# Synthesis and Transformations of some (Heteroaryl)acetylazides, (Heteroaryl)methyl Isocyanates and Alkyl (Heteroaryl)methyl Carbamates



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The synthesis of two complex acetyl azides **6** and **10** having an heteroaryl residue bound to the acetyl group through the ring nitrogen, and their further transformations into the corresponding carbamates **7a-b** and **11a-b** and isocyanates **16** and **14** are described. Hydrolysis of these products results in the elimination of the substituted methyl group from the heterocyclic residue and formation of 1-unsubstituted heterocycles. A similar transformation was also observed under mass measurement conditions.

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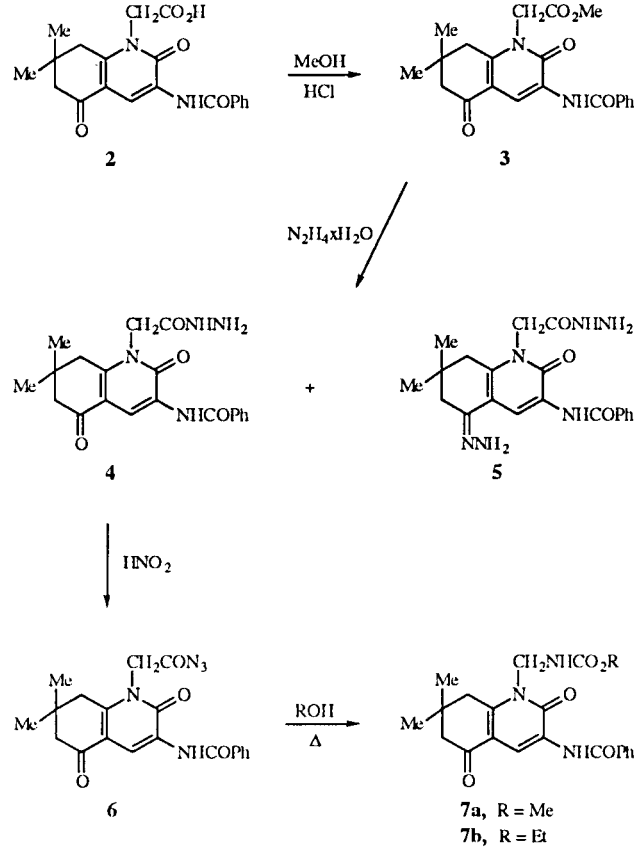
Several approaches towards the synthesis of acylazides and their conversion through isocyanates (The Curtius rearrangement) have been described [1a-h]. There are, however, not many contributions describing acylazides **1a** and the corresponding isocyanates **1b** or carbamates **1c** having an acetyl group substituted by an heterocyclic ring. Among them there is a very small group of compounds **1a-c** having a heterocyclic ring connected to the methylene group *via* the ring nitrogen [2a-c]. It is well known that hydrolysis of isocyanates and carbamates gives either the corresponding amines or urea derivatives [1]. In the case of the hydrolysis of a compound of type **1b** or **1c** one would also expect the formation of the compound **1d**, or possibly the formation of the urea derivative which is the result of the addition of amino compound **1d** onto the isocyanate **1b** [1e,2c]. The proposed final products of the hydrolysis, **1d**, are in these cases less stable than amines in which the aminomethyl group is connected to the carbon atom and therefore may lose the aminomethyl group yielding the final products of type Het-H. This assumption is in agreement with the known low stability of aminals towards hydrolysis and with some observations in the Curtius and Hofmann rearrangements, where in some cases, instead of amino compounds, the corresponding carbonyl compounds were isolated [3].

Het-$CH_2$-X

**1a**, X = $CON_3$,
**1b**, X = NCO,
**1c**, X = $NHCO_2R$,
**1d**, X = $NH_2$

As the starting acylazides in these investigations, 1-(azidocarbonyl)methyl derivatives **6** and **10** were prepared (Schemes 1 and 2). The azido compound **6** was prepared by a known reaction sequence [1e] from 1(2*H*)-quinolineacetic acid **2** [4] through the ester **3** [4], which, upon reaction with hydrazine hydrate, gave the carbazoylmethyl derivative **4**, accompanied by its hydrazono derivative **5**. Diazotization of derivative **4** with nitrous acid in hydrochloric acid solution gave compound **6** in high yield. Similarly,

Scheme 1



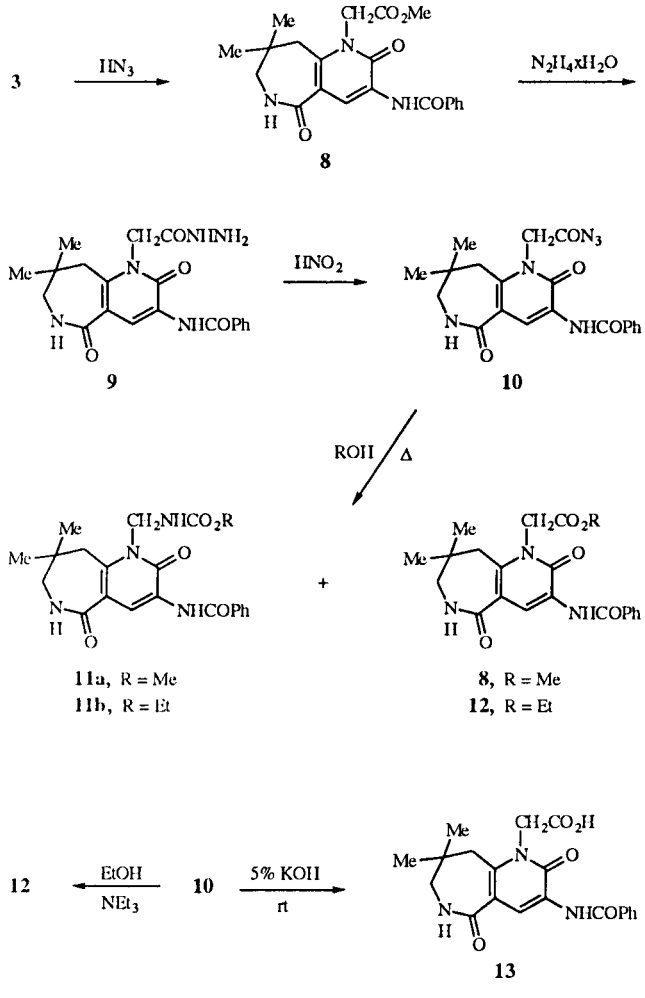

2 3 4 5 6

**7a**, R = Me
**7b**, R = Et

azido compound **10** was prepared *via* the corresponding ester **8** [4] and hydrazide **9**.

The Curtius rearrangement of the azides **6** and **10** was carried out in boiling methanol and ethanol. In the quinoline series the corresponding rearranged products **7a-b** were formed in reasonable yields. In the case of the azide **10** the expected products **11a-b** were accompanied by the

Scheme 2

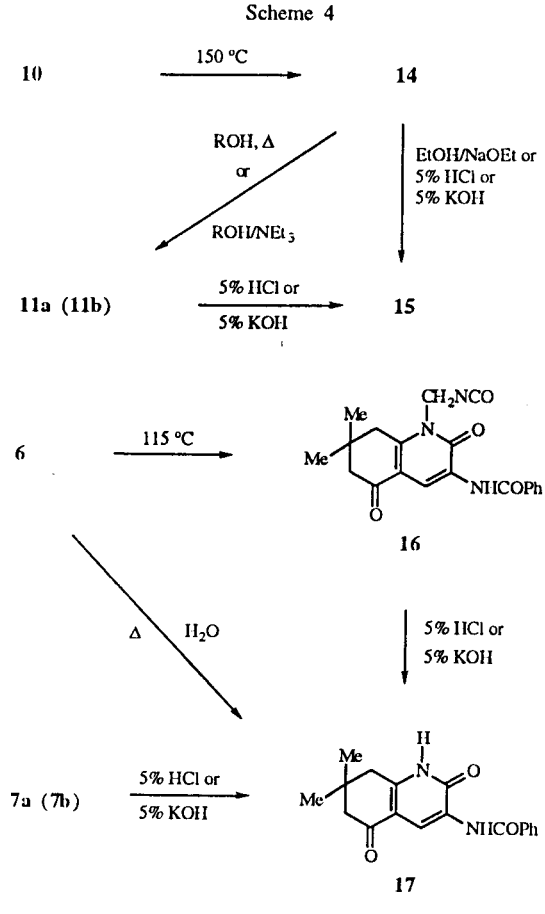


products of substitution of the azido group with the alkoxy group, **8** and **12**. The ratio between isolated compounds **11a** and **8** was 2:3 and between products **11b** and **12** 1.6:1, as determined on the basis of the $^1H$ nmr spectroscopy.

When refluxing the acylazide **10** in distilled water for 7 hours, 1-unsubstituted derivative **15** was isolated in 20% yield (Scheme 3). The ir spectrum of the solid part was taken after 2 hours of heating and, besides the azide signal at 2158 $cm^{-1}$, also showed a small signal at 2262 $cm^{-1}$, which could be ascribed to the isocyanate **14**.

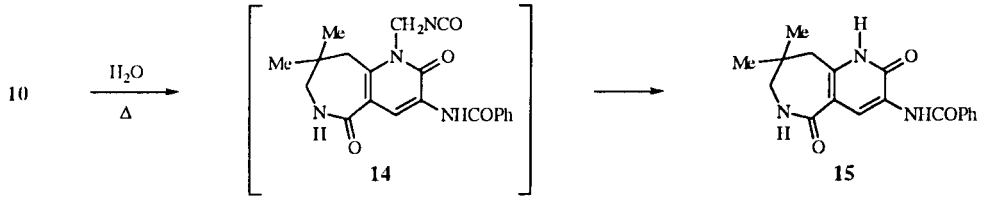
This fact was the reason for some attempts towards the synthesis of the isocyanates **14** and **16** in the pure state (Scheme 4). They were successfully prepared on short heating of the azides **10** and **6** on the Kofler micro hot stage at 150° and 115°, respectively. The compounds show

Scheme 4



in their ir spectra typically strong isocyanate signals at 2262 and 2255 $cm^{-1}$, respectively. In the solid state they are stable compounds (in closed bottles unchanged after several months), insoluble in many common solvents (alcohols, chloroform, water etc); but they are soluble in DMSO and DMF and rapidly decompose. For this reason good nmr spectra for them were not recorded. In the mass spectrum of compound **14** there are the following important peaks: m/z 380 (2.5%, $M^+$), 325 (36%) and 105 (100%).

Scheme 3



Similarly, compound **16** gave the following peaks: m/z 365 ($M^+$), 310 and 105. The structure of the isocyanate **14** was tested by heating in methanol or ethanol. The corresponding carbamates **11a-b** were isolated in 70% and 45% yield. In addition, methyl carbamate **11a** was also formed after 2 hours at room temperature from **14** and methanol in the presence of triethylamine. On the other hand, in ethanol in the presence of triethylamine the isocyanate **14** did not completely disappear even after 10 days at room temperature. When the ethanol/triethylamine mixture was replaced by sodium ethoxide in ethanol, after aqueous workup compound **15** was isolated in 88% yield.

Treating of the isocyanates **14** and **16** with 5% potassium hydroxide solution at room temperature resulted in the formation of compounds **15** and **17**, which were isolated in 82 and 78% yield, respectively. The same products were also formed in even higher yields after brief heating of the isocyanates with 5% hydrochloric acid. Similarly, methyl carbamates **11a** and **7a** were also easily converted to the corresponding final products **15** and **17**, respectively. But ethyl carbamates are much more stable than methyl carbamates. For example, compound **7b** was converted to the final **17** in 53% yield after 100 minutes of heating in boiling 12% hydrochloric acid solution. Severe conditions, of course, might cause reactions in other parts of the molecule. The azido compound **6** was, on heating in water, also directly transformed to **17**. Since the reactivity of the azido compound **10** under basic conditions was tested by its transformations into the ester **12** and the acid **13** (Scheme 2), the appearance of the compound **14** is probably responsible for the transformation of the azide **10** into the product **15**. On the other hand, the transformations of isocyanates and carbamates into the final products **15** and **17** most probably take place *via* intermediates of the type **1d**, which are unstable under the applied conditions, thus yielding the final **15** or **17**, respectively.

The appearance of the peaks with the mass 325 and 310 in the mass spectra of the isocyanates **14** and **16**, which also appear in the spectra of the carbamates **11a-b** and **7a-b**, could be an additional sign for the facility of the formation of the compounds **15** and **17**. This statement was confirmed by high-resolution mass measurements of the fragment with mass 325 in compound **14** and the fragment with mass 310 in **7a**. The exact mass of the fragment 325 is 325.1432 and the calculated mass of this fragment ($C_{18}H_{19}N_3O_3$) is 325.1426. Similarly, in the case of the compound **7a** the exact mass of the fragment 310 is 310.1305 and the calculated mass of $C_{18}H_{18}N_2O_3$ is 310.1317. On the other hand, the exact mass measurements of the fragment ion m/z 310 of **7a** and m/z 310 of **17** show that they have the same elemental composition ($C_{18}H_{18}N_2O_3$). The ms/ms examination of the fragment ion $310^{+\cdot}$ of **7a** and the molecular ion of **17** indicate that these ions have an identical structure. The $^1$H nmr spectra of the isocyanates in DMSO-$d_6$ or DMF-$d_7$ also show rapid formation of the compounds **15** and **17** from the isocyanates **14** and **16**, respectively. All these facts reveal the instability of compounds of the type **1d**.

## 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 **2** was prepared as described in the literature [4]. All other reagents and solvents were used as received from commercial sources.

Methyl 3-(Benzoylamino)-5,6,7,8-tetrahydro-7,7-dimethyl-2,5-dioxo-1(2*H*)-quinolineacetate (**3**) [4].

Into the stirred suspension of the acid **2** [4] (3.5 g, 9.5 mmoles) in methanol (120 ml) dry hydrogen chloride was introduced over 1 hour at room temperature (rt). The resulting solution was evaporated to dryness and the residue suspended in water (40 ml) and neutralized with solid sodium bicarbonate. The solid part was filtered off and washed with water followed by ethanol. The crude product (3 g, 83%) was crystallized from methanol yielding yellow crystals, mp 192-194° (lit [4] 192-194°); $^1$H nmr: (90 MHz) $\delta$ 1.06 (s, 6H, two Me), 2.44 (s, 2H) and 2.85 (s, 2H) (6-$CH_2$, 8-$CH_2$), 3.73 (s, 3H, OMe), 5.03 (s, 2H, $CH_2$), 7.58 (m, 3H, Ph), 7.95 (m, 2H, Ph), 8.70 (s, 1H, 4-H), 9.36 (br s, 1H, NH).

*Anal.* Calcd. for $C_{21}H_{22}N_2O_5$: C, 65.96; H, 5.80; N, 7.33. Found: C, 65.62; H, 6.14; N, 7.28.

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

A mixture of 3 g (7.85 mmoles) of **3** and 1.5 g (29.7 mmoles) of 99% hydrazine hydrate in 60 ml of methanol was refluxed for 2 hours. Upon cooling the solid was filtered off and washed with methanol yielding 2 g (about 67%) of the crude **4** accompanied by tlc traces of **5**, mp 215-218° dec (from methanol); ms: m/z 382 (20, $M^+$); $^1$H nmr: (90 MHz, 60°) $\delta$ 1.06 (s, 6H, two Me), 2.41 (s, 2H) and 2.83 (s, 2H) (6-$CH_2$, 8-$CH_2$), 4.27 (br s, 2H, $NH_2$), 4.83 (s, 2H, $CH_2$), 7.55 (m, 3H, Ph), 7.90 (m, 2H, Ph), 8.69 (s, 1H, 4-H), 9.20 (s, 1H, NH), 9.33 (s, 1H, NH).

*Anal.* Calcd. for $C_{20}H_{22}N_4O_4$ (382.42): C, 62.82; H, 5.80; N, 14.65. Found: C, 62.52; H, 5.91; N, 14.35.

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

A mixture of 400 mg (1.05 mmoles) of **3** and 800 mg (16 mmoles) of 99% hydrazine hydrate in 5 ml of absolute ethanol was refluxed for 5 hours. Upon cooling the solid, a mixture of **4** and **5**, it was filtered off and refluxed again in a mixture of 1.55 g (30.6 mmoles) of hydrazine hydrate and 5 ml of DMF. Charcoal was added to the mixture after 2.5 hours of reflux and the hot mixture was filtered. Upon cooling the separated product was filtered off and crystallized from a mixture of DMF and methanol yielding 60 mg (15%) of white product, mp 272-274°; $^1$H nmr: (90 MHz, 60°) $\delta$ 1.01 (s, 6H, two Me), 2.24 (s, 2H) and 3.53 (s, 2H) (6-$CH_2$, 8-$CH_2$), 4.25 (br s, 2H, $NH_2$), 4.76 (s, 2H, $CH_2$), 6.09 (br s,

2H, $NH_2$), 7.55 (m, 3H, Ph), 7.89 (m, 2H, Ph), 8.90 (s, 1H, 4-H), 9.16 (s, 1H, NH), 9.21 (s, 1H, NH).

*Anal.* Calcd. for $C_{20}H_{24}N_6O_3$: C, 60.59; H, 6.10; N, 21.20. Found: C, 60.72; H, 6.01; N, 21.04.

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

A stirred mixture of 700 mg (1.83 mmoles) of crude **4** in 3 ml of 36% hydrochloric acid and 9 ml of water was treated at 0° with 160 mg (2.31 mmoles) of sodium nitrite in 1 ml of water over 3 minutes. After standing at 0° for 30 minutes the solid material was filtered off and washed with water and ethanol, yield 620 mg (86%). For elemental analysis, for ir and nmr spectra and for conversion into **16** the compound was dissolved in DMSO at about 35° and precipitated with ethanol to give a product which at above 96° is transformed into **16**; ir (potassium bromide): $\nu$ 2137 ($N_3$) $cm^{-1}$; $^1H$ nmr: (90 MHz) $\delta$ 1.07 (s, 6H, two Me), 2.46 (s, 2H) and 2.88 (s, 2H) (6-$CH_2$, 8-$CH_2$), 5.07 (s, 2H, $CH_2$), 7.59 (m, 3H, Ph), 7.95 (m, 2H, Ph), 8.70 (s, 1H, 4-H), 9.38 (s, 1H, NH).

*Anal.* Calcd. for $C_{20}H_{19}N_5O_4$: C, 61.06; H, 4.87; N, 17.80. Found: C, 61.07; H, 5.12; N, 17.45.

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

A mixture of 150 mg (0.38 mmole) of **6** in 7.5 ml of methanol was refluxed for 3.5 hours. After evaporation the solid residue was crystallized from methanol to give 75 mg (50%) of white powder, mp 203-206° dec; ms: m/z 397 (15, $M^+$), 310 (80), 105 (100); $^1H$ nmr: (90 MHz, 60°) $\delta$ 1.08 (s, 6H, two Me), 2.41 (s, 2H) and 3.15 (s, 2H) (6-$CH_2$, 8-$CH_2$), 3.58 (s, 3H), OMe), 5.44 (d, J = 6.3 Hz, 2H, C$H_2$NH), 7.54 (m, 3H, Ph), 7.90 (m, 3H, $CH_2$N*H*, Ph), 8.66 (s, 1H, 4-H), 9.24 (br s, 1H, NH).

*Anal.* Calcd. for $C_{21}H_{23}N_3O_5$ (397.43): C, 63.47; H, 5.83; N, 10.57. Found: C, 63.47; H, 5.93; N, 10.64.

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

A mixture of 600 mg (1.53 mmoles) of **6** in 20 ml of absolute ethanol was refluxed for 135 minutes, then the volume was reduced to 10 ml and the mixture was cooled. The solid product was filtered off and washed with ethanol to give 500 mg (79%) of white powder, mp 172-175° (ethanol) ms: m/z 411 (4, $M^+$), 310 (78), 105 (100); $^1H$ nmr: (90 MHz, 60°) $\delta$ 1.07 (s, 6H, two Me), 1.16 (t, J = 7.1 Hz, 3H, $OCH_2CH_3$), 2.40 (s, 2H) and 3.14 (s, 2H) (6-$CH_2$, 8-$CH_2$), 4.04 (q, J = 7.1 Hz, 2H, $OCH_2CH_3$), 5.44 (d, J = 6.3 Hz, 2H, C$H_2$NH), 7.54 (m, 3H, Ph), 7.78 (t, J = 6.3 Hz, 1H, $CH_2$N*H*), 7.89 (m, 2H, Ph), 8.66 (s, 1H, 4-H), 9.24 (br s, 1H, NH).

*Anal.* Calcd. for $C_{22}H_{25}N_3O_5$ (411.46): C, 64.22; H, 6.12; N, 10.21. Found: C, 64.21; H, 6.25; N, 10.26.

Methyl 3-(Benzoylamino)-2,5,6,7,8,9-hexahydro-8,8-dimethyl-2,5-dioxo-1*H*-pyrido[3,2-*c*]azepine-1-acetate (**8**) [4].

Sodium azide (4 g, 6.12 mmoles) was added over a period of 40 minutes to a stirred mixture of the ester **3** (3 g, 7.85 mmoles) in chloroform (400 ml) and concentrated sulfuric acid (13 ml) at 0°. The reaction mixture was then stirred 1.5 hours at 0° and 2 hours at rt. After the addition of ice and water (200 g) and neutralization of the mixture with solid sodium bicarbonate the layers were separated and the water layer was extracted with chloroform (3 x 140 ml). Methanol (30 ml) was added to the solid product, the solid part was filtered off and washed with a small amount of methanol, yield 2.2 g (71%), mp 277-281° dec (from methanol) (lit [4] 277-281° dec); $^1H$ nmr: (90 MHz) $\delta$ 0.99 (s, 6H, two Me), 2.67 (s, 2H, 9-$CH_2$), 2.70 (d, J = 5.7 Hz, 2H, 7-$CH_2$), 3.71 (s, 3H, OMe), 5.00 (s, 2H, $CH_2$), 7.59 (m, 3H, Ph), 7.92 (m, 2H, Ph), 8.34 (t, J = 5.7 Hz, 1H, 6-H), 8.44 (s, 1H, 4-H), 9.31 (s, 1H, NH).

*Anal.* Calcd. for $C_{21}H_{23}N_3O_5$: C, 63.47; H, 5.83; N, 10.57. Found: C, 63.64; H, 6.00; N, 10.70.

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

A mixture of 2 g (5.03 mmoles) of the ester **8** and 3 g (59.3 mmoles) of 99% hydrazine hydrate in 30 ml of absolute ethanol was refluxed for 4 hours. Upon cooling the solid product was filtered off and washed with ethanol to give 1.8 g (90%) of tlc pure product, mp 275-277° (DMF/methanol); $^1H$ nmr: (90 MHz, 120°) $\delta$ 1.00 (s, 6H, two Me), 2.57 (s, 2H, 9-$CH_2$), 2.73 (d, J = 5.6 Hz, 2H, 7-$CH_2$), 4.18 (br s, 2H, $NH_2$), 4.89 (s, 2H, $CH_2$), 7.56 (m, 3H, Ph), 7.88 (m, 3H, 6-H, 2H of Ph), 8.43 (s, 1H, 4-H), 9.09 (br s, 2H, two NH).

*Anal.* Calcd. for $C_{20}H_{23}N_5O_4$: C, 60.44; H, 5.83; N, 17.62. Found: C, 60.05; H, 5.89; N, 17.41.

*N*-[1-[(Azidocarbonyl)methyl]-2,5,6,7,8,9-hexahydro-8,8-dimethyl-2,5-dioxo-1*H*-pyrido[3,2-*c*]azepin-3-yl]benzamide (**10**).

A stirred mixture of 1.6 g (4.03 mmoles) of **9** in 6 ml of 36% hydrochloric acid and 18 ml of water was treated over 5 minutes at 0° with 370 mg (5.36 mmoles) of sodium nitrite in 2 ml of water. After standing at 0° for 30 minutes the *p*H of the mixture was adjusted with solid sodium bicarbonate to **6**, the solid material was filtered off and washed with water and ethanol, yield 1.6 g (97%). For elemental analysis, for ir and nmr spectra and for conversion into **14** the compound was dissolved in DMSO at rt and precipitated with ethanol to give product which is above 120° transformed into **14**; ir (potassium bromide): $\nu$ 2158 ($N_3$) $cm^{-1}$; $^1H$ nmr: (90 MHz) $\delta$ 0.99 (s, 6H, two Me), 2.68 (s, 2H, 9-$CH_2$), 2.71 (d, J = 5.4 Hz, 2H, 7-$CH_2$), 5.03 (s, 2H, $CH_2$), 7.56 (m, 3H, Ph), 7.80 (m, 2H, Ph), 8.35 (t, J = 5.4 Hz, 1H, 6-H), 8.44 (s, 1H, 4-H), 9.32 (br s, 1H, NH).

*Anal.* Calcd. for $C_{20}H_{20}N_6O_4$: C, 58.82; H, 4.94; N, 20.58. Found: C, 58.44; H, 5.18; N, 20.22.

Methyl [[3-(Benzoylamino)-2,5,6,7,8,9-hexahydro-8,8-dimethyl-2,5-dioxo-1*H*-pyrido[3,2-*c*]azepin-3-yl]methyl]carbamate (**11a**).

A.

A mixture of 95 mg (0.25 mmole) of isocyanate **14** in 4 ml of methanol was refluxed and stirred for 4 minutes. Upon cooling the solid product was filtered off and washed with a small amount of methanol to give 72 mg (70%) of white product, mp about 235° dec (methanol); ms: m/z 412 (5, $M^+$), 325 (74), 105 (100); $^1H$ nmr: (60 MHz) $\delta$ 1.00 (s, 6H, two Me), 2.70 (d, J = 6 Hz, 2H, 7-$CH_2$), 2.80 (s, 2H, 9-$CH_2$), 3.57 (s, 3H, OMe), 5.45 (d, J = 6 Hz, 2H, C$H_2$NH), 7.60 (m, 3H, Ph), 7.97 (m, 3H, 6-H or N*H*$CH_2$, two H of Ph), 8.30 (t, J = 6 Hz, 1H, $CH_2$N*H* or 6-H), 8.40 (s, 1H, 4-H), 9.32 (br s, 1H, NH).

*Anal.* Calcd. for $C_{21}H_{24}N_4O_5$ (412.44): C, 61.16; H, 5.86; N, 13.58. Found: C, 61.25; H, 5.85; N, 13.40.

B.

A mixture of 70 mg (0.184 mmole) of **14** in 6 ml of methanol and 45 mg (0.44 mmole) of triethylamine was stirred for 2 hours

at rt. After evaporation *in vacuo* the solid product was crystallized from methanol to give 32 mg (42%) of **11a**.

Ethyl [[3-(Benzoylamino)-2,5,6,7,8,9-hexahydro-8,8-dimethyl-2,5-dioxo-1*H*-pyrido[3,2-*c*]azepin-3-yl]methyl]carbamate (**11b**).

A mixture of 100 mg (0.263 mmole) of **14** in 3 ml of absolute ethanol was stirred and heated at 80° for 7 minutes. After evaporation *in vacuo* the solid product was crystallized from absolute ethanol to give 50 mg (45%) of white product, mp about 230° dec; ms: m/z 426 (4, M$^+$), 325 (33), 105 (100); $^1$H nmr: (60 MHz) $\delta$ 1.00 (s, 6H, two Me), 1.15 (t, J = 7 Hz, 3H, $OCH_2CH_3$), 2.70 (d, J = 6 Hz, 2H, 7-$CH_2$), 2.82 (s, 2H, 9-$CH_2$), 4.05 (q, J = 7 Hz, 2H, $OCH_2CH_3$), 5.47 (d, J = 6 Hz, 2H, $CH_2NH$), 7.62 (m, 3H, Ph), 7.95 (m, 3H, 6-H or $CH_2NH$, two H of Ph), 8.30 (t, J = 6 Hz, 1H, $CH_2NH$ or 6-H), 8.42 (s, 1H, 4-H), 9.32 (s, 1H, NH).

*Anal.* Calcd. for $C_{22}H_{26}N_4O_5$ (426.47): C, 61.96; H, 6.14; N, 13.14. Found: C, 61.81; H, 5.82; N, 12.76.

Reactions of the Azido Compound **10** with Methanol and Ethanol.

A.

A mixture of 200 mg (0.49 mmole) of **10** in 10 ml of methanol was refluxed for 2.5 hours, then charcoal was added and the mixture was filtered. Upon cooling 140 mg (total yield about 71%) of the mixture of compounds **11a** and **8** in a molar ratio 2:3 was separated. The ratio was determined on the basis of $^1$H nmr spectrum of the mixture ($CH_2$ and OMe groups were determining signals).

B.

When a similar reaction was carried out in absolute ethanol for 2 hours, 138 mg (about 67%) of the mixture of compounds **11b** and **12** in a molar ratio 1.6:1 was separated.

Ethyl 3-(Benzoylamino)-2,5,6,7,8,9-hexahydro-8,8-dimethyl-2,5-dioxo-1*H*-pyrido[3,2-*c*]azepine-1-acetate (**12**).

A mixture of 130 mg (0.32 mmole) of the azido compound **10** in 4 ml of absolute ethanol and 60 mg (0.59 mmole) of 99.5% triethylamine was stirred at rt for 4 days. After evaporation *in vacuo* and crystallization from ethanol 60 mg (46%) of white product was isolated, mp 267-269°; $^1$H nmr: (60 MHz) $\delta$ 1.00 (s, 6H, two Me), 1.23 (t, J = 7 Hz, 3H, $OCH_2CH_3$), 2.68 (s, 2H, 9-$CH_2$), 2.72 (d, J = 6 Hz, 2H, 7-$CH_2$), 4.20 (q, J = 7 Hz, 2H, $OCH_2CH_3$), 5.00 (s, 2H, $CH_2$), 7.60 (m, 3H, Ph), 7.98 (m, 2H, Ph), 8.36 (t, J = 6 Hz, 1H, 6-H), 8.50 (s, 1H, 4-H), 9.35 (s, 1H, NH).

*Anal.* Calcd. for $C_{22}H_{25}N_3O_5$: C, 64.22; H, 6.12; N, 10.21. Found: C, 63.86; H, 5.92; N, 10.44.

3-(Benzoylamino)-2,5,6,7,8,9-hexahydro-8,8-dimethyl-2,5-dioxo-1*H*-pyrido[3,2-*c*]azepine-1-acetic Acid (**13**).

A mixture of 50 mg (0.122 mmole) of **10** in 1 ml of 5% potassium hydroxide was stirred for 160 minutes at rt and then heated for 1 minute at 80° (until a clear solution was formed!). Upon cooling the mixture was acidified with 9% hydrochloric acid to *p*H 2. The solid product was filtered off and washed with water to give 32 mg (68%) of orange compound, mp 273-275° (methanol) (lit [4] 273-275°). The substance corresponds in all respects with the compound described in ref [4].

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

This compound was formed quantitatively when 102 mg (0.25 mmole) of **10** was slowly heated on micro hot stage to 145-150° (during about 25 minutes) and then at this temperature for 5 minutes, mp ~200°, it decomposed; ms: m/z 380 (2.3, M$^+$), 325 (36), 307 (36), 105 (100%); ir (potassium bromide): $\nu$ 2262 (NCO), 1675, 1650, 1623, 1520 cm$^{-1}$.

*Anal.* Calcd. for $C_{20}H_{20}N_4O_4$ (380.40): C, 63.15; H, 5.30; N, 14.73. Found: C, 63.39; H, 4.92; N, 14.49.

*N*-[1,2,5,6,7,8-Hexahydro-1-(isocyanatomethyl)-7,7-dimethyl-2,5-dioxo-3-quinolinyl]benzamide (**16**).

This compound was formed quantitatively when 100 mg (0.254 mmole) of **6** was slowly heated to 110-115° (during about 25 minutes) and then for further 5 minutes at this temperature, mp ~145°, it decomposed; ms: m/z 365 (27, M$^+$), 310 (7), 105 (100); ir (potassium bromide): $\nu$ 2255 (NCO), 1680, 1637 (br) cm$^{-1}$.

*Anal.* Calcd. for $C_{20}H_{19}N_3O_4$ (365.39): C, 65.74; H, 5.24; N, 11.50. Found: C, 65.88; H, 5.57; N, 11.42.

Transformations of the Azido Compounds **6** and **10** in Water.

A.

A suspension of 100 mg (0.254 mmole) of **6** in 3 ml of water was refluxed for 55 minutes. Upon cooling the separated product was filtered off and crystallized from methanol to give 25 mg (32%) of compound **17** [4], mp 264-266° (lit [4] 264-266°); ms: m/z 310 (42, M$^+$). The substance corresponds in all respects with the compound described in ref [4].

B.

A suspension of 100 mg (0.245 mmole) of **10** in 5 ml of distilled water was refluxed for 7 hours, then it was evaporated *in vacuo* and the residue was crystallized from methanol to give 16 mg (20%) of **15** [4], mp above 320° (lit [4] above 320°); ms: m/z 325 (36, M$^+$). The substance corresponds in all respects with the compound described in ref [4].

Transformation of Isocyanates **14** and **16** and Carbamates **11a-b** and **7a** into Compounds **15** or **17**.

General Procedure.

A suspension of the starting compound in 5% potassium hydroxide solution (or 5% hydrochloric acid) was stirred at rt (or heated). The *p*H value of the mixture was adjusted with 9% hydrochloric acid (or solid sodium bicarbonate) to *p*H about 4-5. Upon cooling the solid product was filtered off and washed with water.

The following experiments were performed by this procedure:

Compound **14** (40 mg, 0.105 mmole) in 1 ml of potassium hydroxide for 1 hour at rt yielded 28 mg (82%) of **15**.

Compound **14** (90 mg, 0.237 mmole) in 2 ml of hydrochloric acid for 4 hours at rt and 4-5 minutes at reflux yielded 67 mg (87%) of **15**.

Compound **16** (101 mg, 0.276 mmole) in 2 ml of potassium hydroxide for 3.5 hours at rt yielded 67 mg (78%) of **17**.

Compound **16** (100 mg, 0.274 mmole) in 2 ml of hydrochloric acid for 10 minutes at reflux yielded 82 mg (97%) of **17**.

Compound **11a** (25 mg, 0.606 mmole) in 0.6 ml of potassium hydroxide for 1 hour at rt and 5 minutes at 65-70° yielded 16 mg (81%) of **15**.

Compound **11a** (50 mg, 0.121 mmole) in 1 ml of hydrochloric acid for 7 minutes at reflux yielded 35 mg (89%) of **15**.

Compound **7a** (40 mg, 0.101 mmole) in 1 ml of potassium hy-

droxide for 23 hours at rt yielded 30 mg (96%) of **17**.

Compound **7b** (50 mg, 0.122 mmole) in 2 ml of 12% hydrochloric acid for 100 minutes at reflux yielded 20 mg (53%) of **17**.

A mixture of 100 mg (0.263 mmole) of the isocyanate **14** in a solution of sodium ethoxide, prepared from 28 mg (1.217 mmoles) of sodium and 5 ml of absolute ethanol, was stirred at rt for 80 minutes, then it was evaporated *in vacuo*. The residue was dissolved in 1 ml of water, the *p*H was adjusted to about 4 and, upon cooling, 75 mg (88%) of tlc pure **15** was separated.

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