Fused *s*-Triazino Heterocycles. XV. 13*H*-4,6,7,13a,13c-Pentaazabenzo[*hi*]chrysene, 13*H*-4,7,13a,13c-Tetraazabenzo[*hi*]chrysene, and 7*H*-3,7,10,10b-Tetraazacyclohepta[*de*]naphthalene, Three New Ring Systems

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The reaction of *N*-cyano-*N'*-(6-amino-2-pyridyl)acetamidine (**5a**) and homophthalic anhydride followed by ring closure of the 2-[2-(carboxymethyl)phenyl]-5-methyl-1,3,4,6,9b-pentaazaphenalene intermediate (**4a**) gave 5-methyl-13-oxo-13*H*-4,6,7,13a,13c-pentaazabenzo[*hi*]chrysene (**8a**). An analogous series starting with 3-*N*-(6-amino-2-pyridyl)amino-2-cyano-2-butenenitrile (**5b**) in place of **5a** gave in two steps 5-methyl-13-oxo-13-*H*-4,7,13a,13c-tetraazabenzo[*hi*]chrysene-6-carbonitrile (**8b**). Elemental analysis, ir and pmr spectra of **8a**, **8b** and several new model compounds aided in confirming the structures of **8a** and **8b**. The synthesis of one of these model compounds for **5b** and phenylacetic anhydride led surprisingly to 2-methyl-9-phenyl-7*H*-3,7,-10,10b-tetraazacyclohepta[*de*]naphthalene (**10**) in addition to the expected 2-benzyl-4-cyano-5-methyl-1,3,-6,9b-tetraazaphenalene (**7b**).

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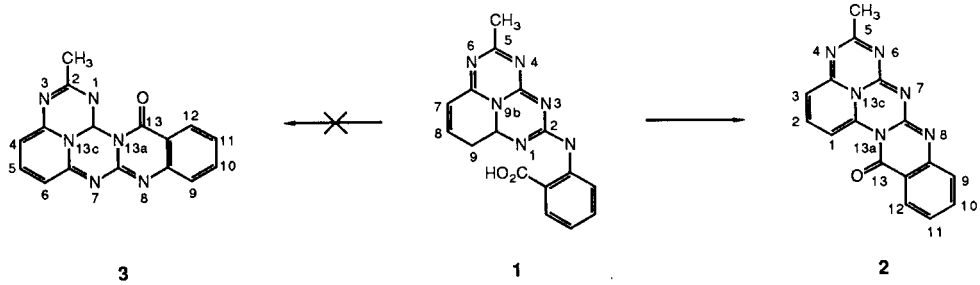
A recent paper [1] described the acetic anhydride catalyzed ring closure of 2-(2-carboxyanilino)-5-methyl-1,3,4,-6,9b-pentaazaphenelene (**1**) to 5-methyl-13*H*-4,6,7,8,13a,-13c-hexaazabenzo[*de*]naphthacen-13-one (**2**). Support for this structure rather than the alternative closure to 2-methyl-13*H*-1,3,7,8,13a,13c-hexaazabenzo[*de*]naphthacen-13-one (**3**) was afforded by pmr data. That is, the rather large downfield shift of the δ values for protons H_7 and H_9 of **1** upon ring closure to **2** (especially when the protons of the anthranilate moiety before and after ring closure remain substantively unchanged) suggested the closer proximity of the electron withdrawing carbonyl group to H_1 and $H_{3'}$ as in **2** rather than the more distant attachment as in **3**.

It was of interest to attempt similar ring closures with structures related to **1**. One such structure is 2-(2-carboxybenzyl)-5-methyl-1,3,4,6,9b-pentaazaphenalene (**6a**). Following an established procedure [2] for preparing this type of ring system, homophthalic anhydride was reacted with *N*-cyano-*N'*-(6-amino-2-pyridyl)acetamidine (**5a**) [2] in refluxing 1,2-dimethoxyethane for 18 hours. Since the anhydride used in the reaction was unsymmetrical, two products are possible: **6a** and 2-[2-(carboxymethyl)phenyl]-5-methyl-1,3,4,6,9b-pentaazaphenalene (**4a**). Thin-layer chromatography of the product isolated showed only one spot and this turned out to be **4a** (46% yield). The structure of **4a** was established by comparing the pmr value of the methylene hydrogens of the product isolated, δ 3.88, with the methylene hydrogens in homophthalic acid (**9**), δ 3.92, (which would be analogous to **4a**) and the methylene hydrogens in 2-benzyl-5-methyl-1,3,4,6,9b-pentaazaphenalene (**7a**), δ 3.56, (which would be analogous to **6a**).

The preparation of the model compound **7a** (32% yield) involved the same methodology used to prepare **4a**; in this case **5a** and phenylacetic anhydride were the reactants. The phenylacetic anhydride was obtained in 66% yield

Scheme 1



3 1 2

from a phase-transfer catalyzed reaction of phenylacetyl chloride and sodium phenylacetate. This procedure is faster and less tedious than the reported method [3].

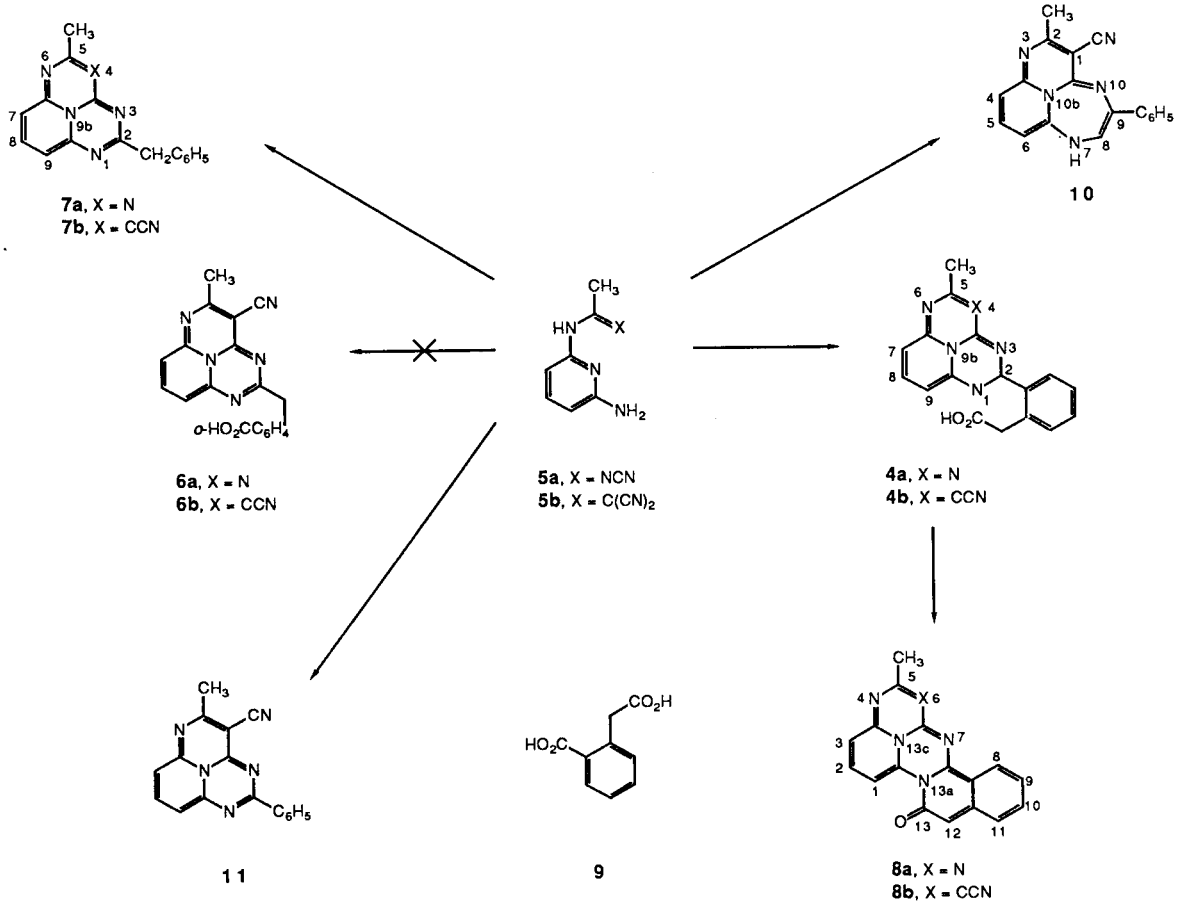
As was the case in the ring closure of **1**, so here also, there are two possible closures for **4a**: the carboxyl group can close on N-1 or N-3 of **4a**. Refluxing **4a** in acetic anhydride for 1.5 hours gave one product only (tlc). Based on pmr data it appears that ring closure took place on N-1 giving rise to 5-methyl-13-oxo-13*H*-4,6,7,13a,13c-pentaazabenzo[*hi*]chrysene (**8a**). The rather large downfield shift of the delta value of protons H_7 and H_9 mentioned above in the preparation of **2** was also observed in the ring colsure of **4a**: the value of H_7 and H_9 in **4a**, shifted from δ 6.04 (a two proton multiplet) to δ 7.09, H_3 and δ 8.41, H_1 in **8a** (each a one proton doublet).

A series of reactions analogous to those just described were carried out using 3-*N*-(6-amino-2-pyridyl)amino-2-cyano-2-butene nitrile (**5b**) [4] and homophthalic anhydride as starting materials. This second set of ring closures proceeded in precisely the same manner as the **5a** series and gave 2-[2-(carboxymethyl)phenyl]-4-cyano-5-methyl-1,3,6,9b-tetraazaphenalene (**4b**) and 5-methyl-13-oxo-13*H*-4,7,13a,13c-tetraazabenzo[*hi*]chrysene-6-carbonitrile (**8b**) in 55 and 51% yields respectively.

To help in determining that the ring closure of **5b** did give **4b** rather **6b**, the pmr delta value for the methylene group of the model compound 2-benzyl-4-cyano-5-methyl-1,3,6,9b-tetraazaphenalene (**7b**) was needed. A 56% yield of **7b** was obtained by reacting **5b** with phenylacetic anhydride. The delta value for the methylene group (δ 3.86) of the phenylacetic anhydride ring-closure product of **5b** was much closer to the value of the methylene group of **9** (δ 3.92) than it was to that of **7b** (δ 3.37), thus supporting **4b** rather than **6b** as the correct structure. Ring closure of **4b** to **8b** caused a downfield shifting of values of peripheral protons H_7 and H_9 of **4b** similar to that described above for the ring closure of **4a** to **8a**.

An additional unexpected product which appears to be 2-methyl-9-phenyl-7*H*-3,7,10,10b-tetraazacyclohepta[*de*]-naphthalene-1-carbonitrile (**10**) (12% yield) was also isolated from the reaction used to prepare **7b**. The proposed structure [5] for this structural isomer of **7b** is supported by the elemental analysis, ir and pmr spectra of **10** and the pmr spectra of the model compound 4-cyano-5-methyl-2-

Scheme 2



phenyl-1,3,6,9b-tetraazaphenalene (**11**). All three compounds, **7b**, **11** and **10** show a CN band in the ir and the expected singlet (methyl group), and a pair of doublets (H_7, H_9 in **7b** and **11**; H_4, H_6 in **10**) in their pmr spectra. However, the typical pmr benzyl pattern (singlet methylene and singlet phenyl) present in **7b** is completely absent in **10**. Instead, the phenyl protons of **10** have a pmr pattern very similar to that of **11**, *i.e.* of a benzene ring attached to an electron-withdrawing group (phenyl protons H_3, H_4 and H_5 appearing as a complex multiplet and protons H_2 and H_6 showing as a two-proton doublet). The integration of the pmr multiplet in **10** suggests that the peripheral protons H_5, H_8 and NH are also present. Similarly the integration of the phenyl multiplet in **7b** suggests the presence of the peripheral proton H_8. The absence of NH-absorption in the ir of **10** is of interest. It may be a peculiarity of the ring system or the result of the diluting effect of several possible CH-tautomers.

The same procedure used to prepare **7b** was utilized in the preparation of **11** (84% yield), by substituting an equivalent amount of benzoic anhydride for phenylacetic anhydride.

EXPERIMENTAL

Melting points were determined in open capillaries on a Thomas-Hoover melting point bath and are uncorrected. Infrared spectra were recorded using a Beckman AccuLab 8 spectrophotometer. The pmr spectra were determined on Varian EM 360 and XL-200 spectrometers using TMS as an internal reference. Analyses were performed by Micro-Analysis Inc., Wilmington, Delaware. All evaporations were carried out on a rotary evaporator at reduced pressure.

Silica gel (70-230 mesh) for column chromatography was obtained from ICN Pharmaceutical Inc. Phenylacetyl chloride, phenylacetic acid, and homophthalic anhydride were purchased from Aldrich Chemical Company.

2-[2-(Carboxymethyl)phenyl]-5-methyl-1,3,4,6,9b-pentaazaphenalene (**4a**).

A stirred mixture of 3.5 g (0.02 mole) of **5a**, 9.72 g (0.06 mole) of homophthalic anhydride and 25 ml of dry 1,2-dimethoxyethane was refluxed for 18 hours. The cooled reaction mixture (room temperature) was filtered and the cake washed well with ether and then oven-dried (60°); tlc, (silica gel, chloroform-methanol (90/10) showed one spot. Recrystallization from 2-methoxyethanol gave red crystals, 2.96 g (46%), mp 264-265° dec; ir (Nujol): λ μm 3-4 (broad, OH) 5.90 (C=O); pmr (DMSO-d_6): δ 1.84 (s, 3H, CH_3), 3.88 (s, 2H, CH_2), 6.04 (m, 2H, H_7, H_9), 7.35-7.85 (m, 5H, H_8 and C_6H_4), 12.88 (s, 1H, CO_2H).

Anal. Calcd. for $C_{17}H_{13}N_5O_2$: C, 63.94; H, 4.10; N, 21.93. Found: C, 63.84; H, 4.29; N, 21.87.

2-Benzyl-5-methyl-1,3,4,6,9b-pentaazaphenalene (**7a**).

A stirred solution of 1.75 g (0.01 mole) of **5a**, 7.62 g (0.03 mole) of phenylacetic anhydride and 10 ml of dry 1,2-dimethoxyethane was refluxed for 22 hours. The reaction mixture was then stirred for 1 hour at room temperature, filtered, washed with ether, and then oven-dried for 2 hours at 100°, 0.88 g (32%), mp 192-195°. Recrystallization from toluene gave red crystals, mp 195-197°; pmr (DMSO-d_6): δ 2.05 (s, 3H, CH_3), 3.56 (s, 2H, CH_2), 6.30 (d, J = 8 Hz, 2H, H_7 and H_9), 7.45-7.72 (s and t overlapping, 6H, H_8 and C_6H_5).

Anal. Calcd. for $C_{16}H_{13}N_5$: C, 69.80; H, 4.76; N, 25.44. Found: C, 69.82; H, 4.71; N, 25.34.

Phenylacetic Anhydride.

A solution of 15.7 g (0.1 mole) of phenylacetyl chloride in 80 ml of methylene dichloride was added to a vigorously stirred aqueous solution of sodium phenyl acetate [20.42 g (0.15 mole) of phenylacetic acid and 6.0 g (0.15 mole) of sodium hydroxide in 80 ml of water] containing 0.4 g (0.0012 mole) of tetrabutyl ammonium bromide. The mixture was vigorously stirred for 30 minutes and then the methylene chloride layer was washed successively with 5% sodium bicarbonate (2 x 80 ml) and brine (1 x 80 ml), dried (sodium sulfate), and evaporated to a colorless oil that solidified to a cream solid, 16.8 g (66%), mp 69-71°, lit value, 68-71° [3].

5-Methyl-13-oxo-13*H*-4,6,7,13a,13c-pentaazabenzo[*hi*]chrysene (**8a**).

A stirred mixture of 1 g (0.003 mole) of **4a** and 10 ml (0.11 mole) of acetic anhydride was refluxed for 1.5 hours and filtered at the boiling point. The filter cake was washed with ether, 0.69 g (74%) mp 328-330° dec. Recrystallization from *o*-dichlorobenzene gave orange crystals, mp 327-329° dec; ir (Nujol): λ μm 5.95 (C=O); pmr (DMSO-d_6): δ 2.23 (s, 3H, CH_3), 6.21 (s, 1H, H_{12}), 7.09 (d, J = 8.6 Hz, 1H, H_3), 7.32-8.11 (m, 5H, H_2, H_8, H_9, H_{10}, H_{11}), 8.41 (d, J = 8.6 Hz, 1H, H_1).

Anal. Calcd. for $C_{17}H_{11}N_5O$: C, 67.77; H, 3.68; N, 23.24. Found: C, 67.88; H, 3.88; N, 23.67.

2-[2-(Carboxymethyl)phenyl]-4-cyano-5-methyl-1,3,6,9b-tetraazaphenalene (**4b**).

A stirred mixture of 3.98 g (0.02 mole) of **5b**, 9.72 g (0.06 mole) of homophthalic anhydride and 25 ml of dry glyme was refluxed for 19 hours. The cooled reaction mixture (room temperature) was filtered, washed well with ether and then oven-dried (60°). Recrystallization from 2-methoxyethanol gave purple crystals, 3.80 g (55%) mp 270-272°; ir (Nujol): λ μm 3-4 (broad, OH), 4.55 (CN), 5.88 (C=O); pmr (DMSO-d_6): δ 1.97 (s, 3H, CH_3), 3.86 (s, 2H, CH_2), 5.84 (d, J = 8 Hz, 1H, H_7 or H_9), 6.17 (d, J = 8 Hz), 1H, H_7 or H_9), 7.27-7.85 (m, 5H, H_8 and C_6H_4), 12.85 (s, 1H, CO_2H).

Anal. Calcd. for $C_{19}H_{13}N_5O_2$: C, 66.46; H, 3.81; N, 20.40. Found: C, 66.28; H, 4.11; N, 20.64.

5-Methyl-13-oxo-13*H*-4,7,13a,13c-tetraazabenzo[*hi*]chrysene-6-carbonitrile (**8b**).

A stirred mixture of 1 g (0.0029 mole) of **4b** and 10 ml of acetic anhydride was refluxed for 20 hours and filtered at the boiling point. The filter cake was washed with ether and oven-dried (60°). Recrystallization from chlorbenzene gave red crystals 0.48 g (51%), mp 316-318°; ir (Nujol): λ μm 4.48 (CN), 5.90 (C=O); pmr (DMSO-d_6): δ 2.37 (s, 3H, CH_3), 6.35 (s, 1H, H_{12}), 7.24 (d, J = 8.4 Hz, 1H, H_3), 7.31-8.12 (m, 5H, H_2, H_8, H_9, H_{10}, H_{11}), 8.34 (d, J = 8.4 Hz, 1H, H_1).

Anal. Calcd. for $C_{19}H_{11}N_5O$: C, 70.14; H, 3.40; N, 21.53. Found: C, 70.04; H, 3.43; N, 21.36.

2-Benzyl-4-cyano-5-methyl-1,3,6,9b-tetraazaphenalene (**7b**) and 2-Methyl-9-phenyl-7*H*-3,7,10,10b-tetraazacyclohepta[*de*]naphthalene-1-carbonitrile (**10**).

A stirred solution of 2 g (0.01 mole) of **5b**, 7.62 g (0.03 mole) of phenylacetic anhydride and 12 ml of dry 1,2-dimethoxyethane was refluxed for 23 hours. The flask containing the chilled reaction mixture was scratched to induce crystallization and the purple solid was collected by suction filtration, the filtrate, "A", being set aside for subsequent work-up. The purple solid was washed with ether and oven-dried (60°), 1.67 g (56%), mp 174-177°. Recrystallization from 1,2-dimethoxyethane gave **7b**, purple crystals, mp 174-176°: ir (Nujol): λ μm 4.46 (CN); pmr (DMSO-d_6): δ 1.96 (s, 3H, CH_3), 3.37 (s, 2H, CH_2), 5.98 (d, J = 8 Hz, 1H, H_7 or H_9), 6.18 (d, J = 8 Hz, 1H, H_7 or H_9), 7.30 (strong s overlapping and obscuring t, 6H, H_8 and C_6H_5).

Anal. Calcd. for $C_{18}H_{13}N_5$, **7b**: C, 72.22; H, 4.38; N, 23.40. Found: C, 72.04; H, 4.37; N, 23.19.

The filtrate, "A", was evaporated and the dark solid that formed upon cooling was stirred with 3 ml of toluene, filtered and washed twice with ether. Recrystallization from 2-methoxyethanol gave 0.37 g (12%) of **10**,

greenish-black crystals, mp 242-244°. Column chromatography over silica gel using chloroform-methanol (95/5) removed a trace yellow impurity and gave the greenish-black analytical sample, mp 243-245°; ir (Nujol): λ μm 4.45 (CN); pmr (DMSO-d_6): δ 2.01 (s, 3H, CH_3), 6.09 (d, J = 8 Hz, 1H, H_4 or H_6), 6.33 (d, J = 8 Hz, 1H, H_4 or H_6), 7.39-7.81 (m, 6H, H_5, H_8, NH, and phenyl H_3, H_4, H_5), 8.16 (d, J = 7 Hz, 2H, benzene H_2 and H_6).

Anal. Calcd. for $C_{18}H_{13}N_5$ (**10**): C, 72.22; H, 4.38; N, 23.40. Found: C, 72.22; H, 4.05; N, 23.09.

4-Cyano-5-methyl-2-phenyl-1,3,6,9b-tetraazaphenalene (**11**).

A stirred solution of 2 g (0.01 mole) of **5b**, 6.79 g (0.03 mole) of benzoic anhydride and 12 ml of 1,2-dimethoxyethane were refluxed for 20 hours. The green precipitate which had formed was collected by suction filtration and washed with ether, 2.38 g, (84%), mp 298-300°. Recrystallization from toluene gave green crystals, mp 297-298°; ir (Nujol): 4.50 (CN); pmr (DMSO-d_6): δ 2.02 (s, 3H, CH_3), 6.14 (d, J = 7.8 Hz, 1H, H_7 or H_9), 6.23 (d, J = 7.8 Hz, 1H, H_7 or H_9), 7.37-7.61 (m, 4H, H_8 and phenyl H_3, H_4, H_5), 8.03 (d, J = 7 Hz, 2H, phenyl H_2, H_6).

Anal. Calcd. for $C_{17}H_{11}N_5$: C, 71.56; H, 3.89; N, 24.55. Found: C, 71.52; H, 3.88; N, 24.82.

Homophthalic Acid (**9**).

A solution of 2 g (0.012 mole) of homophthalic anhydride, 1 ml of concentrated hydrochloric acid and 50 ml of water was refluxed for 1 hour. The white solid that formed on chilling the solution was collected by suction filtration, washed with water and oven-dried (100%), 1.37 g, mp 182-184°: ir (Nujol): 3-4.2 (broad, OH), 5.95 (C=O); pmr (DMSO-d_6): δ 3.92 (s, 2H, CH_2), 7.29-7.53 (m, 3H, H_3, H_4, H_5), 7.87 (d, J = 7.6 Hz, 1H, H_6), 12.48 (s, 2H, CO_2H).

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[5] Other tautomers are also possible.