diastereoisomeric mixture of compound **8a** and **8b** was prepared from 1-benzyl-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline[24] (4.25 g, 15 mmol) and (*R*)-(+)-1-phenylethyl isocyanate (2.45 g, 16.6 mmol) with quantitative yield by the procedure described previously for analogues **4a,b**.

Isomer **8b** was obtained by fractional crystallization from ethyl acetate of the crude reaction product with 24% of yield: mp 162–164 °C; $[\alpha]^{27}_D$ −108.4° (*c* 1.1, $CHCl_3$); ^1H NMR δ 3.75 (s, 3 H, 7-OCH_3), 3.86 (s, 3 H, 6-OCH_3), 4.76–4.91 (m, 2 H, PhC*H*CH_3, 1-H), 6.41, 6.81 (2 s, 1 H each, H-8, H-5); CIMS *m/z* 431 (M^+ + 1, 100), 284 (10). Anal. Calcd for $C_{27}H_{30}N_2O_3$: C, 75.32; H, 7.02; N, 6.50. Found: C, 75.32; H, 7.06; N, 6.51.

Isomer **8a** was isolated from mother liquors by flash chromatography (SiO_2, 1:100, hexane–ethyl acetate, 4:1): yield 23%; mp 123–124 °C; $[\alpha]^{27}_D$ +52.3° (*c* 0.9, $CHCl_3$); ^1H NMR δ 3.80 (s, 3 H, 7-OCH_3), 3.85 (s, 3 H, 6-OCH_3), 4.85 (m, 1 H, pHC*H*CH_3), 5.01 (m, 1 H, 1-H), 6.30, 6.61 (2 s, 1 H each, H-8, M-5); CIMS *m/z* 431 (M^+ + 1, 53), 284 (100), 192 (60). Anal. Calcd for $C_{27}H_{30}N_2O_3 \cdot {}^1/_3H_2O$: C, 74.29; H, 7.08; N, 6.46. Found: C, 74.20; H, 6.97; N, 6.39.

(+)-(1*S*)-1,2,3,4-Tetrahydro-1-benzyl-6,7-dimethoxyquinoline Hydrochloride ((+)-9·HCl). A solution of **8a** (0.446 g, 1 mmol) in 1 M sodium *n*-pentoxide in *n*-pentanol (5 mL) was refluxed for 2 h under argon and worked up according to the procedure previously described for alcoholysis of **4a** to give (−)-**9** in 85% yield. It was characterized in the form of hydrochloride salt (+)-**9**·HCl; mp 185–187 °C (from methanol–isopropyl ether); $[\alpha]^{27}_D$ +27.1° (*c* 1, CH_3OH); ^1H NMR δ 3.43 (s, 3 H, 7-OCH3), 3.43–3.77 (m, 2 H, H-α), 3.83 (s, 3 H, 6-OCH_3), 4.74 (br d, *J* = 7 Hz, 1 H, H-1), 5.89 (s, 1 H, H-8), 6.57 (s, 1 H, H-5); CIMS *m/z* 284 (M^+ + 1, 100), 192 (20). Anal. Calcd for $C_{18}H_{22}NO_2Cl \cdot {}^1/_3H_2O$: C, 66.35; H, 6.80; N, 4.30; Cl, 10.88. Found: C, 66.74; H, 6.96; N, 4.33; Cl, 10.91.

(−)-(1*R*)-1,2,3,4-Tetrahydro-1-benzoyl-6,7-dimethoxyisoquinoline Hydrochloride ((−)-9·HCl). (−)-**9**·HCl was prepared from **8b** in 85% yield according to the above procedure: mp 185–187 °C (from methanol–isopropyl ether); $[\alpha]^{27}_D$ −27.5° (*c* 1, CH_3OH); CD (*c* = 0.005 M, CH_3OH) $[\theta]_{310}$ 0, $[\theta]_{281}$ −5320, $[\theta]_{268}$

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−1480, $[\theta]_{266}$ −1840, $[\theta]_{262}$ −360, $[\theta]_{259}$ −640, $[\theta]_{235}$ −17 200, $[\theta]_{231}$ −16 400, $[\theta]_{211}$ −42 400, $[\theta]_{203}$ 0, $[\theta]_{195}$ +57600. Free base $[\alpha]$ +0.57° (c 1.9, CH_3OH). ^1H NMR and MS spectra are identical with those of compound (+)-**9**·HCl. Anal. Calcd for $C_{18}H_{22}NO_2Cl\cdot{}^1/_3H_2O$: C, 66.35; H, 6.80; N, 4.30; Cl, 10.88. Found: C, 66.30; H, 6.85; N, 4.29; Cl, 10.94.

It is worth noting that (+)-base **9** affords a hydrochloride with a negative specific rotation when measured in methanol.

CD Spectrum of (−)-(1S)-Norreticuline: (c = 0.005 M, CH_3OH) $[\theta]_{310}$ 0, $[\theta]_{291}$ +5360, $[\theta]_{272}$ 0, $[\theta]_{262}$ +160, $[\theta]_{248}$ 0, $[\theta]_{243}$ −620, $[\theta]_{240}$ 0, $[\theta]_{236}$ + 2500, $[\theta]_{227}$ +900, $[\theta]_{213}$ +16 000, $[\theta]_{207}$ 0, $[\theta]_{202}$ −16 800, $[\theta]_{195}$ −8000.

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Registry No. 1, 22190-45-0; (−)-**2**, 120142-61-2; (+)-**2**, 120142-62-3; (±)-**2**, 120034-51-7; (±)-**3**, 120034-52-8; (−)-**4a**, 120034-53-9; (−)-**4b**, 120142-59-8; **5** (isomer 1), 120142-60-1; **5** (isomer 2), 120142-67-8; (+)-**6**, 120142-63-4; (−)-**6**, 120142-64-5; (±)-**6**, 120142-65-6; (±)-**7**, 120142-66-7; (+)-**8a**, 120034-55-1; (−)-**8b**, 120034-56-2; (−)-**9**, 47145-37-9; (+)-**9**·HCl, 14546-74-8; (+)-**9**, 47145-36-8; (−)-**9**·HCl, 14546-73-7; (±)-**9**, 3901-25-5; (±)-**10**, 120034-54-0; (R)-(+)-1-phenylethyl isocyanate, 33375-06-3; (−)-(1S)-norreticuline, 4781-58-2.

Cathodic Acylation of 1,2-Acenaphthenedione

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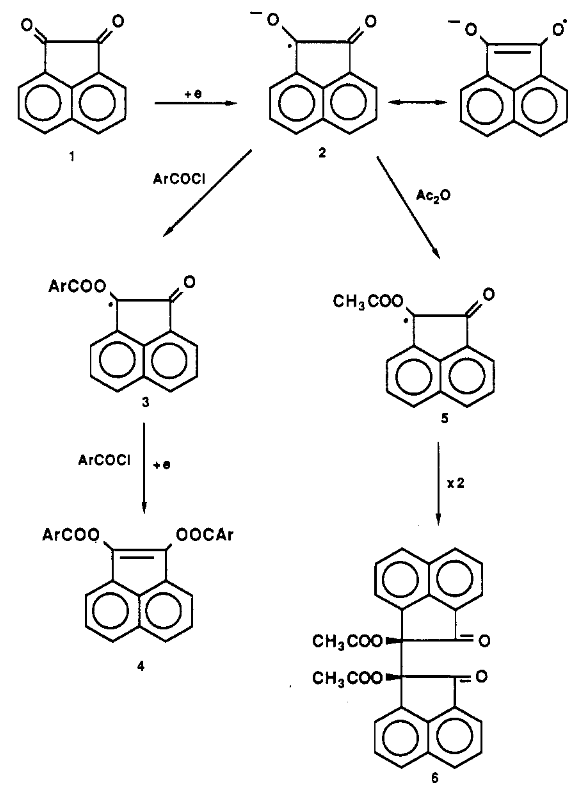
The papers about cathodic reduction of aryl α-diketones have been mainly focused on benzil,[2-6] with the majority of the electrolyses being carried out in protic media. The first products are *cis*- and *trans*-stilbenediols which later are converted into benzoin by ketolization. Overall the reaction corresponds to a two-electron, two-proton process. Either a direct two-electron transfer or two electrochemical steps, each with single-electron transfer, via the semidione radical anion, have been postulated.

The electrochemical reduction of simple carbonyl compounds by single-electron transfer, protonation, and coupling processes lead to the corresponding glycols or pinacols through ketil radical anion intermediates.[7] In contrast, a similar dimerization for aryl 1,2-diketones giving diketopinacols has not been observed. This probably happens because fast protonation of the first radical anion intermediate gives a neutral radical, which is easily reduced to a relatively stable enolate anion. Thus, the radical species is too short-lived to undergo a coupling process.

Scheme I



After studying the cathodic reduction of aroyl chlorides,[8,9] we postulate a ECEC-type reaction mechanism. The first electrochemical step with single-electron transfer leads to the corresponding aroyl free radicals. A second chemical step with coupling of the generated aroyl radicals gives the corresponding aryl 1,2-diketones, which are reduced in the same way as benzil in protic medium but with acylation of the anionic electrogenerated intermediates instead of protonation, e.g. reduction of benzoyl chloride which gives *cis*- and *trans*-stilbenediol dibenzoates in high yield. This mechanism was later studied in detail.[10] In spite of the fact that acylation is relatively slower than protonation, intermolecular coupling giving pinacol derivatives has not been detected.

However, we now report that electroacylation of 1,2-acenaphthenedione by its selective cathodic reduction in the presence of nonelectroactive acylating reagents provides two different types of products in good yields. The compounds are either diacylated two-electron reduction products or a diketopinacol diester, which arises by single-electron transfer and by coupling of the electrogenerated intermediates. The behavior disparity depends exclusively on the acylating reagent used. This is the first time that this peculiar reactivity has been observed in this class of diketones.

Cathodic reductions of 1,2-acenaphthenedione (**1**) were carried out at mercury pool cathode under constant potential with the catholyte solution containing either benzoyl or p-toluyl chlorides. The electricity consumption was 2 F/mol of 1,2-acenaphthenedione. The reaction products were characterized on the basis of their elemental analyses and their MS, IR, and ^1H NMR spectra as the corresponding 1,2-bis(aroyloxy)acenaphthylenes **4**. However,

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