of Canada for financial support.

Supplementary Material Available: Syntheses of diethyl [[1-(methoxymethyl)-2-phenyl-5-imidazolyl]methyl]malonate (**24**), **14**, and **15** (3 pages). Ordering information is given on any current masthead page.

An Efficient Synthesis of the 4a-Aryl-6-oxodecahydroisoquinolines

B. E. Cantrell, J. W. Paschal, and D. M. Zimmerman*

Lilly Research Laboratories, Eli Lilly and Company, Lilly Corporate Center, Indianapolis, Indiana 46285

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The synthesis of part structures of the morphine molecule and structural modification of these fragments has led to the discovery of many important medicinal agents and research tools. Consequently, the efficient synthesis of morphine base structures has been a goal of organic chemists for many years.

Recently the metalated enamines **1** (Figure 1) have proven to be useful in the synthesis of morphine part structures,[1-4] and we have reported that the *trans*-4a-aryldecahydroisoquinoline **2** can be readily synthesized in just two steps from **1**[1,4] by using the metalated enamine approach. Pharmacological evaluation of compound **2** and its *m*-hydroxy and N-substituted analogues identified potent opioid analgesic activities within this series,[4] and further modification of the aryldecahydroisoquinoline molecule was deemed appropriate.

Because several important opioid receptor ligands have been discovered through further functionalization of the 6-keto group in oxycodone (Figure 1) and related molecules,[5-8] the *trans*-4a-aryl-6-oxodecahydroisoquinoline **3** appeared to be a logical intermediate for new analogue synthesis. Though the synthesis of the isoquinoline **3** has been previously reported,[9] we sought a more direct route, which would make the synthesis of large quantities of **3** practical. In this paper we describe an efficient route to the *trans*-4a-aryl-6-oxodecahydroisoquinolines, employing as a key step the use of a metalated enamine. In addition, practical synthesis of the *cis*-4a-aryl-6-oxodecahydroisoquinoline **4** and the *cis*- and *trans*-4a-aryl-6-decahydroisoquinols **5**-**8** (Schemes I and II) was discovered.

Results and Discussion

The synthetic route employed for the synthesis of the oxodecahydroisoquinoline **3** is depicted in Schemes I and II. Alkylation of the metalated enamine **10**[10] with the oxirane derivative **22**, followed by spontaneous addition of the alcohol generated to the immonium moiety, gave in good yield a mixture of the oxa-8-azabicyclononanes **11** and **12**. Separation was achieved by using preparative HPLC,

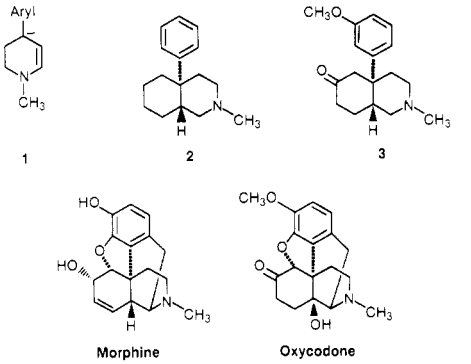
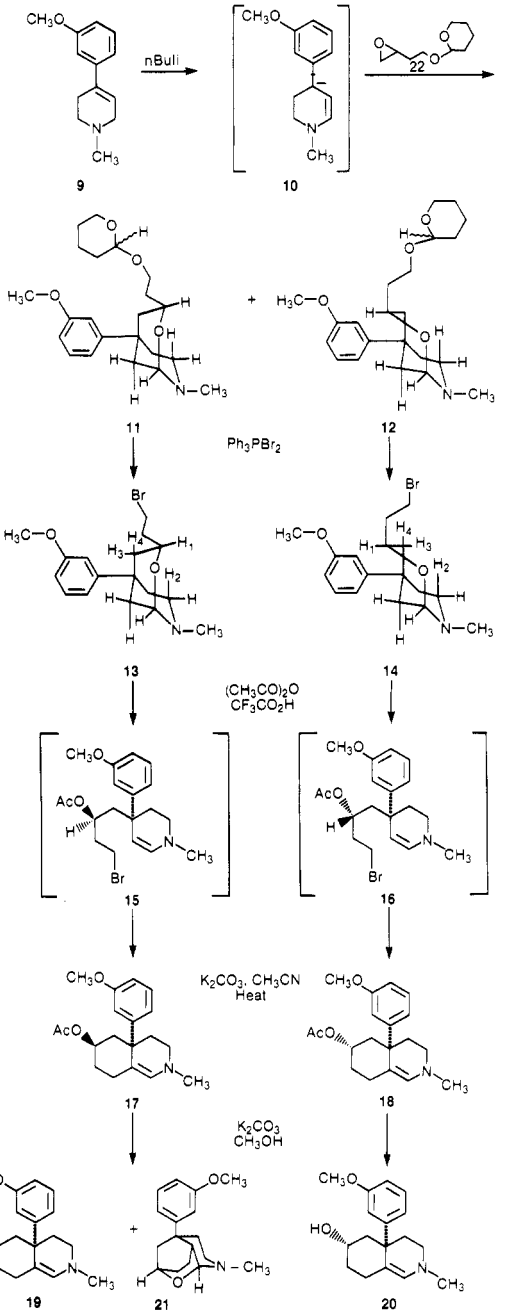


Figure 1.

Scheme I



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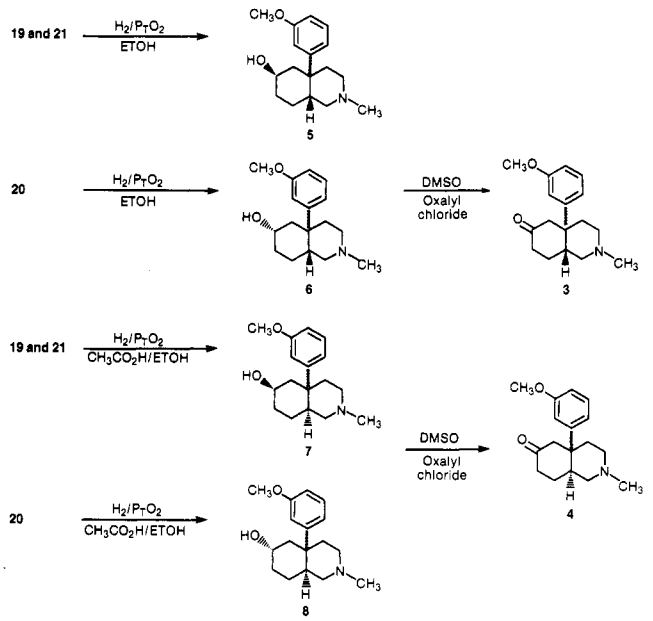
(10) We have since shown that **9**, which is the 3-methoxy analogue of the Parkinsonian-causing agent MPTP, is, like MPTP, highly neurotoxic. We now recommend using the *N*-ethyl derivative as described in Zimmerman, D. M.; Cantrell, B. E.; Reel, J. K.; Hemrick-Luecke, S. K.; Fuller, R. W. *J. Med. Chem.* **1986**, *29*, 1517-1520.

0022-3263/89/1954-1442$01.50/0

Scheme II



providing **11** and **12** in 40% and 34% yield, respectively. Reaction of each with triphenylphosphine dibromide afforded the 3-(2-bromoethyl) derivatives **13** and **14** in good yield.

The relative configurations of **13** and **14**, and consequently those of **11** and **12**, were deduced with ^{1}H NMR. For both compounds, the shape of the resonance for H-1 is the same, and proton decoupling shows that couplings to H-1 are 11.74 and 3.69 Hz. This requires that H-1 have an angle of either approximately 180° or 0° with respect to H-3. With structure **13**, which has both rings in the chair conformation, the H-1/H-3 angle is approximately 180°. In this model H-1 is very close to H-2, and one would expect an NOE between these two protons; this was confirmed experimentally. The other isomer, compound **14**, must surely have a chair/boat conformation, and H-1 would have the same angles to H-3 and H-4 as found with compound **13**. For compound **14**, H-1 is positioned far from H-2. Therefore, no NOE between H-1 and H-2 would be predicted, and none was found.

Treatment of the bicyclo ethyl bromides (**13** and **14**) with trifluoroacetic acid and acetic anhydride at room temperature gave the bromo enamines **15** and **16**,[11] which in acetonitrile (K_2CO_3, reflux) were converted without isolation to the bicyclic enamines **17** and **18** in an overall yield from **13** and **14** of 80 and 82%, respectively. Compounds **17** and **18** were readily deacetylated to the *cis*- and *trans*-6-hydroxybicyclic enamines **19** and **20**. An examination of the ^{1}H NMR spectrum of the material derived from **17** showed that in benzene-d_6 it existed as a mixture of compounds **19** and **21**. The ratio of **19** to **21** initially after dissolution was approximately 2.4:1.0; however, after the mixture stood for 3 days at room temperature, the ratio changed to 1.0:1.3. The structural assignment for **21** was supported by its ^{13}C NMR spectrum which showed the presence of a doublet at a position consistent for a methine, which has an oxygen and a nitrogen attached. Attempts to isolate **21** from **19** were unsuccessful; however, it was found that this mixture could be reduced in near quantitative yield in ethanol with hydrogen and platinum oxide to the trans-fused perhydroisoquinolinol **5** (Scheme II). Similar hydrogenation of **20** gave the isomeric isoquinolinol **6**, also trans-fused.

In contrast, hydrogenation of **19** and **21** or **20** with platinum oxide in acetic acid afforded the cis-fused isoquinolinols **7** and **8**, respectively, in high yield. The rationale for these stereoselective reductions has been previously described in the synthesis of the *trans*-4a-phenyldecahydroisoquinoline (**2**).[1] The relative configurations of compounds **5**–**8** were established by comparison of their ^{1}H NMR spectra and physical properties with those previously described.[9] Oxidation of **5** or **6** under Swern conditions[12] provided the desired *trans*-4a-aryl-6-oxoperhydroisoquinoline **3** in near quantitative yield, while similar oxidation of **7** or **8** afforded the cis-fused analogue **4**, also in high yield.

Thus by this method we have described the synthesis of *trans*-4a-(3-methoxyphenyl)-6-oxodecahydroisoquinoline (**3**) in seven steps from the readily available tetrahydropyridine **9**[10] in an approximate 21% overall yield. Because we wanted to fully characterize all of the intermediates, we have described the synthesis of **3** using the separated isomeric oxoazabicyclononanes **11** and **12**; however, this would not be necessary in a preparative synthesis of **3**.

Experimental Section

Melting points were determined for all solids on a Thomas-Hoover melting point apparatus and are uncorrected. Mass spectra were recorded on a CEC 21-110 mass spectrometer. ^{1}H NMR (300 MHz) and ^{13}C NMR (67.9 MHz) spectra were recorded on a GE QE-300 and a Bruker WM-270 spectrometer, respectively. Infrared spectra were recorded on a Nicolet 10DX FTIR spectrometer. All spectra were consistent with assigned structures. All compounds were elementally analyzed within 0.3% of theoretical value unless otherwise indicated. Where melting points are not indicated, the substance is a liquid at room temperature. Thin-layer chromatography (TLC) was performed on Kieselgel 60 F_{254} plates (0.25 μm) with visualation by UV light and iodine stain. Column chromatography was performed by gravitational flow with use of Allied Fisher silica (70–150 mesh). Preparative liquid chromatography was performed with the Waters Prep LC/500 apparatus and dual silica prep pack cartridges. All temperatures are internal temperatures unless otherwise stated.

Preparation of the 5-(3-Methoxyphenyl)-8-methyl-3-[[(tetrahydro-2*H*-pyran-2-yl)oxy]methyl]-2-oxa-8-azabicyclo[3.3.1]nonanes (11 and 12). A solution of 1-methyl-4-(3-methoxyphenyl)-1,2,3,6-tetrahydropyridine (**9**)[10] (40.0 g, 0.20 mol) in 1000 mL of THF was cooled to 0 °C under nitrogen and treated dropwise with 1.6 M *n*-BuLi (130 mL, 0.21 mol) at a rate to maintain a temperature of 0–5 °C. After the addition was complete, the resulting dark red solution was allowed to stir at 0 °C for 10 min. This solution was then cannulated, using nitrogen pressure, into a solution of tetrahydro-2-(oxiranylethoxy)-2*H*-pyran (33.7 g, 0.20 mol) in 50 mL ether at −10 °C. The resulting solution was stirred for 10 min at −5 °C. A solution of 16.0 g of NaOH pellets and 52.0 g of NaCl in 400 mL of H_2O was then added, maintaining the temperature at 0 °C, and this mixture was immediately poured into 1000 mL of cold H_2O. The desired product was extracted into two 500-mL portions of ether. The ether portions were washed with H_2O, dried over K_2CO_3, and concentrated under reduced pressure to yield 70.0 g of the crude mixture of isomers as a viscous oil. TLC showed the presence of two separable fractions, R_f values of 0.18 and 0.14 (ethyl acetate). The isomers were separated by preparative liquid chromatography with a gradient solvent system, (toluene–toluene/ethyl acetate, 1:1).

For **11**: yield 29.7 g (40%); R_f 0.18 (ethyl acetate); ^{1}H NMR ($CDCl_3$) δ 7.27 (t, 1 H), 6.94 (br d, 1 H), 6.86 (t, 1 H), 6.76 (dd, 1 H), 4.67 (br t, 1 H), 4.62 (br t, 1 H), 4.33 (m, 1 H), 3.88 (m, 2 H), 3.82 (s, 3 H), 3.52 (m, 2 H), 3.25 (m, 1 H), 3.05 (br t, 1 H), 2.57 (d, 3 H), 2.24–1.45 (m, 16 H); mass spectrum, *m/e* (relative

(11) The use of trifluoroacetic anhydride to liberate an enamine of this type was first described by Shenvi and Ciganek in ref 2.

(12) Mancuso, A. J.; Huang, S.-L.; Swern, D. *J. Org. Chem.* **1978**, *43*, 2480.

intensity) 375 (M^+, 8), 346 (2), 318 (2), 290 (13), 246 (30), 202 (100), 189 (25), 96 (15), 70 (25). Anal. Calcd for $C_{22}H_{33}NO_4$: C, 70.37; H, 8.86; N, 3.73. Found: C, 70.10; H, 8.63; N, 3.55.

The hydrochloride salt of **11** was made by using HCl in ether at 0 °C. The salt could be recrystallized from ethyl acetate: mp 109–110 °C. Anal. Calcd for $C_{22}H_{34}NO_4Cl$: C, 64.14; H, 8.32; N, 3.40. Found: C, 64.07; H, 8.18; N, 3.55.

For **12**: yield 25.4 g (34%); R_f 0.14 (ethyl acetate); ^1H NMR ($CDCl_3$) δ 7.25 (t, 1 H), 6.87 (br d, 1 H), 6.81 (t, 1 H), 6.74 (dd, 1 H), 4.82 (br d, 1 H), 4.58 (t, 1 H), 3.85 (m, 3 H), 3.82 (s, 3 H), 3.52 (m, 2 H), 2.83 (dt, 1 H), 2.61 (m, 1 H), 2.46 (m, 1 H), 2.41 (s, 3 H), 2.05 (dd, 1 H), 1.94–1.42 (m, 12 H); mass spectrum, *m/e* (relative intensity) 375 (M^+, 4), 318 (1), 290 (8), 246 (20), 202 (100), 189 (23), 96 (32), 70 (78). Anal. Calcd for $C_{22}H_{33}NO_4$: C, 70.37; H, 8.86; N, 3.73. Found: C, 70.59; H, 8.88; N, 3.54.

The hydrochloride salt of **12** was made with HCl in ether at 0 °C. The salt could be recrystallized from ethyl acetate: mp 123–125 °C. Anal. Calcd for $C_{22}H_{34}NO_4Cl$: C, 64.14; H, 8.32; N, 3.40. Found: C, 64.27; H, 8.29; N, 3.19.

(1*S,3*S**,5*S**)-3-(2-Bromoethyl)-5-(3-methoxyphenyl)-8-methyl-2-oxa-8-azabicyclo[3.3.1]nonane (13).** A solution of 30.0 g (0.073 mol) of the hydrochloride salt of **11** and 33.4 g (0.13 mol) of triphenylphosphine in 350 mL of dry tetrahydrofuran was treated dropwise with 20.5 g (0.13 mol) of bromine under a nitrogen atmosphere while a temperature of 10 °C was maintained. The reaction was allowed to warm to room temperature (15 min) and treated dropwise with 44.0 mL of methanol. After the addition, the reaction mixture was concentrated under reduced pressure, and the resulting crude bromide salt was liberated to the free amine at cold temperature with 1 N NaOH and ether extraction. The ether layer was washed twice with H_2O, dried over K_2CO_3, and concentrated under reduced pressure to yield 53.0 g of semicrystalline material. The crude amine was slurried in 100 mL of cold hexane, and the triphenylphosphine oxide was removed by filtration. The filtrate was concentrated, yield 23.0 g, and further purified by preparative liquid chromatography with use of a gradient solvent system (hexane–hexane/ethyl acetate, 1:1) affording 18.5 g (72%) of a clear viscous oil: R_f 0.28 (ethyl acetate/hexane, 1:1); ^1H NMR ($CDCl_3$) δ 7.27 (t, 1 H), 6.90 (dd, 1 H), 6.85 (t, 1 H), 6.76 (dd, 1 H), 4.66 (br t, 1 H), 4.39 (m, 1 H), 3.80 (s, 3 H), 3.62 (m, 1 H), 3.50 (m, 1 H), 3.27 (m, 1 H), 3.06 (m, 1 H), 2.61 (s, 3 H), 2.19 (br dd, 1 H), 2.12–1.99 (m, 4 H), 1.84 (m, 2 H), 1.55 (ddd, 1 H); mass spectrum, *m/e* (relative intensity) 353 (M^+, 4), 274 (8), 246 (33), 202 (100), 189 (44), 96 (31), 70 (63). Anal. Calcd for $C_{17}H_{24}NO_2Br$: C, 57.63; H, 6.83; N, 3.95. Found: C, 57.44; H, 6.88; N, 3.80.

(1*S,3*R**,5*S**)-3-(2-Bromoethyl)-5-(3-methoxyphenyl)-8-methyl-2-oxa-8-azabicyclo[3.3.1]nonane (14).** This compound was prepared as above from 22.5 g (0.055 mol) of the hydrochloride salt of **12**. Purification was performed by preparative liquid chromatography with use of a gradient solvent system (hexane–hexane/ethyl acetate, 1:1), affording 12.4 g (63%) of crystalline material: mp 84–86 °C; R_f 0.22 (hexane/ethyl acetate, 1:1); ^1H NMR ($CDCl_3$) δ 7.27 (t, 1 H), 6.87 (dd, 1 H), 6.82 (t, 1 H), 6.75 (dd, 1 H), 4.84 (br d, 1 H), 3.90 (m, 1 H), 3.81 (s, 3 H), 3.53 (m, 2 H), 2.79 (ddd, 1 H), 2.63 (m, 1 H), 2.47 (m, 1 H), 2.40 (s, 3 H), 2.10–1.72 (m, 7 H); mass spectrum, *m/e* (relative intensity) 353 (M^+, 4), 274 (10), 246 (32), 202 (100), 189 (26), 96 (23), 70 (50). Anal. Calcd for $C_{17}H_{24}NO_2Br$: C, 57.63; H, 6.83; N, 3.95. Found: C, 57.49; H, 6.73; N, 3.71.

2-Methyl-4aα-(3-methoxyphenyl)-2,3,4,4a,5,6,7,8-octahydro-6β-isoquinolinol Acetate (17). A solution of 10.0 g of **13** was treated with 35.0 mL each of trifluoroacetic acid and acetic anhydride and stirred for 1 h at room temperature. The solution was then made strongly basic with 50% NaOH and ice, and the product was extracted into 300 mL of ether. The ether layer was washed once with H_2O, dried over K_2CO_3, and concentrated under reduced pressure at 0 °C to yield 10.8 g of **15** as a yellow oil. This unstable material was used without further purification and dissolved into 250 mL of acetonitrile containing 11.4 g K_2CO_3 and heated at reflux under a nitrogen atmosphere for 2 h. The mixture was cooled to room temperature and filtered. The resulting solid was washed two times with 50-mL portions of methylene chloride. These extracts were combined with the filtrate and concentrated under reduced vacuum to yield 8.42 g of crude product. Purification was performed by preparative liquid chromatography with use of a gradient solvent system (hexane–hexane/ethyl acetate, 4:1), yielding 5.92 g (75%) crystalline product: mp 83.5–85 °C; R_f 0.31 (hexane/ethyl acetate, 4:1); ^1H NMR ($CDCl_3$) δ 7.25 (t, 1 H), 7.02 (d, 1 H), 7.00 (br d, 1 H), 6.74 (dd, 1 H), 5.91 (s, 1 H), 4.53 (m, 1 H), 3.82 (s, 3 H), 2.83 (ddd, 1 H), 2.63 (m, 1 H), 2.60 (s, 3 H), 2.50 (ddd, 1 H), 2.21–2.00 (m, 2 H), 2.00 (s, 3 H), 1.96–1.80 (m, 3 H), 1.48 (ddd, 1 H), 1.34 (m, 1 H); mass spectrum, *m/e* (relative intensity) 315 (M^+, 53), 272 (4), 256 (67), 214 (15), 148 (100), 122 (9). Anal. Calcd for $C_{19}H_{25}NO_3$: C, 72.35; H, 7.99; N, 4.44. Found: C, 72.08; H, 7.88; N, 4.50.

2-Methyl-4aα-(3-methoxyphenyl)-2,3,4,4a,5,6,7,8-octahydro-6α-isoquinolinol Acetate (18). This compound was prepared as above by starting with 11.0 g of **14**. The only difference was that a 2-h stirring at room temperature was needed for complete conversion to the intermediate **16**. Purification of the 8.25 g of crude **18** was accomplished by preparative liquid chromatography with use of a gradient solvent system (hexane–hexane/ethyl acetate, 1:1), affording 5.90 g (61%) as a viscous oil: R_f 0.22 (hexane/ethyl acetate, 4:1); ^1H NMR ($CDCl_3$) δ 7.20 (t, 1 H), 6.93 (br d, 1 H), 6.92 (br s, 1 H), 6.67 (dd, 1 H), 5.94 (s, 1 H), 4.97 (m, 1 H), 3.80 (s, 3 H), 3.02 (ddd, 1 H), 2.64–2.47 (m, 2 H), 2.57 (s, 3 H), 2.34 (ddd, 1 H), 2.03–1.47 (m, 6 H), 1.30 (s, 3 H); mass spectrum, *m/e* (relative intensity) 315 (m^+, 96), 272 (8), 256 (90), 214 (19), 148 (100), 122 (9). Anal. Calcd for $C_{19}H_{25}NO_3$: C, 72.35; H, 7.99; N, 4.44. Found: C, 72.06; H, 8.05; N, 4.47.

2-Methyl-4aα-(3-methoxyphenyl)-2,3,4,4a,5,6,7,8-octahydro-6β-isoquinolinol (19) and 3-(3-Methoxyphenyl)-6-methyl-11-oxa-6-azatricyclo[5.3.1.0^{3,8}]undecane (21). A solution of 7.20 g (0.023 mol) of **17** and 13.0 g of K_2CO_3 in 200 mL of methanol was stirred at room temperature under nitrogen for 2 h. The mixture was then filtered, and the filtrate was concentrated under reduced vacuum. The resulting residue was taken into 200 mL of methylene chloride, washed twice with brine, dried over K_2CO_3, and concentrated under vacuum to yield 6.80 g of a viscous oil. Purification was performed by column chromatography (hexane/ethyl acetate, 1:1) to give 6.0 g (96%) of **19** and **21**: R_f 0.15 (hexane/ethyl acetate, 1:1); ^1H NMR (C_6D_6) (taken immediately after dissolution) δ 7.18 (m, 1 H), 7.09 (d, 0.7 H), 7.04 (t, 0.7 H), 6.93 (d, 0.3 H), 6.79 (t, 0.3 H), 6.69 (m, 1 H), 5.74 (d, 0.7 H), 4.58 (d, 0.3 H), 3.85 (m, 0.3 H), 3.40 (s, 0.3 H), 3.39 (s, 0.7 H), 3.39 (m, 0.7 H), 2.89 (td, 0.3 H), 2.70 (dt, 0.7 H), 2.50 (s, 0.7 H), 2.29 (s, 0.3 H), 2.48–2.25 (m, 3 H), 2.25–2.08 (m, 2 H), 2.03–1.60 (m, 4 H), 1.46–0.91 (m, 4 H), 0.87–0.65 (br m, 1 H); ^1H NMR (C_6D_6) (after standing for three days at room temperature) δ 7.18 (m, 1 H), 7.09 (d, 0.4 H), 7.04 (t, 0.4 H), 6.93 (d, 0.6 H), 6.79 (t, 0.6 H), 6.69 (m, 1 H), 5.74 (d, 0.4 H), 4.58 (d, 0.6 H), 3.85 (m, 0.6 H), 3.40 (s, 0.6 H), 3.39 (s, 0.4 H), 3.39 (m, 0.4 H), 2.89 (td, 0.6 H), 2.70 (dt, 0.4 H), 2.50 (s, 0.4 H), 2.29 (s, 0.6 H), 2.48–2.25 (m, 3 H), 2.25–2.08 (m, 2 H), 2.03–1.60 (m, 4 H), 1.46–0.91 (m, 4 H), 0.87–0.65 (br m, 1 H); mass spectrum, *m/e* (relative intensity) 273 (M^+, 100), 244 (24), 228 (51), 189 (41), 166 (100), 122 (73), 77 (38). Anal. Calcd for $C_{17}H_{23}NO_2$: C, 74.67; H, 8.48; N, 5.12. Found: C, 74.40; H, 8.41; N, 5.03.

2-Methyl-4aα-(3-methoxyphenyl)-2,3,4,4a,5,6,7,8-octahydro-6α-isoquinolinol (20). This compound was prepared as above from 3.70 g (0.012 mol) of **18**. A 24-h stirring at room temperature was needed to complete the reaction. Purification was performed by column chromatography (hexane/ethyl acetate, 1:1), giving 2.95 g (90%) of **20**: R_f 0.11 (hexane/ethyl acetate, 1:1); ^1H NMR ($CDCl_3$) δ 7.25 (t, 1 H), 7.08 (d, 1 H), 7.04 (t, 1 H), 6.74 (dd, 1 H), 5.94 (s, 1 H), 4.09 (m, 1 H), 3.81 (s, 3 H), 2.82 (m, 1 H), 2.65–2.29 (m, 3 H), 2.57 (s, 3 H), 2.00–1.87 (m, 2 H), 1.80–1.70 (m, 2 H), 1.51 (m, 1 H), 1.03 (d, 1 H); mass spectrum, *m/e* (relative intensity) 273 (M^+, 66), 244 (15), 228 (27), 202 (18), 166 (100), 122 (46), 44 (20). Anal. Calcd for $C_{17}H_{23}NO_2$: C, 74.67; H, 8.48; N, 5.12. Found: C, 74.42; H, 8.60; N, 5.09.

2-Methyl-4aα-(3-methoxyphenyl)-1,2,3,4,4a,5,6,7,8,8aβ-decahydro-6β-isoquinolinol (5). A solution of 2.73 g (0.010 mol) of **19** and **21** in 150 mL of anhydrous ethanol was hydrogenated over PtO_2 at a hydrogen pressure of 60 psi for 16 h. At the end of this period the catalyst was filtered off, and the solvent was removed under reduced pressure to afford 2.70 g of crude product. Purification was performed by chromatography on a silica column with methanol as eluent, giving 2.28 g (84%) of a crystalline material. This was recrystallized from hexane/benzene (1:1): mp

88.5–90 °C; R_f 0.22 (methanol); ^{1}H NMR ($CDCl_3$) δ 7.21 (t, 1 H), 7.03 (d, 1 H), 7.02 (d, 1 H), 6.70 (dd, 1 H), 3.81 (s, 3 H), 3.31 (m, 1 H), 2.71 (m, 2 H), 2.52 (dd, 1 H), 2.40 (ddd, 1 H), 2.25 (s, 3 H), 2.20–1.30 (m, 10 H); mass spectrum, *m/e* (relative intensity) 275 (M^+, 78), 258 (38), 187 (12), 167 (31), 121 (16), 71 (100), 57 (37). Anal. Calcd for $C_{17}H_{25}NO_2$: C, 74.14; H, 9.15; N, 5.09. Found: C, 73.97; H, 9.15; N, 4.81.

2-Methyl-4aα-(3-methoxyphenyl)-1,2,3,4,4a,5,6,7,8,8aβ-decahydro-6α-isoquinolinol (6). This compound was prepared as above from 1.0 g (3.7 mmol) of **20**. Purification was performed by column chromatography (methanol) to yield 0.82 g (82%) of crystalline product that recrystallized from hexane: mp 116–117 °C (lit.[9] mp 117–117.5 °C); R_f 0.23 (methanol); ^{1}H NMR ($CDCl_3$) δ 7.26 (t, 1 H), 7.13 (d, 1 H), 7.11 (br t, 1 H), 6.72 (dd, 1 H), 4.02 (br s, 1 H), 3.80 (s, 3 H), 2.78 (ddd, 1 H), 2.72 (dd, 1 H), 2.54 (m, 2 H), 2.32 (m, 1 H), 2.27 (s, 3 H), 2.09–1.42 (m, 8 H), 0.80 (br s, 1 H); mass spectrum, *m/e* (relative intensity) 275 (M^+, 34), 260 (7), 204 (33), 167 (16), 121 (19), 91 (20), 71 (100), 57 (79). Anal. Calcd for $C_{17}H_{25}NO_2$: C, 74.14; H, 9.15; N, 5.09. Found: C, 73.92; H, 9.06; N, 5.09.

2-Methyl-4aα-(3-methoxyphenyl)-1,2,3,4,4a,5,6,7,8,8aα-decahydro-6β-isoquinolinol (7). A solution of 1.0 g (3.7 mmol) of **19** and **21** in 50 mL anhydrous ethanol/acetic acid (1:1) was hydrogenated over PtO_2 at a hydrogen pressure of 60 psi for 16 h. At the end of this period, the catalyst was filtered off, and the solvent was removed under reduced pressure to afford 0.96 g of crude product. Purification was performed by column chromatography with methanol eluent, yield 0.73 g (73%): R_f 0.30 (methanol); ^{1}H NMR ($CDCl_3$) δ 7.25 (t, 1 H), 7.04 (d, 1 H), 7.00 (t, 1 H), 6.73 (dd, 1 H), 3.80 (s, 3 H), 3.67 (m, 1 H), 2.62 (m, 3 H), 2.50 (ddd, 1 H), 2.32 (s, 3 H), 2.25 (ddd, 1 H), 2.08 (d, 2 H), 1.86–1.32 (m, 7 H); mass spectrum, *m/e* (relative intensity) 275 (M^+, 20), 258 (16), 187 (10), 167 (14), 121 (12), 91 (92), 71 (100), 57 (28). Anal. Calcd for $C_{17}H_{25}NO_2$: C, 74.14; H, 9.15; N, 5.09. Found: C, 74.36; H, 8.93; N, 4.87.

2-Methyl-4aα-(3-methoxyphenyl)-1,2,3,4,4a,5,6,7,8,8aα-decahydro-6α-isoquinolinol (8). This compound was prepared as above from 1.0 g (3.7 mmol) of **20**. Purification was performed by column chromatography with methanol solvent, affording 0.68 g (68%) of **16**, which could be recrystallized from benzene, mp 95–96 °C (lit.[9] mp 95–97 °C), or from hexane/ethyl acetate (4:1), mp 104–106 °C: R_f 0.25 (methanol); ^{1}H NMR ($CDCl_3$) δ 7.27 (t, 1 H), 6.99 (d, 1 H), 6.95 (br t, 1 H), 6.75 (dd, 1 H), 3.92 (m, 1 H), 3.82 (s, 3 H), 2.64 (br d, 1 H), 2.46 (d, 1 H), 2.26 (m, 3 H), 2.11 (s, 3 H), 2.09–1.66 (m, 6 H), 1.35 (m, 3 H); mass spectra, *m/e* (relative intensity) 275 (M^+, 37), 258 (8), 204 (58), 187 (14), 121 (19), 91 (13), 71 (97), 58 (47), 44 (100). Anal. Calcd for $C_{17}H_{25}NO_2$: C, 74.14; H, 9.15; N, 5.09. Found: C, 74.29; H, 9.30; N, 5.18.

General Procedure for the Synthesis of the 6-Oxodecahydroisoquinolines 3 and 4. A solution of 8.7 mL of DMSO in 25 mL of methylene chloride was added dropwise to 5.1 mL of oxalyl chloride in 130 mL of methylene chloride under nitrogen, and a temperature of −55 °C was maintained. After the addition was complete, the reaction was stirred for 2 min at this temperature. A solution of isoquinolinol (15.0 g, 0.055 mol) in 52 mL of methylene chloride was added dropwise to this mixture, and a temperature of −55 °C was maintained. The resulting mixture was then stirred an additional 15 min at −55 °C. Triethylamine (36 mL) was added, and the reaction mixture was allowed to warm to room temperature. Water (250 mL) was added dropwise to the mixture, and the layers were separated. The organic layer was washed two times with brine, dried over K_2CO_3, and concentrated under reduced vacuum. Purification was achieved by either column chromatography or recrystallization.

2-Methyl-4aα-(3-methoxyphenyl)-1,2,3,4,4a,5,6,7,8,8aβ-decahydroisoquinoline (3). This compound was prepared as described above from 15.0 g (0.055 mol) of **5** or 15.5 g (0.056 mol) of **6**. The resulting solids were recrystallized from hexane/ethyl acetate (1:1) to yield 13.7 g (91%) from **5** and 14.2 g (92%) from **6**: mp 90–92 °C; mp 93.5–94.5 °C (hexane/benzene, 1:1; lit.[9] mp 94–95 °C); R_f 0.23 (methanol); ^{1}H NMR ($CDCl_3$) δ 7.22 (t, 1 H), 6.98 (m, 2 H), 6.71 (dd, 1 H), 3.79 (s, 3 H), 2.93 (d, 1 H), 2.84 (dd, 1 H), 2.68 (t, 1 H), 2.59 (d, 1 H), 2.53–2.20 (m, 5 H), 2.33 (s, 3 H), 2.13–1.84 (m, 4 H); mass spectrum, *m/e* (relative intensity) 273 (M^+, 100), 258 (11), 202 (13), 165 (28), 150 (32), 71 (72), 57 (65), 44 (40); IR ($CDCl_3$) 1709.05 (C=O) cm^{-1}. Anal. Calcd for $C_{17}H_{23}NO_2$: C, 74.69; H, 8.48; N, 5.12. Found: C, 74.97; H, 8.68; N, 5.39.

2-Methyl-4aα-(3-methoxyphenyl)-1,2,3,4,4a,5,6,7,8,8aα-decahydro-6-oxadecahydroisoquinoline (4). This compound was prepared as above from 1.90 g (0.0069 mol) of **7** and 1.40 g (0.005 mol) of **8**. The resulting viscous oils were purified by column chromatography with methanol solvent to yield **4**, 1.60 g (84%) from **7** and 1.20 g (86%) from **8**. Material crystallized on standing: mp 66–67.5 °C (hexane); R_f 0.46 (methanol); ^{1}H NMR ($CDCl_3$) δ 7.24 (t, 1 H), 7.00 (m, 2 H), 6.75 (dd, 1 H), 3.79 (s, 3 H), 2.90–2.46 (m, 6 H), 2.36 (s, 3 H), 2.36–2.10 (m, 4 H), 1.86–1.64 (m, 2 H), 1.58 (m, 1 H); mass spectrum, *m/e* (relative intensity) 273 (M^+, 21), 258 (5), 202 (6), 165 (6), 115 (9), 96 (8), 79 (100), 57 (36), 44 (67); IR ($CDCl_3$) 1706.16 cm^{-1} (C=O). Anal. Calcd for $C_{17}H_{23}NO_2$: C, 74.69; H, 8.48; N, 5.12. Found: C, 74.39; H, 8.77; N, 4.94.

Registry No. **3**, 61528-04-9; **4**, 61528-05-0; **5**, 61528-21-0; **6**, 61528-20-9; **7**, 61528-23-2; **8**, 61528-24-3; **9**, 73224-22-3; **11**, 118864-98-5; **11**·HCl, 118724-76-8; **12**, 118864-99-6; **12**·HCl, 118916-31-7; **13**, 118724-77-9; **14**, 118724-78-0; **15**, 118724-79-1; **16**, 118724-80-4; **17**, 118724-81-5; **18**, 118724-82-6; **19**, 118724-83-7; **20**, 118724-84-8; **21**, 118724-85-9; **22**, 88055-58-7.

Electron-Transfer Induced Rearrangement of Spirofluorenebicyclo[6.1.0]nonatriene to Spirofluorenebarbaralane

Tsutomu Miyashi,*[†] Yasutake Takahashi,[†] Akinori Konno,[†] Toshio Mukai,[†,‡] Heinz D. Roth,*[§,∥] Marcia L. Schilling,[§] and Christopher J. Abelt[§,⊥]

Department of Chemistry, Faculty of Science, Tohoku University, Sendai 980, Japan, and AT&T Bell Laboratories, Murray Hill, New Jersey 07974

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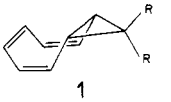
Bicyclo[6.1.0]nonatriene (1) and its derivatives are among the most thoroughly investigated hydrocarbon systems. A multiplicity of thermal and photochemical rearrangements are observed, and substituents at C-9 affect the course of the rearrangement in remarkable fashion.[1] We are interested in the structure and the potential rearrangements of radical cations.[2] Accordingly, we investigated the photoinduced electron transfer reactions of spirofluorenebicyclo[6.1.0]nonatriene (**1a**)[3] and 9,9-diphenylbicyclo[6.1.0]nonatriene (**1b**).[4] In polar solvents, **1a** undergoes a novel rearrangement, chiefly to spirofluorenebarbaralane (**2a**), a type of rearrangement without precedent in radical cation chemistry.



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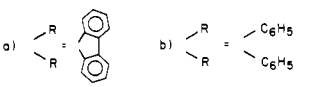

The fluorescence of 9,10-dicyanoanthracene (DCA) was efficiently quenched by either **1a** (k_q = 1.4 × 10^{10} mol^{-1} dm^3 s^{-1}, $E_{1/2}^{ox}$ = 1.52 V vs SCE)[5] or **1b** (k_q = 1.8 × 10^{10}

[†] Tohoku University.
[‡] Current address: College of Industry, Nihon University, Kohriyama 963, Japan.
[§] AT&T Bell Laboratories.
[∥] Current address: Department of Chemistry, Rutgers University, New Brunswick, NJ 08903.
[⊥] Current address: Department of Chemistry, The College of William and Mary, Williamsburg, VA 23185.

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