# The Synthesis of Cycloalkylpyrido[1,2-*a*]benzimidazole Carbonitrile Analogs

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The preparation of various sustituted cycloalkylpyrido[1,2-*a*]benzimidazolecarbonitrile analogs is described as well as the X-ray of the cycloheptyl analog **13a**.

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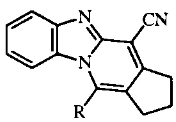
Introduction.

The preparation and biological activity of 11-substituted 2,3-dihydro-1*H*-cyclopenta-[4,5]pyrido[1,2-*a*]benzimidazole-4-carbonitriles (**A**) has been published [1]. This article describes a very limited set of compounds and since there are *no* other literature examples of this type of tetracyclic system, we decided to explore the chemistry of this very interesting pyrido[1,2-*a*]benzimidazole. We report here the preparation of various cycloalkylpyrido-[1,2-*a*]benzimidazole carbonitrile analogs.



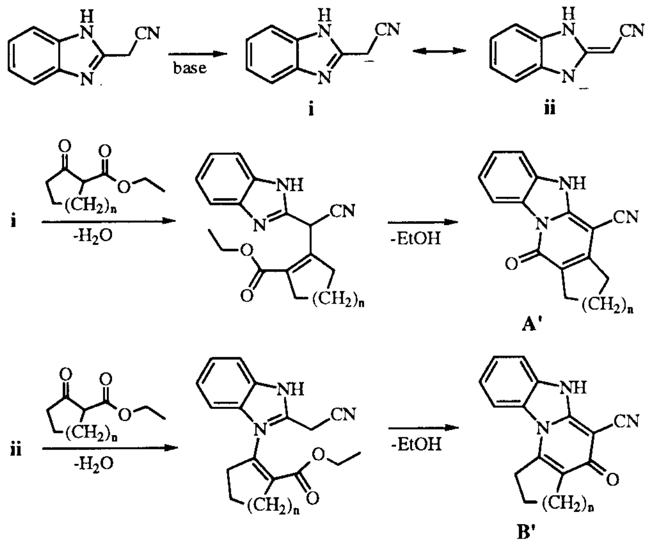
**A**

Discussion.

The reaction of readily available 1*H*-benzimidazole-2-acetonitriles and cyclic β-keto esters in the presence of ammonium acetate gave tetracyclic compounds **1-5** of varying ring sizes (Table 1). When one considers the mechanism of this reaction, it is possible to form either **A'** and/or **B'** (Scheme I). Although our spectral data agreed with that published, we were unsure which isomer we had isolated. To answer this question, compound **13a** was submitted for X-ray crystallographic determination (Figure 1). This X-ray shows the tetracyclic ring fusion is exactly as that depicted in the earlier report.

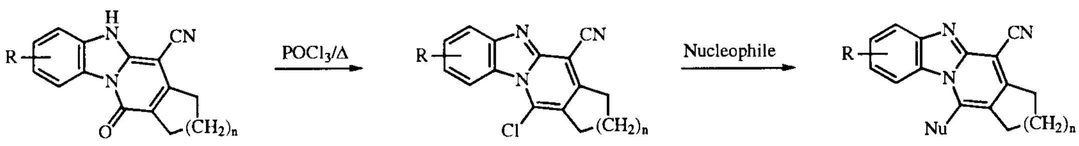
(Scheme II). These chloro compounds (Table 2) were the necessary intermediates for the remaining work. Compounds **6-10** were treated with various nucleophiles to afford either amines, phosphonates, ethers, or sulfides.

Scheme I



An unexpected reaction occurred when trying to displace the chlorine atom on **6** with octylamine to give the amino compound **11c**. Octylamine displaced the chlorine atom, as well as, added to the nitrile moiety to afford the 11-octylamino-4-(*N*-octylimidamido) compound **15** in 58% yield (Scheme III).

Scheme II

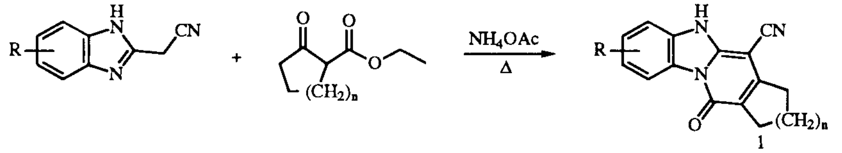


**1-5** **6-10** **11-14**

The pyrido[1,2-*a*]benzimidazolone intermediates **1-5** were converted to their corresponding chloro derivatives by treating them with phosphorous oxychloride at reflux

A primary amine was synthesized by the literature method [1] whereby the chloro compound **6** was reacted with sodium azide, followed by triphenylphosphine

Table 1
Pyrido[1,2-*a*]benzimidazolone Intermediates

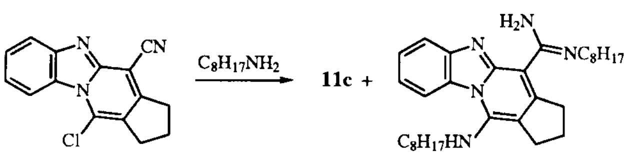


**1-5**

| Product | R | n | Yield [a] (%) | mp [b,c] (°C) | IR (KBr) [d] ν (cm$^{-1}$) | $^1$H NMR [e] (DMSO-d$_6$, TMS) δ, J (Hz) | Molecular Formula (MW) | Analysis | Calcd. | Found |
|---|---|---|---|---|---|---|---|---|---|---|
| **1** | H | 1 | 92 | >310 [f] | 2209, 1666, 1534, 1466, 1132, 759 | 2.09 (p, 2H, J = 7.4, $CH_2CH_2CH_2$), 2.76 (t, 2H, J = 7.4, $CH_2CH_2$), 2.99 (t, 2H, J = 7.4, $CH_2CH_2$), 7.32-7.38 (m, 1H, $H_{6\ arom}$), 7.50-7.52 (m, 2H, $H_{7,8\ arom}$), 8.59 (d, 1H, J = 8.1, $H_{9\ arom}$), 13.53 (br s, 1H, NH) | $C_{15}H_{11}N_3O$ (249.27) | C:<br>H:<br>N: | 72.27<br>4.45<br>16.86 | 71.87<br>4.41<br>16.83 |
| **2** | H | 2 | 39 | >300 | 2205, 1655, 1538, 1466, 1143, 753 | 1.75 (br s, 4H, methylene), 2.48 (br s, 2H, allylic methylene), 2.73 (br s, 2H, allylic methylene), 7.32-7.36 (m, 1H, $H_{7\ arom}$), 7.49-7.50 (m, 2H, $H_{8,9\ arom}$), 8.56 (d, 1H, J = 8.1, $H_{10\ arom}$), 13.35 (br s, 1H, NH) | $C_{16}H_{13}N_3O$ (263.30) | C:<br>H:<br>N: | 72.98<br>4.98<br>15.96 | 72.69<br>4.77<br>16.07 |
| **3** | H | 3 | 63 | >300 | 2207, 1654, 1525, 1464, 1185, 751 | 1.45-1.55 (m, 2H, methylene), 1.61-1.72 (m, 2H, methylene), 1.78-1.90 (m, 2H, methylene), 2.80-2.95 (m, 4H, allylic methylene), 7.33-7.40 (m, 1H, $H_{8\ arom}$), 7.51-7.56 (m, 2H, $H_{9,\ 10\ arom}$), 8.61 (d, 1H, J = 8.1, $H_{11\ arom}$), 13.45 (s, 1H, NH) | $C_{17}H_{15}N_3O$ (277.33) | C:<br>H:<br>N: | 73.62<br>5.45<br>15.15 | 73.45<br>5.35<br>15.08 |
| **4** | H | 4 | 15 | >300 | 2204, 1658, 1533, 1466, 1141, 748 | 1.41 (br s, 4H, methylene), 1.58 (br s, 2H, methylene), 1.77 (br s, 2H, methylene), 2.77 (br s, 2H, allylic methylene), 2.89 (br s, 2H, allylic methylene), 7.37 (br s, 1H, $H_{9\ arom}$), 7.53 (br s, 2H, $H_{10,11\ arom}$), 8.62 (d, 1H, J = 3.7, $H_{12\ arom}$), 13.42 (br s, 1H, NH) | $C_{18}H_{17}N_3O$ (291.36) | C:<br>H:<br>N: | 74.20<br>5.88<br>14.42 | 73.85<br>5.90<br>14.35 |
| **5** | 5,6-diMe [g] | 1 | 43 | >300 | 2211, 1668, 1557, 1475, 1138, 681 | 2.09 (p, 2 H, J = 4.6, $CH_2CH_2CH_2$), 2.36 (s, 6H, $CH_3$), 2.76 (t, 2H, J = 4.6, $CH_2CH_2$), 2.99 (t, 2H, J = 4.6, $CH_2CH_2$), 7.29 (s, 1H, $H_{6\ arom}$), 8.38 (s, 1H, $H_{9\ arom}$), 13.34 (br s, 1H, NH) | $C_{17}H_{15}N_3O$ (277.33) | C:<br>H:<br>N: | 73.62<br>5.45<br>15.15 | 73.49<br>5.62<br>15.35 |

[a] The yields are not optimized. [b] Melting points were taken on a Thomas-Hoover melting point apparatus and are uncorrected. [c] The products were recrystallized from the following solvents: **1**, methanol/dichloromethane; **2**, DMF/methanol; **3**, DMF; **4**, methanol/dichloromethane; **5**, methanol/dichloromethane. [d] The ir spectra were recorded on a Nicolet 5DXC FTIR. [e] The nmr spectra were recorded at 300.2 MHz on a GE QE-300 instrument; all couplings are reported as apparent couplings. [f] Literature mp 300 ° (DMF) [1]. [g] Starting benzimidazole was prepared by literature procedures [3].

Scheme III



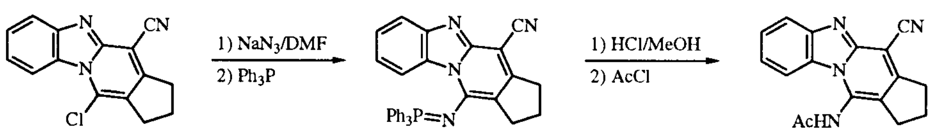
**6** **15**

treatment to afford the triphenylphosphoranylideneamino moiety **16**, and finally hydrolyzing this material to the amine with hydrochloric acid. This crude primary amine was then taken on to make amides, *e.g.* **17** (Scheme IV).

The sulfide compound **13e** was oxidized to its corresponding sulfoxide using *m*-chloroperoxybenzoic acid.

Conversion of the nitrile moiety to other functionality was also investigated. We found that when **13a** was reacted with either potassium hydroxide/DMSO or hydro-

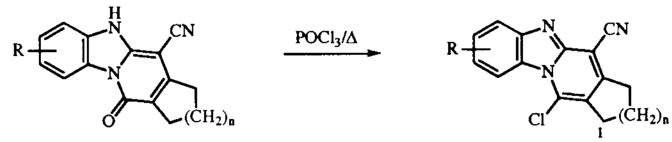
Scheme IV



**6** **16** **17**

Table 2

Chloro Substituted Pyrido[1,2-*a*]benzimidazole Intermediates



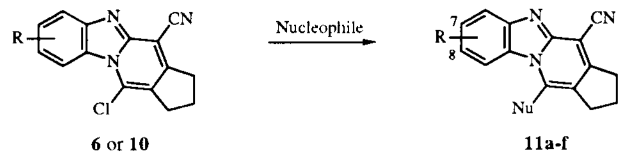

**6-10**

| Product | R | n | Yield [a] (%) | mp [b,c] (°C) | IR (KBr) [d] ν (cm$^{-1}$) | $^1$H NMR [e] (TMS) δ, J (Hz) | Molecular Formula (MW) | Analysis | Calcd. | Found |
|---|---|---|---|---|---|---|---|---|---|---|
| **6** | H | 1 | 99 | 238-241 [f] | 2230, 1635, 1505, 1450, 1304, 1180, 763 | ($CDCl_3$) 2.30 (p, 2H, J = 7.5, $CH_2CH_2CH_2$), 3.09 (t, 2H, J = 7.5, $CH_2CH_2$), 3.31 (t, 2H, J = 7.5, $CH_2CH_2$), 7.38 (dt, 1H, J = 8.5, 1.2, $H_{7/8\ arom}$), 7.57 (dt, 2H, J = 8.3, 1.1, $H_{8/7\ arom}$), 8.00 (dd, 1H, J = 8.3, 0.8, H6 $_{arom}$), 8.52 (dd, 1H, J = 8.6, 0.8, $H_{9\ arom}$) | $C_{15}H_{10}ClN_3$ (267.72) | C:<br>H:<br>N: | 67.29<br>3.77<br>15.70 | 67.11<br>3.49<br>15.85 |
| **7** | H | 2 | 96 | 218-220 | 2227, 1622, 1593, 1466, 1311, 1202, 762 | (DMSO-$d_6$) 1.77-1.90 (m, 4H, methylene), 2.80 (br t, 2H, J = 6.1, allylic methylene), 3.08 (br t, 2H, J = 6.0, allylic methylene), 7.44 (t, 1H, J = 8.4, $H_{8/9\ arom}$), 7.62 (t, 1H, J = 8.1, $H_{9/8\ arom}$), 7.92 (d, 1H, J = 8.3, $H_{7\ arom}$), 8.68 (d, 1H, J = 8.6, $H_{10\ arom}$) | $C_{16}H_{12}ClN_3$ (281.75) | C:<br>H:<br>N: | 68.21<br>4.29<br>14.92 | 68.08<br>4.46<br>14.83 |
| **8** | H | 3 | 91 | 168-170 | 2222, 1623, 1594, 1474, 1444, 1311, 1182, 734 | ($CDCl_3$) 1.73-1.80 (m, 2H, methylene), 1.80-1.95 (m, 4H, methylene), 3.09-3.15 (m, 2H, allylic methylene), 3.24-3.30 (m, 2H, allylic methylene), 7.39 (t, 1H, J = 8.4, $H_{9/10\ arom}$), 7.59 (t, 1H, J = 8.8, $H_{10/9\ arom}$), 8.03 (d, 1H, J = 8.3, $H_{8\ arom}$), 8.60 (d, 1H, J = 8.8, $H_{11\ arom}$) | $C_{17}H_{14}ClN_3$ (295.77) | C:<br>H:<br>N: | 69.03<br>4.77<br>14.21 | 68.77<br>4.69<br>14.12 |
| **9** | H | 4 | 80 | 173.5-176.0 | 2226, 1621, 1470, 1449, 1193, 764 | ($CDCl_3$) 1.38-1.52 (m, 4H, methylene), 1.75-1.83 (m, 2H, methylene), 1.88-1.98 (m, 2H, methylene), 3.05 (t, 2H, J = 6.3, allylic methylene), 3.20 (t, 2H, J = 6.3, allylic methylene), 7.39 (dt, 1H, J = 7.9, 0.8 $H_{10/11\ arom}$), 7.59 (dt, 1H, J = 7.7, 1.0 $H_{11/10\ arom}$), 8.03 (d, 1H, J = 8.2, $H_{9\ arom}$), 8.60 (d, 1H, J = 8.6, $H_{12\ arom}$) | $C_{18}H_{16}ClN_3$ (309.8) | C:<br>H:<br>N: | 69.78<br>5.21<br>13.57 | 69.69<br>5.05<br>13.58 |
| **10** | 7,8-diMe | 1 | 79 | 246-249 | 2229, 1542, 1504, 1463, 1454, 1174 | ($CDCl_3$) 2.27 (p, 2 H, J = 7.5, $CH_2CH_2CH_2$), 2.43 (s, 6H, $CH_3$), 3.04 (t, 2H, J = 7.5, $CH_2CH_2$), 3.25 (t, 2H, J = 7.5, $CH_2CH_2$), 7.71 (s, 1H, $H_{6\ arom}$), 8.20 (s, 1H, $H_{9\ arom}$) | $C_{17}H_{14}ClN_3$ (295.77) | C:<br>H:<br>N: | 69.03<br>4.77<br>14.21 | 68.92<br>4.72<br>13.97 |

[a] The yields are not optimized. [b] Melting points were taken on a Thomas-Hoover melting point apparatus and are uncorrected. [c] The products were recrystallized from the following solvents: **6**, dichloromethane; **7**, dichloromethane; **8**, dichloromethane/ether; **9**, dichloromethane/hexane; **10**, methanol/ether/hexane. [d] The ir spectra were recorded on a Nicolet 5DXC FTIR. [e] The nmr spectra were recorded at 300.2 MHz on a GE QE-300 instrument; all couplings are reported as apparent couplings. [f] Literature mp 250-251° (DMF) [1].

Table 3

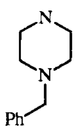
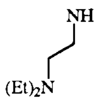
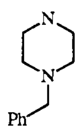
11-Substituted 2,3-Dihydro-1*H*-cyclopenta[4,5]pyrido[1,2-*a*]benzimidazole-4-carbonitriles




**6** or **10** **11a-f**

| Product | R | Nu | Yield [a] (%) | mp [b,c] (°C) | IR (KBr) [d] ν (cm$^{-1}$) | $^1$H NMR [e] (TMS) δ, J (Hz) | Molecular Formula (MW) | Analysis | Calcd. | Found |
|---|---|---|---|---|---|---|---|---|---|---|
| **11a** | H | $C_3H_7NH$ | 100 | 246-248 | 2208, 1630, 1553, 1522, 1452, 748 | (DMSO-$d_6$) 0.95 (t, 3H, J = 7.3, $CH_3$), 1.71 (h, 2H, J = 7.3, $CH_3CH_2CH_2$), 2.13 (p, 2H, J = 7.3, $CH_2CH_2CH_2$), 3.06 (t, 2H, J = 7.6, $CH_2CH_2$), 3.17 (t, 2H, J = 7.2, $CH_2CH_2$), 3.57 (t, 2H, J = 7.3, $NCH_2$), 7.00 (br s, 1H, NH), 7.29 (t, 1H, J = 7.5, $H_{7/8\ arom}$), 7.49 (t, 1H, J = 7.5, $H_{8/7\ arom}$), 7.75 (d, 1H, J = 8.1, $H_{6\ arom}$), 8.34 (d, 1H, J = 8.4, $H_{9\ arom}$) | $C_{18}H_{18}N_4$ (290.37) | C:<br>H:<br>N: | 74.45<br>6.25<br>19.30 | 74.00<br>6.42<br>19.17 |

Table 3 (continued)

| Product | R | Nu | Yield [a] (%) | mp [b,c] (°C) | IR (KBr) [d] ν ($cm^{-1}$) | $^1H$ NMR [e] (TMS) δ, J (Hz) | Molecular Formula (MW) | Analysis | Calcd. | Found |
|---|---|---|---|---|---|---|---|---|---|---|
| **11b** | H | $C_5H_{11}NH$ | 97 | 226-229 | 2207, 1631, 1556, 1535, 1458, 1451, 744 | ($CDCl_3$) 0.97 (t, 3H, J = 6.8, $CH_3$), 1.37-1.52 (m, 4H, methylene), 1.75-1.85 (m, 2H, $CH_3CH_2CH_2$), 2.17 (p, 2H, J = 7.4, $CH_2CH_2CH_2$), 3.02 (t, 2H, J = 7.6, $CH_2CH_2$), 3.15 (t, 2H, J = 7.2, $CH_2CH_2$), 3.66 (q, 2H, J = 6.6, $NCH_2$), 5.02 (br t, 1H, J = 5.4, NH), 7.20 (t, 1H, J = 8.0, $H_{7/8\ arom}$), 7.47 (t, 1H, J = 8.0, $H_{8/7\ arom}$), 7.77 (d, 1H, J = 8.4, $H_{6\ arom}$), 7.90 (d, 1H, J = 8.2, $H_{9\ arom}$) | $C_{20}H_{22}N_4$ (318.43) | C:<br>H:<br>N: | 75.44<br>6.96<br>17.60 | 75.37<br>7.33<br>17.52 |
| **11c** | H | $C_8H_{17}NH$ | 90 | 160.5-162.0 | 2206, 1632, 1556, 1517, 1495, 749 | ($CDCl_3$) 0.89 (br t, 3H, J = 7.4, $CH_3$), 1.22-1.53 (m, 10H, methylene), 1.74-1.86 (m, 2H, $CH_3CH_2CH_2$), 2.17 (p, 2H, J = 7.5, $CH_2CH_2CH_2$), 3.02 (t, 2H, J = 7.6, $CH_2CH_2$), 3.15 (t, 2H, J = 7.3, $CH_2CH_2$), 3.65 (q, 2H, J = 6.7, $NCH_2$), 5.01 (br t, 1H, J = 5.5, NH), 7.19 (t, 1H, J = 8.1, $H_{7/8arom}$), 7.47 (t, 1H, J = 8.0, $H_{8/7\ arom}$), 7.77 (d, 1H, J = 8.3, $H_{6\ arom}$), 7.89 (d, 1H, J = 8.2, $H_{9\ arom}$) | $C_{23}H_{28}N_4$ (360.51) | C:<br>H:<br>N: | 76.63<br>7.83<br>15.54 | 76.79<br>7.71<br>15.57 |
| **11d** | H |  | 69 | 237-241 | 2222, 1634, 1551, 1507, 1444, 736 | ($CDCl_3$) 2.23 (p, 2H, J = 7.4, $CH_2CH_2CH_2$), 2.65 (dt, 2H, J = 11.3, 2.3, piperazine methylene), 2.98 (d, 2H, J = 11.6, piperazine methylene), 3.12 (t, 2H, J = 7.6, $CH_2CH_2$), 3.19 (t, 2H, J = 7.4, $CH_2CH_2$), 3.27 (d, 2H, J = 11.4, piperazine methylene), 3.44 (dt, 2H, J = 11.2, 2.1, piperazine methylene), 3.70 (s, 2H, benzylic), 7.26-7.45 (m, 6H, $H_{7/8\ arom}$ and phenyl), 7.51 (t, 1H, J = 8.0, $H_{8/7\ arom}$), 7.94 (d, 1H, J = 8.2, $H_{6\ arom}$), 8.63 (d, 1H, J = 8.4, $H_{9\ arom}$) | $C_{26}H_{25}N_5$ (407.52) | C:<br>H:<br>N: | 76.63<br>6.18<br>17.19 | 76.53<br>6.06<br>17.15 |
| **11e** | H |  | 74 | 231-233 | 2206, 1632, 1597, 1556, 1523, 1460, 744 | ($CDCl_3$) 1.24 (t, 6H, J = 7.1, $CH_3$), 2.12 (p, 2H, J = 7.4, $CH_2CH_2CH_2$), 2.72 (q, 4H, J = 7.1, $CH_2CH_3$), 2.89 (t, 2H, J = 5.8, $NCH_2CH_2$), 3.02 (t, 2H, J = 7.6, $CH_2CH_2$), 3.21 (t, 2H, J = 7.2, $CH_2CH_2$), 3.79-3.85 (m, 2H, $CH_2NH$), 6.92 (s, 1H, NH), 7.20 (t, 1H, J = 8.0, $H_{7/8\ arom}$), 7.48 (t, 1H, J = 8.0, $H_{8/7\ arom}$), 7.92 (d, 1H, J = 8.2, $H_{6\ arom}$), 8.21 (d, 1H, J = 8.4, $H_{9\ arom}$) | $C_{21}H_{25}N_5$ (347.47) | C:<br>H:<br>N: | 72.59<br>7.25<br>20.16 | 72.50<br>7.29<br>20.18 |
| **11f** | 7,8-diMe |  | 71 | 261-263 | 2222, 1548, 1505, 1453, 1007, 728 | ($CDCl_3$) 2.22 (p, 2H, J = 7.5, $CH_2CH_2CH_2$), 2.43 (s, 3H, $CH_3$), 2.44 (s, 3H, $CH_3$), 2.65 (dt, 2H, J = 11.4, 2.7, piperazine methylene), 2.98 (d, 2H, J = 11.9, piperazine methylene), 3.09-3.20 (m, 4H, $CH_2CH_2$), 3.25 (d, 2H, J = 11.6, piperazine methylene), 3.43 (dt, 2H, J = 11.3, 2.6, piperazine methylene), 3.71 (s, 2H, benzylic), 7.26-7.43 (m, 5H, phenyl), 7.68 (s, 1H, $H_{6\ arom}$), 8.40 (s, 1H, $H_{9\ arom}$) | $C_{28}H_{29}N_5$ (435.58) | C:<br>H:<br>N: | 77.21<br>6.71<br>16.08 | 76.82<br>6.84<br>16.13 |

[a] The yields are not optimized. [b] Melting points were taken on a Thomas-Hoover melting point apparatus and are uncorrected. [c] The products were recrystallized from the following solvents: **11a**, dichloromethane/methanol; **11b**, dichloromethane/ether; **11c**, dichloromethane/ether; **11d**, dichloromethane; **11e**, dichloromethane/ether; **11f**, dichloromethane. [d] The ir spectra were recorded on a Nicolet 5DXC FTIR. [e] The nmr spectra were recorded at 300.2 MHz on a GE QE-300 instrument; all couplings are reported as apparent couplings.

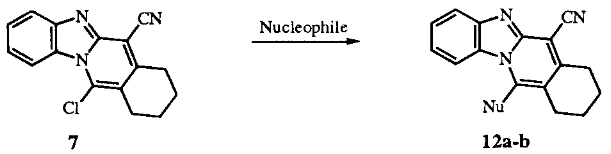
gen chloride/methanol, neither the amide nor the imidate was produced. The tetracyclic compound **13a** was also subjected to basic hydrogen peroxide conditions. Here again, none of the desired amide was isolated. This robust nitrile moiety was found to react with sodium borohydride/zinc chloride to afford the aminomethyl derivative; however, in only a trace amount.

Summary.

This manuscript has demonstrated the ease of preparing a large number of cycloalkylpyrido[1,2-*a*]-benzimidazole carbonitrile analogs. The mechanism of tetracyclic ring formation was investigated. Out of the two possible structures, **A'** or **B'**, an X-ray of compound **13a** confirms the ring system to be that of **A'**. These pyrido[1,2-*a*]benzimidazolone intermediates were converted to their corresponding chloro compounds which were reacted with various nucleophiles to afford either amines, phosphonates, ethers or sulfides.

Table 4

12-Substituted 1,2,3,4-Tetrahydro[5,6]pyrido[1,2-*a*]benzimidazole-5-carbonitriles



| Product | Nu | Yield [a] (%) | mp [b,c] (°C) | IR (KBr) [d] ν (cm$^{-1}$) | $^1$H NMR [e] ($CDCl_3$, TMS) δ, J (Hz) | Molecular Formula (MW) | | Analysis Calcd. | Found |
|---|---|---|---|---|---|---|---|---|---|
| **12a** | $C_5H_{11}NH$ | 56 | 132-135 | 2217, 1628, 1594, 1490, 1446, 1308, 736 | 0.90 (br t, 3H, J = 6.4, $CH_3$), 1.27-1.43 (m, 4H, methylene), 1.64-1.76 (m, 2H, $CH_2CH_2N$), 1.81-1.99 (m, 4 H, cyclohexyl methylene), 2.69 (br t, 2H, J = 6.0, allylic methylene), 3.09 (br t, 2H, J = 6.1, allylic methylene), 3.15-3.22 (m, 2H, $CH_2NH$), 4.03 (t, 1H, J = 6.7, NH), 7.29 (t, 1H, J = 8.2, $H_{8/9\ arom}$), 7.52 (t, 1H, J = 8.1, $H_{9/8\ arom}$), 7.95 (d, 1H, J = 8.2, $H_{7\ arom}$), 8.07 (d, 1H, J = 8.3, $H_{10\ arom}$) | $C_{21}H_{24}N_4$ (332.45) | C:<br>H:<br>N: | 75.87<br>7.28<br>16.86 | 76.02<br>7.23<br>16.86 |
| **12b** | EtO–P(=O)–OEt | 75 | 167-169 | 2229, 1533, 1448, 1283, 1265, 1257, 1036, 1013, 983, 750 | 1.27 (t, 6H, J = 7.0, $CH_3$), 1.83-1.96 (m, 4H, methylene), 3.21 (t, 2H, J = 6.0, allylic methylene), 3.35-3.41 (m, 2H, allylic methylene), 4.13-4.35 (m, 4H, $POCH_2$), 7.32-7.38 (m, 1H, $H_{8/9\ arom}$), 7.51-7.56 (m, 1H, $H_{9/8\ arom}$), 8.01 (d, 1H, J = 8.1, $H_{7\ arom}$), 8.50 (d, 1H, J = 8.8, $H_{10\ arom}$) | $C_{20}H_{22}N_3O_3P$ •1/4 $H_2O$ (383.39) | C:<br>H:<br>N: | 61.93<br>5.85<br>10.83 | 62.08<br>5.72<br>11.07 |

[a] The yields are not optimized. [b] Melting points were taken on a Thomas-Hoover melting point apparatus and are uncorrected. [c] The products were recrystallized from the following solvents: **12a**, dichloromethane/hexane/ether; **12b**, dichloromethane/methanol/ether. [d] The ir spectra were recorded on a Nicolet 5DXC FTIR. [e] The nmr spectra were recorded at 300.2 MHz on a GE QE-300 instrument; all couplings are reported as apparent couplings.

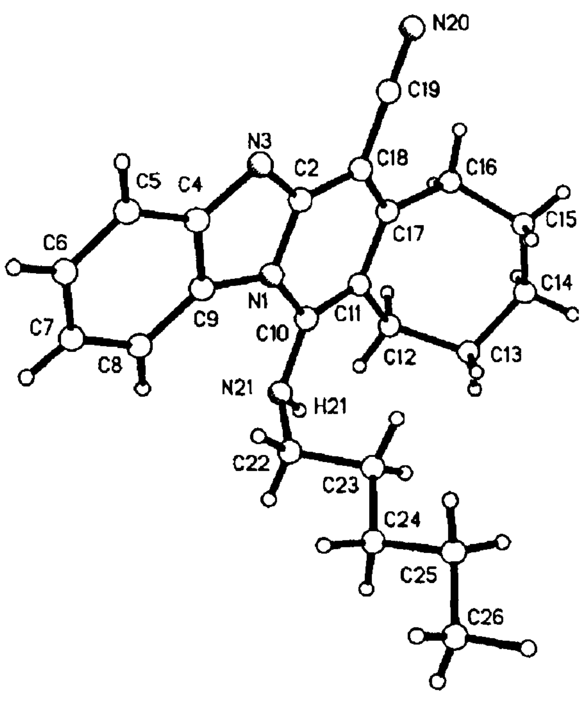



Figure 1. X-Ray perspective drawing of compound **13a**.

## EXPERIMENTAL

Preparation of Compounds **1-5**. General Method.

The 1*H*-benzimidazole-2-acetonitrile (1 mmole) was mixed with the keto ester (1.1 mmoles) and ammonium acetate (2.2 mmoles). The mixture was heated to 150° for 45 minutes cooled to rt and diluted with ethanol. The product was obtained as a tan solid in 15-92% yield and was crystallized from either methanol/dichoromethane, DMF/methanol or DMF.

Preparation of Compounds **6-10**. General Method.

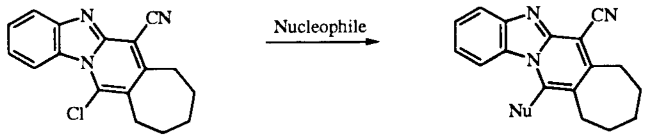
The cycloalkylpyrido[1,2-*a*]benzimidazolones **1-5** (1 mmole) was dissolved in phosphoryl chloride (2 ml). After the solution was warmed to reflux for 0.5-3 hours, it was cooled and the excess phosphoryl chloride removed *in vacuo*. The residue was slurried in ice water and carefully neutralized with base (*e.g.* 2*N* sodium hydroxide solution). The product was collected and air dried (79-99% yield). A portion of this material was further purified by recrystallization from the above solvents.

Displacement Reaction. General Method.

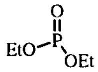
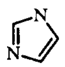
The cycloalkylpyrido[1,2-*a*]benzimidazoles **6-10** (1 mmole) was dissolved in an excess of nucleophilic reagent. The solution was either stirred at rt for 18 hours or warmed to 50-150° for 0.5-6.0 hours and then cooled to rt. For the triethylphosphite reaction, the reflux period was 6-8 hours. The 1-pentanol reaction was accomplished in DMSO/potassium hydroxide at 50° for 1 hour, while the 1-pentanethiol was accomplished in benzene/DBU at rt for 4 hours. Water was added and the solid was collected. This

Table 5

13-Substituted 2,3,4,5-Tetrahydro-1*H*-cyclohepta[6,7]pyrido[1,2-*a*]benzimidazole-6-carbonitriles



8 → 13a-e

| Product | Nu | Yield [a] (%) | mp [b,c] (°C) | IR (KBr) [d] ν ($cm^{-1}$) | $^1H$ NMR [e] ($CDCl_3$, TMS) δ, J (Hz) | Molecular Formula (MW) | Analysis | Calcd. | Found |
|---|---|---|---|---|---|---|---|---|---|
| **13a** | $C_5H_{11}NH$ | 90 | 122-124 | 2220, 1627, 1593, 1501, 1446, 762, 740 | 0.91 (br t, 3H, J = 7.0, $CH_3$), 1.30-1.42 (m, 4H, methylene), 1.66-1.93 (m, 8H, $CH_2CH_2N$ and cycloheptyl methylene), 2.83-2.87 (m, 2H, allylic methylene), 3.10-3.23 (m, 4H, allylic methylene and $CH_2NH$), 4.05 (t, 1H, J = 6.8, NH), 7.32 (t, 1H, J = 8.0, $H_{9/10\ arom}$), 7.52 (t, 1H, J = 8.1, $H_{10/9\ arom}$), 7.99 (d, 1H, J = 8.2, $H_{8\ arom}$), 8.17 (d, 1H, J = 8.4, $H_{11\ arom}$) | $C_{22}H_{26}N4$ (346.48) | C:<br>H:<br>N: | 76.26<br>7.56<br>16.17 | 76.30<br>7.60<br>16.09 |
| **13b** |  | 98 | 153-155 | 2220, 1481, 1457, 1288, 1263, 1176, 1000, 973, 944, 755 | 1.26 (t, 6H, J = 7.1, $CH_3$), 1.86 (br s, 6H, methylene), 3.26-3.30 (m, 2H, allylic methylene), 3.43 (br s, 2H, allylic methylene), 4.12-4.35 (m, 4H, $POCH_2$), 7.35 (t, 1H, J = 8.4, $H_{9/10\ arom}$), 7.52 (t, 1H, J = 7.5, $H_{10/9\ arom}$), 8.01 (d, 1H, J = 8.2, $H_{8\ arom}$), 8.47 (d, 1H, J = 8.8, $H_{11\ arom}$) | $C_{21}H_{24}N_3O_3P$ (397.42) | C:<br>H:<br>N: | 63.47<br>6.09<br>10.57 | 63.70<br>6.03<br>10.47 |
| **13c** |  | 87 | >300 | 2226, 1634, 1517, 1450, 1315, 1238, 740 | 1.62-1.70 (m, 2H, methylene), 1.88 (br s, 4H, methylene), 2.48-2.51 (m, 2H, allylic methylene), 3.25-3.35 (m, 2H, allylic methylene), 5.88 (d, 1H, J = 8.5, $H_{11\ arom}$), 7.15 (dt, 1H, J = 7.9, 1.1, $H_{9/10\ arom}$), 7.22 (t, 1H, J = 1.3, $H_{5\ imidazole}$), 7.49 (dt, 1H, J = 7.7, 0.9, $H_{10/9\ arom}$), 7.56 (t, 1H, J = 1.0, $H_{4\ imidazole}$), 7.77 (t, 1H, J = 0.8, $H_{2\ imidazole}$), 7.99 (d, 1H, J = 8.3, $H_{8\ arom}$) | $C_{20}H_{17}N_5$ (327.39) | C:<br>H:<br>N: | 73.37<br>5.23<br>21.39 | 73.16<br>5.15<br>21.43 |
| **13d** | $C_5H_{11}O$ | 65 | 154.5-157.0 | 2220, 1629, 1504, 740 | 0.99 (t, 3H, J = 7.2, $CH_3$), 1.42-1.62 (m, 4H, methylene), 1.72-1.93 (m, 6H, cycloheptyl methylene), 2.05 (p, 2H, J = 6.9, $CH_2CH_2O$), 2.90-2.95 (m, 2H, allylic methylene), 3.20-3.25 (m, 2H, allylic methylene), 4.19 (t, 2H, J = 6.8, $CH_2O$), 7.36 (dt, 1H, J = 7.7, 1.2, $H_{9/10\ arom}$), 7.54 (dt, 1H, J = 7.7, 1.1, $H_{10/9\ arom}$), 7.99 (d, 1H, J = 8.2, $H_{8\ arom}$), 8.13 (d, 1H, J = 8.4, $H_{11\ arom}$) | $C_{22}H_{25}N_3O$ •1/4 $H_2O$ (347.46) | C:<br>H:<br>N: | 75.08<br>7.30<br>11.94 | 75.27<br>6.99<br>12.06 |
| **13e** | $C_5H_{11}S$ | 98 | 129-131 | 2221, 1587, 1471, 1442, 1299, 1182, 741 | 0.85 (t, 3H, J = 7.0, $CH_3$), 1.20-1.40 (m, 4H, methylene), 1.60 (p, 2H, J = 7.5, $CH_2CH_2S$), 1.70-1.90 (m, 6H, cycloheptyl methylene), 2.87 (t, 2H, J = 7.4, $CH_2S$), 3.23-3.28 (m, 2H, allylic methylene), 3.37-3.43 (m, 2H, allylic methylene), 7.38 (dt, 1H, J = 7.8, 1.1, $H_{9/10\ arom}$), 7.56 (dt, 1H, J = 7.7, 1.0, $H_{10/9\ arom}$), 8.03 (d, 1H, J = 8.2, $H_{8\ arom}$), 8.98 (d, 1H, J = 8.6, $H_{11\ arom}$) | $C_{22}H_{25}N_3S$ (363.53) | C:<br>H:<br>N: | 72.70<br>6.93<br>11.56 | 72.62<br>6.91<br>11.61 |

[a] The yields are not optimized. [b] Melting points were taken on a Thomas-Hoover melting point apparatus and are uncorrected. [c] The products were recrystallized from the following solvents: **13a**, dichloromethane/ether; **13b**, dichloromethane/hexane/ether; **13c**, dichloromethane/hexane; **13d**, dichloromethane/hexane; **13e**, dichloromethane/hexane/ether. [d] The IR spectra were recorded on a Nicolet 5DXC FTIR. [e] The nmr spectra were recorded at 300.2 MHz on a GE QE-300 instrument; all couplings are reported as apparent couplings.

crude material was purified by filtration through a silica gel plug using 0.5-1% methanol in dichloromethane.

2,3-Dihydro-11-octylamino-4-(*N*-octylimidamido)-1*H*-cyclopenta[4,5]pyrido[1,2-*a*]benzimidazole (**15**).

The crude reaction product was purified by flash silica gel column chromatography using 0-1% methanol in dichloromethane. The product was isolated as a solid (1.07 g, 58%). Crystallization from dichloromethane afforded a tan solid, mp 137.0-139.5°; ir (potassium bromide): ν 3453, 3412, 1603, 1585, 1506, 1448, 1407, 1373, 1273, 751 $cm^{-1}$; pmr (deuteriochloroform/TMS) δ 0.85-0.90 (m, 6H, $CH_3$), 1.20-1.55 (m, 20H, methylene), 1.60-1.77 (m, 4H, $CH_2CH_2N$), 2.13-2.23 (m, 2H, cyclopentyl methylene), 2.59 (t, 2H, J = 7.1 Hz, allylic methylene), 3.17 (t, 2H, J = 7.1 Hz, allylic methylene), 3.48-3.54 (m, 2H, $CH_2NH$), 3.59 (t, 2H, J = 7.1 Hz, $CH_2N=$), 4.14 (br s, 1 H, $CH_2NH$), 7.17-7.25 (m, 2H, $H_{arom}$), 7.35 (v br s, 1H, $H_{arom}$), 7.68 (v br s, 1H, $H_{arom}$), 8.90 (v br s, 1H, NH), 9.50 (v br s, 1H, NH).

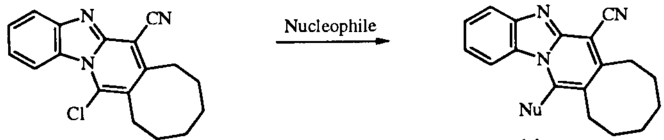
*Anal.* Calcd. for $C_{31}H_{47}N_5$: C, 76.03; H, 9.67; N, 14.30. Found: C, 76.07; H, 9.78; N, 14.22.

2,3-Dihydro-11-(triphenylphosphoranylideneamino)-1*H*-cyclopenta[4,5]pyrido[1,2-*a*]benzimidazole-4-carbonitrile (**16**).

The chloro compound **6** (6.12 g, 23 mmoles) was treated with

Table 6

14-Substituted 1, 2,3,4,5,6-Hexahydrocycloocta[7,8]pyrido[1,2-*a*]benzimidazole-7-carbonitriles




**9** **14a**

| Product | Nu | Yield [a] (%) | mp [b,c] (°C) | IR (KBr) [d] ν (cm$^{-1}$) | $^1$H NMR [e] ($CDCl_3$, TMS) δ, J (Hz) | Molecular Formula (MW) | Analysis | Calcd. | Found |
|---|---|---|---|---|---|---|---|---|---|
| **14a** | $C_5H_{11}NH$ | 64 | 105.5-109.0 | 2219, 1625, 1593, 1491, 1473, 742 | 0.92 (br t, 3H, J = 7.0, $CH_3$), 1.31-1.40 (m, 4H, methylene), 1.41-1.49 (m, 4H, methylene), 1.67-1.80 (m, 4H, methylene), 1.88 (br s, 2H, methylene), 2.89-2.90 (m, 2H, allylic methylene), 3.12-3.20 (m, 4H, allylic methylene and $CH_2N$), 4.11 (t, 1H, J = 6.9, NH), 7.34 (dt, 1H, J = 7.8, 1.1 $H_{10/11\ arom}$), 7.54 (dt, 1H, J =7.7, 1.0 $H_{11/10\ arom}$), 7.99 (d, 1H, J = 8.1, $H_{9\ arom}$), 8.16 (d, 1H, J = 8.4, $H_{12\ arom}$) | $C_{23}H_{28}N4$ (360.51) | C: | 76.63 | 76.40 |
| | | | | | | | H: | 7.83 | 7.84 |
| | | | | | | | N: | 15.54 | 15.52 |

[a] The yield is not optimized. [b] Melting point was taken on a Thomas-Hoover melting point apparatus and are uncorrected. [c] The product **14a** was recrystallized from dichloromethane/hexane. [c] The ir spectrum was recorded on a Nicolet 5DXC FTIR. [e] The nmr spectrum was recorded at 300.2 MHz on a GE QE-300 instnument; all couplings are reported as apparent couplings.

Table 7

Bond Lengths Involving Nonhydrogen Atoms in Crystalline $C_{22}H_{26}N_4$ [a]

| Type [b,c] | Length,Å | Type [b,c] | Length, Å |
|---|---|---|---|
| $N_1$-$C_2$ | 1.405(2) | $C_{19}$-$N_{20}$ | 1.146(2) |
| $N_1$-$C_9$ | 1.405(2) | | |
| $N_1$-$C_{10}$ | 1.386(2) | $C_{12}$-$C_{13}$ | 1.526(3) |
| $N_3$-$C_2$ | 1.320(2) | $C_{13}$-$C_{14}$ | 1.528(3) |
| $N_3$-$C_4$ | 1.382(2) | $C_{14}$-$C_{15}$ | 1.518(3) |
| $N_{21}$-$C_{10}$ | 1.381(2) | $C_{15}$-$C_{16}$ | 1.536(3) |
| $N_{21}$-$C_{22}$ | 1.465(2) | $C_{22}$-$C_{23}$ | 1.496(3) |
| | | $C_{23}$-$C_{24}$ | 1.539(4) |
| $C_2$-$C_{18}$ | 1.413(2) | $C_{23}$-$C_{24'}$ | 1.529(11) |
| $C_4$-$C_5$ | 1.397(3) | $C_{24}$-$C_{25}$ | 1.501(4) |
| $C_4$-$C_9$ | 1.405(2) | $C_{24'}$-$C_{25'}$ | 1.553(14) |
| $C_5$-$C_6$ | 1.370(3) | $C_{25}$-$C_{26}$ | 1.536(4) |
| $C_6$-$C_7$ | 1.389(3) | $C_{25'}$-$C_{26}$ | 1.654(13) |
| $C_7$-$C_8$ | 1.378(3) | | |
| $C_8$-$C_9$ | 1.396(2) | $C_{18}$-$C_{19}$ | 1.430(2) |
| $C_{10}$-$C_{11}$ | 1.378(2) | | |
| $C_{11}$-$C_{17}$ | 1.419(2) | $C_{11}$-$C_{12}$ | 1.519(2) |
| $C_{17}$-$C_{18}$ | 1.386(2) | $C_{16}$-$C_{17}$ | 1.505(2) |
| $N_{21}$-$H_{21}$ | 0.86(3) | $C_{25}$-$H_{25a}$ | 1.02(3) |
| | | $C_{25}$-$H_{25b}$ | 1.05(3) |
| $C_{23}$-$H_{23a}$ | 0.93(3) | $C_{26}$-$H_{26a}$ | 0.87(4) |
| $C_{23}$-$H_{23b}$ | 1.00(2) | $C_{26}$-$H_{26b}$ | 0.93(3) |
| $C_{24}$-$H_{24a}$ | 1.01(3) | $C_{26}$-$H_{26c}$ | 1.23(4) |
| $C_{24}$-$H_{24b}$ | 1.05(3) | | |

[a] The numbers in parentheses are the estimated standard deviations in the last significant digit. [b] Atoms are labeled in agreement with Figure 1. [c] The alkyl chain appears to have 2 alternate orientations in the lattice. The major (81%) orientation for the second and third carbons is specified by carbon atoms $C_{24}$ and $C_{25}$ while the minor (19%) orientation is specified by $C_{24'}$ and $C_{25'}$ (not shown). Hydrogen atoms were included and refined for the major but not the minor orientation. Hydrogen atoms on $C_{23}$-$C_{26}$ were included in the refinement with occupancies of 0.81.

Table 8

Bond Angles Involving Nonhydrogen Atoms in Crystalline $C_{22}H_{26}N_4$ [a]

| Type [b,c] | Angle, (deg) | Type [b,c] | Angle, (deg) |
|---|---|---|---|
| $C_2N_1C_9$ | 105.4(1) | $C_2N_3C_4$ | 104.4(1) |
| $C_2N_1C_{10}$ | 122.2(1) | $C_{10}N_{21}C_{22}$ | 120.5(1) |
| $C_9N_1C_{10}$ | 132.5(1) | $C_{18}C_{19}N_{20}$ | 179.2(2) |
| $N_1C_2N_3$ | 113.5(1) | $N_1C_{10}C_{11}$ | 118.8(1) |
| $N_1C_2C_{18}$ | 117.7(1) | $N_1C_{10}N_{21}$ | 115.7(1) |
| $N_3C_2C_{18}$ | 128.8(1) | $C_{11}C_{10}N_{21}$ | 125.5(1) |
| $N_3C_4C_5$ | 128.2(1) | $C_{10}C_{11}C_{12}$ | 120.7(1) |
| $N_3C_4C_9$ | 111.8(2) | $C_{10}C_{11}C_{17}$ | 120.5(1) |
| $C_5C_4C_9$ | 119.8(1) | $C_{12}C_{11}C_{17}$ | 118.7(1) |
| $C_4C_5C_6$ | 118.2(2) | $C_{11}C_{17}C_{16}$ | 120.1(1) |
| $C_5C_6C_7$ | 121.7(2) | $C_{11}C_{17}C_{18}$ | 119.6(1) |
| $C_6C_7C_8$ | 121.6(2) | $C_{16}C_{17}C_{18}$ | 120.1(1) |
| $C_7C_8C_9$ | 117.1(2) | $C_2C_{18}C_{17}$ | 120.6(1) |
| $N_1C_9C_4$ | 104.7(1) | $C_2C_{18}C_{19}$ | 116.7(1) |
| $N_1C_9C_8$ | 133.4(2) | $C_{17}C_{18}C_{19}$ | 122.8(2) |
| $C_4C_9C_8$ | 121.5(2) | | |
| $C_{11}C_{12}C_{13}$ | 114.7(1) | $C_{22}C_{23}C_{24}$ | 108.1(2) |
| $C_{12}C_{13}C_{14}$ | 113.9(2) | $C_{22}C_{23}C_{24'}$ | 139.1(5) |
| $C_{13}C_{14}C_{15}$ | 115.9(2) | $C_{23}C_{24}C_{25}$ | 113.2(2) |
| $C_{14}C_{15}C_{16}$ | 114.7(2) | $C_{23}C_{24'}C_{25'}$ | 110.1(8) |
| $C_{15}C_{16}C_{17}$ | 113.4(1) | $C_{24}C_{25}C_{26}$ | 110.7(2) |
| $N_{21}C_{22}C_{23}$ | 116.5(2) | $C_{24'}C_{25'}C_{26}$ | 102.0(8) |
| $C_{10}N_{21}H_{21}$ | 109(2) | $C_{22}N_{21}H_{21}$ | 108(2) |
| $C_{22}C_{23}H_{23a}$ | 111(2) | $C_{23}C_{24}H_{24a}$ | 107(2) |
| $C_{22}C_{23}H_{23b}$ | 110(2) | $C_{23}C_{24}H_{24b}$ | 115(2) |
| $C_{24}C_{23}H_{23a}$ | 114(1) | $C_{25}C_{24}H_{24a}$ | 109(2) |
| $C_{24}C_{23}H_{23b}$ | 114(2) | $C_{25}C_{24}H_{24b}$ | 107(2) |
| $H_{23a}C_{23}H_{23b}$ | 100(2) | $H_{24a}C_{24}H_{24b}$ | 105(2) |
| $C_{24}C_{25}H_{25a}$ | 111(2) | $C_{25}C_{26}H_{26a}$ | 110(2) |
| $C_{24}C_{25}H_{25b}$ | 100(2) | $C_{25}C_{26}H_{26b}$ | 112(2) |
| $C_{26}C_{25}H_{25a}$ | 116(2) | $C_{25}C_{26}H_{26c}$ | 109(2) |
| $C_{26}C_{25}H_{25b}$ | 111(2) | $H_{26a}C_{26}H_{26b}$ | 105(3) |
| $H_{25a}C_{25}H_{25b}$ | 107(2) | $H_{26a}C_{26}H_{26c}$ | 108(3) |
| | | $H_{26b}C_{26}H_{26c}$ | 113(3) |

Table 8 (continued)

[a] The numbers in parentheses are the estimated standard deviations in the last significant digit. [b] Atoms are labeled in agreement with Figure 1. [c] The alkyl chain appears to have 2 alternate orientations in the lattice. The major (81%) orientation for the second and third carbons is specified by carbon atoms $C_{24}$ and $C_{25}$ while the minor (19%) orientation is specified by $C_{24'}$ and $C_{25'}$ (not shown). Hydrogen atoms were included and refined for the major, but not the minor, orientation. Hydrogen atoms bonded to $C_{23}$-$C_{26}$ were included in the refinement with occupancies of 0.81.

sodium azide (2.97 g, 46 mmoles) in DMF (30 ml) and stirred at rt for 4 hours. Water was added to dissolve the salts and the mixture was filtered. The crude azide (6.75 g, 100%) was isolated as a tan/green solid that was dried in the oven. Without further storage, this material was slurried in dry benzene (100 ml) and treated with a benzene solution (40 ml) of triphenylphosphine (7.07 g, 27 mmoles). The orange solution was stirred at rt for 3 days. The orange-red solid was collected (9.65 g, 78%) and a portion was recrystallized from dichloromethane to afford a yellow solid, mp >300° (lit [1] mp 300°); ir (potassium bromide): ν 2209, 1589, 1475, 1434, 1256, 1109, 753 $cm^{-1}$; pmr (DMSO-$d_6$/TMS): δ 1.66 (p, 2H, J = 7.0 Hz, $CH_2CH_2CH_2$), 1.98 (t, 2H, J = 7.0 Hz, $CH_2CH_2$), 2.91 (t, 2H, J = 7.3 Hz, $CH_2CH_2$), 6.82 (t, 1H, J = 8.0 Hz, $H_{7/8\ arom}$), 7.33 (t, 1H, J = 8.0 Hz, $H_{8/7arom}$), 7.63-7.83 (m, 16H, phenyl and $H_{6\ arom}$), 8.38 (d, 1H, J = 8.3 Hz, $H_{9\ arom}$).

*Anal.* Calcd. for $C_{33}H_{25}N_4P$: C, 77.94; H, 4.96; N, 11.02. Found: C, 77.73; H, 4.80; N, 10.97.

11-Acetylamino-1*H*-cyclopenta[4,5]pyrido[1,2-*a*]benzimidazole-4-carbonitrile (**17**).

A methanol (85 ml) solution of **16** (4.25 g, 8.36 mmoles) was treated with 2*N* hydrochloric acid (170 ml). The resulting brown solution was warmed to reflux for 2 hours. After the methanol was removed *in vacuo*, the aqueous residue was treated with concentrated ammonium hydroxide to a *p*H of 8. Acetone (5 ml) was added and the crude tan solid was isolated by filtration (3.25 g, >100%). A portion of this material (1.62 g, 6.52 mmoles) was dissolved in dichloromethane and treated with triethylamine (2.7 ml, 19 mmoles) and 4-dimethylaminopyridine (0.39 g, 3.26 mmoles). After this solution was cooled to 0° under nitrogen, it was treated with acetyl chloride (0.51 ml, 7.18 mmoles). The solution was allowed to warm to rt and stirred for 16 hours. Water was added and the solids were removed by filtration. The filtrate was condensed *in vacuo* and the residue was purified by flash silica gel column chromatography using 0.5-2% methanol in dichloromethane. The product was obtained as a solid (0.72 g, 38%). This material was recrystallized from dichloromethane to afford a yellow solid, mp 267-269°; ir (potassium bromide): ν 2220, 1685, 1647, 1517, 1450, 1305, 761, 748 $cm^{-1}$; pmr (DMSO-$d_6$/TMS): δ 2.17 (p, 2H, J = 7.4 Hz, $CH_2CH_2CH_2$), 2.32 (s, 3H, $CH_3$), 2.86 (t, 2H, J = 7.3 Hz, $CH_2CH_2$), 3.25 (t, 2H, J = 7.4 Hz, $CH_2CH_2$), 7.39 (t, 1H, J = 7.3 Hz, $H_{7/8\ arom}$), 7.55 (t, 1H, J = 7.2 Hz, $H_{8/7\ arom}$), 7.87 (d, 1H, J = 8.2 Hz, $H_{6\ arom}$), 8.14 (d, 1H, J = 8.4 Hz, $H_{9\ arom}$), 11.07 (br s, 1H, NH).

*Anal.* Calcd. for $C_{17}H_{14}N_4O$: C, 70.33; H, 4.86; N, 19.30. Found: C, 70.47; H, 5.15; N, 19.05.

2,3,4,5-Tetrahydro-13-pentylsulfinyl-1*H*-cyclohepta[6,7]pyrido-[1,2-*a*]benzimidazole-6-carbonitrile (**18**).

The pentylsulfide compound **13e** (1.0 g, 2.75 mmoles) was dissolved in dichloromethane, cooled to -30° under nitrogen and treated with 85% *m*-chloroperoxybenzoic acid (0.56, 2.75 mmoles). After the mixture warmed to rt, it was filtered. The filtrate was condensed *in vacuo* and the crude waxy solid was crystallized from dichloromethane/hexane/ether. The product was isolated as a yellow solid (0.77 g, 74%), mp 163-165°; ir (potassium bromide): ν 2225, 1478, 1445, 1182, 1091, 1054, 738 $cm^{-1}$; pmr (deuteriochloroform/TMS): δ 0.91 (t, 3H, J = 7.2 Hz, $CH_3$), 1.30-2.00 (m, 12H, methylene), 3.17-3.70 (m, 6H, methylene), 7.42 (dt, 1H, J = 7.8, 1.1 Hz, $H_{9/10\ arom}$), 7.57 (dt, 1H, J = 7.6, 0.9 Hz, $H_{10/9\ arom}$), 8.05 (d, 1H, J = 8.0 Hz, $H_{8\ arom}$), 8.53 (v br lump, 1/2 H, $H_{11\ arom}$).

*Anal.* Calcd. for $C_{22}H_{25}N_3OS$: C, 69.63; H, 6.64; N, 11.07. Found: C, 69.73; H, 6.61; N, 11.06.

Description of the X-ray Determination.

Single crystals of $C_{22}H_{26}N_4$ are, at 20±1°, monoclinic, space group $P2_1/n$ (an alternate setting of $P2_1/c$ - $C_{2}^{5}h$ (No. 14)) with $a$ = 12.478(2)Å, $b$ = 9.231(2)Å, $c$ = 16.782(3)Å, β = 103.87(1)°, V = 1876.7(7)$Å^3$, and Z = 4 {$d_{calcd}$ = 1.226$gcm^{-3}$; $\mu_a(CuK\bar{\alpha})$ = 0.57$mm^{-1}$}. A total of 2788 independent reflections having 2Θ($CuK\bar{\alpha}$)< 120.0° (the equivalent of 0.65 limiting $CuK\bar{\alpha}$ spheres) were collected on a computer-controlled Nicolet autodiffractometer using Θ-2Θ scans and Nickel-filtered $CuK_{\bar{\alpha}}$ radiation. The structure was solved using Direct Methods techniques with the Siemens SHELXTL-PLUS software package as modified at Crystalytics Company. The resulting structural parameters have been refined to convergence {$\underline{R}_1$ (unweighted, based on F) = 0.039 for 2359 independent reflections having 2Θ($CuK_{\bar{\alpha}}$)< 120° and I>3σ(I)} using counter-weighted full-matrix least-squares techniques and a structural model which incorporated anisotropic thermal parameters for all nonhydrogen atoms and isotropic thermal parameters for all hydrogen atoms. Hydrogen atoms $H_{21}$, $H_{23a}$, $H_{23b}$, $H_{24a}$, $H_{24b}$, $H_{25a}$, $H_{25b}$, $H_{26a}$, $H_{26b}$ and $H_{26c}$ were located from a difference Fourier map and refined as independent isotropic atoms. The remaining hydrogen atoms were fixed at idealized $sp^3$- or $sp^2$-hybridized positions with a C-H bond length of 0.96Å. The alkyl chain appears to have 2 alternate orientations in the lattice. The major (81%) orientation for the second and third carbons is specified by carbon atoms $C_{24}$ and $C_{25}$ while the minor (19%) orientation (not shown) is specified by $C_{24'}$ and $C_{25'}$. Hydrogen atoms were included and refined for the major, but not the minor, orientation. Hydrogen atoms bonded to $C_{23}$-$C_{26}$ were included in the refinement with occupancies of 0.81.

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REFERENCES AND NOTES

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