Alkyl 3-amino-5-aryl-2-benzoyl-5-oxo-2-pentenoates as new chelating ligands and reagents of heterocyclic synthesis

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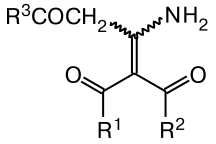
A method for the synthesis of alkyl 3-amino-5-aryl-2-benzoyl-5-oxo-2-pentenoates from Ni chelates of alkyl benzoylacetates and aroylacetonitriles was proposed. The compounds obtained were used for preparation of ethyl 4-amino-6-aryl-2-phenylnicotinates and Ni and B chelates.

Key words: aroylacetonitriles, diphenylboron chelates, nickel chelates, pyran-2-ones, pyrylium salts, pyridines.

Within the scope of studies dealing with the search for new promising reagents for organic synthesis and chelating ligands, our attention was attracted by aminovinyl carbonyl compounds of structural type **A**, which can formally be represented as the products of addition of methylene-active β-diketones or esters of β-oxocarboxylic acids to the C≡N bond of acylacetonitriles.



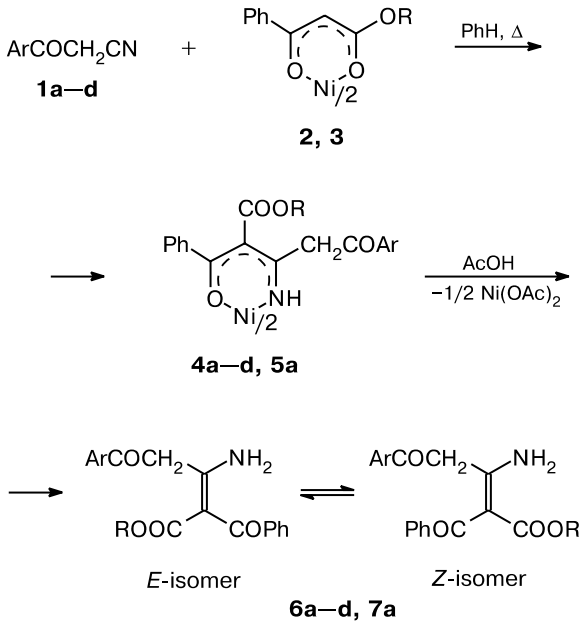
A

R^1 = Alk, OAlk; R^2, R^3 = Alk, Ar

As noted previously,[1—3] adducts of type **A** cannot be prepared directly from nitriles and β-dicarbonyl compounds; therefore, instead of the latter reagents, we proposed performing the reaction with their chelates. For example, we found that the Ni chelate of ethyl acetoacetate can add to aroylacetonitriles in boiling xylene to give Ni complexes incorporating the corresponding compounds **A** (R^1 = OEt, R^2 = Me, R^3 = Ar) as ligands. It was found, however, that destruction of the chelates on treatment with AcOH is accompanied by partial or complete intramolecular cyclization of the evolved free ligands to give 3-acetyl-4-amino-6-arylpyran-2-ones.[3] In this study, we report that more stable adducts of **A** can be obtained from the Ni complexes of benzoylacetates.

It was found that refluxing of a mixture of aroylacetonitriles **1a—d** and chelates **2** or **3** in benzene gives nickel complexes **4a—d** or **5a** in 50—75% yields. On treatment with AcOH, these complexes are smoothly converted into free ligands, namely, 3-amino-5-aryl-2-benzoyl-5-oxo-2-pentenoates **6a—d** and **7a**, which exist in solutions at 20—30 °C as mixtures of *E*- and *Z*-isomers in ~1 : 1 ratio (Scheme 1).

Scheme 1



R = Et (**2**, **4**, **6**), Bu (**3**, **5**, **7**);
Ar = Ph (**a**), 4-MeC_6H_4 (**b**), 4-ClC_6H_4 (**c**), 4-$MeOC_6H_4$ (**d**)

Compounds **6a—d** and **7a** display a much higher thermal stability than their analogs obtained from the Ni chelates of ethyl acetoaceate; they cyclize to pyranones only on refluxing in xylene (for more details, see below).

Ketoesters **6a—d** and **7a** are white crystalline solids readily soluble in most organic solvents. The mass spectra of these compounds exhibit $[M]^+$ peaks, and the ^1H and ^{13}C NMR spectra (in DMSO-d_6 and $CDCl_3$ at 20—30 °C)

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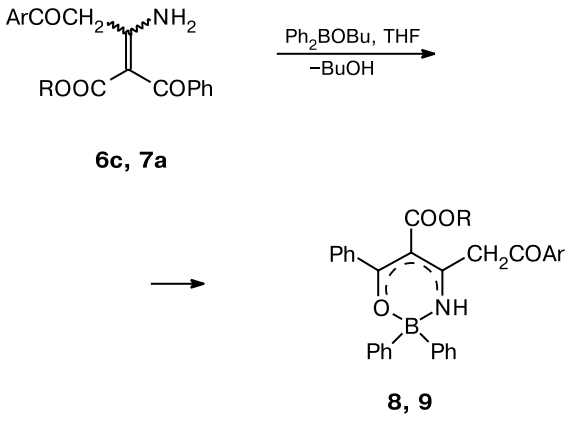
are characterized by double sets of signals with almost equal intensities. The ^{1}H NMR spectrum of compound **6a** in DMSO-d_6 recorded at 70 °C exhibits one set of broadened signals, which confirms the occurrence of an equilibrium between isomers.

Compounds **6** and **7** can evidently be used as chelating ligands, which clearly follows from the method by which they were synthesized (see Scheme 1).

Complexes **4a—d** and **5a** are high-melting red-colored powders poorly soluble in most organic solvents. It is difficult to free them completely from impurities. Although chelates **4b,c** were finally obtained in an analytically pure state, crude compounds **4** and **5** were still used to isolate the free ligands. Apparently, the metal atom in the molecules of complexes **4a—d** and **5a** is coordinated to the O and N atoms of the deprotonated enaminone fragment. The data of IR spectroscopy are in line with the structures **4a—d** and **5a**. The IR spectra (KBr) exhibit narrow absorption bands at 3288—3252 cm^{-1} (NH) and intense absorption in the regions of 1692—1684 (C=O) and 1590—1580 cm^{-1} (delocalized system of multiple bonds in the chelate ring).

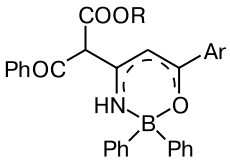
As a rule, boron complexes are more readily soluble in organic solvents than nickel complexes, which facilitates spectroscopic studies. Therefore, we prepared diphenylboron chelates **8** and **9**, which were pale-yellow crystalline compounds readily soluble in most organic solvents (Scheme 2). They are stable in air in the solid state and as solutions in DMSO (for several weeks).

Scheme 2



8: R = Et, Ar = 4-ClC$_6$H$_4$
9: R = Bu, Ar = Ph

The structure of complexes **8** and **9** was confirmed by IR spectroscopy, ^{1}H NMR spectroscopy, and mass spectrometry. The mass spectra of these compounds exhibit a pattern typical of boron chelates, namely, no molecular ion peak and the peak of the $[M - Ph]^+$ ion as the most intense. The ^{11}B NMR signals at δ 4.66—5.46 correspond to four-coordinate boron. The ^{1}H NMR spectra (in DMSO-d_6) exhibit singlets at δ 10.50—10.51 (NH) and δ 4.77—4.80 ($COCH_2$); hence, the alternative structures of type **B** (with a different coordination of boron) can be ruled out. These data also confirm indirectly the structure attributed to chelates **4** and **5** (with a similar coordination of the Ni atom).

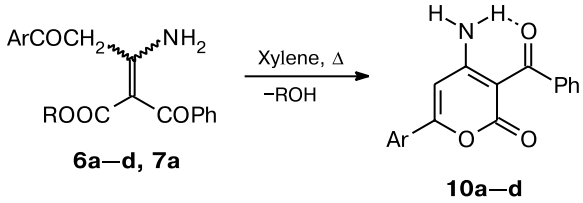


B

In addition, esters **6a—d** and **7a** are new, promising polyfunctional reagents, which can be used in heterocyclic synthesis.

As noted above, on refluxing in xylene, ketoesters **6a—d** and **7a** cyclize to give aminopyranones **10a—d** in ~50% yields (Scheme 3).

Scheme 3



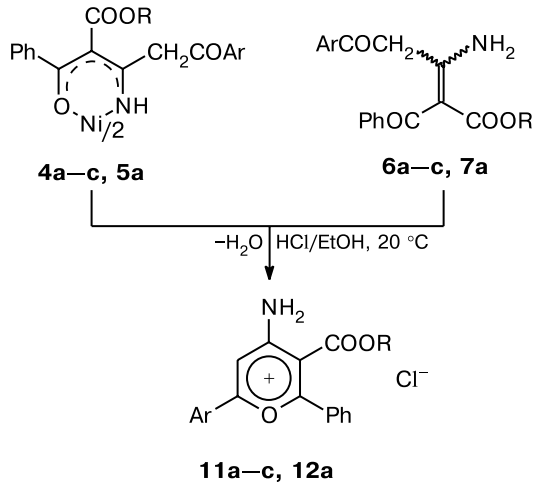
Ar = Ph (**a**), 4-MeC$_6$H$_4$ (**b**), 4-ClC$_6$H$_4$ (**c**), 4-MeOC$_6$H$_4$ (**d**)

Pyranones **10a—d** are white crystalline solids moderately soluble in most organic solvents; they crystallize from benzene, xylene, and ethanol. The mass spectra of these compounds tend to exhibit $[M]^+$ peaks. The IR spectra (KBr) contain narrow absorption bands in the region of 3385—3372 cm^{-1} (free NH) and broadened bands at 3284—3230 cm^{-1} (bound NH). In the ^{1}H NMR spectrum of compound **10a**, the proton signals of the NH_2 group occur as broadened singlets with δ 9.67 (bound NH) and δ 5.63 (free NH), which points to the formation of an N—H...O intramolecular hydrogen bond.

On treatment of ketoesters **6a—c** and **7a** with an ethanolic solution of HCl, previously unknown pyrylium salts **11a—c** and **12a** were synthesized in high yields (Scheme 4). These compounds are prepared even more conveniently using Ni chelates **4a—c** and **5a**, *i.e.*, intermediates in the synthesis of compounds **6** and **7**.

Salts **11a—c** and **12a** are colorless crystalline solids readily soluble in DMSO, EtOH, and $CHCl_3$ and sparingly soluble in most other organic solvents including acetone and MeCN and in water. In the mass spectra of these compounds, the peaks corresponding to the $[M - HCl]^+$ ion are most intense. A specific feature of the ^{1}H NMR spectra (in $CDCl_3$) is the presence of broadened singlets with δ 12.32—12.80 and 8.87—9.17 (NH_2) and characteristic singlets with δ 8.66—8.76 (H(5)).

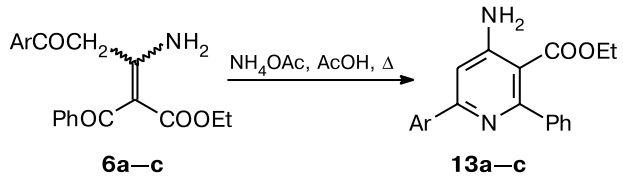
Scheme 4



R = Et (**11**), Bu (**12**);
Ar = Ph (**a**), 4-MeC_6H_4 (**b**), 4-ClC_6H_4 (**c**)

Heating of compounds **6a—c** with ammonium acetate in AcOH gives 4-amino-6-aryl-2-phenylpyridine-3-carboxylates **13a—c** (Scheme 5).

Scheme 5



Ar = Ph (**a**), 4-MeC_6H_4 (**b**), 4-ClC_6H_4 (**c**)

The mass spectra of compounds **13** contain peaks for the $[M]^+$ ions, while the ^1H NMR spectra (in $CDCl_3$) tend to exhibit singlets in the region of δ 6.87—6.93 (H(5)) and broadened signals at δ 5.67—5.71 (NH_2). Only few multistep syntheses of 4-aminonicotinic acid derivatives based on modification of picolines are known.[4,5] Meanwhile, derivatives of 4-aminonicotinic acid are of interest as potential biologically active substances[6] and as naphthyridine precursors.[5]

There is every reason for believing that the above examples are far from exhausting the scope of using compounds **6** and **7** as reagents and chelating ligands.

Experimental

^1H and ^{13}C NMR spectra were recorded on a Bruker WM-250 instrument (250.13 and 62.9 MHz, respectively) using Me_4Si as the internal standard. ^{11}B NMR spectra were recorded on a Bruker AC-200P instrument (64.21 MHz) with $Et_2O \cdot BF_3$ as the internal standard. IR spectra were measured on a Specord M-80 instrument in KBr pellets or in solutions in $CHCl_3$. Mass spectra (EI, 70 eV) were run on a Kratos MS-30 mass spectrometer. The elemental analysis for C, H, N, B, and Cl was performed in the Laboratory for Microanalysis at the N. D. Zelinsky Institute of Organic Chemistry of the RAS. All solvents were dehydrated. Butyl benzoylacetate was synthesized by a known procedure.[7]

Nickel(2+) chelate of ethyl benzoylacetate (2) was prepared similarly to a known method[8] of the synthesis of the nickel chelate of ethyl acetoacetate. The salt $NiCl_2 \cdot 6H_2O$ (12.0 g, 50 mmol) was dissolved in 80 mL of a 4 *M* solution of ammonia. Ethyl benzoylacetate (19.2 g, 100 mmol) was added to the resulting solution and the mixture was stirred for 15 min. The light-blue precipitate that formed was filtered off, washed with water (5×150 mL), and dried *in vacuo* for 4 h (100 °C, 2 Torr) to give 15.7 g (71%) of complex **2** as a green oil readily soluble in most organic solvents (hexane, benzene, chloroform, ethanol, *etc.*) and decomposing on heating above 153 °C. No further purification of the resulting chelate was performed. Found (%): Ni, 12.52. $C_{22}H_{22}NiO_6$. Calculated (%): Ni, 13.31. IR (KBr), ν/cm^{-1}: 1625, 1545, 1480, 1275, 1190. IR ($CHCl_3$), ν/cm^{-1}: 1620, 1530, 1485, 1272, 1192.

Nickel(2+) chelate of butyl benzoylacetate (3). As in the synthesis of complex **2**, butyl benzoylacetate (22.0 g, 100 mmol) was converted into chelate **3**, yield 16.9 g (68%), green oil (dec.p. >134 °C). This product was also used without further purification. Found (%): Ni, 11.37. $C_{26}H_{30}NiO_6$. Calculated (%): Ni, 11.81. IR (KBr), ν/cm^{-1}: 1620, 1536, 1488, 1276, 1192. IR ($CHCl_3$), ν/cm^{-1}: 1624, 1520, 1488, 1276, 1188.

Nickel(2+) chelates of ethyl 3-amino-5-aryl-2-benzoyl-5-oxo-2-pentenoates 4a—d, 5a (general procedure). Nitrile **1a—d** (20 mmol) was added in portions at 70 °C to a solution of 10 mmol of complex **2** or **3** in 25 mL of benzene. The reaction mixture was refluxed for 8 h, and the red precipitates that formed were filtered off, washed with benzene (3×15 mL) and Et_2O (3×10 mL), and dried *in vacuo*.

Nickel(2+) chelate of ethyl 3-amino-2-benzoyl-5-(4-methylphenyl)-5-oxo-2-pentenoate (4b). Yield 75%. For the preparation of an analytically pure specimen, the complex was recrystallized from a large amount of benzene, dec.p. >220 °C. Found (%): C, 66.31; H, 5.30; N, 3.68; Ni, 7.36. $C_{42}H_{40}N_2NiO_8$. Calculated (%): C, 66.42; H, 5.31; N, 3.69; Ni, 7.73. IR (KBr), ν/cm^{-1}: 3288 nar (NH), 1684, 1580, 1448, 1416.

Nickel(2+) chelate of ethyl 3-amino-2-benzoyl-5-(4-chlorophenyl)-5-oxo-2-pentenoate (4c). Yield 82%. For the preparation of an analytically pure specimen, the complex was recrystallized from a large amount of benzene, dec.p. >230 °C. Found (%): C, 60.08; H, 4.38; Cl, 8.87; N, 3.67; Ni, 7.20. $C_{40}H_{34}Cl_2N_2NiO_8$. Calculated (%): C, 60.03; H, 4.28; Cl, 8.86; N, 3.50; Ni, 7.34. IR (KBr), ν/cm^{-1}: 3252 nar (NH), 1692, 1584, 1448, 1408.

Nickel(2+) chelate of ethyl 3-amino-2-benzoyl-5-oxo-5-phenyl-2-pentenoate (4a) (yield 65%, dec.p. >203 °C), **nickel(2+) chelate of ethyl 3-amino-2-benzoyl-5-(4-methoxyphenyl)-5-oxo-2-pentenoate (4d)** (yield 57%, dec.p. >195 °C), and **nickel(2+) chelate of butyl 3-amino-2-benzoyl-5-oxo-5-phenyl-2-pentenoate (5a)** (yield 50%, dec.p. >190 °C) no further purification. IR, chelate **4a** (KBr), ν/cm^{-1}: 3275 nar (NH), 1685, 1695, 1585, 1460, 1414. IR, chelate **4d** (KBr), ν/cm^{-1}: 3260 nar (NH),

1690, 1600, 1590, 1452, 1425. IR, chelate **5a** (KBr), ν/cm^{-1}: 3265 nar (NH), 1688, 1605, 1588, 1445, 1409.

Esters of 3-amino-5-aryl-2-benzoyl-5-oxo-2-pentenoic acids 6a—d, 7a (general procedure). Acetic acid (3 mL) was added to a suspension of complex **4a—d** or **5a** (5 mmol) in 15 mL of $CHCl_3$. The mixture was heated to reflux, cooled to 20 °C, and stirred for 2 h. The organic layer was washed with water (3×10 mL) and dried over $CaCl_2$. The solvent was evaporated and the residue was recrystallized from benzene or from a benzene—hexane mixture.

Ethyl 3-amino-2-benzoyl-5-oxo-5-phenyl-2-pentenoate (6a). Yield 85%, m.p. 129—130 °C (benzene—hexane, 1 : 1). Found (%): C, 71.16; H, 5.72; N, 3.92. $C_{20}H_{19}NO_4$. Calculated (%): C, 71.20; H, 5.68; N, 4.15. MS, *m/z*: 337 $[M]^+$. IR (KBr), ν/cm^{-1}: 3430 br (free NH); 3205 nar (bound NH); 1680, 1660, 1615 (C=O, C=C). ^{1}H NMR* (DMSO-d_6), δ: 10.32, 9.13, 8.61, 8.41 (all br.s, total 2 H, NH_2); 8.15—7.20 (m, 10 H, 2 Ph); 4.46, 4.26 (both s, total 2 H, PhCOC$\underline{H}_2$); 3.78, 3.49 (both q, total 2 H, OCH_2, J = 7.3 Hz); 0.60, 0.45 (both t, total 3 H, Me, J = 7.3 Hz). ^{1}H NMR (70 °C, DMSO-d_6), δ: 9.30 (br.s, 2 H, NH_2); 8.20—7.20 (m, 10 H, 2 Ph); 4.50 (br.s, 2 H, PhCOC$\underline{H}_2$); 3.75 (br.s, 2 H, OCH_2); 0.75 (br.s, 3 H, Me).

Ethyl 3-amino-2-benzoyl-5-(4-methylphenyl)-5-oxo-2-pentenoate (6b). Yield 88%, m.p. 143—144 °C (benzene—hexane, 3 : 1). Found (%): C, 71.56; H, 6.00; N, 3.82. $C_{21}H_{21}NO_4$. Calculated (%): C, 71.78; H, 6.02; N, 3.99. MS, *m/z*: 351 $[M]^+$. IR (KBr), ν/cm^{-1}: 3400 nar (free NH); 3200 br (bound NH); 1688, 1596 (C=O, C=C); 1480. IR ($CHCl_3$), ν/cm^{-1}: 3450 br (NH_2); 1684, 1604 (C=O, C=C); 1482. ^{1}H NMR (DMSO-d_6), δ: 10.32, 9.10, 8.57, 8.35 (all br.s, total 2 H, NH_2); 7.92—7.83, 7.50—7.24 (both m, total 9 H, Ph, 4-MeC$_6\underline{H}_4$); 4.40, 4.20 (both s, total 2 H, 4-MeC$_6$H$_4$COC$\underline{H}_2$); 3.73, 3.49 (both q, total 2 H, OCH_2, J = 7.3 Hz); 2.38, 2.36 (both s, total 3 H, 4-$\underline{Me}$C$_6$H$_4$); 0.58, 0.43 (both t, total 3 H, 2 $\underline{Me}$CH$_2$, J = 7.3 Hz). ^{1}H NMR ($CDCl_3$), δ: 9.30, 6.40 (both br.s, total 2 H, NH_2); 8.05—7.20 (m, 9 H, Ph, 4-MeC$_6\underline{H}_4$); 4.50, 4.25 (both s, total 2 H, PhCOC$\underline{H}_2$); 3.90, 3.75 (both q, total 2 H, OCH_2, J = 7.2 Hz); 2.50, 2.40 (both s, total 3 H, 4-$\underline{Me}$C$_6$H$_4$); 0.75, 0.60 (both t, total 3 H, $\underline{Me}$CH$_2$, J = 7.2 Hz).

Ethyl 3-amino-2-benzoyl-5-(4-chlorophenyl)-5-oxo-2-pentenoate (6c). Yield 91%, m.p. 142—143 °C (benzene). Found (%): C, 64.53; H, 5.00; Cl, 9.32; N, 3.72. $C_{20}H_{18}ClNO_4$. Calculated (%): C, 64.61; H, 4.88; Cl, 9.53; N, 3.77. MS, *m/z*: 371 $[M]^+$. IR (KBr), ν/cm^{-1}: 3405 nar (free NH); 3210 br (bound NH); 1685, 1610 (C=O, C=C); 1480. IR ($CHCl_3$), ν/cm^{-1}: 3440 br (NH_2); 1688, 1593 (C=O, C=C); 1487. ^{1}H NMR (DMSO-d_6), δ: 10.37, 9.14, 8.55, 8.37 (all br.s, total 2 H, NH_2); 8.20—7.15 (m, total 9 H, Ph, 4-ClC$_6\underline{H}_4$); 4.43, 4.19 (both s, total 2 H, 4-ClC$_6$H$_4$COC$\underline{H}_2$); 3.70, 3.47 (both q, total 2 H, OCH_2, J = 7.3 Hz); 0.61, 0.45 (both t, total 3 H, Me, J = 7.3 Hz). ^{1}H NMR ($CDCl_3$), δ: 9.37, 6.25 (both br.s, total 2 H, NH_2); 8.10—7.23 (m, total 9 H, Ph, 4-ClC$_6\underline{H}_4$); 4.45, 4.17 (both s, total 2 H, PhCOC$\underline{H}_2$); 3.89, 3.73 (both q, total 2 H, OCH_2, J = 7.2 Hz); 0.75, 0.63 (both t, total 3 H, Me, J = 7.2 Hz).

Ethyl 3-amino-2-benzoyl-5-(4-methoxyphenyl)-5-oxo-2-pentenoate (6d). Yield 88%, m.p. 97—98 °C (benzene—hexane, 1 : 1). Found (%): C, 68.56; H, 5.90; N, 3.62. $C_{21}H_{21}NO_5$. Calculated (%): C, 68.65; H, 5.76; N, 3.81. MS, *m/z*: 367 $[M]^+$. IR (KBr), ν/cm^{-1}: 3400 nar (free NH); 3215 br (bound NH); 1680, 1600 (C=O, C=C); 1490. ^{1}H NMR (DMSO-d_6), δ: 10.37, 9.14, 8.65, 8.13 (all br.s, total 2 H, NH_2); 8.10—6.90 (m, total 9 H, Ph, 4-MeOC$_6\underline{H}_4$); 4.46, 4.24 (both s, total 2 H, 4-MeOC$_6$H$_4$COC$\underline{H}_2$); 3.86, 3.84 (both s, total 3 H, 4-$\underline{Me}$OC$_6$H$_4$); 3.78, 3.50 (both q, total 2 H, OCH_2, J = 7.3 Hz); 0.60, 0.46 (both t, total 3 H, $\underline{Me}$CH$_2$, J = 7.3 Hz).

Butyl 3-amino-2-benzoyl-5-oxo-5-phenyl-2-pentenoate (7a). Yield 80%, m.p. 103—104 °C (benzene—hexane, 3 : 1). Found (%): C, 72.31; H, 6.34; N, 3.83. $C_{22}H_{23}NO_4$. Calculated (%): C, 72.04; H, 6.30; N, 3.72. MS, *m/z*: 365 $[M]^+$. IR (KBr), ν/cm^{-1}: 3380 nar (free NH); 3200 br (bound NH); 1690, 1580 (C=O, C=C). IR ($CHCl_3$), ν/cm^{-1}: 3440 br (NH_2); 1690, 1605 (C=O, C=C). ^{1}H NMR (DMSO-d_6), δ: 10.36, 9.19, 8.64, 8.40 (all br.s, total 2 H, NH_2); 8.10—7.25 (m, 10 H, 2 Ph); 4.53, 4.17 (both s, total 2 H, PhCOC$\underline{H}_2$); 3.75, 3.49 (both t, total 2 H, OCH_2, J = 6.7 Hz); 1.05—0.40 (m, 7 H, CH_2CH_2Me). ^{13}C NMR (DMSO-d_6), δ: 193.61 and 193.95 (Ph$\underline{C}$OCH$_2$), 168.66, 168.94, 165.88, 164.84, 142.72, 143.44, 136.09, 133.35, 133.19, 130.54, 129.73, 128.73, 128.67, 127.97, 127.81, 127.69, 127.44, 126.38, 100.16, 97.94, 62.71 and 62.21 (OCH_2), 44.84 and 44.25 ($\underline{C}H_2CH_2$Me), 29.76 and 29.45 ($\underline{C}H_2$Me), 18.26 and 13.43 (Me).

Diphenylboron chelate of ethyl 3-amino-2-benzoyl-5-(4-chlorophenyl)-5-oxo-2-pentenoate (8). Ketoester **6c** (0.37 g, 1 mmol) was dissolved in 5 mL of THF in an atmosphere of dry nitrogen, and Ph_2BOBu (0.24 g, 1 mmol) was added. The mixture was refluxed for 5 min and left for 18 h. The solvent was evaporated *in vacuo* and the residue was twice recrystallized from hexane to give 0.29 g (54%) of chelate **8**, m.p. 137—138 °C (hexane). Found (%): C, 71.74; H, 5.31; B, 1.72; Cl, 6.27; N, 2.80. $C_{23}H_{27}BClNO_4$. Calculated (%): C, 71.73; H, 5.08; B, 2.02; Cl, 6.62; N, 2.61. MS, *m/z*: 458 $[M - Ph]^+$. IR (KBr), ν/cm^{-1}: 3288 (NH); 1684 (C=O); 1616, 1416. IR ($CHCl_3$), ν/cm^{-1}: 3372 (NH); 1688 (C=O); 1608, 1580, 1480. ^{1}H NMR (DMSO-d_6), δ: 10.51 (br.s, 1 H, NH); 8.11—6.94 (m, 19 H, 3 Ph, 4-ClC$_6$H$_4$); 4.77 (s, 2 H, 4-ClC$_6$H$_4$COC$\underline{H}_2$); 3.57 (t, 2 H, OCH_2, J = 7.3 Hz); 0.53 (t, 3 H, Me, J = 7.3 Hz). ^{11}B NMR (DMSO-d_6), δ: 5.46 (br.s).

Diphenylboron chelate of butyl 3-amino-2-benzoyl-5-oxo-5-phenyl-2-pentenoate (9) was prepared from ketoester **7a** (0.37 g, 1 mmol) and Ph_2BOBu (0.24 g, 1 mmol) as described in the synthesis of complex **8**. The yield of chelate **9** was 0.32 g (60%), m.p. 114—115 °C (hexane). Found (%): C, 77.24; H, 6.18; B, 1.95; N, 2.50. $C_{34}H_{32}BNO_4$. Calculated (%): C, 77.13; H, 6.09; B, 2.04; N, 2.65. MS, *m/z*: 452 $[M - Ph]^+$. IR (KBr), ν/cm^{-1}: 3324 (NH); 1700, 1680 (C=O); 1616, 1580. IR ($CHCl_3$), ν/cm^{-1}: 3376 (NH); 1695 (C=O); 1612, 1593, 1470. ^{1}H NMR (DMSO-d_6), δ: 10.50 (br.s, 1 H, NH); 8.11—7.10 (m, 20 H, 4 Ph); 4.80 (s, 2 H, PhCOC$\underline{H}_2$); 3.55 (t, 2 H, OCH_2, J = 6.7 Hz); 1.00—0.50 (m, 7 H, MeCH$_2$CH$_2$). ^{11}B NMR (DMSO-d_6), δ: 4.66 (br.s).

4-Amino-6-aryl-3-benzoylpyran-2-ones 10a—d (general procedure). A solution of ketoester **6a—d** (1 mmol) (ethyl ester **6a** can be replaced by butyl ester **7a**) in 25 mL of *o*-xylene was refluxed for 8 h. The solvent was evaporated *in vacuo* and the residue was successively recrystallized from benzene and ethanol to give the corresponding pyranones **10a—d**.

4-Amino-3-benzoyl-6-phenylpyran-2-one (10a). Yield 45% (with ketoester **7a**, the yield was 40%), m.p. 253—254 °C

* The ratio of signals of the *E*- and *Z*-isomers in this spectrum, like that in the spectra of compounds **6b—d** and **7a** (at 20 °C), is close to 1 : 1.

(EtOH). Found (%): C, 73.94; H, 4.69; N, 4.88. $C_{18}H_{13}NO_3$. Calculated (%): C, 74.22; H, 4.50; N, 4.81. MS, *m/z*: 291 $[M]^+$. IR (KBr), ν/cm^{-1}: 3372 nar (free NH); 3284 br (bound NH); 1674, 1652 (C=O); 1592. ^{1}H NMR (DMSO-d_6), δ: 9.14, 8.48 (both br.s, each 1 H, NH_2); 7.80—7.42 (m, 10 H, 2 Ph); 6.80 (s, 1 H, H(5)). ^{1}H NMR ($CDCl_3$), δ: 9.67, 5.63 (both br.s, each 1 H, NH_2); 7.88—7.50 (m, 10 H, 2 Ph); 6.34 (s, 1 H, H(5)).

4-Amino-3-benzoyl-6-(4-methylphenyl)pyran-2-one (10b). Yield 52%, m.p. 274—275 °C (EtOH). Found (%): C, 74.94; H, 4.86; N, 4.58. $C_{19}H_{15}NO_3$. Calculated (%): C, 74.74; H, 4.95; N, 4.59. MS, *m/z*: 305 $[M]^+$. IR (KBr), ν/cm^{-1}: 3380 nar (free NH); 3220 br (bound NH); 1676, 1648 (C=O); 1596, 1508. ^{1}H NMR (DMSO-d_6), δ: 9.15, 8.45 (both br.s, each 1 H, NH_2); 7.70—7.30 (m, 9 H, Ph, 4-Me$C_6\underline{H}_4$); 6.71 (s, 1 H, H(5)); 2.35 (s, 3 H, Me). ^{13}C NMR (DMSO-d_6), δ: 196.09 (Ph$\underline{C}$O); 162.13, 161.61, 160.52, 142.17, 141.87, 130.98, 130.23, 128.37, 128.07, 126.02, 96.79, 93.49; 21.49 (Me).

4-Amino-3-benzoyl-6-(4-chlorophenyl)pyran-2-one (10c). Yield 58%, m.p. 271—272 °C (EtOH). Found (%): C, 66.30; H, 3.62; Cl, 11.04; N, 4.40. $C_{18}H_{12}NO_3$. Calculated (%): C, 66.37; H, 3.71; Cl, 10.88; N, 4.30. MS, *m/z*: 325 $[M]^+$. IR (KBr), ν/cm^{-1}: 3385 nar (free NH); 3223 br (bound NH); 1681, 1653 (C=O); 1600, 1510. ^{1}H NMR (DMSO-d_6), δ: 9.10, 8.40 (both br.s, each 1 H, NH_2); 7.75, 7.60 (both d, each 2 H, 4-Cl$C_6\underline{H}_4$, J = 7.9 Hz); 7.55—7.30 (m, 5 H, Ph); 6.79 (s, 1 H, H(5)). ^{13}C NMR (DMSO-d_6), δ: 196.03 (Ph$\underline{C}$O); 161.83, 161.36, 160.15, 141.69, 136.62, 131.08, 129.98, 129.82, 128.08, 98.00, 93.61.

4-Amino-3-benzoyl-6-(4-methoxyphenyl)pyran-2-one (10d). Yield 44%, m.p. 215—216 °C (EtOH). Found (%): C, 70.92; H, 4.65; N, 4.20. $C_{19}H_{15}NO_4$. Calculated (%): C, 71.02; H, 4.71; N, 4.36. MS, *m/z*: 321 $[M]^+$. IR (KBr), ν/cm^{-1}: 3385 nar (free NH); 3230 br (bound NH); 1687, 1650 (C=O); 1590, 1511. ^{1}H NMR (DMSO-d_6), δ: 9.25, 8.33 (both br.s, each 1 H, NH_2); 7.80—7.10 (m, 9 H, Ph, 4-MeO$C_6\underline{H}_4$); 6.67 (s, 1 H, H(5)); 3.75 (s, 3 H, MeO).

4-Amino-6-aryl-3-ethoxycarbonyl-2-phenylpyrylium chlorides 11a—c, 12a (general procedure). ***A.*** A solution of ketoester **6a—d** or **7a** (1 mmol) in 5 mL of EtOH and 1 mL of concentrated HCl was stirred for 1—2 h. The solvent was distilled off and the residue was recrystallized from acetone.

B. A mixture of chelate **4a—c** or **5a** (0.5 mmol) and 1 mL of concentrated HCl in 5 mL of EtOH was stirred for 2 h. The solvent was distilled off, the residue was dissolved in 10 mL of $CHCl_3$, and the organic layer was washed with water (3×20 mL) and dried over $CaCl_2$. The solvent was evaporated and the residue was recrystallized from acetone and dried.

4-Amino-3-ethoxycarbonyl-2,6-diphenylpyrylium chloride (11a). Yield 87% (***A***), m.p. 197—198 °C (dec.). Found (%): C, 67.30; H, 5.27; Cl, 10.12; N, 3.81. $C_{20}H_{18}ClNO_3$. Calculated (%): C, 67.51; H, 5.10; Cl, 9.96; N, 3.94. MS, *m/z*: 319 $[M - HCl]^+$. IR (KBr), ν/cm^{-1}: 3410 (NH); 3185 (NH); 1740 (C=O). ^{1}H NMR ($CDCl_3$), δ: 12.80, 9.00 (both s, each 1 H, NH_2); 8.76 (s, 1 H, H(5)); 8.00—7.50 (m, 10 H, 2 Ph); 4.17 (q, 2 H, OCH_2, J = 7.3 Hz); 0.84 (t, 3 H, Me, J = 7.3 Hz).

4-Amino-3-ethoxycarbonyl-6-(4-methylphenyl)-2-phenylpyrylium chloride (11b). Yield 89% (***A***), 78% (***B***), m.p. 183—184 °C (dec.). Found (%): C, 67.99; H, 5.50; Cl, 9.99; N, 3.67. $C_{21}H_{20}ClNO_3$. Calculated (%): C, 68.20; H, 5.45; Cl, 9.59; N, 3.79. MS, *m/z*: 333 $[M - HCl]^+$. IR (KBr), ν/cm^{-1}: 3390 (NH); 3180 (NH); 1736, 1644, 1472. IR ($CHCl_3$), ν/cm^{-1}: 3368 (NH); 3040 (NH); 1712, 1656, 1484. ^{1}H ($CDCl_3$), δ: 12.62, 8.87 (both br.s, each 1 H, NH_2); 8.66 (s, 1 H, H(5)); 7.88, 7.30 (both d, each 2 H, 4-Me$C_6\underline{H}_4$, J = 7.9 Hz); 7.80—7.50 (m, 5 H, Ph); 4.14 (q, 2 H, OCH_2, J = 7.3 Hz); 2.35 (s, 3 H, 4-$\underline{Me}C_6H_4$); 0.93 (t, 3 H, $\underline{Me}CH_2$, J = 7.3 Hz). ^{1}H NMR (DMSO-d_6), δ: 10.95, 9.57 (both br.s, each 1 H, NH_2); 7.90—7.32 (m, 9 H, Ph, 4-Me$C_6\underline{H}_4$); 7.33 (s, 1 H, H(5)); 4.20 (q, 2 H, OCH_2, J = 7.3 Hz); 2.39 (s, 3 H, 4-$\underline{Me}C_6H_4$); 0.98 (t, 3 H, $\underline{Me}CH_2$, J = 7.3 Hz).

4-Amino-6-(4-chlorophenyl)-3-ethoxycarbonyl-2-phenylpyrylium chloride (11c). Yield 91% (***A***), 79% (***B***), m.p. 187—188 °C (dec.). Found (%): C, 61.71; H, 4.43; Cl, 18.35; N, 3.47. $C_{21}H_{17}Cl_2NO_3$. Calculated (%): C, 61.55; H, 4.39; Cl, 18.17; N, 3.59. MS, *m/z*: 353 $[M - HCl]^+$. IR (KBr), ν/cm^{-1}: 3328 nar (free NH); 3080 br (bound NH); 1696, 1656. IR ($CHCl_3$), ν/cm^{-1}: 3368 (NH); 3070 (NH); 1712, 1655, 1498. ^{1}H NMR ($CDCl_3$), δ: 12.32, 9.17 (both br.s, each 1 H, NH_2); 8.63 (s, 1 H, H(5)); 7.97, 7.46 (both d, each 2 H, 4-Cl$C_6\underline{H}_4$, J = 8.5 Hz); 7.75—7.50 (m, 5 H, Ph); 4.18 (q, 2 H, OCH_2, J = 7.0 Hz); 0.76 (t, 3 H, Me, J = 7.0 Hz). ^{1}H NMR (DMSO-d_6), δ: 10.98, 9.73 (both br.s, each 1 H, NH_2); 7.95, 7.63 (both d, each 2 H, 4-Cl$C_6\underline{H}_4$, J = 8.5 Hz); 7.87 (s, 1 H, H(5)); 7.80—7.67 (m, 5 H, Ph); 4.21 (q, 2 H, OCH_2, J = 7.0 Hz); 0.98 (t, 3 H, Me, J = 7.0 Hz). ^{13}C NMR ($CDCl_3$), δ: 171.24, 164.15, 163.43, 161.31, 140.72, 133.56, 131.59, 130.42, 129.53, 129.37, 128.84, 127.07, 108.11, 104.07, 63.67 (OCH_2), 13.68 (Me).

4-Amino-3-butoxycarbonyl-2,6-diphenylpyrylium chloride (12a). Yield 94% (***A***), m.p. 173—174 °C (dec.). Found (%): C, 69.02; H, 5.93; Cl, 9.44; N, 3.55. $C_{22}H_{21}ClNO_4$. Calculated (%): C, 68.84; H, 5.78; Cl, 9.24; N, 3.65. MS, *m/z*: 347 $[M - HCl]^+$. IR (KBr), ν/cm^{-1}: 3400 (NH); 3190 (NH); 1720. ^{1}H NMR (DMSO-d_6), δ: 11.34, 9.72 (both br.s, each 1 H, NH_2); 8.17 (s, 1 H, H(5)); 7.90—7.50 (m, 10 H, 2 Ph); 4.14 (t, 2 H, OCH_2, J = 6.4 Hz); 1.38—0.60 (m, 7 H, CH_2CH_2Me). ^{1}H NMR ($CDCl_3$), δ: 12.63, 8.99 (both br.s, each 1 H, NH_2); 8.67 (s, 1 H, H(5)); 7.90—7.35 (m, 10 H, 2 Ph); 4.21 (t, 2 H, OCH_2, J = 6.4 Hz); 1.25—0.59 (m, 7 H, CH_2CH_2Me). ^{13}C NMR ($CDCl_3$), δ: 171.06, 164.43, 164.30, 161.28, 134.08, 133.41, 131.58, 129.93, 129.51, 129.25, 128.44, 127.36, 107.92, 103.67, 67.30 (OCH_2), 30.02, 19.00, 13.85 (Me).

Ethyl 4-amino-6-aryl-2-phenylpyridine-3-carboxylates 13a—c (general procedure). A mixture of ketoester **6a—c** (1 mmol), AcOH (4 mL), and NH_4OAc (6.4 mmol) was refluxed for 3 h. The solvent was evaporated, and 3 mL of concentrated aqueous NH_3 and 15 mL of H_2O were added to the residue. The precipitated crystals were filtered off, washed with water (2×10 mL), and recrystallized from heptane.

Ethyl 4-amino-2,6-diphenylpyridine-3-carboxylate (13a). Yield 75%, m.p. 108—109 °C (heptane). Found (%): C, 75.26; H, 5.75; N, 8.89. $C_{20}H_{18}N_2O_2$. Calculated (%): C, 75.45; H, 5.70; N, 8.80. MS, *m/z*: 318 $[M]^+$. IR (KBr), ν/cm^{-1}: 3470, 3370 (NH); 1669, 1625, 1540. IR ($CHCl_3$), ν/cm^{-1}: 3500, 3390 (NH); 1690, 1610, 1587, 1560. ^{1}H NMR ($CDCl_3$), δ: 7.99—6.90 (m, 10 H, 2 Ph); 6.87 (s, 1 H, H(5)); 5.71 (br.s, 2 H, NH_2); 4.00 (q, 2 H, OCH_2, J = 6.9 Hz); 0.81 (t, 3 H, Me, J = 6.9 Hz). ^{13}C NMR ($CDCl_3$), δ: 169.65 (C=O); 161.89, 157.97, 155.42, 143.01, 139.30, 131.60—126.50 (CH arom.); 108.69, 107.80 (d, H(5), J = 152 Hz); 61.30 (t, OCH_2, J = 151 Hz); 13.21 (q, Me, J = 127 Hz).

Ethyl 4-amino-6-(4-methylphenyl)-2-phenylpyridine-3-carboxylate (13b). Yield 81%, m.p. 115—116 °C (heptane).

Found (%): C, 75.66; H, 5.97; N, 8.49. $C_{21}H_{20}N_2O_2$. Calculated (%): C, 75.88; H, 6.06; N, 8.43. MS, *m/z*: 332 $[M]^+$. IR (KBr), ν/cm^{-1}: 3472, 3368 (NH); 1672, 1624, 1544. IR ($CHCl_3$), ν/cm^{-1}: 3512, 3392 (NH); 1688, 1608, 1584, 1568. ^{1}H NMR ($CDCl_3$), δ: 7.93, 7.25 (both d, each 2 H, 4-Me$C_6\underline{H}_4$, J = 7.9 Hz); 7.70—7.38 (m, 5 H, Ph); 6.93 (s, 1 H, H(5)); 5.65 (br.s, 2 H, NH_2); 4.00 (q, 2 H, OCH_2, J = 7.0 Hz); 2.40 (s, 3 H, 4-$\underline{Me}C_6H_4$); 0.80 (t, 3 H, $\underline{Me}CH_2$, J = 7.0 Hz). ^{13}C NMR ($CDCl_3$), δ: 169.89 (C=O); 162.00, 158.16, 155.52, 143.33, 140.00, 136.67, 129.94, 129.58, 129.15, 128.68, 128.49, 127.16, 108.73, 105.57, 61.30 (OCH_2); 22.00 (4-$\underline{Me}C_6H_4$); 13.80 (Me).

Ethyl 4-amino-6-(4-chlorophenyl)-2-phenylpyridine-3-carboxylate (13c). Yield 83%, m.p. 119—120 °C (heptane). Found (%): C, 68.06; H, 4.91; Cl, 10.26; N, 8.05. $C_{20}H_{17}ClN_2O_2$. Calculated (%): C, 68.09; H, 4.86; Cl, 10.04; N, 7.94. MS, *m/z*: 352 $[M]^+$. IR (KBr), ν/cm^{-1}: 3472 (NH); 3368 (NH); 1684, 1604, 1576, 1568. IR ($CHCl_3$), ν/cm^{-1}: 3512 (NH); 3392 (NH); 1688, 1608, 1604, 1568. ^{1}H NMR ($CDCl_3$), δ: 7.95—7.39 (m, 9 H, Ph, 4-ClC_6H_4); 6.91 (s, 1 H, H(5)); 5.67 (s, 2 H, NH_2); 4.00 (q, 2 H, OCH_2, J = 7.0 Hz); 0.81 (t, 3 H, Me, J = 7.0 Hz).

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