Reactions of Polyfunctional Amines with 3-Amino-4-(anilinothiomethylidene)-2-cyano-2-pentenedioic Acid Diethyl Ester

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3-Amino-4-(anilinothiomethylidene)-2-cyano-2-pentenedioic acid diethyl ester reacts with ethylenediamine, 1,3-propylenediamine and 1,4-butylenediamine affording bicyclic cyclocondensation products. The title compound reacts with diethylenetriamine and 2-(2-aminoethylamino)ethanol to give new seven membered ring tricyclic compounds. The mechanism for these reactions is discussed.

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Introduction.

Syntheses involving various diamines and 1,2-dihydro-6-chloropyridyl-2-oxopyridines were reported by Kubo *et al.* [1-3]. According to these reports, 6-oxo-1,2,3,4-tetrahydro-6*H*-pyrido[1,2-*a*]pyrimidines and imidazo-[1,2-*a*]pyrimidine were obtained in reactions of 1,2-dihydro-6-chloropyridyl-2-oxopyridines with 1,3-diaminopropane and ethylenediamine, respectively. These reactions consisted of the five following steps: (a) addition-elimination, (b) intramolecular Michael addition, (c) pyridone ring opening, (d) condensation, (e) hydrolysis of the imine intermediate (Scheme 1). In a similar fashion the pyridine derivative **1** reacted with diamines, diethylenetriamine and 2-(2-aminoethylamino)ethanol affording rearrangement products [4]. (Compounds **2** and **3** represent a new heterocyclic ring system, Scheme 2).

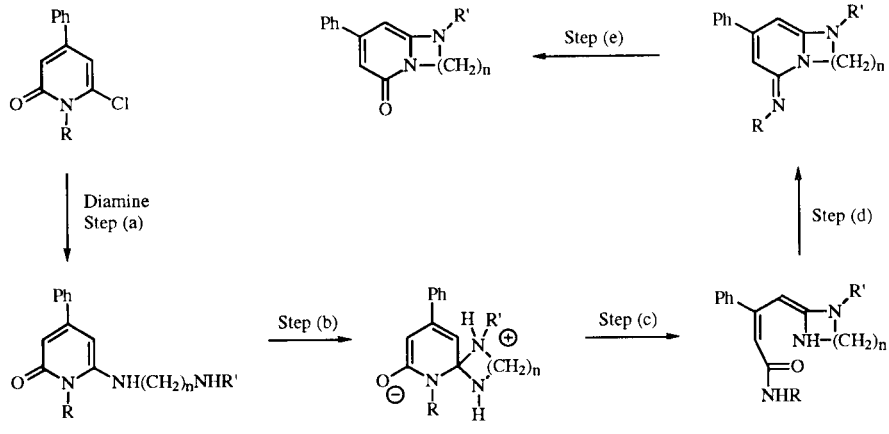
Since compound **4** [5] can be regarded as an open-chain derivative of the pyridone **1**, investigation of the reaction of polyfunctional amines with **4** is a rational continuation of the initial studies of this reaction.

Results and Discussion.

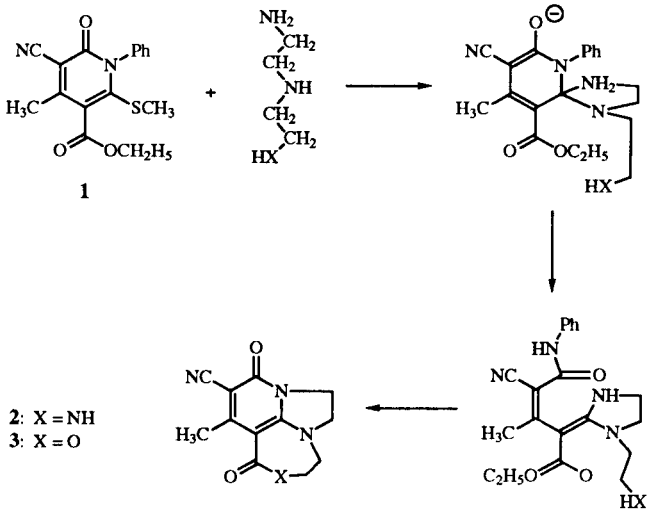
The similar reactivity of compounds **1** and **4** manifests itself in the reaction of **1** and **4** with an aqueous solution of ammonia (Scheme 3). These reactions result in formation of the structurally similar compounds **5** [4] and **6**, respectively. The molecular structure of compound **6** is supported by spectral and experimental data (see Experimental); in particular, the presence of a m/z 119 phenylisocyanate peak in the mass spectrum of **6** demonstrates that the phenylamino group of **6** is attached to the pyridone carbonyl function.

Compound **4** reacts with diamines to give new heterocylic compounds **7-9** (Scheme 4). The reactions are carried out with ethylenediamine, 1,3-propylenediamine and 1,4-butylenediamine at temperatures ranging from room temperature to 140° in good-average product yields. The reaction products are different from what could be expected based on the results of diamine addition reactions to the pyridone derivative **1** in which the phenylamino group is eliminated [4]. Absence of cyano group

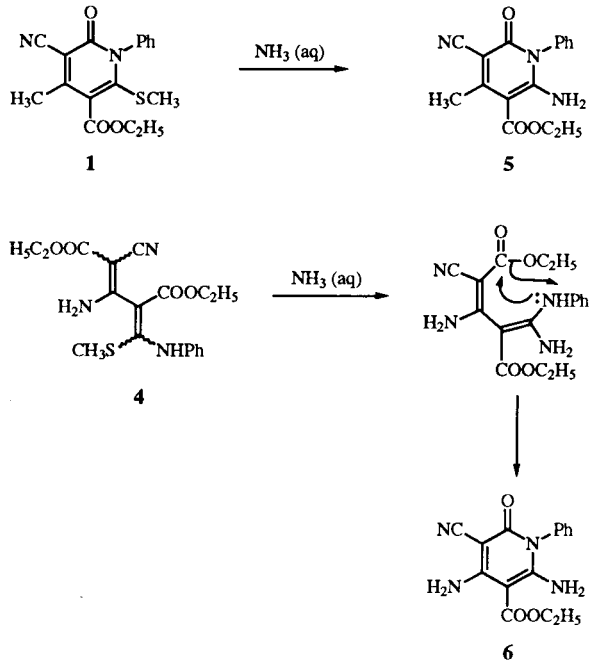
Scheme 1



Scheme 2



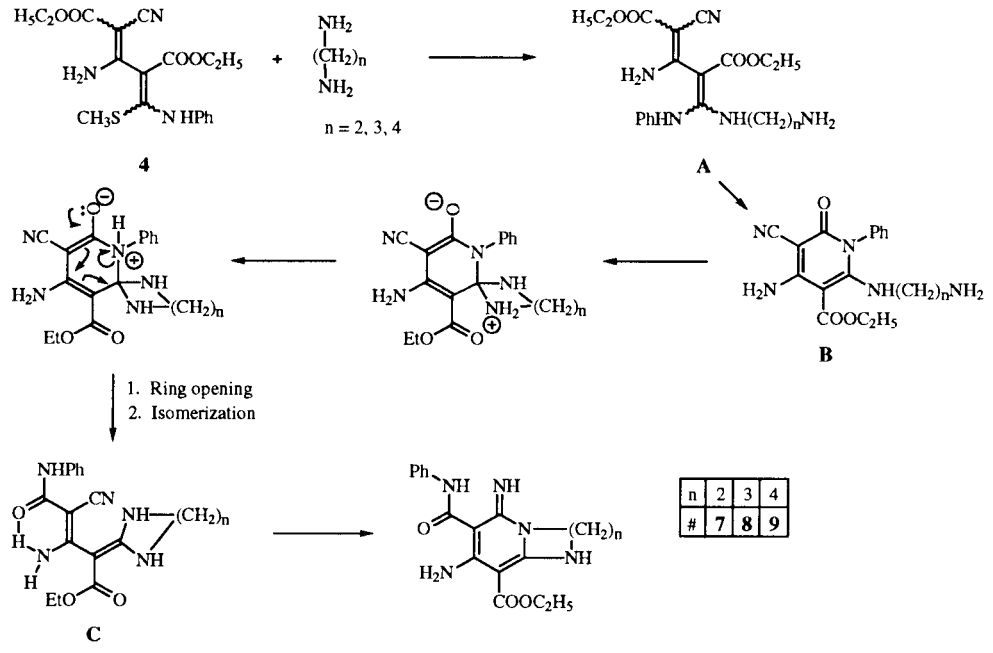
Scheme 3



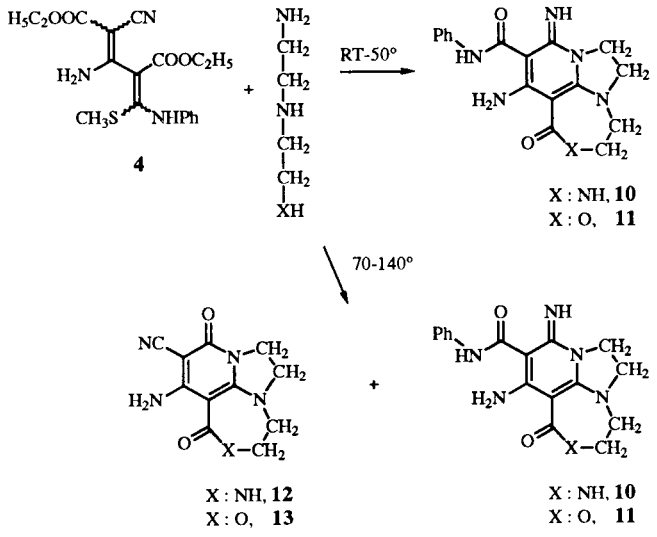
absorption bands in the ir spectra of compounds **7-9** suggests transformation of the cyano group of **4** into the imino function of the cyclization products **7-9**. Also, presence of the prominent peaks (100% R.A.) corresponding to a phenylisocyanate fragment loss in the mass spectra of **7-9** indicates an exocyclic character of the phenylaminocarbanoyl group. The structure of compounds **7-9** is fully supported by the ^{1}H-nmr and ^{13}C-nmr spectra. The nmr spectra interpretation has been aided by the 2D COSY and HETCOR nmr techniques. The ^{1}H-nmr and COSY experiments allow for the following signal identification: NH-CH_2, δ 3.32-3.75; N-CH_2, δ 3.60-4.26; $NCH_2CH_2CH_2N$, δ 1.87-2.02.

The initial addition-elimination step in the reaction mechanism presented in Scheme 4 is consistent with reports that a thioalkyl function can easily be displaced by amines [4,6-8] and with the finding that during the experiments, evolution of methyl mercaptan is observed immediately after the reactants are combined. According to the proposed mechanism (Scheme 4), in the process that follows the initial step involving elimination of a thio-

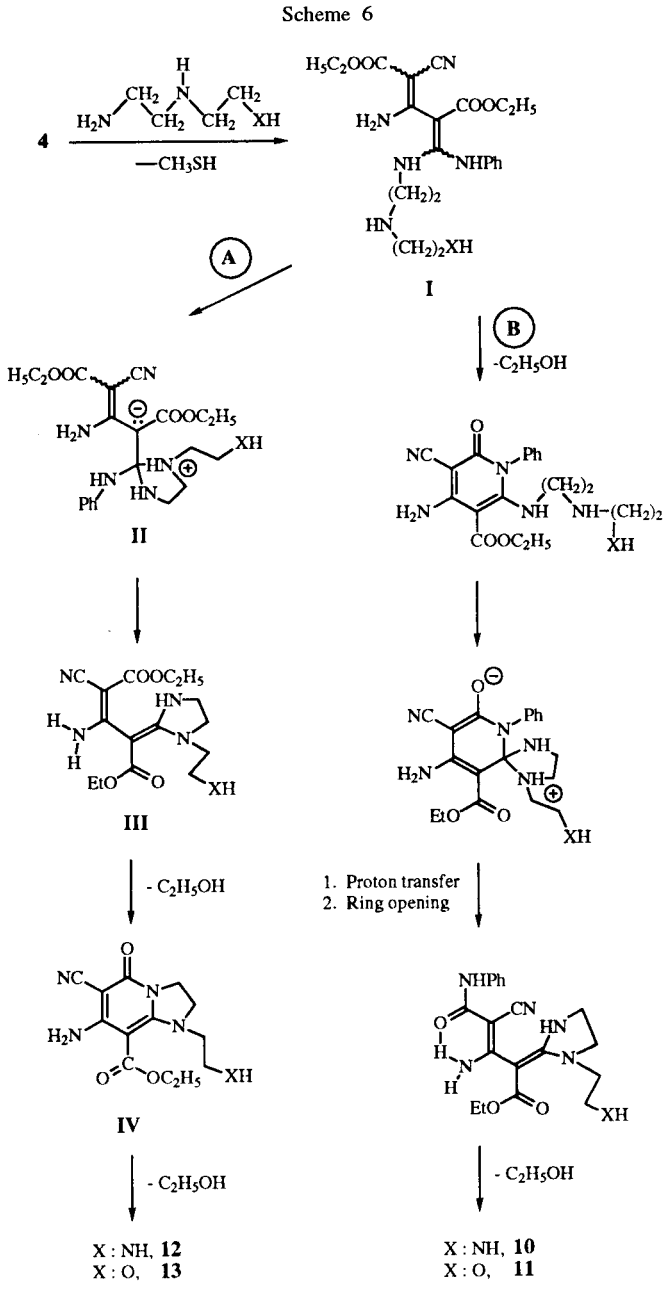
Scheme 4



Scheme 5



Scheme 6



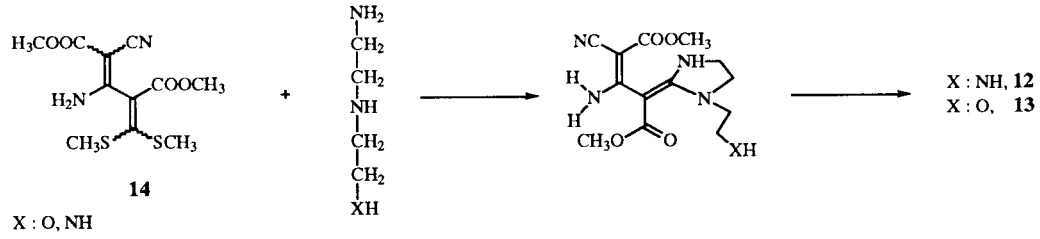
methanol molecule, the nitrogen atom of the phenylamino group of the intermediate product **A** attacks the carbonyl group to produce the pyridine derivative **B**. Intermediate **B** is transformed in the subsequent rearrangement step (similar to that proposed for the reaction of diamines with **1** [4] and 6-chloropyrid-2-ones [1-3]) into an open chain intermediate product **C**. In contrast to the intermediate proposed for the reaction of **1** with diamines [4], **C** possesses an amino function instead of a methyl group. This amino group probably binds the oxygen atom of the neighboring phenylamide group through intramolecular hydrogen bonding that stabilizes the *cis* configuration of the intermediate **C** (Scheme 4). In the final step, cycloaddition of the amine nitrogen atom of **C** to the cyano group completes the reaction to give compounds **7-9**.

Compound **4** reacts with diethylenetriamine and 2-(2-aminoethylamino)ethanol at temperatures ranging from RT to 50° affording heterocyclic compounds **10** and **11**, respectively (Scheme 5). When this reaction is carried out at higher temperatures (70°-140°) the reaction time is reduced to 2 hours but a mixture of products is formed. (With diethylenetriamine **4** produces **10** and **12** while **11** and **13** are formed when **4** reacts with 2-(2-aminoethylamino)ethanol, Scheme 5). These results can be explained by existence of two different reaction pathways (**A** and **B**) leading to formation of the two different products (Scheme 6). Pathway **B** is comparable to the formerly described mechanism that depicts formation of compounds **7-9**. (The difference between these mechanisms is the final closure of an additional seven-membered-ring of **10** and **11**). In contrast, in the reaction proceeding by pathway **A** a molecule of aniline is expelled prior to the cyclocondensation step. Consequently, the reaction follows the route of cyclocondensation in which a molecule of ethanol is eliminated.

(The reaction between compound **4** and ammonia shows that the nucleophilic attack of an amine nitrogen atom on the carbonyl carbon atom is preferred to the attack of the amine nitrogen atom on the carbon atom of the cyano group). This process is then followed by the seven-membered-ring closure to give the final reaction product. It appears that at lower temperatures pathway **B** is the only reaction channel accessible, at higher temperatures, the competing reaction (pathway **A**) opens up.

In order to study further the proposed reaction pathway **A**, an analog of **4**, compound **14**, was synthesized. In this compound the phenylamino group, which is present in **4**,

Scheme 7



is replaced by a thiomethyl function. Since it is already known that a conjugated thiomethyl moiety constitutes a relatively good leaving group [4,6-8] one may predict that both thiomethyl groups of **14** should be eliminated in the initial stage of this reaction (Scheme 6). Compound **14** indeed reacts smoothly with diethylenetriamine or 2-(2-aminoethylamino)ethanol to give the expected cyclocondensation products **12** or **13**, respectively. This result supports the proposed steps **III** and **IV** of the reaction mechanism route **A** (Scheme 6).

Molecular structures of the discussed compounds are clear from their analytical and spectral data. For example, the C^{13}-nmr spectra of compounds **2** [4] and **12** are quite similar, as are **3** [4] and **13**. Each spectrum shows four methylene group signals, and seven downfield signals (δ 69-169), corresponding to sp^2 and sp (cyano group) hybridized carbon atoms. The methylene groups of the diazepine ring of **2**, **10** and **12** attached to the amide nitrogen atom appear in the ^{13}C-nmr spectra at δ 38.0 [4], δ 38.8 and δ 38.9, respectively. The chemical shift of the neighboring methylene group carbon atom is δ 52.7 (**2**) [4], δ 52.2 (**10**) and δ 51.4 (**12**). This signal assignment is supported by comparison of the ^{13}C-nmr spectra of compounds **2**, **10** and **12** with the similar spectra of **3**, **11** and **13**. The signals present in the spectra of the former compounds at δ 37.97-38.86 are replaced by the O-CH_2 signals at δ 63.9 (**3**) [4], δ 63.9 (**11**) and δ 64.2 (**13**). This assignment is also in good agreement with the 2D COSY and HETCOR nmr spectra of compounds **2**, **3** [4] and **10**.

Conclusion.

In conclusion, compound **4** reacts with ethylenediamine, 1,3-propylenediamine and 1,4-butylenediamine affording compounds **7**, **8** and **9**, respectively. In reaction with diethylenetriamine and 2-(2-aminoethylamino)-ethanol **4** yields either a mixture of two products (**10** and **12**, and **11** and **13**, respectively, at the reaction temperatures higher than 70°) or a single compound (**10** and **11**, respectively, at the reaction temperatures below 50°). A derivative of **4**, compound **14** reacts with diethylenetriamine and 2-(2-aminoethylamino)ethanol to give a single product **12** (or **13**). The procedures described here represent convenient methods of synthesis of the relatively complex heterocycles **7-13**.

EXPERIMENTAL

Melting points are uncorrected. The ir spectra were recorded on a Mattson 4020 Galaxy ft/ir as potassium bromide pellets. The ^{1}H- and ^{13}C-nmr spectra were recorded on a Bruker AC 300 spectrometer in deuteriochloroform or DMSO-d_6 (TMS was added as internal standard). Mass spectra were obtained using a Finnigan TSQ-45 Triple Quadrupole Mass Spectrometer. Compound **4** was prepared as described previously [5].

Preparation of 3-Cyano-4,6-diamino-5-ethoxycarbonyl-1-phenyl-1,2-dihydropyridin-2-one (**6**).

Compound **4** (1 g) was dissolved in 5 ml of DMF. To the solution 5 ml of 35% aqueous ammonia solution was added. The reaction mixture was stirred at room temperature for one week and then diluted with 100 ml of distilled water. The crude product was filtered off, dried and recrystallized from a mixture DMF-ethanol yielding a colorless solid, mp 245-246°, yield 0.60 g; ^{1}H-nmr (DMSO-d_6): δ 1.29 (t, 3H), 4.31 (q, 2H), 7.30-7.57 (m, 6H), 8.2-9.5 (br, 3H); ^{13}C-nmr (DMSO-d_6): δ 14.1 (OCH_2CH_3), 60.8 (OCH_2CH_3), 70.1, 78.8, 117.2, 129.2, 129.4, 130.1, 134.1, 157.0, 159.5, 159.6, 166.6; ms: m/z 298 (100%, M^+), 119 (6% , $PhNCO^+$).

Anal. Calcd. for $C_{15}H_{14}N_4O_3$ (298.30): C, 60.40; H, 4.73; N, 18.78. Found: C, 60.51; H, 4.80; N, 18.81.

Preparation of 7-Amino-8-ethoxycarbonyl-5-imino-6-phenylaminocarbonyl-1,2,3,5-tetrahydroimidazo[1,2-*a*]pyridine (**7**).

A mixture of **4** (1.0 g) and 1.0 g (large excess) of ethylenediamine was stirred at 100-110° for 3 hours. The liquid portion of the reaction mixture was removed under reduced pressure. The remaining semi-solid residue was triturated with 10 ml of hot ethanol. (Similar results were obtained by stirring the reaction mixture at room temperature for two weeks followed by usual work up or by diluting the reaction mixture with 5-10 ml of methyl cellosolve used as a solvent.) The colorless precipitate was collected and recrystallized from DMF, mp 210-211°, yield 64%; ^{1}H-nmr (DMSO-d_6): δ 1.28 (t, 3H), 3.75 (t, 2H), 4.00 (q, 2H), 4.26 (q, 2H), 6.66 (s, 1H), 6.93-7.58 (m, 5H), 8.21 (s, 1H), 8.78 (s, 1H), 11.04 (s, 1H), 14.84 (s, 1H); ^{13}C-nmr (DMSO-d_6): δ 14.4 (OCH_2CH_3), 41.4, 43.8 ($2CH_2$), 59.5 (OCH_2CH_3), 80.0, 83.6, 119.4, 121.8, 128.6, 140.2, 153.4, 154.1, 160.4, 166.1, 168.1; ms: m/z 341 (8%, M^+), 222 (100%, M^+-PhNCO), 119 (18%, $PhNCO^+$); ir: ν 3444, 3358, 3172 (NH), 1675 (CO), 1670 (CO).

Anal. Calcd. for $C_{17}H_{19}N_5O_3$ (341.37): C, 59.81; H, 5.61; N, 20.51. Found: C, 59.66; H, 5.64; N, 20.60.

Preparation of 8-Amino-9-ethoxycarbonyl-6-imino-7-phenylaminocarbonyl-1,2,3,4-tetrahydro-6*H*-pyrido[1,2-*a*]pyrimidine (**8**).

The procedure is analogous to that described for synthesis of compound **7**, except that instead of ethylenediamine, 1.0 g of 1,3-

propylenediamine was stirred with 1.0 g of **4**. After removal of liquid under reduced pressure, the oily product was washed several times with small amounts of diethyl ether. To the residue water (10 ml) was added. The mixture was extracted 3 times with 10 ml portions of chloroform. The combined chloroform extracts were dried over anhydrous magnesium sulfate. Chloroform was removed under reduced pressure. The semisolid product was recrystallized from ethanol to give colorless crystals of **8**, mp 179-180°, yield 51%; ^{1}H-nmr (deuteriochloform): δ 1.37 (t, 3H), 2.02 (m, 2H), 3.32 (m, 2H), 3.60 (t, 2H), 4.31 (q, 2H), 6.45 (br s, 1H), 7.00-7.31 (m, 5H), 7.80 (br, 1H), 10.52 (s, 1H), 11.60 (br, 1H), 14.65 (br, 1H); ^{13}C-nmr (deuteriochloroform): δ 14.4 (OCH_2CH_3), 20.5 ($CH_2CH_2CH_3$), 37.8 ($HNCH_2CH_2N$), 41.7 ($HNCH_2CH_2N$), 60.7 (OCH_2CH_3), 78.8, 85.0, 120.8, 122.4, 128.6, 140.2, 153.6, 155.9, 159.1, 168.7, 169.0; ms: m/z 355 (5%, M^+), 236 (100%, M^+-PhNCO), 119 (30%, $PhNCO^+$); ir: ν 3461, 3389, 3086 (NH), 1653 (CO), 1646 (CO).

Anal. Calcd. for $C_{18}H_{21}N_5O_3$ (355.40): C, 60.83; H, 5.96; N, 19.71. Found: C, 61.09; H, 6.00; N, 19.85.

Preparation of 9-Amino-10-ethoxycarbonyl-7-imino-8-phenylaminocarbonyl-1,2,3,4,5,6-hexahydropyrido[1,2-*a*][1,3]diazepine (**9**).

The procedure is analogous to that described for synthesis of compound **8**, except that instead of 1,3-propylenediamine, 1.0 g of 1,4-butylenediamine was stirred with 1.0 g of **4**. Colorless **9** was isolated, mp 173-174°, yield 31%; ^{1}H-nmr (deuteriochloroform): δ 1.38 (t, 3H), 1.87 (m, 2H), 1.94 (m, 2H), 3.40 (t, 2H), 3.90 (t, 2H), 4.32 (q, 2H), 6.35 (br, 1H), 7.1-7.7 (m, 5H), 7.8 (s, 1H), 9.4 (s, 1H), 11.52 (s, 1H), 14.35 (br, 1H); ^{13}C-nmr (deuteriochloroform): δ 14.4 (OCH_2CH_3), 25.6, 26.0 ($2CH2CH_2CH_2CH_2$), 46.3 ($CH2CH_2CH_2CH_2$), 51.6 ($CH2CH_2CH_2CH_2$), 60.9 (OCH_2CH_3), 83.2, 87.5, 120.9, 122.6, 128.6, 139.9, 158.6, 159.7, 161.1, 168.2, 168.5; ms: m/z 369 (22%, M^+), 250 (100%, M^+-PhNCO), 119 (18%, $PhNCO^+$); ir (potassium bromide): ν 3387, 3345, 3122 (NH), 1674 (CO).

Anal. Calcd. for $C_{19}H_{23}N_5O_3$ (369.42): C, 61.77; H, 6.28; N, 18.96. Found: C, 61.43; H, 6.29; N, 18.86.

Preparation of 1-Amino-3-imino-2-phenylaminocarbonyl-5,6,8,9,10,11-hexahydro-3*H*-pyrido[3,2,1-*ij*]-1,3a,6-triazaazulene-11-one (**10**).

Method A.

Compound **4** (1.5 g) and diethylenetriamine (3.3 g) were stirred at 50-60° for 24 hours. (The same results were obtained by stirring the reaction mixture at room temperature for two weeks followed by the usual work up or by diluting the reaction mixture with 5-10 ml of methyl cellosolv used as a solvent). The excess of amine was removed *in vacuo*. A crude solid product was triturated with 25 ml of distilled water. The product was collected in a Buchner funnel, washed with boiling ethanol and recrystallized from DMF, mp 225-227° yield, 52%.

Method B.

Compound **4** (1.5 g) and diethylenetriamine (3.3 g) were stirred at 120-130° for 2.5 hours. The excess of amine was removed *in vacuo*. A crude solid product was washed with 20 ml of boiling ethanol, yield 0.95 g of a mixture of **10** and **12**. (The estimated molar ratio of **10**:**12** was approximately **1**:**1**). The mixture was separated by means of liquid chromatography using silica gel grade 60 (Aldrich) as an immobile phase. Thus 0.2 g of the mixture was dissolved in 20 ml of a solution of acetic acid, ethanol and water (1:1:1) and introduced on top of the lc column. Initially ethanol was used as eluent. After acetic acid was removed from the column, ethanol was replaced by a 9:1 mixture of ethanol and water. After the first component of the reaction mixture was eluted (**12**), a solution of ethanol, water and acetic acid (6:3:1 by volume) was used to elute **10**. Compound **12** was precipitated from the eluate during evaporation of the solvent under reduced pressure. Compound **10** precipitated on standing after removal of the solvent. In order to remove acetic acid from **10** it was triturated with a 10% aqueous solution of ammonia. The colorless solids of **10** and **12** were collected on a Buchner funnel, dried and recrystallized from DMF. Yields after chromatographic separation were: 45% of **10** and 10% of **12**. Compound **10** had ^{1}H-nmr (DMSO-d_6): δ 3.32 (m, 2H), 3.44 (m, 2H), 3.74 (m, 2H), 3.90 (m, 2H), 6.43 (s, 1H), 6.92-7.57 (m, 5H), 7.92 (t, 1H), 9.48 (s, 1H), 10.92 (s, 1H), 15.03 (s, 1H); ^{13}C-nmr (DMSO-d_6): δ 38.8 ($HNCH_2CH_2N$), 42.2 ($HNCH_2CH_2N$), 49.2 (CH_2), 52.2 (CH_2), 79.7, 84.0, 119.3, 121.7, 128.6, 140.4, 149.4, 153.4, 161.9, 168.1, 169.4; ms: m/z 219 (80%, M^+-PhNCO), 119 (32%, $PhNCO^+$), 93 (100%, $PhNH_2^+$); ir (potassium bromide): ν 3411, 3389 (NH), 1653, 1646 cm^{-1} (CO).

Anal. Calcd. for $C_{17}H_{18}N_6O_2$ (338.37): C, 60.34; H; 5.36; N, 24.84. Found: C, 60.25; H, 5.34; N, 24.97.

Preparation of 1-Amino-3-imino-2-phenylaminocarbonyl-5,6,8,9,-tetrahydro-3*H*,11*H*-pyrido[3,2,1-*ij*]-6-oxa-1,3a-diaza-azulene-11-one (**11**).

Method A.

The procedure was analogous to the one previously described but 2-(2-aminoethylamino)ethanol (3.3 g) was used in the reaction instead of diethylenetriaamine, mp 236-237° dec, yield 55% of **11**.

Method B.

The mixture of **4** (1 g) and 0.45 g of 2-(2-aminoethylamino)-ethanol was heated under reflux in 7 ml of methyl cellosolve for 3 hours. The solvent was removed under reduced pressure. A crude semi-solid product was triturated with 15 ml of boiling ethanol, filtered off and recrystallized from DMF, yield 0.47 g of a mixture of compounds **11** and **13** (The ratio of **11**:**13** was estimated as approximately **1**:**1**). The mixture was resolved into its individual components according to the procedure reported for the chromatographic separation of **10** and **12**, yields after the purification: 45-50% for **11**, 10-15% for **13**.

Compound **11** had ^{1}H-nmr (DMSO-d_6): δ 3.63 (m, 2H), 3.79 (m, 2H), 3.96 (m, 2H), 4.45 (m, 2H), 6.69 (s, 1H), 6.96-7.56 (m, 5H), 8.78 (s, 1H), 11.25 (s, 1H); 14.91 (s, 1H); ^{13}C-nmr spectrum (DMSO-d_6): δ 42.7 (CH_2), 48.8 (CH_2), 49.9 (CH_2), 63.9 (OCH_2CH_2), 77.1, 84.1, 119.4, 121.9, 128.6, 140.1, 150.5, 152.9, 161.2, 167.9, 168.4; ms: m/z 220 (25%, M^+-PhNCO), 93 (100%, $PhNH_2^+$); ir: ν 3391, 3341 (NH), 1669 (CO), 1653 (CO).

Anal. Calcd. for $C_{17}H_{17}N_5O_3$ (339.35): C, 60.17; H, 5.05; N, 20.64. Found: C, 60.07; H, 5.00; N, 20.63.

Preparation of 1-Amino-2-cyano-5,6,8,9,10,11-hexahydro-3*H*-pyrido[3,2,1-*ij*]-1,3a-triazaazulene-3,11-dione (**12**).

Method A.

A mixture of **14** (1 g) and 1.5 g of diethylenetriamine was dissolved in 5 ml of methyl cellosolve and then heated under reflux for 2.5 hours. The solvent was removed under reduced pressure.

The crude product was washed with distilled water and recrystallized from DMF, mp: decomposes above 320°, yield 54%.

Method B.

Compound **12** was synthesized as a mixture with **10** according to the procedure B described for synthesis of **10**; ^{1}H-nmr (DMSO-d_6): δ 3.41 (m, 2H), 3.45 (m, 2H), 3.75 (m, 2H), 3.86 (m, 2H), 6.81 (br, 1H), 9.35 (br, 1H), 8.06 (m, 1H); ^{13}C-nmr (DMSO-d_6): δ 38.9 (CH_2), 41.6 (CH_2), 50.4 (CH_2), 51.4 (CH_2), 69.9, 80.4, 117.6, 151.9, 158.6, 163.1, 168.8; ms: m/z 245 (100%, M^+); ir: ν 3383, 3296 (NH), 2198 (CN), 1652, 1646 (CO).

Anal. Calcd. for $C_{11}H_{11}N_5O_2$ (245.24): C, 53.87; H, 4.52. Found: C, 53.98; H, 4.18.

Preparation of 1-Amino-2-cyano-5,6,8,9-tetrahydro-3*H*,11*H*-pyrido[3,2,1-*ij*]-6-oxa-1,3a-diazaazulene-3,11-dione (**13**).

Method A.

A mixture of **14** (1.15 g) and 1.6 g of 2-(2-aminoethylamino)-ethanol was added to 5 ml of methyl cellosolve and then heated under reflux for 2 hours. The solvent was removed under reduced pressure. The crude product was washed with distilled water, filtered and recrystallized from DMF, mp: decomposes above 300°, yield 64%.

Method B.

Compound **13** was synthesized as a mixture with **11** according to the procedure B described for synthesis of **11**; ^{1}H-nmr (DMSO-d_6): δ 3.66 (t, 2H), 3.81 (m, 2H), 3.91 (m, 2H), 4.47 (t, 2H), 7.25 (m, 1H), 8.60 (m, 1H); ^{13}C-nmr (DMSO-d_6): δ 42.1 (CH_2), 49.5 (CH_2), 50.1 (CH_2), 64.2 (OCH_2CH_2), 70.2, 78.1, 117.1, 152.9, 158.4, 161.7, 168.1; ms: m/z (CI/isobutane) 247 (18%, $[M+1]^+$; ir (potassium bromide): ν 3358, 3224 (NH), 2200 (CN), 1662 (CO), 1654 (CO).

Anal. Calcd. for $C_{11}H_{10}N_4O_3$ (246.22): C, 53.66; H, 4.09; N, 22.75. Found: C, 53.96; H, 4.17; N, 22.87.

Preparation of 3-Amino-4-(bisthiomethylmethylidene)-2-cyano-2-pentenedioic Acid Dimethyl Ester (**14**).

To a cooled (0°) suspension of pulverized potassium hydroxide (0.15 mole) in 40 ml of anhydrous dimethylformamide (DMF) 0.075 mole 3-amino-2-cyanopentenedioic acid dimethyl ester [9] was added. To this mixture a solution of carbon disulfide (0.075 mole) in 20 ml of anhydrous DMF was added with stirring. After one hour the ice bath was removed and the reaction mixture was stirred at room temperature for an additional three hours. Then the solution was cooled to 0° in an ice bath and a solution of methyl iodide (0.16 mole) in 20 ml of DMF was slowly added (0.5 hour). The reaction mixture was left overnight at 0°, and its liquid portion was removed *in vacuo* at 50-70°. The oily, orange product was triturated with 150 ml of diethyl ether, and the semi-solid product was collected. It was washed twice with distilled water (50 ml), dried, and recrystallized from a methanol/diethyl ether mixture to give an almost pure, orange, crystalline product. The pure, colorless analytical sample was prepared using either liquid chromatography (chloroform/silica gel) or by dissolving the product sample (1.0 g) in the solution of 40 ml of DMF and 5 ml of the concentrated aqueous ammonia solution. The solution was left overnight at room temperature and then poured over the large amount of water with ice. Thus obtained colorless compound **14** (0.9 g) was collected and recrystallized from methanol, mp 179-180°, total yield 13 g; ^{1}H-nmr (DMSO-d_6): δ 2.44 (s, 3H), 2.52 (s, 3H), 3.67 (s, 3H), 3.68 (s, 3H), 8.98 (s, 1H), 9.05 (s, 1H); ^{13}C-nmr (DMSO-d_6): δ 17.5 (SCH_3), 19.0 (S,CH_3) 51.1 (OCH_3), 52.1 (OCH_3), 70.9, 118.3, 124.3, 161.7, 162.0, 167.2, 167.5; ms: m/z (R.A.) 302 (2%, M^+), 287 (5%, M^+-CH_3), 255 (100%, M^+-CH_3S), 223 (18%), 196 (9%, M^+-CH_3SCSCH_3); ir: ν 3402, 3260, 3199 (NH), 2204 (CN), 1682 (CO).

Anal. Calcd. for $C_{11}H_{14}N_2O_4S_2$ (302.37) C, 43.69; H, 4.67; N, 9.26 S; 21.21. Found: C, 43.69; H, 4.54; N, 9.25; S, 21.50.

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