# 214. 1-Aralkylated Tetrahydro-2-benzazepines[1]). Part III. Synthesis from β-tetralones

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*Summary.* 1-Benzyl-tetrahydro-2-benzazepin-3-ones **4** were prepared by submitting the corresponding 1-benzyl-β-tetralones **3** to the *Schmidt* reaction. On the other hand, the rearrangement of the tetralones **3** by the *Beckmann* procedure gave 1-benzyl-tetrahydro-3-benzazepin-2-ones **5**. The syntheses of some hexahydrophenanthro-azepines of types **10** and **15** are also described.

**Introduction.** – In parts I and II of this study the synthesis of tetrahydro-2-benzazepines carrying methoxy groups in the aromatic nucleus was described. In part I [1], methoxyphenyl-propionamides were used as starting materials, the methoxy groups being necessary to direct the subsequent acylation to the *ortho* position of the propionamide side-chain. Also in part II [2], at least one methoxy group was needed to promote the *Bischler-Napieralski* ring-closure of the intermediate amides. The present synthesis was designed to obtain tetrahydro-2-benzazepines which do not carry methoxy groups in the aromatic ring.

**Results.** – β-Tetralone (**1**) was aralkylated with substituted benzyl chlorides *via* the enamine **2**, giving compounds of type **3**. In a few cases, aralkylated enamine hydrochlorides could be easily separated in crystalline form.

Treatment of the benzylated β-tetralones **3**, usually as crude oils, with sodium azide in concentrated acids (*Schmidt* reaction) gave mainly the readily isolable tetrahydro-2-benzazepin-3-ones **4**, together with some of the isomeric tetrahydro-3-benzazepin-2-ones **5**. When the *Beckmann* rearrangement was used instead, compounds **5** were obtained as the main products.

For dissolving the 1-benzyl-β-tetralones **3** without side reactions, different acidic media were used in the *Schmidt* reaction. For example, the tetralone **3e** was not soluble in polyphosphoric acid (PPA) or in phosphoric acid; concentrated sulfuric acid giving mainly by-products was also found to be unsuitable. A mixture of acetic acid and sulfuric acid gave the best yields. When the tetralone **3d** was dissolved in warm PPA prior to treatment with sodium azide, the compound readily cyclized to 8,9-dimethoxy-6,11-dihydro-5*H*-benzo[*a*]fluorene (m.p. 180–185°) identified by NMR. This cyclodehydration did not occur in 85% phosphoric acid.

In the NMR. spectra of compounds **4**, the proton at the 1-position appeared at about δ 4.8 ppm as an indistinct multiplet which collapsed to a clear double doublet

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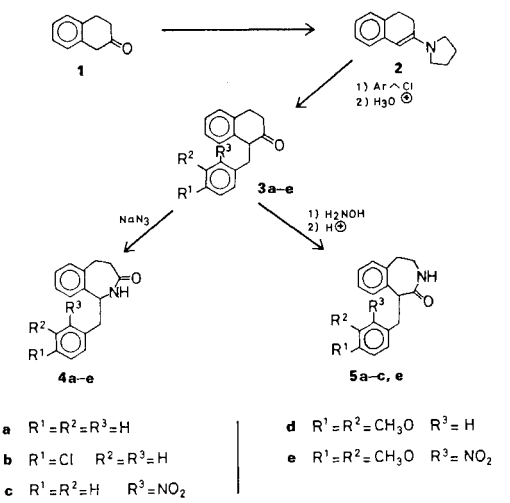
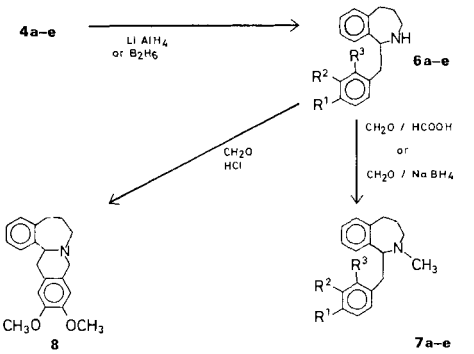
1) 20th Communication on seven-membered heterocycles; 19th Communication: [1].




when the sample was treated with $D_2O$. The corresponding proton in the isomeric products **5** appeared at about $\delta$ 4.4 ppm as a clear double doublet which was not affected by the deuterium exchange technique.

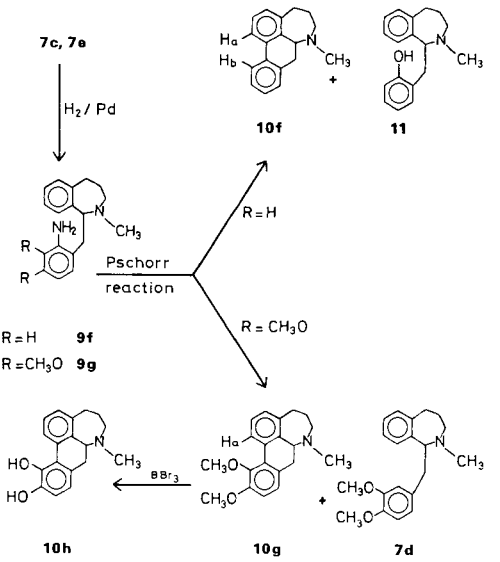
Lactams of type **4** were reduced with $LiAlH_4$, or with diborane when nitro or chloro substituents were present. The resulting 1-benzyl-tetrahydro-2-benzazepines **6** were methylated by the *Clarke-Eschweiler* method to compounds of type **7** or, in the case of **6d**, by $NaBH_4$ reduction of its adduct with formaldehyde, thus avoiding the formation of the tetracyclic compound **8**. The latter could be prepared by treating **6d** with formaldehyde and HCl.




The nitro group of the methylated products **7c** and **7e** was catalytically hydrogenated to give the amino compounds **9f** and **9g**. These were submitted to a modified *Pschorr* reaction [3] to yield small amounts of the hexahydronaphtho-benzazepines **10f** and **10g**. The product **10f** was obtained in 35% yield together with the phenolic

by-product **11**. Compound **10g** was obtained in only 20% yield together with the deaminated compound **7d** as the major product but could be easily separated by crystallization from this mixture.

In analogy to the aporphines the signals for the protons $H_a$ and $H_b$ of compound **10f** appear on the NMR. spectrum significantly more downfield (multiplet centered at $\delta$ 7.8 ppm) than the other aromatic protons (multiplet centered at $\delta$ 7.25 ppm).




With compound **10g**, the deshielding effect on the proton $H_a$ is even bigger (double doublet centered at $\delta$ 8.5 ppm), due mainly to the presence of the methoxy groups.

The 'Homoapomorphine' **10h**[2]) was obtained on treatment of **10g** with $BBr_3$.

Conversion of tetralones **3** to their oximes and subsequent treatment with concentrated acids gave the lactams **5** together with small amounts of lactams **4**. In practice, the lactams **5** were prepared in one step from the tetralones **3** by dissolving the tetralones in PPA, by adding hydroxylamine sulfate and by heating the mixture to approximately 100°. The lactam **5d** could be prepared neither by this one-step procedure nor from the oxime[3]), the above mentioned benzo[*a*]fluorene being the only product that could be isolated. Compound **5e** could be obtained only from the isolated **3e** oxime in PPA, but **5e** and its by-product **4e** could not be separated.

Lactams **5** were successively reduced with $LiAlH_4$ or diborane to **12** and methylated to give compounds **13**. In analogy to the corresponding nitro-2-benzazepines

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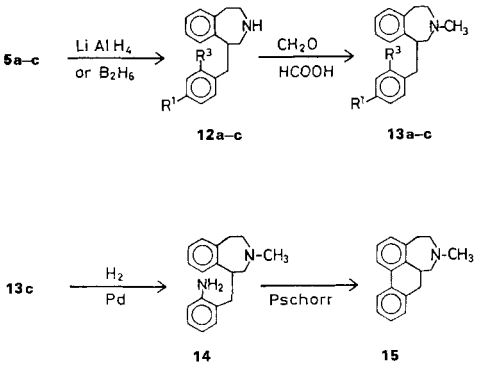
[2]) Concerning the conformation and biological properties of compound **10h**, see *D. Berney et al.* [4].

[3]) The tetralone **3d** treated with $NH_2OH \cdot HCl$ and $Na_2CO_3$ in methanol gave the oxime of **3d**, m.p. 138–140°.




already discussed, the nitro group of the 3-benzazepine **13c** was hydrogenated, yielding the amine **14**. The *Pschorr* reaction on **14** gave the expected tetracyclic compound **15**[4]).

## Experimental Part

*General.* For general remarks on NMR. spectra and microanalyses see part I [1].

*1-Benzyl-3,4-dihydro-1* H-*2-naphthalenone* (**3a**). $\beta$-Tetralone (**1**) [5] (73 g, 0.5 mol) was dissolved in benzene (200 ml) and refluxed in an apparatus equipped with a *Dean-Stark* water-trap. Pyrrolidine (42.7 g, 0.6 mol) was added dropwise and the reaction mixture heated for 1 h under reflux. Benzyl chloride (170 g, 1.35 mol) was then added and the solution was heated for 4 h under reflux. After the addition of water (680 ml) the mixture was heated at reflux for a further 3 h. The organic layer was separated, washed with a saturated aqueous $NaHSO_3$-solution, then with water, dried over $Na_2SO_4$ and evaporated to dryness. The crude oil was distilled under reduced pressure to give 95.5 g (81%) of **3a** as a yellowish product, b.p. 140–145°/0.02 Torr. For preparations, the crude oil could be used. – NMR.: 3.2 (*d*, $J = 6$, 2H, $CH_2$ benzyl); 3.7 (*t*, $J = 6$, 1H, ArCHCO).

*1-(4'-Chlorobenzyl)-3,4-dihydro-1* H-*2-naphthalenone* (**3b**). As for **3a**; $\beta$-tetralone (29.2 g, 0.2 mol), benzene (80 ml), pyrrolidine (17.1 g, 0.24 mol) heated for 2 h under reflux. *p*-Chlorobenzyl chloride (*Fluka*) (57.8 g, 0.34 mol) was added and heated for a further 2.5 h. The solution was then cooled, and the crystalline alkylated enamine hydrochloride was filtered off. After being washed with benzene, it was heated with benzene (80 ml) and water (100 ml) for 3 h under reflux. After work-up as for **3a**, the crude oil **3b** (32.5 g) was used for the next steps.

*1-(2'-Nitrobenzyl)-3,4-dihydro-1* H-*2-naphthalenone* (**3c**). As for **3a**; $\beta$-tetralone (14.6 g, 0.1 mol), benzene (40 ml), pyrrolidine (8.9 g, 0.125 mol) heated for 2 h under reflux. *o*-Nitrobenzyl chloride (*Fluka*) (25.6 g, 0.15 mol) was added, and further heated for 4 h. After cooling, the crystalline enamine salt was filtered off, washed with benzene and refluxed with benzene (40 ml) and water (135 ml) for 3 h, yielding after work-up 20.8 g of a dark brown viscous oil which; for analysis was crystallized twice from ether/petrol ether, yielding 13.6 (48%) of **3c**, m.p. 85–90°. $C_{17}H_{15}NO_3$: C, H, N.

*1-(3',4'-Dimethoxybenzyl)-3,4-dihydro-1* H-*2-naphthalenone* (**3d**). As for **3a**; $\beta$-tetralone (146 g, 1 mol), benzene (500 ml), pyrrolidine (85.3 g, 1.2 mol) refluxed for 2 h. 3,4-Dimethoxybenzyl chloride [6] (260 g, 1.39 mol) was added and the mixture heated for 6 h under reflux. Water (1500 ml) was added and heating was continued for 3 h. After work-up 301 g of crude **3d** as an orange oil were collected.

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[4]) The mixture of the isomeric lactams **5e** and **4e** was reduced with $B_2H_6$ and methylated. The nitro group was hydrogenated and the mixture of the isomers was submitted to the *Pschorr* reaction, which gave a small amount of the 11,12-dimethoxyphenanthro[10,1-*b*,*c*]azepine **10g** (obtained from the by-product **4e**) but none of the desired phenanthro[10,1-*c*,*d*]azepine of the type exemplified by **15** (expected from the major product **5e**).

*1-(3',4'-Dimethoxy-2'-nitrobenzyl)-3,4-dihydro-1*H*-2-naphthalenone* (**3e**). As for **3a**; β-tetralone (438 g, 3 mol), benzene (1200 ml), pyrrolidine (256.5 g, 3.6 mol) heated for 2 h under reflux. 2-Nitro-3,4-dimethoxybenzyl chloride [7] (1042.5 g, 4.5 mol) was added and heating was continued for 4 h. After cooling, the crystalline enamine salt was filtered off, washed with benzene and heated for 3 h with water (4000 ml) and benzene (1200 ml) under reflux. After work-up, 729 g (71%) of crude **3e** were collected as a brownish oil. 7 g of this oil were crystallized twice from ether/petroleum ether yielding 6.25 g of **3e**, m.p. 76–84°. The crude oil was used for the next steps.

*1-Benzyl-1,2,4,5-tetrahydro-3*H*-2-benzazepin-3-one* (**4a**) (Caution: This and all subsequent reactions using sodium azide should be carried out behind a heavy safety screen in the fume hood). During the whole reaction time, the reaction vessel was flushed with nitrogen in order to keep down the concentration of hydrazoic acid. 1-Benzyl-β-tetralone (**3a**) (67 g, 0.28 mol) was added to PPA (700 g) at 40° with mechanical stirring. Sodium azide (22.7 g, 0.35 mol) was added portionwise during a period of 2 h. The reaction mixture was stirred for a further 3 h at 40°, then poured into ice/water and extracted three times with $CHCl_3$. The extract was washed with 2N $KHCO_3$, dried over $Na_2SO_4$ and evaporated to dryness. The residue was dissolved in a small amount of $CHCl_3$, ether was added and the product was allowed to crystallize, giving 40.8 g (m.p. 115-135°) of a mixture of **4a** and **5a**. **4a** could be easily obtained by slow recrystallization of the mixture in ethanol (300 ml), giving 14.2 g (20%) of pure lactam **4a**, m.p. 153–155°. – NMR.: 4.8 (br. *m*, collapses to a sharp $d \times d$ after deuterium exchange, 1H, ArCHN); 6.0 (br. *d*, disappears after deuterium exchange, 1H, NH). – $C_{17}H_{17}NO$: C, H, N.

*1-(4'-Chlorobenzyl)-1,2,4,5-tetrahydro-3*H*-2-benzazepin-3-one* (**4b**). Flushing with nitrogen as for **4a**. Crude **3b** (16 g), was dissolved in stirred glacial acetic acid (160 g) at room temperature. After the slow addition of sodium azide (9.6 g), conc. $H_2SO_4$ (24 ml) was added dropwise. The temperature rose slowly to around 50°. After a further 30 min the reaction mixture was poured into ice/water, and extracted with $CHCl_3$. The extract was washed with 2N $KHCO_3$, dried over $Na_2SO_4$ and evaporated to dryness. The residual oil was crystallized from $CHCl_3$/ether yielding 12.2 g (72%). This product was a mixture of **4b** and **5b**, from which **4b** could be separated by slow recrystallization from $CHCl_3$/ether, yielding 8 g (47%) of pure material, m.p. 156–158°. – $C_{17}H_{16}ClNO$: C, H, N.

*1-(2'-Nitrobenzyl)-1,2,4,5-tetrahydro-3*H*-2-benzazepin-3-one* (**4c**). Flushing with nitrogen as for **4a**. The crude ketone **3c** (16 g) was dissolved in 85% $H_3PO_4$ (150 g) with stirring. Sodium azide (7.5 g) was added in small portions at room temperature, during a period of 45 min. The temperature was then raised to 60° for 1 h. After the work-up as for **4a**, the residue was recrystallized slowly from $CHCl_3$/ether yielding 5.2 g (30%) of pure **4c**, m.p. 200–209°. – $C_{17}H_{16}N_2O_3$: C, H, N.

*1-(3',4'-Dimethoxy)-1,2,4,5-tetrahydro-3*H*-2-benzazepin-3-one* (**4d**). Flushing with nitrogen as for **4a**. Sodium azide (8.3 g, 0.13 mol) was added to $H_3PO_4$ (250 ml, 85%) with stirring at 10° (Caution: Explosion danger!). After the slow addition of the crude ketone **3d** (25 g) the reaction mixture was brought slowly to room temperature and heated to 80° until no more gas evolution could be observed. After a work-up as for **4a**, the residue was recrystallized from $CHCl_3$/ether yielding 6.7 g (25%) of **4d**, m.p. 207–210°. – $C_{19}H_{21}NO_3$: C, H, N.

*1-(3',4'-Dimethoxy-2'-nitrobenzyl)-1,2,4,5-tetrahydro-3*H*-2-benzazepin-3-one* (**4e**). As for **4b**. The crude ketone **3e** (20 g) was diluted at room temperature with glacial acetic acid (200 g). After the slow addition of sodium azide (9.7 g), conc. $H_2SO_4$ (30 ml) was added dropwise during a period of 30 min. Stirring was continued for 2 h at 50°, then the reaction mixture was worked up and the residue recrystallized from $CHCl_3$/ether yielding 9.0 g (42% from **3e**) of pure **4e**, m.p. 153–158°. – $C_{19}H_{20}N_2O_5$: C, H, N.

*1-Benzyl-2,3,4,5-tetrahydro-1*H*-2-benzazepine* (**6a**) *hydrogen maleate*. Compound **4a** (10 g, 0.04 mol) was suspended in tetrahydrofuran (THF) (100 ml). $LiAlH_4$ (3.8 g, 0.1 mol) was added portionwise. The mixture was heated for 2 h under reflux and cooled; water (6 ml) was then added dropwise. After the addition of $CHCl_3$ the mixture was filtered, dried and evaporated. The crude oily amine was converted to its hydrogen maleate by dissolving in a small amount of ethanol and by adding a solution of maleic acid in ethanol; ether was then added and the compound was allowed to crystallize. It was recrystallized from ethanol/ether, yielding 3.9 g (27%) of **6a** hydrogen maleate, m.p. 106–110°. – NMR.: 3.2 (br. *s*, 1H, NH); 4.2 ($d \times d$, 1H, ArCHN). – $C_{21}H_{23}NO_4$: C, H, N.

*1-(4'-Chlorobenzyl)-2,3,4,5-tetrahydro-1* H-*2-benzazepine* (**6b**) *hydrochloride*. The entire reaction was made under nitrogen. The lactam **4b** (25 g, 0.0875 mol) was suspended in dry THF (100 ml), and the reaction flask was cooled in ice/water. 1 M solution of $B_2H_6$/THF (*Aldrich*) (175 ml) was added slowly with stirring. The mixture was kept for 30 min at 0–5°, then 2.5 h at room temperature. Then water was added very slowly to destroy the excess of diborane. The solution was then evaporated almost to dryness, 2 N HCl (700 ml) was added, and the mixture was heated for 30 min under reflux. The crystalline chlorhydrate which separated was filtrated off from the hot solution and recrystallized from ethanol/water, yielding 20.2 g (75%) of **6b** hydrochloride, m.p. 268–272°. – $C_{17}H_{19}Cl_2N$: C, H, N.

*1-(2'-Nitrobenzyl)-2,3,4,5-tetrahydro-1* H-*2-benzazepine* (**6c**). As for the reduction of **4b**. The lactam **4c** (10 g, 0.034 mol), THF (100 ml) and 1 M $B_2H_6$/THF solution (100 ml) were kept for 30 min at 0–5°, then 2 h at room temperature. Water was added and the reaction mixture evaporated. 2 N HCl (250 ml) was added and the mixture heated for 30 min under reflux, made alkaline with 5 N NaOH and extracted with $CHCl_3$. The organic phase was dried and evaporated. The residue was recrystallized from petroleum/ether, yielding 5 g (53%) of **6c**, m.p. 62–67°. – $C_{17}H_{18}N_2O_2$: C, H, N.

*1-(3',4'-Dimethoxybenzyl)-2,3,4,5-tetrahydro-1* H-*2-benzazepine* (**6d**) *naphthalene-1,5-disulfonate*. As for the reduction of **4a**. Compound **4d** (5 g, 16 mmol), THF (100 ml), $LiAlH_4$ (1.5 g, 40 mmol), heated for 2 h under reflux. After work-up the oily crude amine was converted to its naphthalene-1,5-disulfonate by dissolving it in a small amount of ethanol and adding a warm solution of the calculated amount of naphthalene-1,5-disulfonic acid (NDS) [8] in ethanol. The salt which crystallized after the addition of ether was recrystallized from dimethylformamide/$H_2O$ on addition of ethanol/ether, yielding 3.8 g (54%) of **6d** NDS salt, m.p. 295–297°. – $C_{24}H_{27}NO_5S$: C, H, N.

*1-(3',4'-Dimethoxy-2'-nitrobenzyl)-2,3,4,5-tetrahydro-1* H-*2-benzazepine* (**6e**). As for the reduction of **4b**, but using dry dimethoxyethane (DME) instead of THF. Lactam **4e** (17.8 g, 0.05 mol), DME (150 ml), 1 M $B_2H_6$/THF solution (150 ml) were kept at 0–5° for 30 min, followed by 2 h at room temperature. Water was added. After evaporation the residue was heated with 2 N HCl (250 ml) for 30 min under reflux and filtered to remove some insoluble impurities. The filtrate was made alkaline and was extracted with $CHCl_3$. The organic layer was dried, evaporated to dryness, and the residue was recrystallized from petroleum/ether, yielding 10 g (58%) of **6e**, m.p. 107–110°. – $C_{19}H_{22}N_2O_4$: C, H, N.

*1-Benzyl-2-methyl-2,3,4,5-tetrahydro-1* H-*2-benzazepine* (**7a**) *hydrochloride*. The amine **6a** (5 g, 21 mmol) was heated for 2 h with formic acid (15 ml) and with 35% aqueous formaldehyde solution (10 ml) under reflux. The solution was then poured into water, made alkaline with 5 N NaOH and extracted with $CHCl_3$. The organic layer was dried and evaporated to dryness. The oil was diluted with ethanol, and a slight excess of a solution of HCl gas in ether was added; more ether was then added, and the solution was allowed to crystallize. The salt was recrystallized from ethanol/ether yielding 4.5 g (74%) of **7a** hydrochloride, m.p. 233–240°. – NMR.: 2.2 (*s*, 3H, $NCH_3$); 3.2 (*d*, $J$ = 6, 2H, $CH_2$ benzyl); 4.1 (*t*, $J$ = 6, 1H, ArCHN). – $C_{18}H_{22}ClN$: C, H, N.

*1-(4'-Chlorobenzyl)-2-methyl-2,3,4,5-tetrahydro-1* H-*2-benzazepine* (**7b**) *hydrochloride*. As for the methylation of **6a**. The amine **6b** (10 g, 0.033 mol), formic acid (15 ml), and 38% formaldehyde solution (10 ml) were heated for 1 h under reflux. After work-up, the crude amine was converted to its HCl salt which was recrystallized from $H_2O$/ethanol/ether, yielding 7.5 g (71%) of **7b** hydrochloride, m.p. 224–231°. – $C_{18}H_{21}Cl_2N$: C, H, N.

*1-(2'-Nitrobenzyl)-2-methyl-2,3,4,5-tetrahydro-1* H-*2-benzazepine* (**7c**) *hydrochloride*. As for the methylation of **6a**. The amine **6c** (14.2 g, 0.05 mol), formic acid (25 ml), 35% formaldehyde solution (15 ml) were heated for 1 h under reflux. After work-up, the crude amine was converted to its HCl salt, yielding after recrystallization from ethanol/ether 12.5 g (75%) of **7c** hydrochloride, m.p. 236–240°. – $C_{18}H_{21}ClN_2O_2$: C, H, N.

*1-(3',4'-Dimethoxybenzyl)-2-methyl-2,3,4,5-tetrahydro-1* H-*2-benzazepine* (**7d**) *naphthalene-1,5-disulfonate*. The amine **6d** (29.7 g, 0.1 mol) was dissolved in ethanol (100 ml) and a 35% aqueous solution of formaldehyde (150 ml) was added. The solution was then heated for 1 h under reflux and cooled to 0–5°. $NaBH_4$ (39.5 g, 1.05 mol) was added portionwise and the reaction mixture

was brought slowly to room temperature. After work-up, the amine was converted to its NDS salt (see preparation of **6d** NDS salt) yielding 20 g (44%) of **7d** salt, m.p. 180–185°. – $C_{25}H_{29}NO_5S$: C, H, N.

*11,12-Dimethoxy-6,7,14,14a-tetrahydro-isoquino[3,2-a][2]benzazepine* (**8**). The amine **6d** (12 g, 0.041 mol) was dissolved in 2N HCl (75 ml) and 35% aqueous formaldehyde solution (24 ml) was added. The solution was heated for 1 h under reflux, cooled, made alkaline with 5N NaOH and extracted with $CHCl_3$. The organic extract was dried and evaporated to dryness. The residue was recrystallized from methanol, yielding 8.4 g (67%) of **8**, m.p. 156–158°. – NMR.: 3.6 (*s*, 2H, $ArCH_2N$); 3.75 (*s*, 3H, $OCH_3$); 3.85 (*s*, 3H, $OCH_3$); 4.4 (*t*, 1H, ArCHN); 6.5 (*s*, 1H, ArH); 6.75 (*s*, 1H, ArH). – $C_{20}H_{19}NO_2$: C, H, N.

*1-(3',4'-Dimethoxy-2'-nitrobenzyl)-2-methyl-2,3,4,5-tetrahydro-1*H*-2-benzazepine* (**7e**). As for the methylation of **6a**. Amine **6e** (80 g, 0.23 mol), formic acid (120 ml), 35% formaldehyde solution (80 ml), heated for 1 h under reflux. After work-up the product was recrystallized from ether/petroleum ether, yielding 78 g (94%) of **7e**, m.p. 112–115°. – $C_{20}H_{24}N_2O_4$: C, H, N.

*1-(2'-Aminobenzyl)-2-methyl-2,3,4,5-tetrahydro-1*H*-2-benzazepine* (**9f**) *hydrochloride*. The nitro compound **7c** HCl salt (14 g, 0.04 mol) was dissolved in acetic acid (300 ml) and Pd/C 5.4% (3 g) was added. The solution was hydrogenated at normal pressure and temperature. After filtration, ether was added (250 ml) and the product was allowed to crystallize, yielding 12 g (95%) of **9f** hydrochloride, m.p. 263–270°. – $C_{18}H_{23}ClN_2$: C, H, N.

*1-(3',4'-Dimethoxy-2'-aminobenzyl)-2-methyl-2,3,4,5-tetrahydro-1*H*-2-benzazepine* (**9g**). The nitro compound **7e** (133 g, 0.373 mol) was dissolved in ethanol (1000 ml), Pd/C 5.4% (10 g) was added, and the mixture was hydrogenated for about 24 h at normal pressure and temperature, yielding after work-up 125 g of crude oily **9g** which was used without purification. – NMR.: 2.1 (*s*, 3H, $NCH_3$); 3.8 (*s*, 6H, $2OCH_3$); 4.2 (*t*, 1H, ArCHN); 4.4 (br., 1H, $NH_2$); 6.2 (*d*, $J = 8$, 1H, ArH); 6.6 (*d*, $J = 8$, 1H, ArH).

*1-(2'-Hydroxybenzyl)-2-methyl-2,3,4,5-tetrahydro-1*H*-2-benzazepine* (**11**) *and 7-methyl-4,5,6,7,-7a,8-hexahydro-phenanthro[10,1-*b,c*]azepine* (**10f**) *naphthalene-1,5-disulfonate*. A solution of sodium nitrite (3.3 g) in water (30 ml) was added dropwise to a cold, stirred solution of amino compound **9f** hydrochloride (12 g) in acetic acid (190 ml) and conc. sulfuric acid (14 ml). The mixture was kept at 5–10° for 15 min, sulfamic acid (0.8 g) and cold 3N sulfuric acid (270 ml) were added. The mixture was stirred at 90° for 30 min. Zinc-dust (15.5 g) was added and the stirring and warming continued for an additional 30 min. The hot solution was filtered, cooled with ice, made alkaline with ammonia and extracted with chloroform. The extract was washed with saturated sodium chloride solution, dried over sodium sulfate and taken to dryness *in vacuo*. The dark, oily residue (13 g) was dissolved in ether, treated with charcoal and filtered. On cooling, **11** crystallized (4.7 g, 45%). Recrystallization from ether yielded an analytical sample, m.p. 147–149°. – $C_{18}H_{21}NO$: C, H, N.

The filtrate, after collecting **9h** was taken to dryness and the residue (4,5 g) was dissolved in warm ethanol. On adding a concentrated ethanolic solution of naphthalene-1,5-disulfonic acid (2.6 g), the NDS salt of **10f** was obtained; recrystallized from a mixture of dimethylformamid, water and ethanol by adding ether. Yield: 3.7 g (24%) of **10f** NDS salt, m.p. 263–266°. – NMR.: 1.85 (*s*, 3H, $NCH_3$); 4.45 ($d \times d$, 1H, ArCHN); 7.25 (*m*, 5H, arom); 7.8 (*m*, 2H, arom). – $C_{23}H_{23}NSO_3$: C, H, N.

*11,12-Dimethoxy-7-methyl-4,5,6,7,7a,8-hexahydro-phenanthro[10,1-*b,c*]azepine* (**10g**) *and 1-(3',4'-dimethoxybenzyl)-2-methyl-2,3,4,5-tetrahydro-1*H*-2-benzazepine* (**7d**) *naphthalene-1,5-disulfonate*. As for **10f**. A solution of sodium nitrite (14 g) in water (130 ml) was added dropwise to a cold, stirred solution of amino compound **9g** (60 g) in glacial acetic acid (790 ml) and conc. sulfuric acid (60 ml). The mixture was kept at 5–10° for 15 min. Sulfamic acid (3.3 g) and cold 3N sulfuric acid (1150 ml) were added. The mixture was stirred at 90° for 1 h. Zinc-dust (66 g) was added, and the stirring and heating continued for an additional 30 min.

The hot solution was filtered, the filtrate cooled and made alkaline with ammonia. The mixture was extracted with chloroform, the extract was washed with saturated sodium chloride solution, dried and evaporated. The dark oil was dissolved in ether (500 ml), treated with charcoal and filtered. The filtrate was concentrated to a volume of 150 ml. On cooling, **10g** (11.6 g, 20%) crystallized. Recrystallization from chloroform/ether yielded an analytical sample, m.p. 138–140°. –

NMR. of **10g**: 1.85 (*s*, 3H, $NCH_3$); 3.65 (*s*, 3H, $OCH_3$); 3.85 (*s*, 3H, $OCH_3$); 4.3 (*t*, 1H, ArCHN); 7.0 (*m*, 4H, arom); 8.5 ($d \times d$, $J = 2$ and 7, 1H, arom). – $C_{20}H_{23}NO_2$: C, H, N.

The mother liquor was evaporated, the residue (22 g) dissolved in warm ethanol (220 ml), and a solution of naphthalene-1,5-disulfonic acid (9,7 g) in ethanol (100 ml) was added. On cooling the NDS salt of **7d** crystallized giving 8.4 g, m.p. 183–188°. – $C_{25}H_{29}NO_5S$: C, H, N. Identical with the product obtained from **6d** (superimposable NMR. spectra).

*11,12-Dihydroxy-7-methyl-4,5,6,7,7a,8-hexahydro-phenanthro[10,1-b,c]azepine* (**10h**) *hydrochloride*. A solution of **10g** (16 g, 0.05 ml) in methylene chloride (500 ml) was added to a cold stirred solution of boron tribromide (38.8 g, 0.15 mol) in methylene chloride (500 ml). Stirring was continued for 2 h at 5° and for 20 h at room temperature. The reaction mixture was evaporated to dryness, and the residue boiled for a short time with 2N HCl (250 ml). After the addition of ethanol (250 ml) the hot solution was filtered. On cooling **10h** hydrochloride crystallized (10.3 g, 62%). Recrystallization from ethanol/water yielded an analytical sample, m.p. 255–260° (dec.). – $C_{18}H_{20}ClNO_2$: C, H, N.

*1-Benzyl-1,3,4,5-tetrahydro-2H-3-benzazepin-2-one* (**5a**). Hydroxylamine sulfate (65.5 g, 0.8 mol of $NH_2OH$) was dissolved with efficient stirring in PPA (900 g), kept at 55°. Distilled tetralone **3a** (91 g, 0.39 mol) was then slowly added whereby the temperature rose to about 95°. The reaction mixture was then heated in an oil bath to 100–110° for 30 min and allowed to cool. The mixture was poured into ice/water and extracted with $CHCl_3$. The organic layer was washed with $H_2O$, dried and evaporated to dryness. The crude product was crystallized from $CHCl_3$/ether, yielding 26.2 g (27%) of **5a**, m.p. 142–143°. – NMR.: 4.3 (*t*, 1H, ArCHCO); 6.4 (br., 1H, NH). – $C_{17}H_{17}NO$: C, H, N.

*1-(4'-Chlorobenzyl)-1,3,4,5-tetrahydro-2H-3-benzazepin-2-one* (**5b**). As for the preparation of **5a**; PPA (1600 g), hydroxylamine sulfate (97 g), crude **3b** (155 g). The compound was recrystallized from $CHCl_3$/ether, yielding 59 g (36%) of pure **5b**, m.p. 142–148°. – $C_{17}H_{16}ClNO$: C, H, N.

*1-(2'-Nitrobenzyl)-1,3,4,5-tetrahydro-2H-3-benzazepin-2-one* (**5c**). As for the preparation of **5a**; PPA (1000 g), hydroxylamine sulfate (57.5 g), crude **3c** (90 g). The temperature rose to 55° and the mixture was then maintained at 95° for 30 min. After work-up the crude compound was recrystallized from $CHCl_3$/ether, yielding 27.3 g (29%) of a 3:1 mixture of lactams **5c** and **4c**, m.p. 165–175°. Pure compound **5c** could be isolated by slow recrystallization from toluene, m.p. 178–180°. – $C_{17}H_{16}N_2O_3$: C, H, N.

*1-(3',4'-Dimethoxy-2'-nitrobenzyl)-β-tetralone* (**3e**) *oxime*. Tetralone **3e** (15 g, 0.044 ml) was dissolved in hot methanol (100 ml), water was added (50 ml) and hydroxylamine hydrochloride (5.25 g, 0.075 mol) was added portionwise. After the addition of $K_2CO_3$ (10.5 g, 0.075 mol) the mixture was heated for 15 min under reflux. After cooling, the crystalline solid formed was filtered off, washed with methanol/water and dried *in vacuo*, yielding 11.9 g (75%) of **3e** oxime, m.p. 167–177°. – $C_{19}H_{20}N_2O_5$: C, H, N.

*1-(3',4'-Dimethoxy-2'-nitrobenzyl)-1,3,4,5-tetrahydro-2H-3-benzazepin-2-one* (**5e**) *and 1-(3',4'-dimethoxy-2'-nitrobenzyl)-1,2,4,5-tetrahydro-3H-2-benzazepin-3-one* (**4e**). PPA (1000 g) was heated to 70° with efficient stirring, **3e** oxime (110 g) was added portionwise and the mixture was kept at 70° for 45 min. The reaction mixture was allowed to cool, then poured into ice/water and extracted with $CHCl_3$. The organic layer was dried and evaporated to dryness. The residue was recrystallized from $CHCl_3$/ether, yielding 51 g (51%) of a 3:2 mixture of **5e** and **4e**, m.p. 150–165°. These isomers could not be separated. – $C_{19}H_{20}N_2O_5$: C, H, N.

*1-Benzyl-2,3,4,5-tetrahydro-1H-3-benzazepine* (**12a**) *hydrochloride*. As for the reduction of **4a**; lactam **5a** (16 g, 0.064 mol) was dissolved in THF (200 ml), $LiAlH_4$ (5.9 g, 0.16 mol) was added, and the mixture was heated for 2 h under reflux. After work-up 15.4 g of the crude base was converted to the HCl salt (as for **7a**), yielding 11.7 g (67%) of **12a** hydrochloride, m.p. 247–253°. – NMR.: 2.1 (br., 1H, NH); 3.0 (*m*, 9H, 5 benzylic H and $2CH_2N$). – $C_{17}H_{20}NCl$: C, H, N.

*1-(4'-Chlorobenzyl-2,3,4,5-tetrahydro-1H-3-benzazepine* (**12b**) *naphthalene-1,5-disulfonate*. As for the reduction of **4b**; lactam **5b** (20 g, 0.07 mol), THF (100 ml), 1M $B_2H_6$/THF solution (140 ml, 0.14 mol). After treatment with 2N HCl (600 ml) the solution was made alkaline and the product extracted with $CHCl_3$; 15.8 g of crude base were obtained and were converted to the NDS salt

(as for **6d**), yielding 16 g (55%) of **12b** NDS salt, m.p. 273–276°. – $C_{22}H_{22}ClNO_3S$: C, H, N. – Hydrochloride, m.p. 195–205°.

*1-(2'-Nitrobenzyl)-2,3,4,5-tetrahydro-1*H*-3-benzazepine* (**12c**). As for the reduction of **4b**; lactam **5c** (38 g, 0.13 mol), THF (380 ml), 1 M $B_2H_6$/THF solution (200 ml). After treatment with 2 N HCl (800 ml) the solution was made alkaline and the product extracted with $CHCl_3$. The organic layer was dried, evaporated, and the residue was recrystallized from $CHCl_3$/ether, yielding 19.7 g (54.5%) of **12c**, m.p. 112–115°. – $C_{17}H_{18}N_2O_2$: C, H, N.

*1-Benzyl-3-methyl-2,3,4,5-tetrahydro-1*H*-3-benzazepine* (**13a**) *naphthalene-1,5-disulfonate*. As for the methylation of **6a**. Amine **12a** (7.5 g), formic acid (12 ml), 35% formaldehyde solution (7.5 ml). Yield: 8.2 g (65%) of **13a** NDS salt, m.p. 257–259°. – NMR.: 2.3 (*s*, 3H, $NCH_3$). – $C_{23}H_{25}NO_3S$: C, H, N.

*1-(4'-Chlorobenzyl)-3-methyl-2,3,4,5-tetrahydro-1*H*-3-benzazepine* (**13b**) *hydrochloride*. As for the methylation of **6a**. Amine **12b** (7.9 g), formic acid (12 ml), 35% formaldehyde solution (8 ml). Yield: 6.1 g (65%) of **13b** HCl salt, m.p. 200–213°. – $C_{18}H_{21}Cl_2N$: C, H, N.

*1-(2'-Nitrobenzyl)-3-methyl-2,3,4,5-tetrahydro-1*H*-3-benzazepine* (**13c**) *hydrochloride*. As for methylation of **6a**. Amine **12c** (19.7 g), formic acid (30 ml), 35% formaldehyde solution (20 ml). Yield: 20.5 g (90%) of **13c** hydrochloride, m.p. 195–205°. – $C_{18}H_{21}ClN_2O_2$: C, H, N.

*1-(2'-Aminobenzyl)-3-methyl-2,3,4,5-tetrahydro-1*H*-3-benzazepine* (**14**) *hydrochloride*. As for the hydrogenation of **7c**. Nitro-compound **13c** HCl salt (24.5 g), glacial acetic acid (500 ml), Pd/C 5.4% (5 g), hydrogenation time 2 h. The crude oily **14** HCl salt was used for the *Pschorr* reaction. – NMR.: 2.3 (*s*, 3H, $NCH_3$); 4.5 (br. *s*, 2H, $NH_2$).

*6-Methyl-4,5,6,7,7a,8-hexahydro-phenanthro[10,1-c,d]azepine* (**15**) *naphthalene-1,5-disulfonate*. As for the preparation of **10f**. A solution of sodium nitrite (6.2 g, 0.09 mol) was added slowly to a cold, stirred solution of **14** HCl salt (31 g, crude) in glacial acetic acid (310 ml) and conc. sulfuric acid (23 ml). The mixture was kept at 5–10° for 15 min then sulfamic acid (1.5 g, 0.015 mol) and cold 3 N sulfuric acid (460 ml) were added. The mixture was stirred at 90° for 30 min, zinc dust (29 g) was added and the stirring and warming continued for an additional 30 min. The hot solution was filtered, cooled with ice and made alkaline with ammonia. Extraction with chloroform yielded 20 g of a dark oil. This was dissolved in ethanol (150 ml) and a solution of NDS (8,5 g) in ethanol (50 ml) was added. The salt was recrystallized from DMF, ethanol and water by adding ether, yielding 4.4 g (15% calc. from **13c**) of **15** NDS salt, m.p. 278–281°. – NMR.: 2.3 (*s*, 3H, $NCH_3$); 7.15 (*m*, 5H, arom); 7.65 (*m*, 2H, arom). – $C_{23}H_{23}NO_3S$: C, H, N.

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