Synthesis and Transformations of some Quinolines and 1*H*-Pyrido[3,2-*c*]azepines Containing Amino Acid Units

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The synthesis of two complex acetyl azides **5** and **12** having quinoline or pyrido[3,2-*c*]azepine ring bound to the acetyl group through the ring nitrogen, and their further transformations into the corresponding carbamates **6** and **13**, isocyanates **7** and **14** and 1-unsubstituted heterocyclic compounds **8** and **15** are described. The later compounds were debenzoylated on heating in concentrated sulfuric acid to give the corresponding products **9** and **16**.

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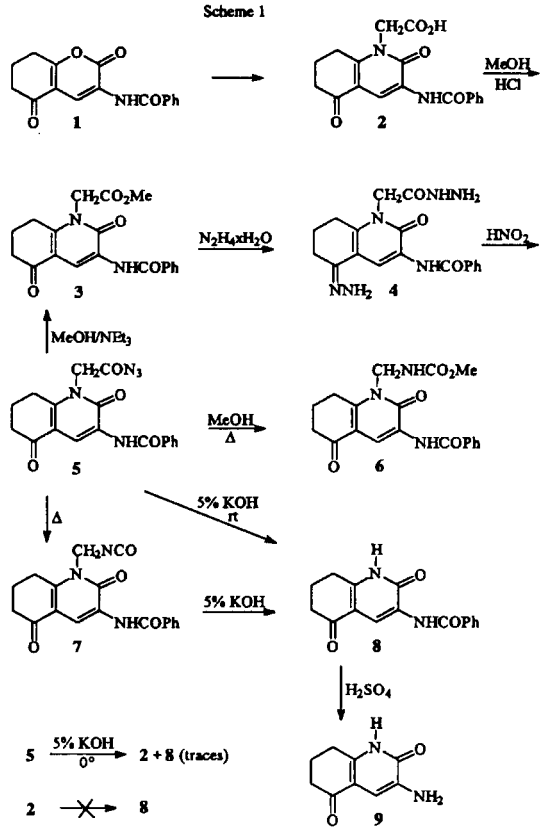
Synthetic approaches to the quinoline system and its hydrogenated derivatives are well documented [1a-b]. On the other hand, only a few papers are dealing with the pyrido[3,2-*c*]azepine system and its derivatives [2]. Many representatives of these two systems exhibit different biological activities [1c,2d]. Some heterocyclic lactams containing an amino acid unit in their structure are also known for their activities. For example, nootropics are used in the therapy of primary dementia, since they improve learning and memory [3].

In this report we would like to describe the synthesis of a quinolinacetic acid derivative **2**, its further transformation into the azides **5** and **12**, some conversions of both azides, mostly *via* the corresponding isocyanates, and some other transformations in the quinoline or pyrido[3,2-*c*]azepine series.

The starting quinolinacetic acid **2** was formed from the benzopyran derivative **1** and sodium salt of glycine in boiling DMF in 91% yield (Scheme 1). This methodology was preliminarily applied for the synthesis of a dimethyl derivative of a quinolinacetic acid [2a]. Compound **2** was transformed by a known reaction sequence [4] through the ester **3**, which, in reaction with hydrazine hydrate, reacted at both sites, at the ester group and the 5-oxo group, to give the corresponding carbazoylmethyl derivative **4**. Diazotization of derivative **4** with nitrous acid in hydrochloric acid solution resulted in the formation of an acylazido group and in the elimination of the hydrazono group from the position 5 yielding compound **5** in high yield. The quinoline system was transformed to the pyrido[3,2-*c*]azepine system by the application of the Schmidt reaction [5,2a] to compound **3**, which gave ester **10** in 54% isolated yield (Scheme 2). The previously described procedure transformed ester **10** to the azide **12** *via* the corresponding hydrazide **11**.

The Curtius rearrangement [4,5b,6] of the azides **5** and **12** was carried out in boiling methanol. In the quinoline series the corresponding rearranged product **6** was formed in reasonable yields. In the case of the azide **12** the

Scheme 1

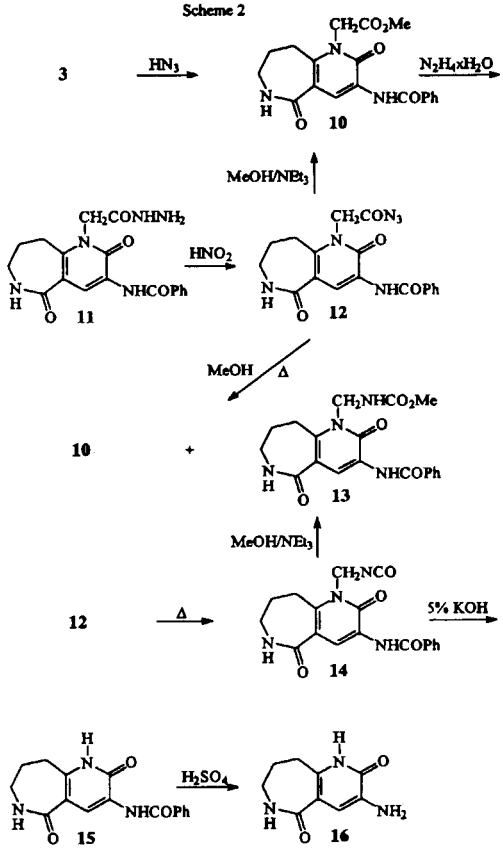


expected product **13** was accompanied by the product **10**, which was the result of the substitution of the azido group by the alkoxy moiety. The compounds were separated by the fractional crystallization.

Some attempts were carried out towards the synthesis of the isocyanates **7** and **14** in the pure state. They were successfully prepared on heating the azides **5** and **12** on the Kofler micro hot stage at about 100° and 110°, respectively. The compounds show in their ir spectra strong isocyanate signals at 2250 and 2280 cm^{-1}, respectively. In the solid state they are stable compounds, slightly soluble in common solvents (alcohols, chloroform, water *etc*), but

they rapidly decompose in DMSO. For this reason both compounds were not crystallized and a good nmr spectrum for the compound **7** was not obtained. The highest peak in the mass spectrum of the compound **7**, 282, probably represents compound **8**. Compound **14** gave under FAB conditions MH^+ peak with 7% intensity. The structure of the isocyanate **14** was also tested by the transformation to the corresponding carbamate **13** in methanolic solution in the presence of triethylamine.

Scheme 2



Treating of the isocyanates **7** and **14** with 5% potassium hydroxide solution at room temperature resulted in the formation of compounds **8** and **15**, which were isolated in good yields. In the quinoline series compound **8** was formed even from the azide **5** under the influence of potassium hydroxide solution. In the pyrido[3,2-*c*]azepine series we have not observed a similar transformation of the azide **12** into the compound **15**. Since the acid **2** is stable under basic conditions, the transformation of azide **5** into quinolone **8** does not take place *via* **2**, but probably *via* the isocyanate **7**. This means that the azide **5** is more easily transformed at room temperature into the isocyanate **7** than to the acid **2** even in alkaline solution. When the reaction was carried out at 0°, the expected acid **2** was accompanied by only traces of **8**. In a corresponding previous observation [7], transformation of isocyanates to the products of the type Het-H probably takes place *via* the unstable carbamic acid derivative, Het-CH_2NHCO_2H, and the aminal, Het-CH_2NH_2, which have a heterocyclic ring bound to the methylene group *via* the ring nitrogen. The aminal hydrolyzes under the influence of the alkaline solution into the final product.

The azido group in compounds **5** and **12** was also replaced by the methoxy group in methanolic solution in the presence of triethylamine yielding products **3** and **10**, respectively.

Finally, the benzoyl group was removed from compounds **8** and **15** to give amino derivatives **9** and **16**, respectively. This reaction took place on heating compounds **8** and **15** in concentrated sulfuric acid at 70-80°.

EXPERIMENTAL

Melting points were determined on a Kofler micro hot stage, and are uncorrected. The nmr spectra were recorded in DMSO-d_6 with a JEOL JNM FX90Q and Varian EM360L instruments, using TMS as an internal standard. Mass spectra were recorded with a VG-Analytical AutoSpec Q and CEC 21-110 B instruments. Elemental analyses (C,H,N) were performed with a Perkin Elmer 2400 CHN Analyzer. Compound **1** was prepared as described in the literature [8]. All other reagents and solvents were used as received from commercial sources.

3-(Benzoylamino)-5,6,7,8-tetrahydro-2,5-dioxo-1(2*H*)-quinolineacetic Acid (**2**).

A.

To a solution of sodium methoxide, prepared from 738 mg (32.1 g-atoms) of sodium and 64 ml of methanol, 2.41 g (32.1 mmoles) of glycine was added and the resulting solution was evaporated *in vacuo* to dryness. The residue was treated with 3.04 g (10.7 mmoles) of *N*-(5,6,7,8-tetrahydro-2,5-dioxo-2*H*-1-benzopyran-3-yl)benzamide (**1**) and 60 ml of *N,N*-dimethylformamide. The resulting mixture was refluxed for 25 minutes and then evaporated *in vacuo*. The remaining residue was suspended in 30 ml of water, the suspension was cooled and acidified to *p*H 2-3. The separated product was filtered off, washed with water and a small amount of ethanol to give 3.31 g (91%) of crude product, mp 253-258° dec (from methanol); ir (potassium bromide): ν 1740, 1680, 1630 cm^{-1}; ^1H nmr: (90 MHz) δ 2.11 (deg p, 2H, 7-CH_2), 2.48 (deg t, 2H) and 2.93 (deg t, 2H) (6-CH_2, 8-CH_2), 4.94 (s, 2H, CH_2), 7.56 (m, 3H, Ph), 7.93 (m, 2H, Ph), 8.70 (s, 1H, 4-H), 9.33 (s, 1H, NH).

Anal. Calcd. for $C_{18}H_{16}N_2O_5$ (340.34): C, 63.52; H, 4.74; N, 8.23. Found: C, 63.31; H, 4.97; N, 7.86.

B.

A mixture of 25 mg (0.068 mmole) of the azide **5** in 1 ml of 5% potassium hydroxide was stirred at 0° for 30 minutes. The *p*H of the mixture was then adjusted to 2-3 with 9% hydrochloric acid solution and the separated product was filtered off and washed with water to give 18 mg (about 77%) of crude acid **2**, accompanied by tlc traces of **8**.

C.

When 170 mg (0.50 mmole) of **2** in 10 ml of 5% potassium hydroxide solution was allowed to stand for 30 minutes at room temperature, or heated for 30 minutes at 50°, upon acidification of the solution with 9% hydrochloric acid to *p*H 2-3, 143 mg (84%) of **2** was recovered.

Methyl 3-(Benzoylamino)-5,6,7,8-tetrahydro-2,5-dioxo-1(2*H*)-quinolineacetate (**3**).

A.

Into a stirred suspension of the acid **2** (5.8 g, 17.04 mmoles) in methanol (235 ml) dry hydrogen chloride was introduced over 15 minutes at room temperature. The resulting solution was evaporated *in vacuo* to dryness and the residue suspended in water (70 ml) and neutralized with solid sodium bicarbonate, while cooling in an ice-bath. The solid part was filtered off and washed with water. The crude product (4.79 g, 79%) was crystallized from methanol and *N,N*-dimethylformamide yielding yellow crystals, mp 221-224°; ir (potassium bromide): ν 1740, 1683, 1645 cm^{-1}; ^1H nmr: (60 MHz) δ 2.12 (m, 2H, 7-CH_2), 2.50 (m, 2H) and 2.92 (m, 2H) (6-CH_2, 8-CH_2), 3.74 (s, 3H, Me), 5.02 (s, 2H, CH_2), 7.60 (m, 3H, Ph), 7.97 (m, 2H, Ph), 8.74 (s, 1H, 4-H), 9.40 (br s, 1H, NH).

Anal. Calcd. for $C_{19}H_{18}N_2O_5$ (354.36): C, 64.40; H, 5.12; N, 7.91. Found: C, 64.46; H, 5.34; N, 8.05.

B.

A mixture of 50 mg (0.137 mmole) of the azide **5** in 2 ml of methanol and 47 mg (0.462 mmole) of 99.5% triethylamine was stirred for 1 hour at room temperature. Upon cooling the separated product was filtered off and washed with a small amount of methanol to give 33 mg (72%) of **3**.

N-[1-(Carbazoylmethyl)-1,2,5,6,7,8-hexahydro-5-hydrazono-2-oxo-3-quinolinyl]benzamide (**4**).

A mixture of 960 mg (2.71 mmoles) of the ester **3** and 615 mg (12.2 mmoles) of 99% hydrazine hydrate in 27 ml of absolute ethanol was refluxed for 16 hours. Upon cooling the solid was filtered off and washed with ethanol yielding 812 mg (81%) of crude **4**, mp 249-251° dec (from methanol and *N,N*-dimethylformamide); ir (potassium bromide): ν 1682, 1640, 1595 cm^{-1}; ^1H nmr: (60 MHz) δ 1.85 (m, 2H, 7-CH_2), 2.25-2.90 (m, 4H, 6-CH_2, 8-CH_2), 3.40 (br s, 4H, two NH_2), 4.79 (s, 2H, CH_2), 7.62 (m, 3H, Ph), 7.98 (m, 2H, Ph), 8.96 (s, 1H, 4-H), 9.27 (s, 1H, NH), 9.42 (s, 1H, NH).

Anal. Calcd. for $C_{18}H_{20}N_6O_3$ (386.40): C, 58.69; H, 5.47; N, 22.81. Found: C, 59.03; H, 5.63; N, 22.72.

N-[1-[(Azidocarbonyl)methyl]-1,2,5,6,7,8-hexahydro-2,5-dioxo-3-quinolinyl]benzamide (**5**).

A stirred mixture of 500 mg (1.36 mmoles) of crude **4** in 2.2 ml of 36% hydrochloric acid and 6.4 ml of water was treated at 0° with 270 mg (3.91 mmoles) of sodium nitrite in 0.8 ml of water over 3 minutes. After standing at 0° for 5 minutes the solid material was filtered off and washed with water, yield 462 mg (93%). For elemental analysis, for ir and nmr spectra and for conversion into **7** the compound was crystallized from methanol to give product which is above 95° transformed into **7**; ms: FAB m/z 366 (5, MH^+), 105 (100); ir (potassium bromide): ν 3350, 2152 (N_3), 1720, 1670, 1637 cm^{-1}; ^1H nmr: (60 MHz) δ 2.05 (m, 2H, 7-CH_2), 2.95 (m, 2H) and 3.45 (m, 2H) (6-CH_2, 8-CH_2), 5.07 (s, 2H, CH_2), 7.62 (m, 3H, Ph), 8.00 (m, 2H, Ph), 8.74 (s, 1H, 4-H), 9.40 (s, 1H, NH).

Anal. Calcd. for $C_{18}H_{15}N_5O_4$ (365.35): C, 59.18; H, 4.14. Found: C, 59.02; H, 4.09.

Methyl [[3-(Benzoylamino)-1,2,5,6,7,8-hexahydro-2,5-dioxo-1-quinolinyl]methyl]carbamate (**6**).

A mixture of 160 mg (0.438 mmole) of **5** in 7 ml of methanol was refluxed for 2 hours. Upon cooling the solid product was filtered off to give 61 mg (37%) of white product, mp 193-195° (methanol); ir (potassium bromide): ν 1708, 1680, 1635 cm^{-1}; ^1H nmr: (60 MHz) δ 2.10 (m, 2H, 7-CH_2), 2.50 (m, 2H) and 3.21 (m, 2H) (6-CH_2, 8-CH_2), 3.58 (s, 3H, Me), 5.44 (d, J = 5.6 Hz, 2H, CH_2NH), 7.64 (m, 3H, Ph), 8.00 (m, 3H, CH_2N*H*, two H of Ph), 8.70 (s, 1H, 4-H), 9.38 (br s, 1H, NH).

Anal. Calcd. for $C_{19}H_{19}N_3O_5$ (369.38): C, 61.78; H, 5.18; N, 11.38. Found: C, 62.23; H, 4.91; N, 11.45.

N-[1,2,5,6,7,8-Hexahydro-1-(isocyanatomethyl)-2,5-dioxo-3-quinolinyl]benzamide (**7**).

This compound was formed quantitatively when 200 mg (0.547 mmole) of azide **5** was heated on micro hot stage at 98-100° for 10 minutes, mp about 110° dec; ms: m/z 282 (78, M^+ -55, corresponding to compound **8**), 105 (100); ir (potassium bromide): ν 3350, 2250 (NCO), 1675, 1630 cm^{-1}.

Anal. Calcd. for $C_{18}H_{15}N_3O_4 \cdot 0.5H_2O$: C, 62.42; H, 4.66; N, 12.13. Found: C, 62.77; H, 4.38; N, 11.98.

N-(1,2,5,6,7,8-Hexahydro-2,5-dioxo-3-quinolinyl)benzamide (**8**).

A.

A mixture of 315 mg (0.862 mmole) of the azide **5** in 14 ml of 5% potassium hydroxide was allowed to stand at room temperature for 30 minutes, then it was acidified with 9% hydrochloric acid solution to *p*H 2-3. Upon cooling the separated product was filtered off and washed with water to give 194 mg (80%) of crude white product, mp 273-276° (ethanol); ir (potassium bromide): ν 1625 (br) cm^{-1}; ^1H nmr: (60 MHz) δ 2.06 (m, 2H, 7-CH_2), 2.45 (m, 2H) and 2.82 (m, 2H) (6-CH_2, 8-CH_2), 7.62 (m, 3H, Ph), 7.98 (m, 2H, Ph), 8.65 (s, 1H, 4-H), 9.28 (s, 1H, NH), 12.6 (br s, 1H, NH).

Anal. Calcd. for $C_{16}H_{14}N_2O_3$ (282.30): C, 68.08; H, 5.00; N, 9.92. Found: C, 68.15; H, 5.21; N, 9.74.

B.

A mixture of 55 mg (0.163 mmole) of isocyanate **7** in 4 ml of 5% potassium hydroxide was allowed to stand at room temperature for 30 minutes, then it was acidified with 9% hydrochloric acid solution to *p*H 2-3. Upon cooling the separated product was filtered off and washed with water to give 36 mg (78%) of product **8**.

3-Amino-7,8-dihydroquinoline-2,5(1*H*,6*H*)-dione (**9**).

A mixture of 245 mg (0.868 mmole) of **8** in 1 ml of concentrated sulfuric acid was heated for 2 hours at 70-80°. Upon cooling the mixture was added to 10 g of ice and water, the separated solid was filtered off and washed with a small amount of water to give 81 mg (90%) of benzoic acid, corresponding in all respect with an authentic sample of Fluka, mp 122-123°. The filtrate was neutralized with solid sodium bicarbonate, evaporated *in vacuo* and the solid residue was extracted with hot ethyl

acetate (3 x 15 ml) to give 80 mg (45%) of white product, mp 267-268° (ethanol); ms: m/z 178 (100, M^+); hrms: Calcd. mass 178.0742, exact mass 178.0748; ir (potassium bromide): ν 1620 (br) cm^{-1}; ^1H nmr: (60 MHz) δ 1.95 (deg p, 2H, 7-CH_2), 2.37 (deg t, 2H) and 2.68 (deg t, 2H) (6-CH_2, 8-CH_2), 5.02 br s, 2H, NH_2), 6.83 (s, 1H, 4-H), 11.84 (br s, 1H, 1-H).

Anal. Calcd. for $C_9H_{10}N_2O_2$ (178.19): C, 60.66; H, 5.66. Found: C, 60.55; H, 5.56.

Methyl 3-(Benzoylamino)-2,5,6,7,8,9-hexahydro-2,5-dioxo-1*H*-pyrido[3,2-*c*]azepine-1-acetate (**10**).

A.

Sodium azide (871 mg, 13.4 mmoles) was added over a period of 30 minutes to a stirred mixture of the ester **3** (436 mg, 1.23 mmoles) in chloroform (65 ml) and concentrated sulfuric acid (2.15 ml) at 0°. The reaction mixture was then stirred for 1 hour at 0° and 80 minutes at room temperature. After the addition of ice and water (37 g) and neutralization of the mixture with solid sodium bicarbonate the layers were separated and the water layer was extracted with chloroform (2 x 40 ml). Methanol (5 ml) was added to the solid product, the solid part was filtered off and washed with a small amount of methanol, yield 246 mg (54%), mp 238-240° (methanol and *N,N*-dimethylformamide); ir (potassium bromide): ν 1723, 1668, 1645, 1622 cm^{-1}; ^1H nmr: (60 MHz) δ 1.90 (m, 2H, 8-CH_2), 2.30-3.12 (m, 4H, 7-CH_2, 9-CH_2), 3.73 (s, 3H, Me), 5.12 (s, 2H, CH_2), 7.62 (m, 3H, Ph), 8.00 (m, 2H, Ph), 8.15 (t, J = 5.6 Hz, 1H, 6-H), 8.46 (s, 1H, 4-H), 9.32 (s, 1H, NH).

Anal. Calcd. for $C_{19}H_{19}N_3O_5$ (369.38): C, 61.78; H, 5.18; N, 11.38. Found: C, 62.11; H, 5.37; N, 11.44.

B.

A mixture of 50 mg (0.132 mmole) of the azide **12** in 2 ml of methanol and 47 mg (0.462 mmole) of 99.5% triethylamine was stirred for 2 days at room temperature. Upon cooling the separated product was filtered off and washed with a small amount of methanol to give 32 mg (66%) of **10**.

N-[1-(Carbazoylmethyl)-2,5,6,7,8,9-hexahydro-2,5-dioxo-1*H*-pyrido[3,2-*c*]azepin-3-yl]benzamide (**11**).

A mixture of 1 g (2.71 mmoles) of the ester **10** and 1.162 g (23 mmoles) of 99% hydrazine hydrate in 15 ml of absolute ethanol was refluxed for 4 hours. Upon cooling the solid product was filtered off and washed with ethanol to give 928 mg (93%) of white product, mp 281-283° (*N,N*-dimethylformamide/methanol); ir (potassium bromide): ν 1695, 1645 cm^{-1}; ^1H nmr: (60 MHz) δ 1.90 (m, 2H, 8-CH_2), 2.45-3.10 (m, 4H, 7-CH_2, 9-CH_2), 4.31 (br s, 2H, NH_2), 4.94 (s, 2H, CH_2), 7.60 (m, 3H, Ph), 7.98 (m, 2H, Ph), 8.11 (t, J = 5.6 Hz, 1H, 6-H), 8.44 (s, 1H, 4-H), 9.31 (br s, 1H, NH), 9.48 (br s, 1H, NH).

Anal. Calcd. for $C_{18}H_{19}N_5O_4$ (369.38): C, 58.53; H, 5.18; N, 18.96. Found: C, 58.39; H, 5.18; N, 18.88.

N-[1-[(Azidocarbonyl)methyl]-2,5,6,7,8,9-hexahydro-2,5-dioxo-1*H*-pyrido[3,2-*c*]azepin-3-yl]benzamide (**12**).

A stirred mixture of 400 mg (1.08 mmole) of **11** in 1.7 ml of 36% hydrochloric acid and 5.1 ml of water was treated over 3 minutes at 0° with 240 mg (3.48 mmoles) of sodium nitrite in 0.6 ml of water. After standing at 0° for 4-5 hours the solid material was filtered off and washed with water to give 356 mg (86%) of product **12**, mp above 100° it transformed into **14**; ms: FAB m/z 381 (13, MH^+); ir (potassium bromide): ν 2145 (N_3), 1700, 1660, 1625 cm^{-1}; ^1H nmr: (60 MHz) δ 1.95 (m, 2H, 8-CH_2), 2.60-3.20 (m, 4H, 7-CH_2, 9-CH_2), 5.18 (s, 2H, CH_2), 7.62 (m, 3H, Ph), 8.00 (m, 2H, Ph), 8.20 (t, J = 5.5 Hz, 1H, 6-H), 8.46 (s, 1H, 4-H), 9.35 (br s, 1H, NH).

Anal. Calcd. for $C_{18}H_{16}N_6O_4$ (380.36): C, 56.84; H, 4.24; N, 22.09. Found: C, 57.30; H, 4.07; N, 21.93.

Methyl [[3-(Benzoylamino)-2,5,6,7,8,9-hexahydro-2,5-dioxo-1*H*-pyrido[3,2-*c*]azepin-3-yl]methyl]carbamate (**13**).

A mixture of 150 mg (0.426 mmole) of the isocyanate **14** in 5 ml of methanol and 47 mg (0.462 mmole) of triethylamine was stirred for 2 hours at room temperature. After evaporation *in vacuo* the solid product was crystallized from a mixture of *N,N*-dimethylformamide and methanol to give 35 mg (21%) of **13**, mp 233-235°; ir (potassium bromide): ν 1725, 1670, 1620 (br) cm^{-1}; ^1H nmr: (60 MHz) δ 2.00 (m, 2H, 8-CH_2), 3.00 (m, 4H, 7-CH_2, 9-CH_2), 3.58 (s, 3H, Me), 5.52 (d, J = 6.0 Hz, 2H, CH_2NH), 7.60 (m, 3H, Ph), 8.00 (m, 3H, CH_2N*H*, two H of Ph), 8.12 (t, J = 5.5 Hz, 1H, 6-H), 8.42 (s, 1H, 4-H), 9.33 (br s, 1H, NH).

Anal. Calcd. for $C_{19}H_{20}N_4O_5$ (384.39): C, 59.37; H, 5.24; N, 14.58. Found: C, 59.70; H, 5.10; N, 14.57.

Transformation of the Azide **12** in Methanol.

A mixture of 152 mg (0.40 mmole) of the azide **12** in 7 ml of methanol was refluxed for 2 hours. Upon careful cooling 69.5 mg (45%) of the carbamate **13** was separated. An additional cooling gave 42 mg (28%) of the ester **10**.

N-[2,5,6,7,8,9-Hexahydro-1-(isocyanatomethyl)-2,5-dioxo-1*H*-pyrido-[3,2-*c*]azepin-3-yl]benzamide (**14**).

This compound was formed quantitatively when 200 mg (0.53 mmole) of **12** was heated on micro hot stage or in a bottle in an oil bath at 110° for about 4 hours (until the azido signal disappeared and the isocyanato signal appeared in the ir spectrum), mp about 145° dec; ms: FAB m/z 353 (7, MH^+); ir (potassium bromide): ν 2280 (NCO), 1640 (br), 1520 cm^{-1}; ^1H nmr: (60 MHz) δ 2.00 (m, 2H, 8-CH_2), 3.0 (m, 4H, 7-CH_2, 9-CH_2), 5.17 (s, 2H, CH_2), 7.62 (m, 3H, Ph), 8.00 (m, 2H, Ph), 8.18 (t, J = 5.5 Hz, 1H, 6-H), 8.50 (s, 1H, 4-H), 9.37 (br s, 1H, NH).

Anal. Calcd. for $C_{18}H_{16}N_4O_4 \cdot H_2O$: C, 58.37; H, 4.90; N, 15.13. Found: C, 58.70; H, 4.75; N, 14.93.

N-(2,5,6,7,8,9-Hexahydro-2,5-dioxo-1*H*-pyrido[3,2-*c*]azepin-3-yl)-benzamide (**15**).

A mixture of 86 mg (0.244 mmole) of isocyanate **14** in 2.5 ml of 5% potassium hydroxide was allowed to stand at room temperature for 30 minutes, then it was acidified with 9% hydrochloric acid solution to *p*H 2-3. Upon cooling the separated product was filtered off and washed with water to give 51 mg (70%) of crude product **15**, which was crystallized from a mixture of *N,N*-dimethylformamide and methanol, mp 322-325°; ir (potassium bromide): ν 1660 (br), 1615 cm^{-1}; ^1H nmr: (90 MHz) δ 1.94 (m, 2H, 8-CH_2), 2.75 (m, 2H, 9-CH_2), 3.08 (m, 2H, 7-CH_2), 7.58 (m, 3H, Ph), 7.95 (m, 3H, two H of Ph, 6-H), 8.45 (s, 1H, 4-H), 9.24 (br s, 1H, NH).

Anal. Calcd. for $C_{16}H_{15}N_3O_3$ (297.31): C, 64.64; H, 5.09; N, 14.13. Found: C, 64.68; H, 5.18; N, 14.05.

3-Amino-6,7,8,9-tetrahydropyrido[3,2-*c*]azepine-2,5(1*H*)-dione (**16**).

A mixture of 190 mg (0.639 mmole) of **15** in 0.8 ml of concentrated sulfuric acid was heated for 2 hours at 70-80°. Upon cooling the mixture was added to 8 g of ice and water, the separated solid was filtered off and washed with a small amount of water to give 51 mg (77%) of benzoic acid. The *p*H of the filtrate was adjusted with solid sodium bicarbonate to 6, the solid product was filtered off and washed with water to give 107 mg (87%) of white product, mp 315-317° (water); ms: m/z 193 (100, M^+); hrms: Calcd. mass 193.0851, exact mass 193.0858; ir (potassium bromide): ν 1672, 1640 (br), 1610 cm^{-1}; ^1H nmr: (60 MHz) δ 1.85 (deg p, 2H, 8-CH_2), 2.65 (deg t, 2H, 9-CH_2), and 3.00 (deg q, 2H, 7-CH_2), 4.95 (br s, 2H, NH_2), 6.68 (s, 1H, 4-H), 7.77 (t, J = 5.5 Hz, 1H, 6-H), 11.65 (br s, 1H, 1-H).

Anal. Calcd. for $C_9H_{11}N_3O_2$ (193.21): C, 55.95; H, 5.74. Found: C, 55.57; H, 5.50.

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REFERENCES AND NOTES

[1a] G. Jones, in Comprehensive Heterocyclic Chemistry, Vol **2**, A. R. Katritzky and C. W. Rees, eds, Pergamon Press, Oxford, 1984, p 395; [b] G. Jones, in The Chemistry of Heterocyclic Compounds, Vol **32** (**1**), A. Weissberger and E. C. Taylor, eds, John Wiley & Sons, London, 1977, p 93; [c] F. S. Yates, ref [1a], p 511.

[2a] M. Kočevar, S. Polanc, M. Tišler, and B. Verček, *Heterocycles*, **30**, 227 (1990); [b] Ref [2a], literature sources under ref [6]; [c] M. Kočevar, *J. Heterocyclic Chem.*, **31**, 265 (1994); [d] A. D. Cale, Jr., US 4,746,657 (1988); *Chem. Abstr.*, **109**, 230988b (1988).

[3] J. F. Almeida, M. Grande, J. R. Moran, J. Anaya, M. L. Mussons and M. C. Caballero, *Tetrahedron: Asymmetry*, **4**, 2483 (1993).

[4] P. A. S. Smith, *Org. React.*, **3**, 337 (1949).

[5a] D. V. Banthorp, The Chemistry of the Azido Group, S. Patai, ed, Interscience, New York, 1971, pp 397-440; [b] T. Shioiri, in Comprehensive Organic Synthesis, Vol **6**, B. M. Trost and I. Fleming, eds, Pergamon Press, Oxford, 1991, pp 795-828.

[6a] E. F. V. Scriven and K. Turnbull, *Chem. Rev.*, **88**, 297 (1988); [b] R. Richter and H. Ulrich, The Chemistry of Cyanates and their Thio Derivatives, S. Patai, ed, Interscience, Chichester, 1977, Part 2, pp 619-818.

[7] C. L. Arcus and D. A. Greenwood, *J. Chem. Soc.*, 1937 (1953).

[8] M. Kočevar, S. Polanc, M. Tišler, and B. Verček, *Synth. Commun.*, **19**, 1713 (1989).