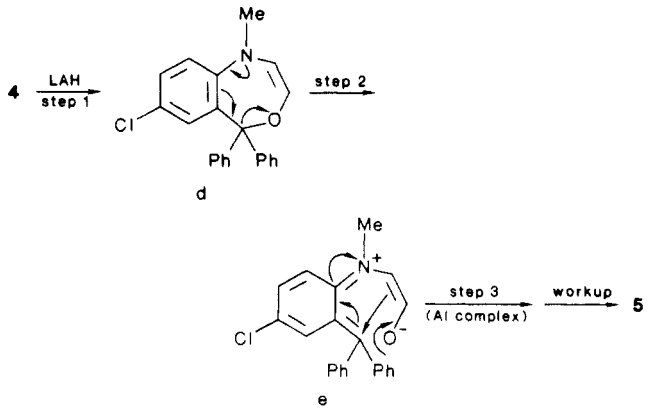
Scheme IV

mechanism B



filtered, and the solid washed with H_2O and ether to give 8.15 g of compound **2**, mp 185–186.5 °C. The filtrate was separated into layers, and the aqueous layer was extracted once with ether. The combined ether extract was washed with cold solvents as follows: H_2O (100 mL), 10% HCl (3 × 50 mL), H_2O, $NaHCO_3$ solution (3 × 50 mL), and saturated salt solution. It was dried ($MgSO_4$) and evaporated. Crystallization from ether gave 5.05 of **2**, g mp 184–185 °C. Yield: 68%. The analytical sample melted at 186–187 °C (from ether): UV (EtOH) λ_{max} 252 nm (ϵ 14 450), 289 sh (1050); IR 3410, 3280 (NH/OH), 3060 (=CH), 1650 (C=O), 1600, 1585, 1495 (C=C), 1535 (amide H), 1445, 1395, 1270 (CH/C-N), 835, 765, 750, 700, 655 (Ar/ether) cm^{-1}; ^1H NMR (Me_2SO-d_6) δ 3.92 (C(=O)CH_2Cl, A_2, s), 6.5 (H_3, d, $J_{3,4}$ = 3 Hz), 7.4 (H_5, d of d, $J_{5,6}$ = 8 Hz), 8.18 (H_6, d), 7.35 (Ph's), 10.4 (NH-C=O); mass spectrum, *m/e* 385.

Anal. Calcd for $C_{21}H_{17}Cl_2NO_2$: C, 65.29; H, 4.44; Cl, 18.36; N, 3.63. Found: C, 65.24; H, 4.61; Cl, 18.46; N, 3.60.

7-Chloro-1,5-dihydro-5,5-diphenyl-4,1-benzoxazepin-2-(3*H*)-one (3). A solution of **2** (88.84 g; 0.230 mol) in 460 mL of THF was added during 15 min to a suspension of NaH (19.36 g; 0.46 mol of 57% dispersion in mineral oil, washed with ether) in 2300 mL of THF. The mixture was stirred at room temperature for 20 h and then refluxed for 1.75 h. It was evaporated, and the residue was cooled in ice and stirred with 2 L of H_2O for 30 min (200 mL of ether was added to aid solidification). The suspension was filtered and the solid washed with H_2O and ether. Crystallization from MeOH gave 48.53 g of compound **3** as prisms, mp 211.5–212.5 °C. Second crop, 11.1 g, mp 197–198 °C. Yield: 74%. Both crops were identical by NMR, TLC and mixed mp with the polymorph obtained from a previous run which melted at 197–198 °C (from MeOH) and was analyzed: UV (EtOH) λ_{max} 254 nm (ϵ 15 950), 287 sh (2200), 294 sh (1600); IR 3210, 3120, 3080 (NH/=CH), 1690, 1675 (C=O), 1600, 1575, 1685 (C=C), 1415, 1400 (CH), 1220, 1110 (C-N/C-O), 885, 835, 760, 700 (Ar) cm^{-1}; ^1H NMR (Me_2SO-d_6) δ 4.28 (H_3, s), 6.48 (H_6, d, J = 2.5 Hz), 7.45 (H_8, d of d), 7.0–7.5 (H_9), 7.0–7.5 (Ph's), 10.1 (NHC=O); mass spectrum, *m/e* 349.

Anal. Calcd for $C_{21}H_{16}ClNO_2$: C, 72.10; H, 4.61; Cl, 10.13; N, 4.01. Found: C, 71.95; H, 4.48; Cl, 10.22; N, 4.02.

7-Chloro-1,5-dihydro-1-methyl-5,5-diphenyl-4,1-benzoxazepin-2(3*H*)-one (4). Sodium hydride (0.421 g; 0.01 mol of 57% dispersion in mineral oil) was added to a solution of **3** (3.49 g; 0.01 mol) in 100 mL of DMF, and the mixture was stirred for 2.25 h. The resulting solution was treated with methyl iodide (2.84 g; 0.02 mol) during 2 min and then stirred for 24 h (allowed to stand 48 h). It was evaporated, the residue was taken up in CH_2Cl_2–H_2O, and the organic layer was washed with H_2O and saturated salt solution, dried ($MgSO_4$), and evaporated. The residue was crystallized from ether–petroleum ether (30–60 °C) to give 2.60 g of compound **4**, mp 163.5–164.5 °C. Second crop: 0.261 g, mp 164–165 °C. Yield: 79%.

The analytical sample melted at 164–165 °C: UV (EtOH) λ_{max} 253 nm (ϵ 12 900), 258 sh (11 450), 264 sh (8350), 271 sh (4900), 287 sh (1050), 291 sh (800); IR (C=O), 1685, 1640, 1590, 1565, 1475 (C=C), 1445, 1410 (CH), 1095, 1075 (C-O), 835, 770, 755, 700 (Ar) cm^{-1}; NMR ($CDCl_3$) δ 2.59 (CH_3NC=O), 4.3 (H_3, s), 6.65 (H_6, d, J = 2.5 Hz), 7.1 (H_9, d, J = 9 Hz), 7.3 (Ph's), 7.4 (H_8, dd, J = 2.5, 9 Hz); mass spectrum, *m/e* 363.

Anal. Calcd for $C_{22}H_{18}ClNO_2$: C, 72.62; H, 4.99; Cl, 9.74; N, 3.85. Found: C, 72,57; H, 5.22; Cl, 9.63; N, 3.92.

5-Chloro-1-methyl-3,3-diphenyl-2-indolinecarboxaldehyde (5). A solution of **4** (4.57 g; 0.0126 mol) in 100 mL of THF was added to a solution of LAH (4.57 g) in 250 mL of THF during 10 min, and the mixture was stirred at room temperature for 19.5 h. It was cooled in ice and decomposed in succession with 4.6 mL of H_2O, 4.6 mL of 15% aqueous NaOH, and 13.8 mL of H_2O. The suspension was then stirred for 1 h and filtered and the cake washed with THF. The filtrate was dried ($MgSO_4$) and evaporated to give 4.6 g of an amorphous yellow solid. Crystallization from MeOH at −70 °C gave a solid which showed two spots on TLC (silica gel, 50% ethyl acetate–cyclohexane). The total product was therefore chromatographed on 450 g of silica gel by using 10% ethyl acetate–cyclohexane. Fractions 1–5 (625 mL) gave no material. Fractions 6–124 (25 mL each) gave 3.0 g of compound **5** (pure by TLC and identical by TLC and MNR with the crystallized sample below). Crystallization from MeOH at −70 °C gave 1.5 g of **5**: mp 111–117 °C; UV (EtOH) λ_{max} 258 nm (ϵ 9250), 319 (2850); IR (C=O), 1720 1600, 1480 (C=C), (C-N), 1300, 1210, 1100, 820, 700 (Ar) cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.98 (NCH_3), 4.55 (H_2, d, J = 4.0 Hz), 6.5 (H_7, $J_{6,7}$ = 9 Hz), 7.0–7.6 (H_4, H_6, Ph's, m), 9.1 (CHO, d, J = 4.0 Hz); mass spectrum, *m/e* 347.

Anal. Calcd for $C_{22}H_{18}ClNO$: C, 75.96; H, 5.22; Cl, 10.19; N, 4.03. Found: C, 76.24; H, 5.34; Cl, 10.26; N, 4.13.

Better crystals were obtained for X-ray by crystallization from ethyl acetate–petroleum ether (30–60 °C), mp 126–127 °C.

5-Chloro-1-methyl-3,3-diphenyl-2-indolinemethanol (6). Sodium borohydride (0.3 g) was added to a solution of **5** (0.3 g) in 10 mL of EtOH and stirred for 21 h. EtOH was evaporated at 35 °C in vacuo, 10 mL of H_2O and 25 mL of ether were added, and the aqueous layer was extracted once more with ether. The combined ether extract was washed once with H_2O and saturated salt solution, dried ($MgSO_4$), and evaporated to give 0.286 g of an oily solid. The product (0.256 g) was chromatographed on 25.6 g of silica gel using 10% ethyl acetate–cyclohexane. Fractions 1–3 (220 mL) gave no material. Fractions 4–7 (10 mL each) gave a trace. Fractions 8–18 (10 mL each) gave no material. Fractions 19–39 (10 mL each) gave 0.195 g of compound **6** (single spot on TLC). Crystallization from petroleum ether (30–60 °C) gave 0.113 g: mp 58 °C (effervesces); UV (EtOH) λ_{max} 262 nm (ϵ 9600), 266 sh (9300), 272 sh (7760), 318 (2660); IR 3370 (OH), 1595, 1490, 1480 (C=C), 1045, 1035 (C-O), 815, 700 (Ar) cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.9 (OH, exchangeable), 2.95 (NCH_3, 3.6 (CH_2O, m), 4.27 (H_2, t), 6.45 (H_7, d, $J_{6,7}$ = 9 Hz), 7.0–7.5 (H_4, H_6, Ph's, m); mass spectrum, *m/e* 349.

Anal. Calcd for $C_{22}H_{20}ClNO$: C, 75.52; H, 5.76; Cl, 10.13; N, 4.00. Found: C, 75.49; H, 5.98; Cl, 10.02; N, 4.00.

In another experiment the product was obtained after chromatography without crystallization as a polymorph melting at 104–107 °C. It was identical with the above crystallized sample as shown by IR, UV, and TLC.

Registry No. 1, 21741-00-4; **2**, 98414-59-6; **3**, 98414-60-9; **4**, 105104-37-8; **5**, 105104-38-9; **6**, 105104-39-0.

An Unusual Isomerization of a Furan-Containing Compound

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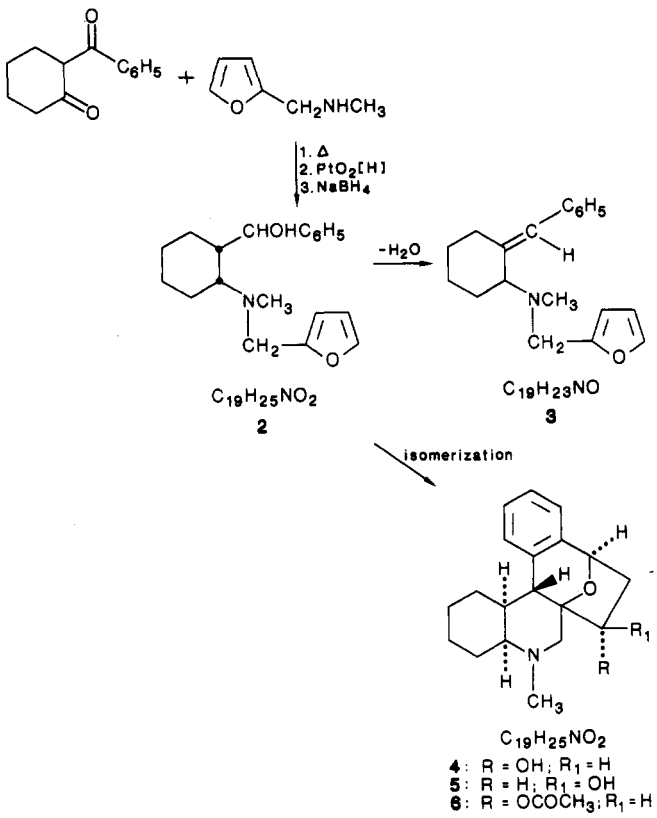
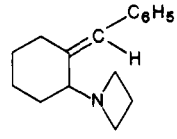
In connection with our interest in tazadolene succinate, a structurally novel nonopioid analgesic with antidepressant properties[1] (1), we became interested in compound

0022-3263/86/1951-5002$01.50/0

Scheme I



which incorporates the furanoid-type allylic system as a substituent on the nitrogen atom and could provide a transition from an agonist to the antagonist in its biological profile.



To this end, 2-benzoylcyclohexanone was reacted with *N*-methylfurfurylamine, and the intermediate was reduced first by catalytic hydrogenation, and then with sodium borohydride to give the amino alcohol **2** (see Scheme I).

Attempted dehydration of **2** did not produce compound **3** but instead gave a small yield of compound **4**. Extended experimentation culminated in using 9% aqueous hydrochloric acid for 4.5 h at 96 °C, and produced a reasonable yield of **4** along with a small amount of isomer. We assign tentatively structure **5** to this isomer.

Compound **4** is isomeric with its precursor, compound **2**, and its structure was established by single-crystal X-ray crystallography.[2] We propose the mechanism shown in Scheme II[2a] to account for the transformation **2** → **4**.

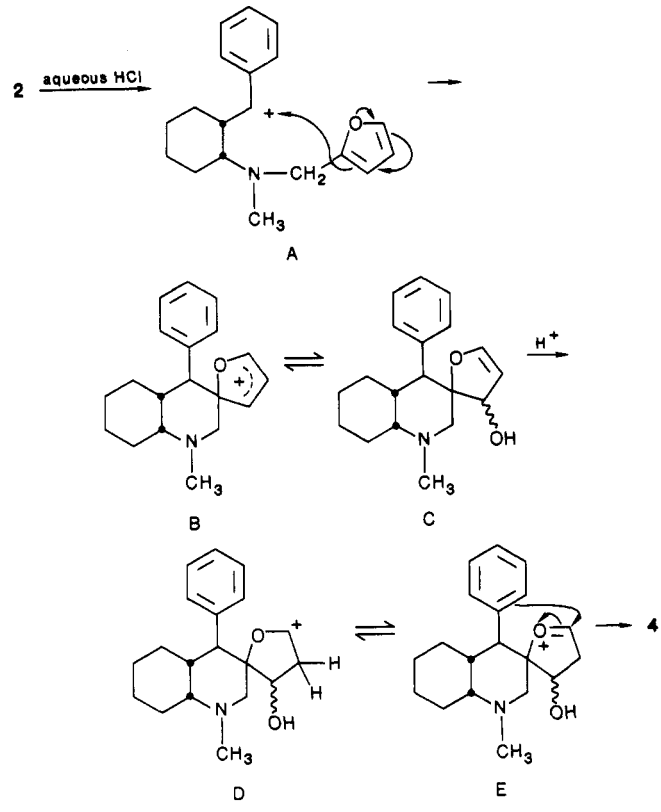
Intermediates A and B are responsible for C–C bond formation between the furan and the benzylic carbon. Intermediates C–E set the stage for the C–C bond formation between the five-membered ring and the aromatic carbon.

Formation of both isomers **4** and **5** is not surprising in view of the relatively nonspecific transformation B → C.

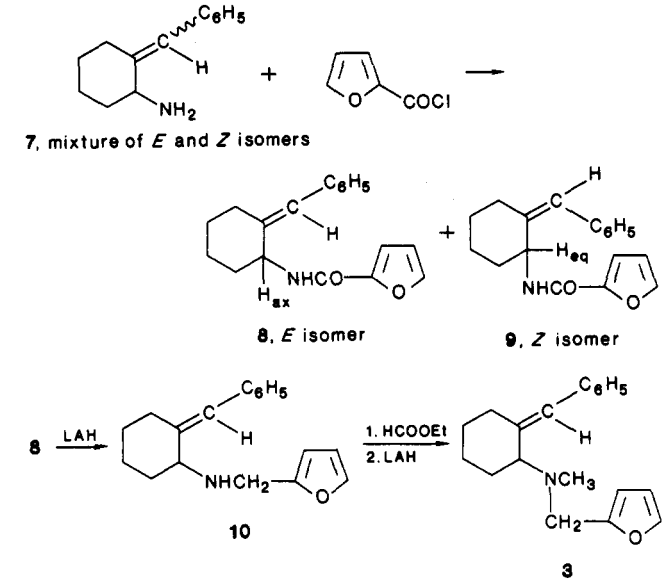
Furan chemistry is well-known for a number of intricate transformations,[3] and the above described reaction is a new addition to this class.

Our original goal, namely, synthesis of compound **3**, was accomplished as shown in Scheme III, and proceeded without mishaps.

Scheme II



Scheme III



(1) Von Voigtlander, P. F.; Chidester, C. G.; Kane, M. P.; Szmuszkovicz, J. accepted for publication in *Drug Design and Delivery*.

(2) To be submitted to *Acta Crystallog. Sect. C: Cryst. Struct. Commun.* (a) We thank the referee for pointing out the need for defining the nature of the nitrogen in Scheme II. The nitrogen could be present either in the nonprotonated form or in the protonated form (which will create a doubly charged intermediate). The third possibility would involve the protonated species, but the rearrangement could proceed without the generation of the carbonium ion.

(3) Meyers, A. I. *Heterocycles in Organic Syntheses*; Wiley-Interscience: New York, 1974. For a summary of furan equivalencies, see a recent paper by: Tanis, S. P.; Herrington, P. M. *J. Org. Chem.* **1985**, *48*, 4572.

Experimental Section

Melting points were taken in capillary tubes and are corrected. Ultraviolet spectra were determined on a Cary Model 14 spectrophotometer, IR spectra on a Perkin-Elmer Model 421 spectrophotometer, mass spectra at 70 eV on an Atlas Model CH-4 spectrometer, and NMR spectra on a Varian Model XL-100 spectrometer. NMR peaks are recorded in parts per million downfield from tetramethylsilane.

***cis*-α-[2-[(2-Furanylmethyl)methylamino]cyclohexyl]-benzenemethanol (2).** A mixture of 2-benzoylcyclohexanone[4] (20.2 g, 0.1 mol), *N*-methylfurfurylamine (22.23 g, 0.2 mol, purchased from ROC), *p*-toluenesulfonic acid (0.5 g), and 200 mL of benzene was refluxed for 18 h with an azeotropic separator filled with 200 g of molecular sieve (4A). The mixture was concentrated, dissolved in 200 mL of absolute ethanol, and hydrogenated in presence of 1 g of PtO_2 at 52.5 psi initial pressure of 6.5 h. It was then filtered and concentrated, and the residue was stirred for 1.5 h with 200 mL of 10% HOAc and 200 mL of ether. The acid layer was separated, backwashed with ether, cooled in ice, and basified with 20% NaOH. The product was extracted with $CHCl_3$ and worked up as usual.[5] The residue (11.82 g) showed a strong 1675-cm^{-1} absorption in the infrared and very little alcohol by NMR. It was dissolved in 200 mL of absolute EtOH and $NaBH_4$ (11 g) was added portionwise during 10 min. The mixture was stirred for 18 h and concentrated. The residue was taken up in ether and H_2O and worked up as usual.[5] The residue showed no carbonyl in the infrared spectrum, and the NMR spectrum was compatible with a mixture of alcohols. Crystallization from ether gave 3 g of colorless microcrystals, mp 116–117 °C. The filtrate was rich in this compound and showed four other spots by TLC (silica gel, 10% MeOH–$CHCl_3$): UV (EtOH) λ_{max} 212 nm (ε 32500), 216 (sh, 29800), 247 (s, 515), 252 (476), 257 (491), 261 (sh, 383), 264 (371), 267 (249); mass spectrum, *m/e* 299; IR 3120 (OH), 2800 (N–C–H), 1625, 1600, 1585, 1495, 1490 (C=C), 1045, 1020, 775, 760, 750, 715, 700 (C–O, C–N, other) cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.9–2.1 (CH_2,CH), 2.5 (3 H, s, NCH_3), 3.24 (1 H, m, NCH), 3.6–4.0 (2 H, AB, NCH_2), 5.0 (1 H, s, CHO), 6.3 (2 H, m, C=C*H*C*H*=CHO), 6.7 (1 H, br, OH exchangeable), 7.1–7.4 (6 H, m, Aromatic + C=CHCH=C*H*O). The line width of CHN suggests an equatorial H; the pattern and $\nu_{1/2}$ are not similar to those observed in 1,2-diaxial (trans) systems. We cannot assign the CH adjacent to CHOH. On the other hand the coupling for CHCHOH is small (less than 1 Hz) so that the dihedral angle is close to 90°. We suggest that the compound is cis and the configuration of side chain asymmetric center is analogous to a similar case described by us in detail previously.[6]

Anal. Calcd for $C_{19}H_{25}NO_2$: C, 76.22; H, 8.42; N, 4.68. Found: C, 76.08; H, 8.80; N, 4.36.

1,2,3,4,4a,5,6,8,12b,12c-Decahydro-5-methyl-[4a*S*-(4aα,8α,12bβ,12cα,14aα)]-6a,8-ethano-6a*H*-[2]benzopyrano-[3,4-*c*]quinolin-14-ol. (4). A mixture of **2** (15.7 g, 0.053 mol) and 280 mL of 9% aqueous HCl was heated on the steam bath with mechanical stirring for 4.5 h. The inside temperature was 96 °C, and a solution resulted after 3 h. It was cooled in ice, basified with 20% NaOH, extracted well with $CHCl_3$, and worked up as usual.[5] The residue (14 g) was triturated with ether to give 6.44 g of **4** as colorless needles, mp 248–250 °C raised to 249–250 °C on recrystallization from MeOH. The second crop, 3.13 g, mp 235–237 °C, slightly impure. Yield: 61%.

The filtrate was concentrated to give 0.84 g, mp 212–214 °C, of a mixture of **4** and **5**. Chromatography of 0.8 g on 80 g of natural alumina in 3% MeOH–ether gave 0.34 g of **5**, which was crystallized from MeOH, mp 212–213 °C.

Compound 4: UV (EtOH) 215 nm (sh, ε 8671), 258 (sh, 296), λ_{max} 264 nm (ε 358), 272 (319), 290 (sh, 62), 300 (sh, 56); HR mass spectrum, found 299.1875, calcd $C_{19}H_{25}NO_2$ 299.1885; IR 3160 (OH), 2780 (N–C–H), 1605, 1585, 1485 (C=C), 1220, 1095, 1055, 1030, 865, 790, 755, 735, (C–O, other) cm^{-1}; ^1H NMR

	mult	δ Me$_2$SO	δ $CDCl_3$
Ph'S		6.8–7.2	6.8–7.2
PhCHO	doublet	4.96	5.08 (J = 6 Hz)
CHOH	triplet	3.92	4.24 (J = 7 Hz)
CH_3N		2.3	2.45

^{13}C NMR ($CDCl_3$) 140 (s), 134 (s), 132 (d), 127 (d), 126 (d), 124 (d) [Ph's], 82 (s, >CO), 76 (d), 75 (d) [CHO], 62 (d, CHN), 54 (t, $>CH_2N$), 48.5 (t CH_2CHO), [CH's], 40 (d), 39 (d) 16 (t), 21 (t), 25.5 (t), 27 ppm (t) [cyclohexyl].

Anal. Calcd for $C_{19}H_{25}NO_3 \cdot {}^1/_3H_2O$: C, 74.72; H, 8.47; N, 4.59. Found: C, 74.77; H, 8.38; N, 4.58.

Compound 5: UV (EtOH) 259 nm (sh, ε 296), λ_{max} 265 nm (ε 386), 272 (350); mass spectrum, *m/e* 299; IR 3160 (OH), 2800, 2790 (N–C–H), 1605, 1580, 1490 (C=C), 1080, 1055, 1025, 1010, 870, 825, 760 (C–O, other) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.0–2.28 (CH_2's, cyclohexyl), 2.4 (CH_3N), 2.9 (CHN), 3.0 (CH_2N), 3.96 (CHOHCH$_2$, d, J = 9 Hz), 5.02 (PhCHO, d, J = 6 Hz), 6.9–7.25 (Ph's).

Anal. Calcd for $C_{19}H_{25}NO_2$: C, 76.22; H, 8.42; N, 4.68. Found: C, 76.13; H, 8.45; N, 4.65.

Preparation of Acetate 6. A mixture of compound **4** (1 g) and acetic anhydride (5 mL) was heated at 95 °C for 15 min. The resulting solution was concentrated, and the residue was warmed with H_2O for 5 min, cooled, and brought to pH 8 with Na_2CO_3. The product was extracted with $CHCl_3$ and worked up as usual.[5] The residue (1.2 g) crystallized from ether: mp 148–149 °C; UV (EtOH) 264 nm (sh, ε 294), λ_{max} 272 nm (ε 236); mass spectrum, *m/e* 341; IR 2800, 2760 (N–C–H), 1725 (C=O), 1600, 1580, 1985 (C=C), 1365, 1285, 1265, 1255, 1220, 1045, 1040, 1030, 755, 740 (C–O, other) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.0–1.8 (CH_2's), 2.06 (CH_3C), 2.46 (CH_3N), 2.6–2.9 (CH_2N AB), 2.86 (CHN), 5.1–5.25 (PhCHO and CHOC), 6.9–7.2 (Ph's).

Anal. Calcd for $C_{21}H_{27}NO_3$: C, 73.87; H, 7.97; N, 4.10. Found: C, 73.73; H, 7.98; N, 4.07.

(*E*)- and (*Z*)-*N*-[2-(Phenylmethylene)cyclohexyl]-2-furancarboxamide (8 and 9). A solution of 2-furoyl chloride (7.05 g, 0.054 mol) in 50 mL of ether was added dropwise during 1 h to a solution of compound **7**[1] (mixture of *E* and *Z* isomers, 10 g, 0.054 mol) and triethylamine (5.45 g, 0.054 mol) in 200 mL of ether. The initially formed suspension became a solution after 6 h. The mixture was stirred for a total of 22 h. Saturated $NaHCO_3$ (200 mL) was added, and the organic layer was worked up as usual.[5] The resulting oil (13.6 g) was crystallized from ether–petroleum ether (30–60 °C) to give 7 g of the *E* isomer **8**, mp 117–118 °C. The filtrate was concentrated and the residue (6.6 g) chromatographed on 660 g of silica gel by using 25% EtOAc–cyclohexane–1% NH_4OH and collecting 30-mL fractions. Fractions 1–40 gave no material. Elution with 50% EtOAc–cyclohexane–1% NH_4OH, fractions 41–55 gave no material. Fractions 56–66 gave 0.98 g of the *Z* isomer **9**. Crystallization from ether–petroleum ether (30–60 °C) gave colorless needles, mp 99.5–100.5 °C. Fractions 67–73 gave no material. Fractions 74–89 gave 1.82 g of additional *E* isomer **8**. Fractions 90–110 gave no material. Elution with 5% MeOH–EtOAc–1% NH_4OH, fractions 111–214, gave no material. Fractions 215–260 gave 2.2 g of starting material.

***E* isomer 8**: UV (EtOH) λ_{max} 246 nm (ε 25800); mass spectrum, *m/e* 281; IR 3280 (NH), 1645 (C=O), 1595, 1535, 1500, 1005, 750, 705 (C=C/amide II/other) cm^{-1}; ^1H NMR ($CDCl_3$) [the pattern of CHN suggests that NHC(=O)–furan group is equatorial] δ 1.4–2.2 (CH_2's, cyclohexyl), 2.8 (C*H*CH=C, axial), 4.7 (CHNC=O, axial), 6.4 (CH=C), 6.5 (NHC=O), 6.5 (C=CHC*H*=CHO), 7.2 (C=CHCH=C*H*O), 7.2 (Ph's).

Anal. Calcd for $C_{18}H_{19}NO_2$: C, 76.84; H, 6.81; N, 4.98. Found: C, 76.73; H, 6.79; N, 5.01.

***Z* isomer 9**: UV (EtOH) λ_{max} 248 nm (ε 24750); mass spectrum, *m/e* 281; IR 3320, 3280 (NH), 1640, 1630 (C=O), 1600, 1570, 1530, 760, 700 (C=C/amide II, other) cm^{-1}; ^1H NMR ($CDCl_3$) [the pattern of CHN suggests that NHC(=O)–furan group is axial] δ 1.6–2.2 (CH_2's, cyclohexyl), (CH_2CH=C), 2.4 (C*H*NHC=O, equatorial), 5.2 6.4, 7.1, 7.4 (C=CHCH=CHO), 6.6 (NHC=O), (Ph's) 7.3.

Anal. Calcd for $C_{18}H_{19}NO_2$: C, 76.84; N, 6.81; N, 4.98. Found: C, 76.58; H, 6.94; N, 5.00.

(4) Campbell, R. D.; Gilow, H. M. *J. Am. Chem. Soc.* **1962**, *84*, 1440. Eistert, B.; Reiss, W.; Wurzler, H. *Ann.* **1961**, *650*, 146.

(5) The organic layer was washed with H_2O saturated NaCl solution, dried ($MgSO_4$), and concentrated.

(6) Compare to amino alcohol **4A** described by: Szmuszkovicz, J.; Skaletzky, L. L. *J. Org. Chem.* **1967**, *32*, 3300.

(*E*)-*N*-[2-(Phenylmethylene)cyclohexyl]-2-furanmethanamine Maleate (10). A solution of compound **8** (7 g, 0.025 mol) in 100 mL of THF was added to a solution of LAH (7 g) in 200 mL of THF, and the mixture was refluxed 6 h. It was cooled in ice and decomposed in succession with 7 mL of H_2O, 7 mL of 15% NaOH, and 21 mL of H_2O. The mixture was stirred 1 h and filtered and the filtrate dried ($MgSO_4$) and concentrated. The residue (5 g) was dissolved in ether, extracted with cold 10% HCl (3 × 20 mL). The acid extract was basified with 20% NaOH, extracted with ether, and worked up as usual[5] to give 1.3 g of yellow oil. The "neutral" component was examined by TLC only. The basic fraction was converted to the maleate. It was crystallized from MeOH–ether: mp 162–163 °C; UV (EtOH) λ_{max} 241 nm (ϵ 16 050); mass spectrum, *m/e* 267; IR 2800, 2720, 2620, 2560, 2480 (NH/acid OH), 1705 (C=O), 1640, 1620, 1525 (C=C/CO_2^-/NH_2^+), 1395, 1365, 1215, 1155, 805, 750, 700 (C–O/other) cm^{-1}; ^1H NMR (Me_2SO-d_6) [the pattern of CHN suggests that $NHCH_2$–furan group is axial] δ 1.4–2.2 (CH_2's, cyclohexyl), 4.2 (NCH_2C=CHCH=CHO), 3.8 (CHN, equatorial), 6.6 (C=CH-CH=CHO), 6.6 (CH=C), 6.05 (HOOCCH=CHCOOH), 7.3 (C=CHCH=CHO), 7.3 (Ph's).

Anal. Calcd for $C_{18}H_{21}NO{\cdot}C_4H_4O_4$: C, 68.91; H, 6.57; N, 3.65. Found: C, 68.64; H, 6.75; N, 3.84.

(*E*)-*N*-Methyl-*N*-[2-(phenylmethylene)cyclohexyl]-2-furanmethanamine (3). A solution of compound **10** (1.1 g, 0.0041 mol) in 10 mL of ethyl formate was refluxed 23 h and concentrated. The residue was dissolved in ether, washed with 10% HOAc (3 × 10 mL) and saturated $NaHCO_3$, and worked up as usual.[5] The resulting *N*-formyl compound (0.86 g) showed a reasonable IR and NMR: HR mass spectrum; found 295.15867, calcd for $C_{19}H_{21}NO_2$ 295.15721.

A solution of the *N*-formyl compound in 10 mL of ether was added to a solution of LAH (0.9 g) in 25 mL of ether and refluxed 18 h. It was cooled and decomposed as described above. The residue was dissolved in 1% MeOH–$CHCl_3$, filtered through a short column of silica gel, and concentrated to give 0.54 g of compound **3**, which showed one spot on TLC (silica gel 5% MeOH–$CHCl_3$): GC (1% QF-1 column) t_r 4.52 min; 97.33%; UV (EtOH) 229 nm (sh, ϵ 11 650), λ_{max} 242 nm (ϵ 12 450); IR 2790 (N–C–H), 1655, 1600, 1575, 1495 (C=C), 1150, 1015, 1005, 740, 735 700 (C–O/other) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.4–2.1 (CH_2's cyclohexyl), 2.25 (CH_3N), 2.5 (CH_2CH=C), 2.86 (CHN, equatorial), 6.2, 6.3 (C=CHCH=CHO), 6.46 (CH=C), 7.25 (Ph's), 7.36 (C=CHCH=CHO); HR mass spectrum, found 281.176939, calcd for $C_{19}H_{23}NO$, 281.177953.

Registry No. **2**, 105206-07-3; **3**, 105229-44-5; **4**, 105206-08-4; **5**, 105307-21-9; **6**, 105229-45-6; (*E*)-**7**, 105206-09-5; (*Z*)-**7**, 105206-14-2; **8**, 105206-10-8; **9**, 105206-11-9; **10**, 105206-13-1; **10** (*N*-formyl deriv), 105206-15-3; 2-benzoylcyclohexanone, 3580-38-9; *N*-methylfurfurylamine, 4753-75-7; 2-furoyl chloride, 527-69-5.

Electrosynthesis in a Beaker: An Efficient Route to Morphinandienones Avoiding Potentiostats for Control of Electrode Potentials

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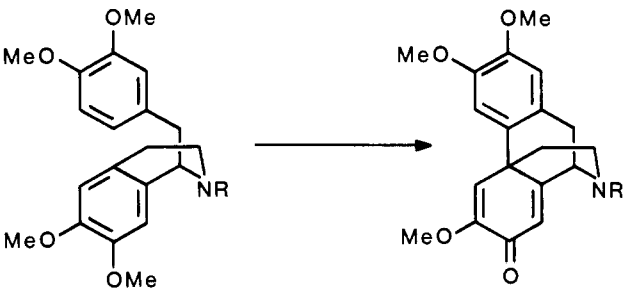
Reproducible electrosyntheses require control of the electrode potentials; potentiostats achieve this directly, but extra apparatus and specialized techniques are then required.[1a] Indirect control of electrode potentials can be carried out with much simpler apparatus, if the resistance of the solution and either the applied voltage or the current is controlled.[1b] We illustrate this general approach by the electrosynthesis of *O*-methylflavinantine (**4**) from laudanosine (**2**), which has previously been carried out at constant electrode potential.[2,3] It is a mechanistically complex process,[2c,e] and the product **4** is oxidized at an electrode potential only 0.1 V above that of the starting material **2**.[2f] Consequently, it provides a severe test of the scope of electrosynthesis by indirect control of electrode potentials.

Scheme I



(1) R = H (2) R = Me (3) R = H (4) R = Me

Results

In our most detailed studies we investigated the conversion of (±)-laudanosine (**2**) to (±)-*O*-methylflavinantine (**4**) in acetonitrile containing aqueous HBF_4 (Scheme I). This electrochemical reaction is reported to produce a yellow oil,[2,3] but we obtained a white crystalline product in over 70% isolated yield after flash chromatography. Analysis (^1H NMR, HPLC) of crude electrolysis mixtures showed higher yields, and a control experiment showed that about 10% loss of material occurred on the chromatographic column.

Experiments carried out at constant electrode potential showed decreasing currents as the reaction proceeded.[4] Currents for subsequent constant-*current* electrolyses were those continuing to flow after passing 1.1 equiv of electricity under optimum conditions for controlled-*potential* electrolysis (electrode potential 1.03–1.1 V, reference 0.1 M Ag^+/Ag). Therefore, in the constant-current experiments, the electrode potential will be less than or at most equal to the potential applied in corresponding controlled-potential experiments. Consequently overoxidation should be minimized. Experiments at constant current (but otherwise under the same reaction conditions and geometrical arrangement of the electrodes) gave virtually the same yields (ca. 80%) as the constant-potential experiments but required 50% longer electrolysis times. However, constant-current experiments were successful (ca. 70% yield) at higher concentrations of substrate (0.1 M) than the constant-potential experiments, which gave good yields below 0.02 M substrate but gave a dark intractable

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