Combination of the Claisen—Schmidt reaction, the Michael addition, and the Hantzsch reaction in the synthesis of 2′,6′-bis-aryl-3,4′-bipyridines*

V. A. Mamedov, L. V. Mustakimova, O. A. Gerasimov, and A. T. Gubaidullin*

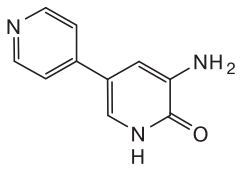
A. E. Arbuzov Institute of Organic and Physical Chemistry,
Federal Research Center "Kazan Scientific Center of the Russian Academy of Sciences,"
8 ul. Arbuzova, 420088 Kazan, Russian Federation.
Fax: +7 (843) 273 2253. E-mail: mamedov@iopc.ru

Pyridine-3-carbaldehyde reacted with 1-(aryl)ethan-1-ones to give 1,5-diaryl-3-(pyridin-3-yl)pentane-1,5-diones, which were further converted to 2′,6′-bis-aryl-3,4′-bipyridines.

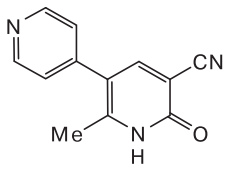
Key words: pyridine-3-carbaldehyde, 1-(aryl)ethan-1-ones, ammonium acetate, the Claisen—Schmidt reaction, the Michael addition, the Hantzsch pyridine synthesis, 2′,6′-bis-aryl-3,4′-bipyridines.

Bipyridines are of great interest due to their catalytic activity, broad applications in industry, medicine, and as the analytical reagents and ligands for the metal complex synthesis.[1—4] Symmetrical bipyridines can be synthesized under the modified Ullmann-type reaction conditions, namely, by metal-catalyzed cross-coupling of halopyridines.[5,6] Only few cases of the synthesis of unsymmetrical bipyridines by the Kröhnke reaction,[7—10] the Hantzsch pyridine synthesis,[11,12] the Suzuki—Miyaura coupling,[13—15] other cross-couplings,[16,17] and the coupling reactions[18,19] of halopyridines have been described.

Comparing with other bipyridines, 3,4′-bipyridines are still poorly studied biheterocyclic systems although they attract a considerable interest[15,20—25] of the researchers as cardiotonics.[26,27] Amrinone (5-amino-1*H*-3,4′-bipyridin-6-one) and milrinone (2-methyl-6-oxo-1,6-dihydro-3,4′-bipyridine-5-carbonitrile) have pronounced positive inotropic effect in myocardium and also function as vasodilators.[28—33]



Amrinone



Milrinone

As for the synthesis of 3,4′-bipyridines, it is very difficult to find the publications devoted to the synthesis of compounds of this precise type. The known methods to access 3,4′-bipyridines are mainly given as the separate examples together with the syntheses of other pyridine derivatives. The key step of the Kröhnke-type[7—10] and the Hantzsch-type[11,12] syntheses is the condensation of 1,5-dicarbonyl compounds with ammonium acetate or other nitrogen sources. In general, 1,5-dicarbonyl compounds are generated *in situ* by either the reactions of enones with the pyridinium salts (accessible by the reaction between pyridine and ketones in the presence of iodine under the Ortoleva—King conditions) or the reactions of acetoacetic ester (or its analogs) with aldehydes in the presence of ammonium acetate.

Our approach to 3,4′-bipyridines is shown in Scheme 1.

3,4′-Bipyridines **5** can be synthesized from 1,5-dicarbonyl compounds **4** by cyclization with NH_4OAc as the nitrogen source. In turn, 1,5-dicarbonyl compounds **4** can be prepared from enones **3** and 1-(aryl)ethan-1-ones **2** under the Michael reaction conditions. We assumed that depending on the reaction conditions 1-(aryl)ethan-1-ones **2** bearing active methyl group can be used as the starting material not only in the Claisen—Schmidt synthesis of enone **3** from pyridine-3-carbaldehyde (**1**), but also in the Michael addition reaction with enones **3** to give 1,5-dicarbonyl compounds **4**.

Indeed, pyridine-3-carbaldehyde reacts with 4-chloro-, 4-bromo-, and 3-bromoacetophenones in a 10% solution of KOH in MeOH for 18 h followed by dilution with water and acidification with 10% HCl to give 1,5-diaryl-3-(pyridin-3-yl)pentane-1,5-diones **4a—c** (Scheme 2). Formation of these compounds was confirmed by ^1H NMR spectroscopy showing the characteristic signals of the A_2B_2X spin system for the $—CH(CH_2)_2$ moiety, the signals of the aryl ring, and 3-substituted pyridine ring. In the IR spectra of these compounds, the carbonyl group absorptions are

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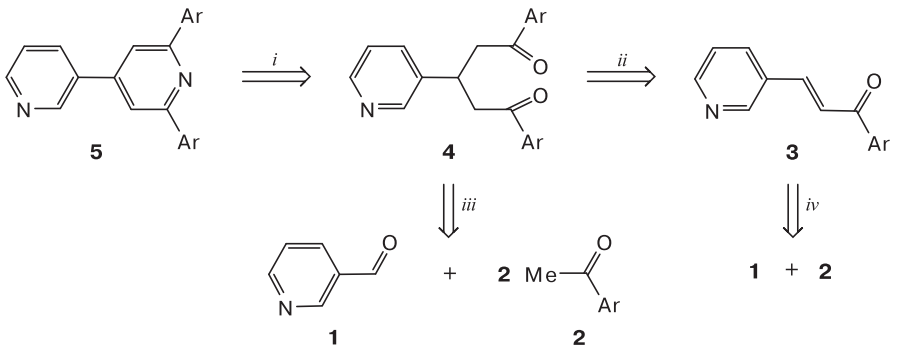
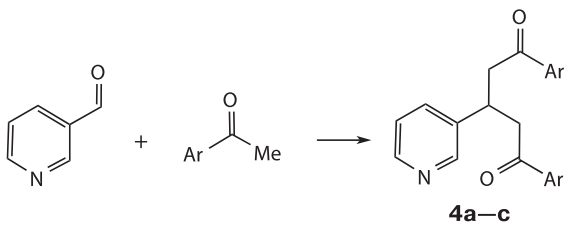
Scheme 1



i. Cyclization with the N atom source. *ii*. The Michael addition. *iii*. The Claisen—Schmidt condensation + the Michael addition. *iv*. The Claisen—Schmidt condensation.

observed at the 1678—1692 cm^{-1} range that is shifted to the shorter wavelengths by 20—30 cm^{-1} compared to the standard values. This deviation from the standard values is apparently due to the –I and –M effects as well as the steric effect of the substituted benzene rings.

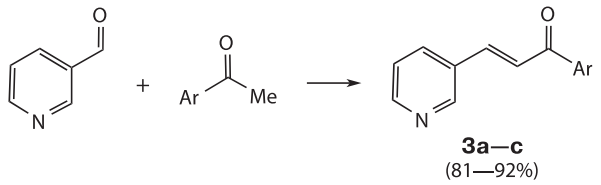
Scheme 2



4	Ar	Yield (%)
a	4-ClC_6H_4	77
b	4-BrC_6H_4	79
c	3-BrC_6H_4	75

Reagents and conditions: 10% KOH/MeOH, MeOH, 0—5 °C, ~18 h.

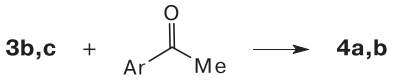
Scheme 3



Ar = Ph (**a**), 4-ClC_6H_4 (**b**), 4-BrC_6H_4 (**c**)

Reagents and conditions: 10% KOH/MeOH, MeOH, 0—5 °C, ~30—40 min.

Scheme 4



Ar = 4-ClC_6H_4 (**3b**, **4a**), 4-BrC_6H_4 (**3c**, **4b**)

Reagents and conditions: 10% KOH/MeOH, MeOH, ~20 °C, ~18 h.

When the reaction time was shorten to 30—40 min, the intermediate 1-aryl-3-(pyridin-3-yl)prop-2-en-1-ones **3a—c** were isolated in good yields (Scheme 3). Compounds **3b,c** were also converted into 1,5-diaryl-3-(pyridin-3-yl)pentane-1,5-diones **4a,b** (Scheme 4).

Structure of the substituted 1,5-diaryl-3-(pyridin-3-yl) pentane-1,5-dione (**4a**) was established by X-ray diffraction analysis. The obtained X-ray diffraction data show that compound **4a** crystallizes in the orthorhombic crystal system in the chiral space group $P2_12_12_1$ with one molecule in the asymmetric unit of the unit cell. The molecular geometry of compound **4a** is shown in Fig. 1, the bond lengths and bond angles agree with the standard values within the experimental errors. Selected bonds lengths for compound **4a** are given in Table 1. The dihedral angles between the pyridine ring plane and the planes of the aryl substituents are 86.3(2)° and 74.2(2)°. The aryl substituents are almost coplanar; the dihedral angle between their planes is 12.7(2)°.

In the crystal of pentane-1,5-dione **4a**, no classical H-bonding is observed and the main structure-forming interactions are the C—H...O and C—H...N hydrogen bonds that have connected the molecules of **4a** into a 3D hydrogen-bonding network. The parameters of intermolecular contacts are given in Table 2. It is of interest that in this case the directions of the intermolecular interactions are dictated by all the three O and N hydrogen bond acceptors. Thus, along the 0*a* axis, the shortest axial direction in the unit cell, the bifurcated H-bonds that involved the O(1) atom of the carbonyl group are realized

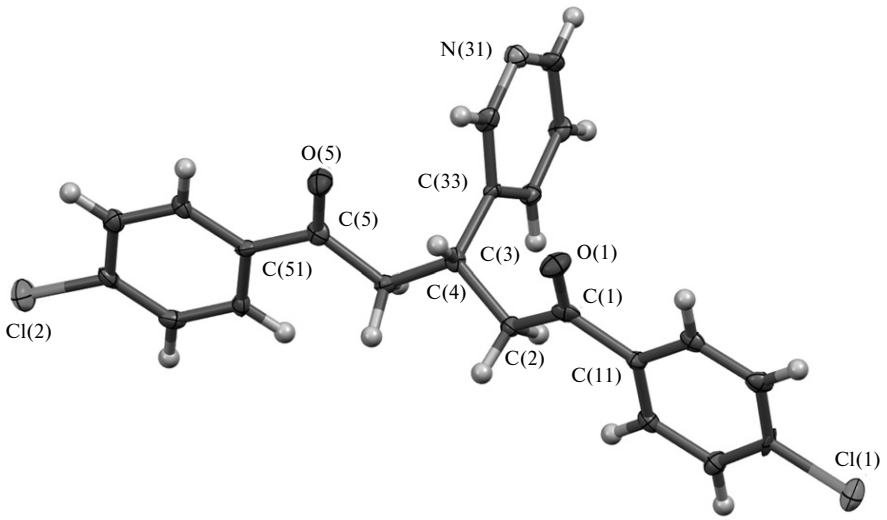


Fig. 1. Crystal geometry of compound **4a** with partial atomic numbering scheme. Nonhydrogen atoms are drawn as displacement ellipsoids at the 50% probability level, hydrogen atoms are drawn as spheres with arbitrary radii.

Table 1. Bond lengths (*d*) in compound **4a**

Bond	*d*/Å
C(3)—C(33)	1.505(7)
C(3)—C(4)	1.537(7)
C(3)—C(2)	1.535(7)
C(5)—O(5)	1.216(6)
C(1)—O(1)	1.227(6)
N(31)—C(32)	1.328(6)
N(31)—C(36)	1.328(7)
C(14)—Cl(1)	1.744(5)
C(54)—Cl(2)	1.732(6)

(see Table 2 and Fig. 2, *a*). Along the 0*c* axis, the similar H-bonded chains of the molecules are formed due to the bifurcated H-bonds that involve the N(31) pyridine ring atom (see Fig. 2). The thus formed 2D H-bonded layers of the molecules are linked along the 0*b* crystallographic axis *via* the hydrogen bonds involving the O(5) atom of the second carbonyl group of the molecule (see Fig. 2, *b*). Nonequivalence of two carbonyl oxygen atoms O(1) and O(5) in the intermolecular H-bonding is the exact reason why pentane-1,5-dione **4a** is chiral and crystallizes in the Sohncke space group.

It should be noted that in such molecular packing the crystal lacks the solvent-accessible void space and a sufficiently dense packing is achieved. The calculated packing efficiency is equal to 71.6%, which is within the highest values characteristic of the organic compounds (0.65—0.75).

1,5-Diketones **4a—c** react with 5-fold excess of ammonium acetate on refluxing in acetic acid in the presence of pyridine for 12 h to give high yields of 2′,6′-bis-aryl-3,4′-bipyridines **5a—c** that are not contaminated with any 1,4-dihydropyridine derivatives **A**, the precursors of compounds **5** (Scheme 5).

Structures of 2′,6′-bis-aryl-3,4′-bipyridines **5a—c** were unambiguously confirmed by their ^{1}H NMR spectra showing the characteristic signals of differently substituted pyridine rings and *para*- (compounds **5a,b**) and *meta*-substituted (compound **5c**) benzene rings. In ^{1}H NMR spectra of compounds **5a** and **5b**, the proton signals of the *meta*-substituted pyridine ring have the same chemical shifts and multiplicities and appear at δ 7.60 (dd, H(5), J = 8.1, 4.8 Hz), 8.47 (ddd, H(4), J = 8.1, 2.1, 1.4 Hz), 8.71 (dd, H(6), J = 4.8, 1.4 Hz), and 9.27 (d, H(2),

Table 2. Intermolecular interactions in the crystal of compound **4a**

Fragment D—H...A	Distance/Å		Angle/deg D—H—A	Symmetry codes
	H...A	D...A		
C(15)—H(15)...O(5′)	2.49	3.368(7)	154	$1/2 - x$, $2 - y$, $1/2 + z$
C(2)—H(21)...N(31″)	2.60	3.474(7)	147	$1 - x$, $-1/2 + y$, $1/2 - z$
C(4)—H(42)...N(31″)	2.67	3.517(7)	144	$1 - x$, $-1/2 + y$, $1/2 - z$
C(34)—H(34)...O(1*)	2.50	3.441(7)	172	$1 + x$, y, z
C(2)—H(22)...O(1*)	2.64	3.585(7)	159	$1 + x$, y, z

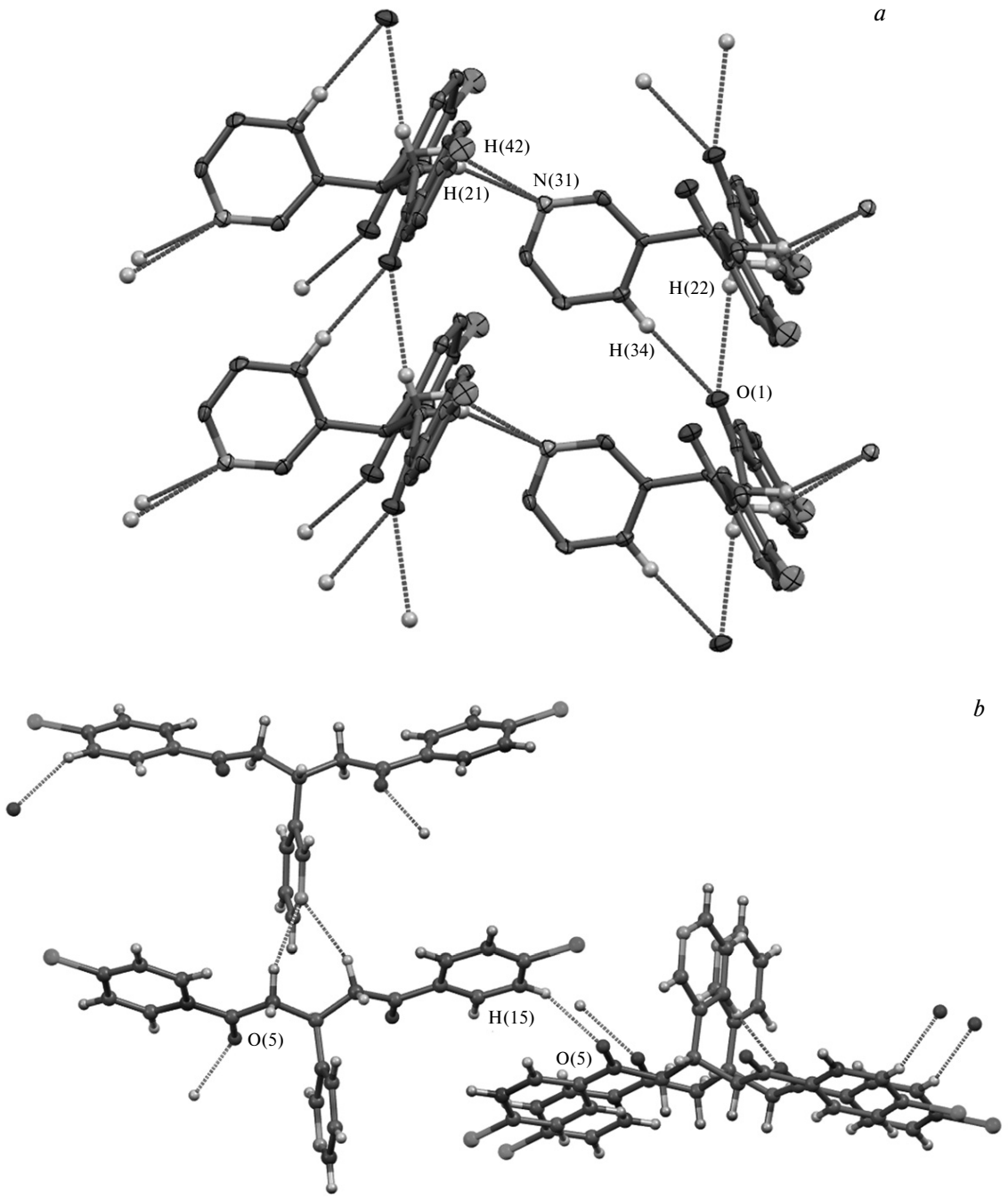
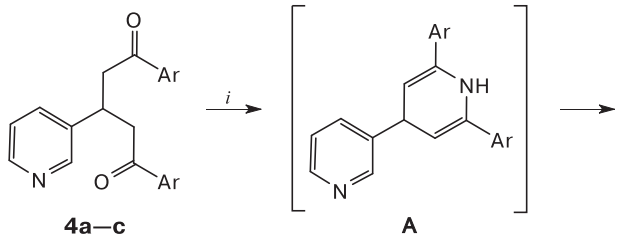


Fig. 2. Two projections of the supramolecular crystal structure of compound **4a** drawn along the 0*a* axis (*a*) and approximately along the 0*c* axis. Only the hydrogen atoms involved in the hydrogen bonding are shown, H-bonds are shown by dotted lines.

J = 2.1 Hz). The H(3′) and H(5′) protons of the trisubstituted pyridine rings of both compounds resonate as the singlets at almost the same range at δ 8.35 and 8.36, respectively. The signals of *para*-substituted benzene ring of *para*-chloro-substituted derivatives **5a** are shifted to the lower filed by 0.1 ppm. The H(3′) and H(5′) protons of compound **5c** bearing *meta*-bromo-substituted benzene rings resonate as the singlets at δ 8.42. The protons of *meta*-substituted benzene rings of these compounds are observed at δ 7.57 (dd, H(5), $J_1 = J_2$ = 7.9 Hz), 7.71 (dd, H(6), J = 7.9, 1.0 Hz), 8.38 (d, H(4), J = 7.9 Hz), and 8.55 (dd, H(2), J = 1.8, 1.0 Hz).

These data indicate that the chemical shifts of the H(3′) and H(5′) pyridine rings depend on the nature and the position of the substituents in the benzene rings, which is an agreement with the published data. For instance, the

Scheme 5



5	Ar	Yield (%)
a	4-ClC_6H_4	83
b	4-BrC_6H_4	84
c	3-BrC_6H_4	72

Reagents and conditions: $AcONH_4$, Py, AcOH, Δ, ~12 h.

H(3′) and H(5′) protons of trisubstituted pyridine ring of dihydroxy analog of compounds **5a** and **5b** resonate at δ 8.03.[34]

In summary, we developed simple and efficient method for synthesizing three dihalo-substituted 2′,6′-diaryl-3-pyridin-4′-ylpyridine derivatives that initiated by the Claisen—Schmidt reaction and the Michael addition and finalized by the Hantzsch pyridine synthesis. The transformations started by the reaction of pyridine-3-carbaldehyde with 1-(aryl)ethan-1-ones to give α,β-unsaturated ketones. In the next step, α,β-unsaturated ketones react with the second molecule of 1-(aryl)ethan-1-ones to afford 1,5-diaryl-3-(pyridin-3-yl)pentane-1,5-dione derivatives. The last compounds undergo cyclization in the presence of ammonium acetate followed by aromatization of the plausible dihydropyridine intermediate to give 2′,6′-bis-aryl-3,4′-bipyridines.

Experimental

IR spectra were recorded with a Bruker Tensor 27 FT-IR spectrometer (Germany) in KBr pellets in the frequency range from 4000 to 400 cm^{-1}. Data collection and primary analysis were accomplished using OPUS 7/2012 software. ^1H NMR spectra were run on Avance-400 (working frequency of 399.93 MHz), Avance-600 (working frequency of 600.1 MHz), and Avance-500 (working frequency of 500.1 MHz) spectrometers. The chemical shifts are given in the δ scale relative to the residual solvent signals. Melting points were measured with an IA 9200 apparatus.

Single crystal X-ray diffraction analysis of compound **4a** was carried out in the Laboratory of diffraction research methods of the A. E. Arbuzov Institute of Organic and Physical Chemistry, the Federal Research Center "Kazan Scientific Center of the Russian Academy of Sciences" using the equipment of the Collective spectral and analytical center for physicochemical studies of the structure, properties, and composition of compounds and materials.

X-ray diffraction data were collected with a Bruker Kappa Apex II CCD diffractometer (λ(Mo-Kα) = 0.71073 Å, graphite monochromator, φ and ω scan modes). The main crystallographic data and refinement details are given in Table 3.

The data were collected, processed, and the unit cell parameters were refined using APEX2 software.[35] Semiempirical absorption corrections (μMo = 0.373 mm^{-1}) were applied using SADABS program.[36] The structure was solved by the direct method and refined by the full-matrix least-squares method first in isotropic and then in anisotropic approximations (for all non-hydrogen atoms) with SHELXL program.[37] The positions of hydrogen atoms were calculated based on stereochemical considerations and refined using the corresponding riding models.

The Flack parameter is equal to 0.07(11). All calculations were performed with WinGX program.[38] Intermolecular interactions were analyzed and the crystal structures were visualized using PLATON[39] and Mercury software.[40] The atomic coordinates and structural parameters of compound **4a** were deposited with the Cambridge Crystallographic Data Centre (CCDC 1957532) and are available free of charge at www.ccdc.cam.ac.uk/data_request/cif.

Synthesis of 1,5-diaryl-3-(pyridin-3-yl)pentane-1,5-diones 4a—c (general procedure). ***A***. To a stirred mixture of 3-pyridinecarboxaldehyde (10 mmol) and the appropriately substituted acetophenone (20 mmol) in MeOH cooled to 0—5 °C, a 10% solution of KOH in MeOH (5 mL) was slowly added dropwise. The mixture was kept at room temperature for 18 h, poured into water, and acidified with 10% HCl to pH ~7. The crystals formed were collected by filtration, washed with water, dried in air, and crystallized from EtOH.

B. To a stirred mixture of the appropriate 1-aryl-3-(pyridin-3-yl)prop-2-en-1-one **3b,c** (10 mmol) and the appropriately substituted acetophenone (20 mmol) in MeOH, a 10% solution of KOH in MeOH (5 mL) was slowly added dropwise at room temperature. The mixture was kept at room temperature for 18 h, poured into water, and acidified with 10% HCl to pH ~7. The crystals formed were collected by filtration, washed with water, dried in air, and crystallized from EtOH.

1,5-Bis(4-chlorophenyl)-3-(pyridin-3-yl)pentane-1,5-dione (4a). White powder. Yield 3.1 g (77%), m.p. 163—165 °C. Found (%): C, 66.34; H, 4.30; Cl, 17.80; N, 3.52; O, 8.04. $C_{22}H_{17}Cl_2NO_2$. Calculated (%): C, 66.44; H, 4.19; Cl, 17.61; N, 3.39; O, 8.37. IR, ν/cm^{-1}: 3349, 3063, 3031, 3001, 2901, 1920, 1793, 1691, 1680, 1589, 1573, 1486, 1475, 1430, 1419, 1400, 1364, 1330, 1273, 1231, 1211, 1169, 1090, 1056, 1026, 1011, 990, 922, 903, 826, 808, 790, 773, 718, 634, 611, 583, 533, 519. ^1H NMR ($CDCl_3$), δ: 3.35 (dd, 2 H, $CH(\underline{CH_2})_2$, J_{AB} = 17.0 Hz, J_{BX} = 7.1 Hz); 3.52 (dd, 2 H, $CH(\underline{CH_2})_2$, J_{AB} = 17.0 Hz, J_{AX} = 6.8 Hz); 4.02—4.12 (m, 1 H, $\underline{CH}(CH_2)_2$, J_{AX} + J_{BX} = = 13.9 Hz); 7.22 (dd, 1 H, H(5), Py, J = 7.8 Hz, J = 4.8 Hz); 7.44, 7.88 (both d, 4 H each, ArCO, J = 8.7 Hz); 7.65 (ddd, 1 H, H(6), pyridyl, J = 7.8 Hz, J = 2.0 Hz, J = 1.6 Hz); 8.46 (dd, 1 H, H(4), pyridyl, J = 4.8 Hz, J = 1.6 Hz); 8.57 (d, 1 H, H(2), pyridyl, J = 2.0 Hz).

1,5-Bis(4-bromophenyl)-3-(pyridin-3-yl)pentane-1,5-dione (4b). White powder. Yield 3.8 g (79%), m.p. 178—180 °C. Found (%): C, 54.63; H, 3.82; Br, 32.39; N, 2.46; O, 6.70.

Table 3. Crystallographic parameters and X-ray data collection and structure refinement statistics for compound **4a**

Parameter	**4**
Molecular formula	$C_{22}H_{17}Cl_2NO_2$
T/K	100
M	398.26
Crystal system	Orthorhombic
Space group	$P2_12_12_1$
a/Å	5.6710(9)
b/Å	14.901(2)
c/Å	21.647(3)
V/Å^3	1829.2(5)
λ/Å	0.71073
Z	4
d_{calc}/g cm^{-3}	1.446
Crystal size/mm^3	0.075×0.123×0.540
Scanning range, θ/deg	2.89—28.33
Index ranges h, k, l	$-5 \le h \le 7$, $-17 \le k \le 19$, $-26 \le l \le 28$
Number of refined parameters	244
Number of reflections	
measured	18311
independent	4458
R_{int}	0.1194
with $I > 2\sigma(I)$	2212
R Factors (based on 2212 reflections with $F^2 \ge 2\sigma$)	
R_1	0.0628
wR_2	0.0953
R Factors (based on all independent reflections)	
R_1	0.1640
wR_2	0.1201
GOOF	0.913
Residual electron density (max/min)/e Å^{-3}	0.337/−0.336

$C_{22}H_{17}Br_2NO_2$. Calculated (%): C, 54.24; H, 3.52; Br, 32.80; N, 2.88; O, 6.57. IR, ν/cm^{-1}: 3366, 3085, 3060, 3030, 3001, 2930, 2900, 2570, 1920, 1794, 1692, 1585, 1479, 1429, 1418, 1397, 1362, 1273, 1229, 1210, 1169, 1070, 1027, 1008, 989, 903, 822, 806, 772, 717, 633, 610, 579, 534, 495. ^{1}H NMR (DMSO-d$_6$), δ: 3.34 (dd, 2 H, CH(C$\underline{H}_2$)$_2$, J_{AB} = 17.4 Hz, J_{BX} = 7.6 Hz); 3.48 (dd, 2 H, CH(C$\underline{H}_2$)$_2$, J_{AB} = 17.4 Hz, J_{AX} = 6.3 Hz); 3.92—3.99 (m, 1 H, C$\underline{H}$(CH$_2$)$_2$, $J_{AX} + J_{BX}$ = 13.9 Hz); 7.18 (dd, 1 H, H(5), pyridyl, J = 7.8 Hz, J = 4.8 Hz); 7.56, 7.78 (both d, 4 H each, ArCO, J = 8.4 Hz); 7.64 (br.d, 1 H, H(6), pyridyl, $J \approx$ 7.8 Hz); 8.33 (br.d, 1 H, H(4) pyridyl, $J \approx$ 4.8 Hz); 8.50 (br.d, 1 H, H(2), pyridyl, $J \approx$ 2.0 Hz).

1,5-Bis(3-bromophenyl)-3-(pyridin-3-yl)pentane-1,5-dione (4c). Yellowish crystals. Yield 3.7 g (75%), m.p. 226—228 °C. Found (%): C, 54.63; H, 3.82; Br, 32.39; N, 2.46; O, 6.70. $C_{22}H_{17}Br_2NO_2$. Calculated (%): C, 54.24; H, 3.52; Br, 32.80; N, 2.88; O, 6.57. IR, ν/cm^{-1}: 3338, 3074, 3052, 3028, 2989, 2934, 2902, 1957, 1817, 1678, 1566, 1470, 1421, 1354, 1279, 1261, 1202, 1173, 1104, 1068, 1025, 1013, 994, 971, 912, 833, 807, 789, 770, 720, 707, 679, 556. ^{1}H NMR ($CDCl_3$), δ: 3.51 (dd, 2 H, CH(C$\underline{H}_2$)$_2$, J_{AB} = 17.8 Hz, J_{BX} = 7.7 Hz); 3.58 (dd, 2 H, CH(C$\underline{H}_2$)$_2$, J_{AB} = 17.8 Hz, J_{AX} = 6.2 Hz); 3.84—3.91 (m, 1 H C$\underline{H}$(CH$_2$)$_2$, $J_{AX} + J_{BX}$ = 13.9 Hz); 7.27 (dd, 1 H, H(5), pyridyl, J = 7.8 Hz, J = 4.7 Hz); 7.48 (dd, 2 H, H(5), ArCO, J = 7.9 Hz, J = 7.9 Hz); 7.79 (ddd, 1 H, H(6), pyridyl, J = 7.8 Hz, J = 2.0 Hz, J = 1.0 Hz); 7.82 (dd, 2 H, H(4), ArCO, J = 7.9 Hz, J = 1.0 Hz); 7.92 (br.d, 1 H, H(6), ArCO, $J \approx$ 7.9 Hz); 8.07 (dd, 2 H, H(2), ArCO, J = 1.7 Hz, J = 1.6 Hz); 8.46 (dd, 1 H, H(4), pyridyl, J = 4.7 Hz, J = 1.0 Hz); 8.54 (d, 1 H, H(2), pyridyl, J = 2.0 Hz).

Synthesis of 1-aryl-3-(pyridin-3-yl)prop-2-en-1-ones 3a—c (general procedure). To a stirred mixture of 3-pyridinecarboxaldehyde (10 mmol) and the appropriately substituted acetophenone (10 mmol) in MeOH cooled to 0—5 °C, a 10% solution of KOH in MeOH (5 mL) was slowly added dropwise. The reaction mixture was kept at room temperature for 30—40 min, poured into water, acidified with 10% aqueous HCl to pH ~7, and extracted with dichloromethane (3½50 mL). The combined organic layers were dried with $MgSO_4$, concentrated *in vacuo*, and the obtained residue was triturated with diethyl ether. The crystals formed were collected by filtration, washed with diethyl ether, and dried in air.

3-(Pyridin-3-yl)-1-phenylprop-2-en-1-one (3a). White powder. Yield 1.7 g (83%), m.p. 104—106 °C. Found (%): C, 80.14; H, 5.42; N, 6.73; O, 7.71. $C_{14}H_{11}NO$. Calculated (%): C, 80.36;

H, 5.30; N, 6.69; O, 7.65. IR, ν/cm^{-1}: 3473, 3086, 3062, 1958, 1902, 1661, 1604, 1579, 1564, 1474, 1447, 1423, 1346, 1338, 1309, 1221, 1182, 1122, 1098, 1044, 1015, 993, 982, 928, 869, 811, 768, 683, 626, 574, 517. ^{1}H NMR (DMSO-d_6), δ: 7.48—7.52 (m, 1 H, H(5), pyridyl); 7.58 (dd, 2 H, H(3), H(5), Ph, *J* = 7.8 Hz, *J* = 7.5 Hz); 7.67 (ddd, 1 H, H(4), Ph, *J* = 7.4 Hz, *J* = 7.3 Hz, *J* = 1.0 Hz); 7.78 (d, 1 H, CH=, *J* = 15.7 Hz); 8.07 (d, 1 H, CH=, *J* = 15.7 Hz); 8.17 (d, 2 H, H(2), H(6), Ph, *J* = 8.1 Hz); 8.35 (br.d, 1 H, H(4), pyridyl, *J* ≈ 7.8 Hz); 8.62 (br.d, 1 H, H(6), pyridyl, *J* ≈ 4.6 Hz); 9.03 (br.s, 1 H, H(2), pyridyl).

1-(4-Chlorophenyl)-3-(pyridin-3-yl)prop-2-en-1-one (3b). White powder. Yield 2.0 g (82%), m.p. 157—159 °C. Found (%): C, 69.12; H, 4.28; Cl, 14.49; N, 5.59; O, 6.52. $C_{14}H_{10}ClNO$. Calculated (%): C, 69.00; H, 4.14; Cl, 14.55; N, 5.75; O, 6.57. IR, ν/cm^{-1}: 3064, 3032, 1930, 1798, 1668, 1609, 1589, 1570, 1476, 1401, 1341, 1312, 1223, 1178, 1090, 1028, 1011, 986, 837, 798, 698, 667, 631, 584. ^{1}H NMR (DMSO-d_6), δ: 7.51 (dd, 1 H, H(5), pyridyl, *J* = 7.8 Hz, *J* = 4.7 Hz); 7.67, 8.21 (both d, 4 Heach, ArCO, *J* = 8.6 Hz); 7.80 (d, 1 H, CH=, *J* = 15.7 Hz); 8.08 (d, 1 H, CH=, *J* = 15.7 Hz); 8.37 (ddd, 1 H, H(6), pyridyl, *J* = 7.8 Hz, *J* = 2.0 Hz, *J* = 1.5 Hz); 8.63 (dd, 1 H, H(4), pyridyl, *J* = 4.7 Hz, *J* = 1.5 Hz); 9.04 (d, 1 H, H(2), pyridyl, *J* = 2.0 Hz).

1-(4-Bromophenyl)-3-(pyridin-3-yl)prop-2-en-1-one (3c). Yellowish crystals. Yield 2.4 g (84%), m.p. 127—129 °C. Found (%): C, 58.31; H, 3.46; Br, 27.76; N, 4.91; O, 5.56. $C_{14}H_{10}BrNO$. Calculated (%): C, 58.36; H, 3.50; Br, 27.73; N, 4.86; O, 5.55. IR, ν/cm^{-1}: 3319, 3258, 3064, 3029, 1931, 1874, 1796, 1730, 1682, 1667, 1609, 1586, 1568, 1475, 1426, 1396, 1340, 1311, 1274, 1223, 1178, 1126, 1109, 1071, 1026, 1007, 986, 889, 835, 799, 729, 698, 666, 630, 609, 581. ^{1}H NMR (DMSO-d_6), δ: 7.50 (dd, 1 H, H(5), pyridyl, *J* = 7.7 Hz, *J* = 4.8 Hz); 7.74—7.84 (m, 3 H, H(2), H(6), ArCO, CH=); 8.07 (d, 1 H, CH=, *J* = 15.8 Hz); 8.12 (d, 2 H, H(3), H(5), ArCO, *J* = 8.5 Hz); 8.36 (br.d, 1 H, H(4), pyridyl, *J* ≈ 7.7 Hz); 8.63 (br.d, 1 H, H(6), pyridyl, *J* ≈ 4.8 Hz); 9.04 (br.s, 1 H, H(2), pyridyl).

Synthesis of 3,4′-bipyridine derivatives 5a—c (general procedure). To a stirred mixture of the appropriately substituted 1,5-diaryl-3-(pyridin-3-yl)pentane-1,5-dione **4a—c** (10 mmol) and ammonium acetate (50 mmol) in glacial AcOH, pyridine (4 drops) was added. The reaction mixture was refluxed for 12 h and concentrated *in vacuo*. The resulting residue was triturated with diethyl ether, the crystals formed were collected by filtration, washed with diethyl ether, and dried in air.

2′,6′-Bis(4-chlorophenyl)-3,4′-bipyridine (5a). White crystals. Yield 3.1 g (83%), m.p. 235—237 °C. Found (%): C, 70.06; H, 3.72; Br, 18.74; N, 7.48. $C_{22}H_{14}Cl_2N_2$. Calculated (%): C, 70.04; H, 3.74; Cl, 18.79; N, 7.43. IR, ν/cm^{-1}: 3432, 3035, 2922, 2852, 1903, 1749, 1647, 1601, 1579, 1547, 1495, 1485, 1406, 1382, 1339, 1299, 1258, 1191, 1177, 1122, 1090, 1011, 878, 831, 799, 742, 727, 703, 653, 653, 631, 616, 575, 495, 419. ^{1}H NMR (DMSO-d_6), δ: 7.54—7.58 (m, 1 H, H(5), pyridyl); 7.61, 8.40 (both d, 4 H each, Ar, *J* = 8.3 Hz); 8.35 (s, 2 H, H(3′), H(5′), pyridyl); 8.48 (br.d, 1 H, H(4), pyridyl, *J* ≈ 8.0 Hz); 8.72 (br.d, 1 H, H(6), pyridyl, *J* ≈ 4.8 Hz); 9.27 (d, 1 H, H(2), pyridyl, *J* = 2.0 Hz).

2′,6′-Bis(4-bromophenyl)-3,4′-bipyridine (5b). White crystals. Yield 3.9 g (84%), m.p. 236—238 °C. Found (%): C, 56.71; H, 3.00; Br, 34.23; N, 6.06. $C_{22}H_{14}Br_2N_2$. Calculated (%): C, 56.68; H, 3.03; Br, 34.28; N, 6.01. IR, ν/cm^{-1}: 3419, 3035, 1604, 1577, 1547, 1483, 1429, 1403, 1379, 1251, 1180, 1122, 1072, 1007, 879, 830, 801, 742, 706, 650, 631, 614, 498. ^{1}H NMR (DMSO-d_6), δ: 7.61 (ddd, 1 H, H(5), pyridyl, *J* = 8.1 Hz, *J* = 4.8 Hz, *J* = 0.7 Hz); 7.75, 8.33 (both d, 4 H each, Ar, *J* = 8.6 Hz); 8.36 (s, 2 H, H(3′), H(5′), pyridyl); 8.47 (ddd, 1 H, H(4), pyridyl, *J* = 8.1 Hz, *J* = 2.4 Hz, *J* = 1.5 Hz); 8.71 (dd, 1 H, H(6), pyridyl, *J* = 4.8 Hz, *J* = 1.5 Hz); 9.27 (dd, 1 H, H(2), pyridyl, *J* = 2.4 Hz, *J* = 0.7 Hz).

2′,6′-Bis(3-bromophenyl)-3,4′-bipyridine (5c). White powder. Yield 3.4 g (72%), m.p. 268—270 °C. Found (%): C, 56.71; H, 3.00; Br, 34.23; N, 6.06. $C_{22}H_{14}Br_2N_2$. Calculated (%): C, 56.68; H, 3.03; Br, 34.28; N, 6.01. IR, ν/cm^{-1}: 3124, 3057, 1939, 1713, 1653, 1608, 1590, 1565, 1544, 1475, 1446, 1427, 1377, 1333, 1274, 1252, 1242, 1191, 1161, 1127, 1092, 1071, 1052, 1022, 996, 958, 917, 874, 838, 801, 777, 750, 721, 712, 696, 683, 661, 631, 614, 506. ^{1}H NMR (DMSO-d_6), δ: 7.57 (dd, 2 H, H(5′), Ar, *J* = 7.9 Hz, *J* = 7.9 Hz); 7.62 (dd, 1 H, H(5), pyridyl, *J* = 8.1 Hz, *J* = 4.8 Hz); 7.71 (dd, 2 H, H(6), Ar, *J* = 7.9 Hz, *J* = 1.0 Hz); 8.38 (br.d, 2 H, H(4), Ar, *J* ≈ 7.9 Hz); 8.42 (s, 2 H, H(3′), H(5′), pyridyl); 8.52 (ddd, 1 H, H(4), pyridyl, *J* = 8.1 Hz, *J* = 2.2 Hz, *J* = 1.5 Hz); 8.55 (dd, 2 H, H(2), Ar, *J* = 1.8 Hz, *J* = 1.0 Hz); 8.73 (dd, 1 H, H(6), pyridyl, *J* = 4.8 Hz, *J* = 1.5 Hz); 9.32 (d, 1 H, H(2), pyridyl, *J* = 2.2 Hz).

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