Imino-Bridged Heterocycles. III [1a]. Synthesis of Mono-Bridgehead Substituted 11*H*-Benzo[5,6]cyclohepta[1,2-*c*]pyridin-6,11-imines by Regiospecific Amine to Olefin Cyclizations

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Employing regiospecific amine to endocyclic olefin and hydroxylamine to exocyclic olefin cyclizations, we have developed pathways to two isomeric, bridgehead methyl-substituted benzo[5,6]cyclohepta[1,2-*c*]pyridin-6,11-imines. Acid catalyzed cyclization of **5** to **6** was accomplished under exceedingly mild conditions (silica gel/chloroform), whereas, thermal cyclization of **20** to generate **21** was performed analogously to the dibenzo[*a,d*]cyclohepten-5,10-imine system.

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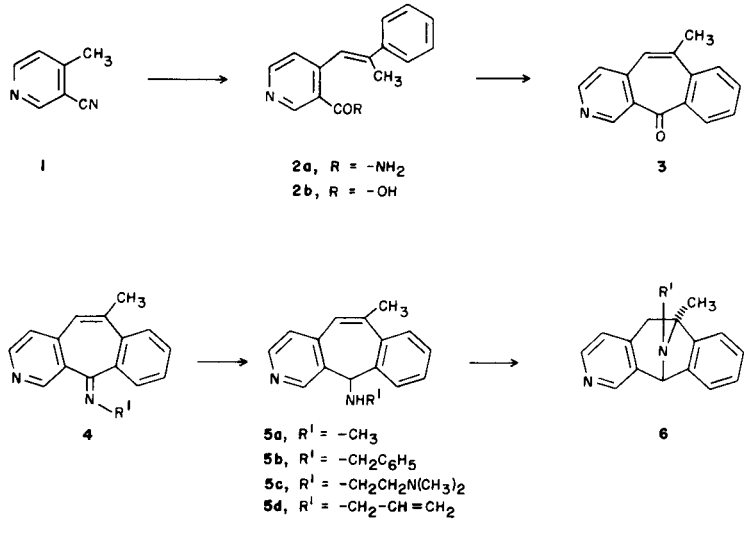
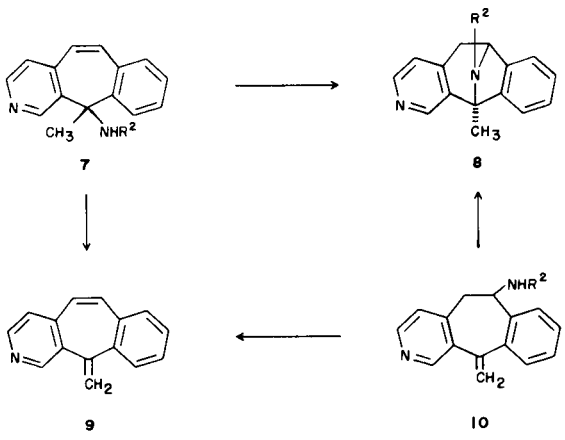
In earlier papers of this series we described methods for the preparation of isomeric benzocycloheptapyridinimines [1a,2]. Because the biological profiles of these derivatives were similar to those of anthracenimines, dibenzo[*a,d*]-cyclooctenimines and dibenzo[*a,d*]cyclohepten-5,10-imines [3-5], we were prompted to investigate the biological consequences of bridgehead methyl group introduction into selected benzocycloheptapyridines. In this paper we describe in detail the methods of the regiospecific syntheses of **6** and **22**, the two types of bridgehead mono-substituted products in the benzo[5,6]cyclohepta[1,2-*c*]pyridin-6,11-imine system.

Our earlier preparation of benzo[5,6]cyclohepta[1,2-*c*]-pyridin-6,11-imines took advantage of a regiospecific, acid-catalyzed amine to internal olefin cyclization [1a]. We envisaged a similar route for the preparation of the 6-substituted analogs **6**. The requisite tricyclic ketone **3** was prepared using a modification of the procedure for the unsubstituted derivative **11**. Attempts to condense acetophenone with the methylpyridinecarbonitrile (**1**) using a variety of bases were unsuccessful. Conditions that provided condensation between **1** and benzaldehyde [6] gave no appreciable reaction with acetophenone. Using the more basic system, sodium *t*-butoxide in DMF, the olefinic amide **2a** was generated in good yield at 25°. As seen in earlier reactions of this type, the nitrile underwent concomitant conversion to the carboxamide **2a** [1a,6]. Hydrolysis of the amide to the carboxylic acid **2b** followed by PPA cyclization provided the ketone **3**. Using the previously reported ketimine forming procedure [1a,7], the ketone **3** was converted to the imines **4a-d** which subsequently were reduced to the amines **5a-d** with sodium borohydride in acetonitrile. Two of the crude reduction products, **5a** and **5c**, were subjected to silica gel chromatography with mixed chloroform solvents as the eluant. In both cases, this treatment was sufficiently acidic to cyclize the amines to the corresponding bridged structures, **6a** and **6c**. The position of cyclization was indicated clearly by the ^{1}H nmr spectra. The methyl group in **6a** was a sharp singlet, thus confirming that cyclization indeed had occurred at the bridge carbon β to the pyridine ring. There was a large coupling constant (J = 18 Hz) for H5β and H5α as would be expected for



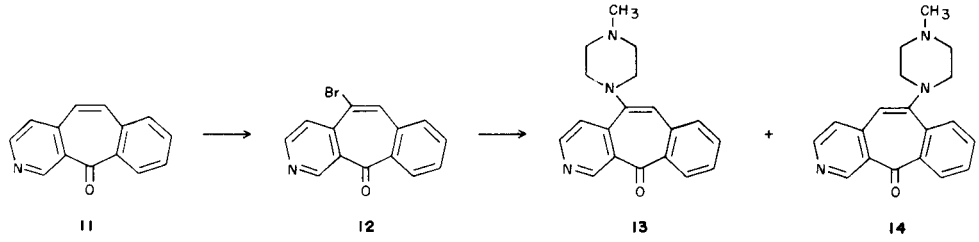


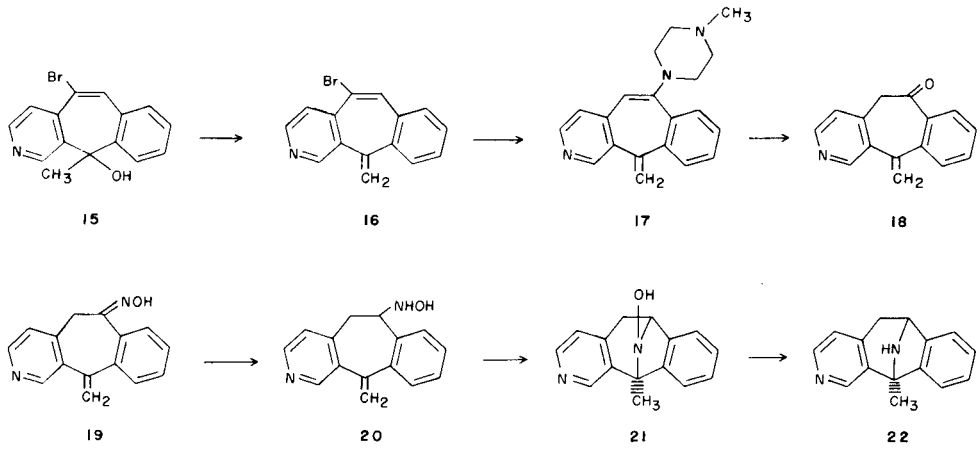
protons of this type. From analogy with the unsubstituted derivatives reported earlier, the higher field proton was assigned to be H5α. The remaining two amines, **5b** and **5d**, were cyclized using ethanolic hydrogen chloride to give **6b** and **6d**, respectively.

Two different strategies were available for the synthesis of the 11-methyl isomer **22**. The amine function and methyl group could be introduced onto C-11 followed by cyclization into the endocyclic olefin, **7** to **8**, or a hydroxylamine function could be introduced selectively at C-6 with subsequent cyclization into an exocyclic olefin at C-11, **10** to **8**. *A priori*, each of these strategies has limitations. The former (**7**) would be susceptible to elimination of the amine to generate an exocyclic olefin **9**, whereas, **10** would require regioselective introduction of the amine function which also would be susceptible to elimination to **9**. Although we investigated both approaches, the latter (**10** to **8**) is described below; results of the former will be described in a subsequent communication devoted to dimethyl analogs.

By analogy with the preparation of dibenzo[*a*,*d*]cyclohepten-5,10-imines [4], it was anticipated that a 6-hydroxylamino function (**20**) would thermally cyclize regiospecifically into an exocyclic olefin to give the desired product **21**. Thus the preparation of **20** became an immediate goal. The bromination of **11** in acetic acid gave the 5-bromoketone **12** as the major product, presumably through an addition-elimination mechanism. In an effort to generate **14**, treatment of **12** with potassium *t*-butoxide and 4-methylpiperazine provided minimal regioselectivity. The isomers **13** and **14** were isolated in an approximate 2:3 ratio (^{1}H nmr). Although the enaminoketones could be separated chromatographically, the observed nonselectivity made this route totally unattractive. For other synthetic purposes, we previously had treated **11** with methyl magnesium bromide to give the carbinol **15**, and dehydrated this material to the exocyclic methylene derivative **16**. With the conversion of the keto function to methylene, we anticipated that the pyridine ring might provide the sole influence on the addition of a nucleophile to an "yne" intermediate. Treatment of **16** with the *t*-butoxide/4-methylpiperazine mixture gave **17** as the exclusive product. This result is attributed to the pronounced influence of the pyridine ring on the β-carbon in the methylene case, whereas, the 5-keto function apparently activates both positions to nucleophilic addition. Acid hydrolysis of **17** to **18** followed by oxime formation was straightforward. With the oxime **19** in hand, methods of reduction to the hydroxylamino function necessary for cyclization were explored. The reduction could be effected with sodium cyanoborohydride [8] or pyridine-borane [9] in ethanolic THF under acid catalysis. However, under strongly acidic conditions, **20** eliminated the elements of hydroxylamine to generate **9**. It was necessary to add the acid to a cold solution of **19** containing the reducing agent and to monitor the reaction by tlc. The reduction failed to go to completion before elimination was observed; therefore, the reaction was allowed to proceed until the first evidence of **9** was observed and then was worked up. The starting material could be separated from **20** by a simple extraction procedure and recycled. Once **20** was isolated free of acid, it was less susceptible to elimination, as evidenced by its thermal cyclization to **21** in excellent yield. Zinc and acetic acid reductive cleavage of the N-O bond of **21** produced the desired 11-methyl isomer **22**.

It is noteworthy that each scheme is regiospecific at critical operations in the synthesis. Ring closure of **5** to **6**, as in our earlier analogs, produced only the desired bridge isomer. In the preparation of **18**, advantage was taken of the directing influence of the pyridine ring to generate the required regio isomer. Subsequent thermal cyclization of **20** occurred exclusively at the substituted carbon of the methylene function, in direct analogy with the dibenzocycloheptene case [4].





15 16 17 18

19 20 21 22

EXPERIMENTAL

Melting points were taken on a Thomas-Hoover melting point apparatus in open capillaries and are uncorrected values. The ^{1}H nmr spectra were recorded on a Varian T-60 spectrometer using TMS as an internal standard. Mass spectra were run on an AEI MS 902 by Mr. Shoji Date and microanalyses were performed under the direction of Dr. William C. Randall.

E-4-(2-Phenylpropen-1-yl)pyridine-3-carboxamide (**2a**).

A suspension of sodium hydride (12.6 g, 57% oil dispersion, 0.3 mole) and *t*-butyl alcohol (29.6 g, 0.40 mole) in DMF (325 ml) was warmed on the steam bath until gas evolution ceased (*ca.* 0.5 hour). The mixture was cooled to 0° and a solution of **1** [10] (23.6 g, 0.20 mole) in DMF (100 ml) was added dropwise (0.5-1 hour). After an additional hour at 0°, a solution of acetophenone (24 g, 0.20 mole) in DMF (100 ml) was added. The reaction mixture was allowed to come to room temperature overnight, poured over ice (1 kg) and acidified by the addition of glacial acetic acid (20 ml). The light yellow solid was filtered, washed with water and air-dried, 38 g, mp 149-154°. Recrystallization from ethyl acetate produced white salt-like crystals, mp 152.5-154.5°.

Anal. Calcd. for $C_{15}H_{14}N_2O$: C, 75.60; H, 5.92; N, 11.76. Found: C, 75.76; H, 5.94; N, 11.67.

E-4-(2-Phenylpropen-1-yl)pyridine-3-carboxylic Acid (**2b**).

A mixture of **2a** (5.1 g), potassium hydroxide (5 g) in 50% aqueous ethanol (100 ml) was heated on the steam bath overnight. The ethanol was removed and the resulting aqueous solution was chilled and acidified with glacial acetic acid (5 ml). The white solid was collected, washed well with water and dried, 4.5 g, mp 150-157°. Recrystallization from methanol raised the mp to 159-160.5°.

Anal. Calcd. for $C_{15}H_{13}NO_2$: C, 75.30; H, 5.48; N, 5.85. Found: C, 75.35; H, 5.66; N, 5.80.

6-Methylbenzo[5,6]cyclohepta[1,2-*c*]pyridin-11-one (**3**).

The acid **2b** (2 g) was added to hot polyphosphoric acid (PPA, 20 g, 200°) and the temperature was raised to 220-225° for 0.25 hour. The mixture was cooled to 50° followed by addition of ice. The aqueous mixture was made alkaline by the addition of 40% sodium hydroxide solution. The alkaline solution was extracted with dichloromethane and the organic extracts were washed with water until the washings were neutral, saturated brine and dried (sodium sulfate). After removal of the solvent and trituration with hexane, there was obtained 0.5 g of brown solid, mp 114-117°. Recrystallization from cyclohexane gave mp 117-118.5°; ^{1}H nmr (deuteriochloroform): δ 2.52 (d, 3H, J = 1 Hz, =C-CH_3), 6.95 (br s, 1H, H-C=), 4.41 (d, 1H, J = 6 Hz, H_3), 7.45-8.18 (m, 4H, aromatic), 8.67 (d, 1H, J = 6 Hz, H_2), 9.12 (s, 1H, H_1).

Anal. Calcd. for $C_{15}H_{14}NO$: C, 81.43; H, 5.01; N, 6.33. Found: C, 81.76; H, 5.42; N, 6.49.

6-Methyl-11-methyliminobenzo[5,6]cyclohepta[1,2-*c*]pyridine (**4a**).

To a stirred solution of methyl amine (2.5 g) and **3** (4.2 g) in toluene (250 ml) was added a solution of titanium tetrachloride (1.4 ml) in toluene (50 ml). After stirring for *ca.* 5 hours, anhydrous potassium carbonate was added and the mixture was filtered. The filtered cake was washed with toluene and the combined filtrates were evaporated to a clear viscous oil that solidified on standing 4.7 g, mp 158-159°; ^{1}H nmr (deuteriochloroform): δ 2.33 (d, 3H, J = 1 Hz, =C-CH_3), 3.32 (s, 3H, =N-CH_3).

5,6-Dihydro-6,12-dimethylbenzo[5,6]cyclohepta[1,2-*c*]pyridin-6,11-imine (**6a**).

A mixture of **4a** (4.7 g), sodium borohydride (0.60 g) and acetonitrile (200 ml) was heated under reflux for 4 hours. The solvent was removed *in vacuo* and the residual solid was dissolved in 3*N* hydrochloric acid (200 ml). After extraction of the acidic solution with ether, it was made alkaline by the addition of 40% sodium hydroxide solution. The alkaline solution was extracted with dichloromethane (4 × 100 ml) and the organic layer was washed with water until the washings were neutral, saturated sodium chloride solution and dried (anhydrous potassium carbonate). The residue [11], after filtration and evaporation of the solvent, was chromatographed over silica gel (50 g) using chloroform/ethyl acetate (60:40) until the product appeared, then using ethyl acetate alone. The fractions containing the desired product were pooled and rechromatographed on silica gel using a pressurized column and eluting with 5% methanol in chloroform. The fractions containing the product were pooled, evaporated and the residue triturated with hexane. The resulting solid was extracted with boiling petroleum ether to give 1.5 g of white solid, mp 77-82°; ^{1}H nmr (deuteriochloroform): δ 1.60 (s, 3H, CCH_3), 2.32 (s, 3H, N-CH_3), 2.50 (d, 1H, J = 18 Hz, $H_{5\alpha}$), 3.05 (d, J = 18 Hz, $H_{5\beta}$), 4.82 (s, 1H, H_{11}), 6.87 (d, 1H, J = 4 Hz, H_4), 7.20 (s, 4H, aromatic), 8.33 (d, 1H, J = 4 Hz, H_3), 8.43 (s, 1H, H_1).

Anal. Calcd. for $C_{16}H_{16}N_2$: C, 81.32; H, 6.83; N, 11.86. Found: C, 81.40; H, 6.80; N, 11.74.

11-Benzylimino-6-methylbenzo[5,6]cyclohepta[1,2-*c*]pyridine (**4b**).

Following the procedure for **4a** and using **3** (6.0 g, 0.071 mole), benzylamine (11.66 g, 0.109 mole) and titanium tetrachloride (3.42 g, 0.018 mole) in toluene (250 ml), there was obtained 4.64 g of a light yellow viscous oil.

12-Benzyl-5,6-dihydro-6-methylbenzo[5,6]cyclohepta[1,2-*a*]pyridin-6,11-imine (**6b**).

A mixture of **4b** (4.64 g, 0.015 mole), sodium borohydride (0.59 g, 0.015 mole) and acetonitrile (150 ml) was stirred at 25° for 2 hours. Excess hydride was destroyed by addition of 3*N* hydrochloric acid and the solvent was removed *in vacuo*. The residue was dissolved in 3*N* hydrochloric acid (150 ml), extracted with ether and the solution was made alkaline by the addition of 40% sodium hydroxide solution. The basic solu-

tion was extracted with ether (4 × 150 ml) and the combined organic extracts were washed with water (250 ml), saturated sodium chloride solution (2 × 300 ml) and dried (sodium sulfate). The residue (4.0 g) after filtration and removal of the solvent was dissolved in ethanol (75 ml). Excess 9*N* hydrogen chloride in ethanol was added and the solution heated under reflux for 24 hours. The ethanol was removed *in vacuo*, the residue was dissolved in water (100 ml) and extracted with ether (4 × 75 ml). The aqueous solution was made alkaline by the addition of 40% sodium hydroxide solution and extracted with ether (4 × 100 ml). These extracts were washed with water (150 ml), saturated sodium chloride solution (2 × 150 ml) and dried (sodium sulfate). The residue after evaporation was dissolved in chloroform and chromatographed over silica (250 g) under medium pressure (50 psi) using 90% chloroform-10% ethyl acetate as eluant. The fractions containing the product (tlc) were combined, stripped to a viscous oil that was dissolved in acetone (25 ml) and mixed with a hot solution of fumaric acid (1.16 g) in acetone (75 ml). The resulting solution was treated with Darco, filtered and concentrated to a volume of 75 ml. Filtration and drying gave 3.1 g, mp 193-196° dec with effervesence; ^{1}H nmr (DMSO-d_6): δ 1.60 (s, 3H, -C-CH_3), 2.48 (d, 1H, J = 18 Hz, $H_{5\alpha}$), 3.07 (d, 1H, J = 18 Hz, $H_{5\beta}$), 3.16 (d, 1H, J = 13 Hz, benzyl-CH), 3.53 (d, 1H, J = 13 Hz, benzyl-C-H), 4.67 (s, 1H, H_{11}), 6.60 (s, 2H, fumaric acid olefinic), 6.87-7.43 (m, 10H, benzyl, aromatic, H_4), 8.22 (d, 1H, J = 4 Hz, H_3), 8.27 (s, 1H, H_1).

Anal. Calcd. for $C_{22}H_{20}N_2 + C_4H_4O_4$: C, 72.88; H, 5.65; N, 6.54. Found: C, 72.68; H, 5.72; N, 6.48.

11-(2-Dimethylaminoethyl)imino-6-methylbenzo[5,6]cyclohepta[1,2-*c*]pyridine (**4c**).

Following the procedure for **4a** and using **3** (6.0 g, 0.0271 mole), 2-dimethylaminoethylamine (9.59 g, 0.109 mole) and titanium tetrachloride (3.42 g, 0.018 mole) in toluene (250 ml) there was obtained 3.12 g of a viscous light yellow oil; ^{1}H nmr (deuteriochloroform): δ 2.22 (d, 6H, J = 2 Hz, -N(CH_3)$_2$), 2.42 (d, 3H, J = 2 Hz, C=C-CH_3).

5,6-Dihydro-12-(2-dimethylaminoethyl)-6-methylbenzo[5,6]cyclohepta-[1,2-*c*]pyridin-6,11-imine (**6c**).

A mixture of **4c** (3.12 g, 0.0107 mole), sodium borohydride (0.40 g, 0.0105 mole) and acetonitrile (150 ml) was treated as described for **4a**. After chromatogaphy over silica (90 g) eluting with chloroform then 90% chloroform-10% methanol the product (1.5 g) was dissolved in acetone (25 ml) and treated with a hot solution of fumaric acid (0.60 g, 0.0052 mole) in acetone (100 ml) to give 1.43 g of white crystals, mp 168-169.5° dec; ^{1}H nmr (DMSO-d_6): δ 1.55 (s, 3H, ≡CH-CH_3), 2.60 (s, 6H, -N(CH_3)$_2$), 5.17 (s, 1H, H_{11}), 6.53 (s, 3H, fumaric acid olefinic), 6.93 (d, 1H, J = 2.5 Hz, H_4), 8.24 (d, J = 2.5 Hz, H_3), 8.43 (s, 1H, H_1).

Anal. Calcd. for $C_{19}H_{23}N_3 + 1.5C_4H_4O_4$: C, 64.22; H, 6.25; N, 8.99. Found: C, 64.23; H, 6.39; N, 8.76.

11-Allylimino-6-methylbenzo[5,6]cyclohepta[1,2-*c*]pyridine (**4d**).

Following the procedure for **4a** and using **3** (4.0 g, 0.0181 mole), allylamine (4.14 g, 0.0725 mole) and titanium tetrachloride (1.4 ml, 0.012 mole) in toluene (300 ml) there was obtained 3.0 g of viscous yellow oil; ^{1}H nmr (deuteriochloroform): δ 2.40 (d, 3H, J = 1 Hz, =C-CH_3), 6.80 (br s, 1H, =C-H).

12-Allyl-5,6-dihydro-6-methylbenzo[5,6]cyclohepta[1,2-*c*]pyridin-6,11-imine (**6d**).

A mixture of **4d** (3.0 g, 0.00115 mole), sodium borohydride (0.44 g, 0.0016 mole) and chloroform (150 ml) was stirred at 25° for 3 hours. The residue (2.72 g) after work-up as described in the preparation of **6b** was dissolved in ethanol (100 ml) and 5 ml of 9*N* hydrogen chloride in ethanol was added. The mixture was heated to reflux overnight and the hot mixture was filtered to give 2.4 g of white solid, mp 197-202° dec; ^{1}H nmr (deuterium oxide): δ 2.13 (s, 3H, ≡C-CH_3), 6.27 (s, 1H, H_{11}), 7.55 (br s, 4H, aromatic), 7.78 (d, 1H, J = 3 Hz, H_4), 8.72 (d, 1H, J = 3 Hz, H_3), 9.0 (s, 1H, H_1).

Anal. Calcd. for $C_{18}H_{18}N_2$ + 2HCl + 1.5H_2O: C, 59.67; H, 6.40; N, 7.73; Cl, 19.57. Found: C, 59.38; H, 6.34; N, 7.61; Cl, 19.43.

5-Bromobenzo[5,6]cyclohepta[1,2-*c*]pyridin-11-one (**12**).

A solution of bromine (4.18 ml) in acetic acid (50 ml) was added dropwise to **11** [8] (12.35 g, 0.60 mole) in acetic acid and the resulting mixture was heated on the steam bath for 24 hours. After the solvent was removed under reduced pressure, the residue was treated with saturated sodium carbonate solution (500 ml) and the resulting yellow solid was filtered, washed with water and dried. Recrystallization from 1-chlorobutane gave 9.3 g, mp 167-169°.

Anal. Calcd. for $C_{14}H_8BrNO$: C, 58.76; H, 2.82; N, 4.89; Br, 27.93. Found: C, 58.79; H, 3.07; N, 4.83; Br, 27.54.

5-Bromo-11-methoxybenzo[5,6]cyclohepta[1,2-*c*]pyridin-11-ol (**15**).

Methyl magnesium bromide (27.6 ml, 2.9 *M* in ether) was added dropwise to a solution of **12** (20.02 g, 0.070 mole) in THF (300 ml) with cooling. The resulting mixture was stirred at 25° for 24 hours. The solvent was removed *in vacuo*, the residue was taken up in water (300 ml) and acidified with acetic acid. The resulting solid was filtered, washed with water and recrystallized from 2-propanol to give 16.25 g, mp 226.5-229.5°.

5-Bromo-11-methylenebenzo[5,6]cyclohepta[1,2-*c*]pyridine (**16**).

Concentrated sulfuric acid (15 ml) was added gradually to a stirred solution of **15** (6.1 g) in acetic acid (50 ml). After 24 hours, water (500 ml) was added and the solution was made alkaline by the addition of 20% sodium hydroxide solution. The basic mixture was extracted with ethyl acetate (4 × 150 ml) and the combined extracts were washed with water, saturated sodium chloride solution and dried (sodium sulfate). After removal of the solvent *in vacuo* the product, 5.65 g, was obtained as a dark brown oil that was used directly in the next step without purification; ms: (M^+/e) 282.9995. Calcd: $C_{15}H_{10}NBr^{79}$: 283.256.

11-Methylene-6-(4-methylpiperazinyl)benzo[5,6]cyclohepta[1,2-*c*]pyridine (**17**).

A mixture of **16** (11.0 g) methylpiperazine (7.8 ml), potassium *t*-butoxide (8.4 g) and *t*-butanol (150 ml) was heated under reflux for 4 hours. The *t*-butanol was removed *in vacuo* and the residue was taken up in methylene chloride (600 ml). After washing with 10% sodium chloride solution, saturated sodium chloride solution and drying (sodium sulfate), the solvent was removed to give 10.76 g of a dark amber oil that was used directly in the next step.

11-Methylenebenzo[5,6]cyclohepta[1,2-*c*]pyridin-6-one (**18**).

A mixture of **17** (10.76 g) and 3*N* hydrochloric acid (150 ml) was stirred at room temperature for approximately 24 hours. The dark brown solution was made alkaline by the addition of 20% sodium hydroxide solution and extracted with methylene chloride. The extracts were washed with water, saturated sodium chloride solution and dried (sodium sulfate). Removal of the solvent *in vacuo* followed by trituration with petroleum ether (30-60°) gave 6.2 g, mp 98-110°.

11-Methylenebenzo[5,6]cyclohepta[1,2-*c*]pyridin-6-one Oxime (**19**).

A mixture of **18** (6.2 g), anhydrous sodium acetate (3.1 g), hydroxylamine hydrochloride (2.48 g) and methanol (130 ml) was heated under reflux for 24 hours. The solvent was removed *in vacuo*, water (100 ml) was added and the resulting yellow-orange solid was filtered and dried, 6.4 g, mp 183-205°. Recrystallization from toluene gave material with mp 218.5-221° dec.

Anal. Calcd. for $C_{15}H_{12}N_2O$: C, 76.25; H, 5.12; N, 11.86. Found: C, 76.45; H, 5.16; N, 11.87.

N-(5,6-Dihydro-11-methylenebenzo[5,6]cyclohepta[1,2-*c*]pyridin-6-yl)hydroxylamine (**20**).

A 10% hydrochloric acid solution (50 ml) was added dropwise to a cold (0-5°) solution of **19** (2.60 g), sodium cyanoborohydride (5.0 g), ethanol (50 ml) and THF (100 ml). When addition was complete, the cooling bath was removed and the resulting mixture was stirred overnight. The reaction mixture was diluted with water (250 ml) and extracted with ethyl

acetate to remove unreacted oxime (recovery 0.70 g). The resulting aqueous layer was brought to *p*H 8 with dilute sodium hydroxide solution and re-extracted with ethyl acetate. The combined extracts of the basic solution were washed (water, saturated sodium chloride solution) and dried (sodium sulfate). Evaporation of the solvent after filtration gave 1.7 g of yellow solid, mp 130-136°. Recrystallization from ethyl acetate gave material with mp 138-141°; ^{1}H nmr (deuteriochloroform): δ 3.33 (d, 2H, J = 6 Hz, $H_{5\alpha,5\beta}$), 4.50 (t, 1H, J = 6 Hz, H_6), 5.50, 5.57 (d, 2H, J = 1 Hz, $=CH_2$), 7.13 (d, 1H, J = 2.5 Hz, H_4), 7.34 (s, 4H, H_{7-10}), 8.42 (d, 1H, J = 2.5 Hz, H_3), 8.61 (s, 1H, H_1).

Anal. Calcd. for $C_{15}H_4N_2O$: C, 75.61; H, 5.92; N, 11.76. Found: C, 75.65; H, 6.02; N, 11.53.

12-Hydroxy-11-methylbenzo[5,6]cyclohepta[1,2-*c*]pyridin-6,11-imine (**21**).

A mixture of **20** (1.8 g) and toluene (40 ml) was heated to reflux for 4.5 hours. The solvent was removed under reduced pressure and the residue was chromatographed over silica gel (50 g). After removal of some by-product by elution with methylene chloride-ethyl acetate (1:1), the product was eluted with ethyl acetate. Removal of the solvent *in vacuo* gave 1.4 g of light yellow flakes; ^{1}H nmr (deuteriochloroform): δ 1.95 (s, 3H, C_{11}-CH_3), 2.47 (d, 1H, J = 18 Hz, $H_{5\alpha}$), 3.60 (dd, 1H, J = 18, 3 Hz, $H_{5\beta}$), 4.60 (d, J = 3 Hz, H_6), 6.79 (d, 1H, J = 2.5 Hz, H_4), 6.91-7.28 (m, 4H, H_{7-10}), 8.23 (d, 1H, J = 2.5 Hz, H_3), 8.40 (s, 1H, H_1).

5,6-Dihydro-11-methylbenzo[5,6]cyclohepta[1,2-*c*]pyridine-6,11-imine (**22**).

Zinc dust (1.4 g) was added to a solution of **21** (1.4 g) in acetic acid (40 ml) and the resulting mixture was heated (80-100°) for 4 hours. The reaction mixture was cooled, diluted with water (300 ml) and filtered. The filtrate was made alkaline with 20% sodium hydroxide solution and extracted with ethyl acetate. The extracts were washed with saturated sodium chloride solution and dried (sodium sulfate). Filtration and evaporation of the solvent gave 1.1 g of a straw-colored foam that was converted to a fumarate salt by treatment with 1.1 g of fumaric acid in 150 ml of boiling acetone, yield 1.3 g, mp 194-195.5°; ^{1}H nmr (DMSO-d_6): δ 2.03 (s, 3H, C_{11}-CH_3), 2.72 (d, 1H, J = 18 Hz, $H_{5\alpha}$), 3.47 (dd, 1H, J = 18, 3 Hz, $H_{5\beta}$), 4.88 (d, 1H, J = 3 Hz, H_6), 6.93-7.43 (m, 5H, H_{7-10}, H_4), 8.24 (d, 1H, J = 2.5 Hz, H_3), 8.53 (s, 1H, H_1).

Anal. Calcd. for $C_{15}H_{14}N_2 + C_4H_4O_4$: C, 67.45; H, 5.36; N, 8.28. Found; C, 67.52; H, 5.40; N, 8.25.

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[11] The ^{1}H nmr analysis of this oil indicated it to be the uncyclized amine **5a**.