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Synthesis of Chalcones on the Basis of Pyridin-2(1*H*)-one

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Abstract—Pyridin-2(1*H*)-one derivatives form chalcones in the Claisen–Schmidt condensation with aromatic and heteroaromatic aldehydes in the presence of bases. For various aldehydes and pyridinones, four main methods are developed. They allow expected chalcones to be prepared in the highest yields.

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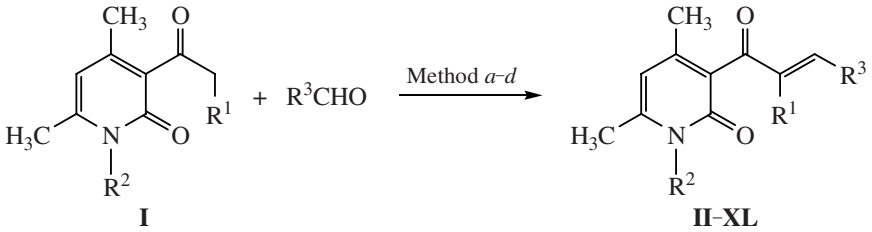
Chalcones, analogs of 1,3-diarylprop-2-en-1-one, form a wide class of compounds containing two aromatic or heteroaromatic rings bound with the vinylketone fragment. Some natural chalcones of plant origin are known [1]. Synthetic chalcones present great interest as compounds exhibiting antiphlogistic [2, 3], antibacterial [4], antimalarial [5], antituberculous, and anticancer activity [7–11]. Furthermore, chalcones are starting compounds for preparing potentially biologically active substances [12].

The aim of this work was to optimize conditions for the synthesis of heterocyclic chalcones derived from pyridin-2(1*H*)-one, depending on the structure of the starting reagents. Such compounds are most commonly prepared by the condensation of aldehydes and ketones in presence of KOH in ethanol [13]. However, this method is not universal and does not work with certain aromatic and heterocyclic aldehydes and ketones, since many reactive systems under these conditions form polycondensation products, while less reactive ones fail to react. The synthesis of chalcones is presented in the scheme.



I **II–XL**

R^1 = H, R^2 = H (**a**), R^1 = Me, R^2 = H (**b**), R^1 = Pr, R^2 = H (**c**), R^1 = C_6H_5, R^2 = H (**d**), R^1 = H, R^2 = 4-$CH_3OC_6H_4$ (**e**).
Method *a*: KOH, H_2O – THF; *b*: KOH, H_2O, 0°C; *c*: CH_3ONa; *d*: $TiCl_4$, Et_3N.

We have studied the condensation conditions for pyridin-2(1*H*)-one analogs with alkyl radical of different size. Compound **Id** containing benzyl radical instead of alkyl, and compound **Ie**, an N-substituted analog of pyridin-2(1*H*)-one, were also investigated.

3-Acetyl-4,6-dimethylpyridin-2(1*H*)-one (**Ia**), 4,6-dimethyl-3-(1-oxopropyl)pyridin-2(1*H*)-one (**Ib**), 4,8-dimethyl-3-(phenylacetyl)pyridin-2(1*H*)-one (**Id**), and 3-acetyl-1-(4-methoxyphenyl)-4,6-dimethylpyridin-2(1*H*)-one (**Ie**) were synthesized as described in [13]. 4,6-Dimethyl-3-(1-oxopentyl)pyridin-2(1*H*)-one (**Ic**), a butyl-containing analog, was prepared similarly in 76% yield.

The yields of chalcones by a popular procedure in the presence of ethanolic KOH at room or elevated temperatures are reportedly about 60% [13]. We used

aqueous THF as a solvent, and the reaction temperature was maintained at 35°C. This allowed the yields to be improved to 65–90%. Such reaction conditions proved to be optimal for the condensation of pyridone **Ia** with benzaldehyde and also with alkyl-, alkoxyl-, and halogen-substituted aromatic aldehydes. It was found that under these conditions pyridone **Ia** readily reacts with 1-naphthaldehyde and anthracene-9-carbaldelyde, as well as with furan- and thiophene-2-carbaldehydes. Elongation of the hydrocarbon fragment by one $–CH_2–$ group (compound **Ib**) slightly decreases the activity of the ketone. At a longer reaction time (48 h), yields of about 50–70% can be achieved. In the case of furfural and thiophene-2-carbaldehyde, the yields are especially high and reach 87 and 91%, respectively. With a benzyl-containing analog of pyridin-2(1*H*)-one, compound **Id**, the best results were obtained as the reaction time was prolonged to 72 h. The yields of chalcones in this case were 30–70%. Pyridones **Ic** and **Ie** fail to react with aromatic aldehydes in the presence of KOH. The conversion of the starting compounds was always close to zero, and they almost completely recovered from the reaction mixture. This finding suggests that the elongation of hydrocarbon radical R_1 significant decreases the reactivity of pyridones. Due to the inductive effect of the electron-donor alkyl radical, the α-protons of pyridin-2(1*H*)-one are activated insufficiently. Successful synthesis of chalcones from compound **Ic** could be performed, when sodium methylate in methanol was used, and the reaction mixture was refluxed for 4 h.

Ketone **Ie** containing a substituted pyridine nitrogen atom was found to be the least reactive in the process under investigation. No condensation was observed in the presence of either alkali or sodium methylate. Attempted synthsis in the presence of piperidine, according to the procedure in [14], also failed. As known, titanium tetrachloride can be also used as a condensing agent [15, 16]. We developed a procedure for preparing of chalcones from ketone **Ie** in the presence of the titanium tetrachloride and excess triethylamine in yields of 30–60%. Note that $TiCl_4$ is quite difficult to operate with, and fully moisture-proof conditions are required.

In the case of the most reactive ketones **Ia, Ib**, and **Id**, synthetic procedures and condensation conditions with a great number of aromatic ketones were explored. The structure of the aldehyde strongly affects the reaction progress, synthesis conditions, and conversion.

As mention above, many aldehydes easily react with pyridones **Ia, Ib**, and **Id** to form chalcones in high yields. At the same time, aldehydes with strong electron-donor substituents, such as *p*-dimethylaminobenzaldehyde, *o*-vanillin on the one side, and aldehydes containing strong electron–acceptor groups, such as picolinic, nicotinic, and isonicotinic aldehydes, on the other, fail, by different reasons, to react with pyridones **Ia, Ib**, and **Id** in the presence of KOH to form chalcones. Strong electron-donor substituents in the aromatic ring hinder carbanion addition by decreasing the effective positive charge on the aldehyde carbon atom, which decelerates condensation. It was found that sodium methylate is an effective catalyst for the reaction of compounds **Ia, Ib**, and **Id** with such aldehydes.

Picolinic, nicotinic, and isonicotinic aldehydes containing a strong acceptor in the aromatic ring fast react at room temperature in an alkaline medium, but the resulting chalcones undergo further transformations, thus complicating isolation of the target substances. We found that dropwise addition of a pyridine-containing aldehyde to an ice-cooled solution of pyridin-2(1*H*)-one in aqueous KOH permits to the desired chalcones to be obtained in 30–57% yields.

The prepared chalcones are, as a rule, solids havinga bright yellow color, which is accounted for by the conjugation of π electrons of the double bond and the aromatic ring. In the case of anthracenecarbaldehyde, a batochromic shift of coloration is observed, and the corresponding chalcone is orange red.

The products are generally soluble in ethanol or DMF at elevated temperatures. The melting points of chalcones prepared from ketone **Ib** having a methyl substitient at the double bond are lower than those of their analogs prepared from ketones **Ia** and **Id**.

The experimetal procedures, yields, and melting points of the synthesized compounds are presented in Table 1. The ^1H NMR spectra of compounds having no substituents at the double bond show a well-defined doublet of doublets of the –CH=CH– fragment. The coupling constant of about 16 Hz points to *trans* isomers. The position of the pyridone H^5 signal remains the same (near 6 ppm). The ^1H NMR spectra of the synthesized chalcones are listed in Table 2.

Table 1. Methods of synthesis, melting points, and elemental analyses of chalcones **II–XL**

Comp. no.	R_1	R_2	R_3	Method	mp, °C (EtOH)	Calculated, %			Formula	Found, %			Yield, %
						C	H	N		C	H	N	
II	H	H	Ph	*a*	204–206	75.87	5.97	5.53	$C_{16}H_{15}NO_2$	75.95	5.90	5.50	67
III	Me	H	Ph	*a*	199–202	76.38	6.41	5.24	$C_{17}H_{17}NO_2$	76.46	6.44	5.30	58
IV	Ph	H	Ph	*a*	206–208	80.22	5.81	4.25	$C_{22}H_{19}NO_2$	80.20	5.88	4.19	51
V	H	H	4-$CH_3OC_6H_4$	*a*	213–215	72.07	6.05	4.94	$C_{17}H_{17}NO_3$	72.12	6.05	4.97	67
VI	Me	H	4-$CH_3OC_6H_4$	*a*	184–186	72.71	6.44	4.71	$C_{18}H_{19}NO_3$	72.77	6.40	4.80	51
VII	Ph	H	4-$CH_3OC_6H_4$	*a*	221–222	76.86	5.89	3.90	$C_{23}H_{21}NO_3$	76.90	5.90	3.90	40
VIII	H	H	4-BrC_6H_4	*a*	289–290[a]	57.85	4.25	4.22	$C_{16}H_{14}BrNO_2$	57.85	4.25	4.25	65
IX	Me	H	4-BrC_6H_4	*a*	214–215[a]	58.98	4.66	4.05	$C_{17}H_{16}BrNO_2$	59.07	4.62	4.09	58
X	Ph	H	4-BrC_6H_4	*a*	198–200	64.72	4.44	3.43	$C_{22}H_{18}BrNO_2$	64.79	4.47	3.40	66
XI	H	H	2-ClC_6H_4	*a*	218–220[a]	66.79	4.90	4.87	$C_{16}H_{14}ClNO_2$	66.83	4.95	4.83	68
XII	Me	H	2-ClC_6H_4	*a*	185–188	67.66	5.34	4.64	$C_{17}H_{16}ClNO_2$	67.70	5.30	4.69	55
XIII	Ph	H	2-ClC_6H_4	*a*	206–209	72.62	4.99	3.85	$C_{22}H_{18}ClNO_2$	72.69	5.00	3.83	50
XIV	H	H	2,3-$(CH_3O)_2C_6H_3$	*a*	207–209[a]	68.99	6.11	4.47	$C_{18}H_{19}NO_4$	69.04	6.10	4.50	68
XV	Me	H	2,3-$(CH_3O)_2C_6H_3$	*a*	160–162	69.71	6.47	4.28	$C_{19}H_{21}NO_4$	69.70	6.42	4.30	62
XVI	Ph	H	2,3-$(CH_3O)_2C_6H_3$	*a*	217–220	74.02	5.95	3.60	$C_{24}H_{23}NO_4$	74.10	5.95	3.65	68
XVII	H	H	1-naphthyl	*a*	246–247[a]	78.66	6.27	4.59	$C_{20}H_{19}NO_2$	78.70	6.30	4.54	80
XVIII	Me	H	1-naphthyl	*a*	198–201	78.97	6.66	4.39	$C_{21}H_{21}NO_2$	79.00	6.69	4.40	70
XIX	Ph	H	1-naphthyl	*a*	264–265	81.86	6.08	3.67	$C_{26}H_{23}NO_2$	81.90	6.06	3.66	54
XX	H	H	9-anthranyl	*a*	312–314[a]	81.10	5.96	3.94	$C_{24}H_{21}NO_2$	81.12	5.95	3.95	69
XXI	H	H	2-pyridyl	*b*	199–201	70.85	5.55	11.02	$C_{15}H_{14}N_2O_2$	70.85	5.55	11.00	49
XXII	H	H	3-pyridyl	*b*	214–215[b]	70.85	5.55	11.02	$C_{15}H_{14}N_2O_2$	70.93	5.60	10.98	57
XXIII	Me	H	3-pyridyl	*b*	165–168[b]	71.62	6.01	10.44	$C_{16}H_{16}N_2O_2$	71.69	6.08	10.50	46
XXIV	Ph	H	3-pyridyl	*b*	218–221[b]	76.34	5.49	8.48	$C_{21}H_{18}N_2O_2$	76.35	5.50	8.50	29
XXV	H	H	4-pyridyl	*b*	264–267[b]	70.85	5.55	11.02	$C_{15}H_{14}N_2O_2$	70.89	5.59	11.00	33
XXVI	H	H	2-thienyl	*a*	242–243	64.84	5.05	5.40	$C_{14}H_{13}NO_2S$	64.80	5.01	5.36	65
XXVII	Me	H	2-thienyl	*a*	222–223[a]	65.91	5.53	5.12	$C_{15}H_{15}NO_2S$	65.90	5.55	5.15	91
XXVIII	Ph	H	2-thienyl	*a*	267–269	71.62	5.11	4.18	$C_{20}H_{17}NO_2S$	71.68	5.10	4.22	71
XXIX	H	H	2-furyl	*a*	217–218[a]	69.12	5.39	5.76	$C_{14}H_{13}NO_3$	69.10	5.42	5.80	72
XXX	Me	H	2-furyl	*a*	202–203[a]	70.02	5.88	5.44	$C_{15}H_{15}NO_3$	70.05	5.92	5.40	87
XXXI	Ph	H	2-furyl	*a*	254–256	75.22	5.31	4.39	$C_{20}H_{17}NO_3$	75.28	5.35	4.43	63
XXXII	H	H	C_6H_5CH=CH	*a*	196–200	77.40	6.13	5.01	$C_{18}H_{17}NO_2$	77.47	6.18	5.00	70
XXXIII	Me	H	C_6H_5CH=CH	*a*	226–229	77.79	6.53	4.77	$C_{19}H_{19}NO_2$	77.84	6.50	4.71	62
XXXIV	Ph	H	C_6H_5CH=CH	*a*	299–303[a]	81.10	5.96	3.94	$C_{24}H_{21}NO_2$	81.15	5.95	3.93	45
XXXV	H	H	4-$(CH_3)_2NC_6H_4$	*c*	242–243	72.95	6.80	9.45	$C_{18}H_{20}N_2O_2$	72.90	6.86	9.48	64
XXXVI	H	H	2-OH.3-$CH_3OC_6H_3$	*c*	233–234	68.21	5.72	4.68	$C_{17}H_{17}NO_4$	68.20	5.70	4.70	40
XXXVII	Pr	H	4-BrC_6H_4	*c*	156–157	60.97	5.39	3.74	$C_{19}H_{20}BrNO_2$	61.04	5.42	3.70	56
XXXVIII	Pr	H	4-ClC_6H_4	*c*	197–200	69.19	6.11	4.25	$C_{19}H_{20}ClNO_2$	69.25	6.14	4.29	36
XXXIX	H	4-$CH_3OC_6H_4$	Ph	*d*	196–197	76.86	5.89	3.90	$C_{23}H_{21}NO_3$	76.76	5.94	3.90	34
XL	H	4-$CH_3OC_6H_4$	4-$CH_3OC_6H_4$	*d*	168–170	74.02	5.95	3.60	$C_{24}H_{23}NO_4$	74.20	5.88	3.57	61

[a] Crystallized from DMF [b] Crystallized from *i*-PrOH.

Table 2. ^{1}H NMR spectra of chalcones **II–XL**

Comp. no.	^{1}H NMR spectrum, δ, ppm (DMSO-d_6)
II	2.08 s (3H, CH_3), 2.18 s (3H, CH_3), 6.02 s (1H, C^5H), 7.15 d (1H, CH, *J* 16.1 Hz), 7.42 m (4H, CH + C_6H_5), 7.70 m (2H, C_6H_5), 11.90 s (1H, NH)
III	1.91 s (3H, CH_3), 2.04 s (3H, CH_3), 2.15 s (3H, CH_3), 5.95 s (1H, C^5H), 7.22 s (1H, CH), 7.44 m (5H, C_6H_5), 11.75 s (1H, NH)
IV	2.05 s (3H, CH_3), 2.16 s (3H, CH_3), 5.96 s (1H, C^5H), 7.05 d (2H, C_6H_5, *J* 8.9 Hz), 7.21 m (5H, C_6H_5), 7.39 m (4H, C_6H_5), 11.78 s (1H, NH)
V	2.05 s (3H, CH_3), 2.19 s (3H, CH_3), 3.80 s (3H, OCH_3), 5.99 s (1H, C^5H), 7.36 d (1H, CH, *J* 16.2 Hz), 6.99 m (3H, CH + + C_6H_4), 7.68 d (2H, C_6H_4, *J* 8.9 Hz), 11.81 s (1H, NH)
VI	1.92 s (3H, CH_3), 2.10 s (3H, CH_3), 2.20 s (3H, CH_3), 3.80 s (3H, OCH_3), 5.98 s (1H, C^5H), 7.01 d (2H, C_6H_4, *J* 8.9 Hz), 7.23 s (1H, CH), 7.48 d (2H, *J* 8.9 Hz), 11.71 s (1H, NH)
VII	2.02 s (3H, CH_3), 2.15 s (3H, CH_3), 3.69 s (3H, OCH_3), 5.98 s (1H, C^5H), 6.77 d (2H, C_6H_4, *J* 9.0 Hz), 6.92 d (2H, C_6H_4, *J* 9.0 Hz), 7.17 m (2H, C_6H_5), 7.39 m (4H, CH + C_6H_5), 11.80 s (1H, NH)
VIII	2.10 s (3H, CH_3), 2.10 s (3H, CH_3), 6.05 s (1H, C^5H), 7.24 d (1H, CH, *J* 16.2 Hz), 7.43 d (1H, CH, *J* 16.2 Hz), 7.67 m (4H, C_6H_4), 11.90 s (1H, NH)
IX	1.99 s (3H, CH_3), 2.09 s (3H, CH_3), 2.20 s (3H, CH_3), 5.90 s (1H, C^5H), 7.18 s (1H, CH), 7.37 d (2H, C_6H_4, *J* 9.3 Hz), 7.56 s (2H, C_6H_4, *J* 9.3 Hz), 11.76 s (1H, NH)
X	2.09 s (3H, CH_3), 2.20 s (3H, CH_3), 5.96 s (1H, C^5H), 6.98 d (2H, C_6H_4, *J* 8.7 Hz), 7.20 m (2H, C_6H_5), 7.35 m (6H, CH + + C_6H_4 + C_6H_5), 11.73 s (1H, NH)
XI	2.18 s (3H, CH_3), 2.23 s (3H, CH_3), 5.97 s (1H, C^5H), 7.26 d (1H, CH, *J* 16.1 Hz), 7.43 m (3H, C_6H_4), 7.80 m (2H, CH + + C_6H_4), 11.96 s (1H, NH)
XII	2.00 s (3H, CH_3), 2.03 s (3H, CH_3), 2.20 s (3H, CH_3), 5.93 s (1H, C^5H), 7.45 m (5H, CH + C_6H_4), 11.76 s (1H, NH)
XIII	2.00 s (3H, CH_3), 2.12 s (3H, CH_3), 6.00 s (1H, C^5H), 6.73 d (1H, arom, *J* 9.0 Hz), 6.98 t (1H, arom), 7.11 m (2H, arom), 7.35 m (3H, arom), 7.52 d (2H, arom, *J* 9.0 Hz), 7.56 s (1H, CH), 11.76 s (1H, NH)
XIV	2.13 s (3H, CH_3), 2.21 s (3H, CH_3), 3.77 s (3H, OCH_3), 3.84 s (3H, OCH_3), 5.99 s (1H, C^5H), 7.10 m (2H, C_6H_3), 7.17 d (1H, CH, *J* 16.3 Hz), 7.26 m (1H, C_6H_3), 7.67 d (1H, CH, *J* 16.3 Hz), 11.89 s (1H, NH)
XV	1.97 s (3H, CH_3), 2.05 s (3H, CH_3), 2.21 s (3H, CH_3), 3.59 s (3H, OCH_3), 3.81 s (3H, OCH_3), 5.96 s (1H, C^5H), 7.12 m (3H, C_6H_3), 7.50 s (1H, CH), 11.76 s (1H, NH)
XVI	2.06 s (3H, CH_3), 2.18 s (3H, CH_3), 3.67 s (3H, OCH_3), 3.73 s (3H, OCH_3), 6.00 s (1H, C^5H), 6.20 d (1H, arom, *J* 9.0 Hz), 6.70 t (1H, arom), 6.93 d (1H, arom, *J* 9.0 Hz), 7.16 m (2H, arom), 7.33 m (3H, arom), 7.60 s (1H, CH), 11.80 s (1H, NH)
XVII	2.18 s (3H, CH_3), 2.23 s (3H, CH_3), 6.04 s (1H, C^5H), 7.28 d (1H, CH, *J* 16.2 Hz), 7.60 m (3H, $C_{10}H_7$), 7.99 m (3H, $C_{10}H_7$), 8.15 m (1H, $C_{10}H_7$), 8.28 d (1H, CH, *J* 16.2 Hz), 11.82 s (1H, NH)
XVIII	1.93 s (3H, CH_3), 2.05 s (3H, CH_3), 2.20 s (3H, CH_3), 6.00 s (1H, C^5H), 7.53 m (4H, $C_{10}H_7$), 7.70 m (2H, $C_{10}H_7$), 7.87 m (2H, CH + $C_{10}H_7$), 11.93 s (1H, NH)
XIX	2.17 s (6H, $2CH_3$), 6.05 s (1H, C^5H), 6.98 m (3H, arom), 7.31 m (4H, arom), 7.58 m (2H, arom), 7.84 m (1H, arom), 8.02 m (3H, CH + arom), 11.88 s (1H, NH)
XX	2.20 s (3H, CH_3), 2.30 s (3H, CH_3), 6.10 s (1H, C^5H), 7.05 d (1H, CH, *J* 16.2 Hz), 7.61 m (4H, $C_{14}H_9$), 8.12 m (2H, $C_{14}H_9$), 8.37 m (3H, CH + $C_{14}H_9$), 8.63 s (1H, $C_{14}H_9$), 11.96 s (1H, NH)
XXI	2.09 s (3H, CH_3), 2.18 s (3H, CH_3), 6.00 s (1H, C^5H), 7.49 m (3H, 2CH + C_5H_4N), 7.82 m (2H, C_5H_4N), 8.69 m (1H, C_5H_4N), 11.90 s (1H, NH)
XXII	2.03 s (3H, CH_3), 2.13 s (3H, CH_3), 6.02 s (1H, C^5H), 7.28 d (1H, CH, *J* 15.9 Hz), 7.38 m (2H, CH + C_5H_4N), 8.15 s (1H, C_6H_4N, *J* 9.0 Hz), 8.56 d (1H, C_5H_4N, *J* 9.0 Hz), 8.80 s (1H, C_6H_4N), 11.83 s (1H, NH)
XXIII	1.98 s (3H, CH_3), 2.07 s (3H, CH_3), 2.17 s (3H, CH_3), 6.00 s (1H, C^5H), 7.27 s (1H, CH), 7.50 m (1H, C_5H_4N), 7.93 m (1H, C_5H_4N), 8.52 m (1H, C_5H_4N), 8.68 s (1H, C_5H_4N), 11.72 s (1H, NH)
XXIV	2.07 s (3H, CH_3), 2.23 s (3H, CH_3), 5.96 s (1H, C^5H), 7.22 m (4H, arom), 7.42 m (4H, arom), 8.28 s (1H, CH), 8.38 m (1H, C_5H_4N), 11.74 s (1H, NH)
XXV	2.07 s (3H, CH_3), 2.18 s (3H, CH_3), 6.03 s (1H, C^5H), 7.40 s (2H, 2CH), 7.61 d (2H, C_6H_4N, *J* 6.0 Hz), 8.62 d (2H, C_6H_4N, *J* 6.0 Hz), 11.89 s (1H, NH)

Table 2. (Contd.)

Comp. no.	^{1}H NMR spectrum, δ, ppm (DMSO-d_6)
XXVI	2.07 s (3H, CH_3), 2.18 s (3H, CH_3), 6.01 s (1H, C^5H), 6.85 d (1H, CH, *J* 16.1 Hz), 7.14 t (1H, C_4H_3S), 7.55 m (1H, C_4H_3S), 7.68 d (1H, CH, *J* 16.1 Hz), 7.75 m (1H, C_4H_3S), 11.78 s (1H, NH)
XXVII	1.93 s (3H, CH_3), 2.14 s (3H, CH_3), 2.20 s (3H, CH_3), 6.00 s (1H, C^5H), 7.21 m (1H, C_4H_3S), 7.50 m (2H, CH + C_4H_3S), 7 88 m (1H, C_4H_3S), 11.71 s (1H, NH)
XXVIII	2.04 s (3H, CH_3), 2.18 s (3H, CH_3), 5.98 s (1H, C^5H), 7.00 m (1H, C_4H_3S), 7.19 m (2H, C_6H_5), 7.42 m (4H, C_4H_3S + C_6H_5), 7.54 m (1H, C_4H_3S), 7.66 s (1H, CH), 11.75 s (1H, NH)
XXIX	2.08 s (3H, CH_3), 2.20 s (3H, CH_3), 6.02 s (1H, C^5H), 6.65 m (1H, C_4H_3O), 6.94 m (2H, CH + C_4H_3O), 7.28 d (1H, CH, *J* 16.0 Hz), 7.86 s (1H, C_4H_3O), 11.93 s (1H, NH)
XXX	1.93 s (3H, CH_3), 2.08 s (3H, CH_3), 2.11 c (3H, CH_3), 6.00 s (1H, C^5H), 6.68 m (1H, C_4H_3O), 6.95 m (1H, C_4H_3O), 7.02 m (1H, C_4H_3O), 7.89 s (1H, CH), 11.57 s (1H, NH)
XXXI	2.02 s (3H, CH_3), 2.17 c (3H, CH_3), 5.97 m (2H, C^5H + C_4H_3O), 6.47 m (1H, C_4H_3O), 7.22 m (3H, C_4H_3O + C_6H_5), 7.42 m (3H, C_6H_5), 7.70 s (1H, CH), 11.80 s (1H, NH)
XXXII	2.08 s (3H, CH_3), 2.21 c (3H, CH_3), 6.00 s (1H, C^5H), 6.68 d (1H, CH, *J* 16.0 Hz), 7.12 d (2H, C_6H_5, *J* 9.1 Hz), 7.22 d (1H, CH, *J* 16.0 Hz), 7.37 m (3H, 2CH + C_6H_5), 7.59 d (2H, C_6H_5, *J* 9.1 Hz), 11.67 s (1H, NH)
XXXIII	1.91 s (3H, CH_3), 2.03 s (3H, CH_3), 2.18 s (3H, CH_3), 6.00 s (1H, C^5H), 7.00 m (2H, CH + C_6H_5), 7.34 m (4H, CH + C_6H_5), 7.65 m (2H, CH + C_6H_5), 11.70 s (1H, NH)
XXXIV	2.01 s (3H, CH_3), 2.17 s (3H, CH_3), 5.98 s (1H, C^5H), 7.15 m (2H, 2CH), 7.24 m (3H, arom), 7.32 m (5H, arom), 7.42 m (3H, CH + arom), 11.63 s (1H, NH)
XXXV	2.03 s (3H, CH_3), 2.18 s (3H, CH_3), 3.00 s [6H, $N(CH_3)_2$], 5.98 s (1H, C^5H), 6.69 d (2H, C_6H_4, *J* 9.2 Hz), 6.83 d (1H, CH, *J* 16.0 Hz), 7.34 d (1H, CH, *J* 16.0 Hz), 7.53 d (2H, C_6H_4, *J* 9.2 Hz), 11.79 s (1H, NH)
XXXVI	2.08 s (3H, CH_3), 2.21 (3H, CH_3), 3.88 s (3H, OCH_3), 6.00 s (1H, C^5H), 6.83 m (1H, C_6H_3), 7.01 d (1H, CH, *J* 15.9 Hz), 7.11 d (1H, CH, *J* 15.9 Hz), 7.24 d (1H, C_6H_3, *J* 8.9 Hz), 7.75 d (1H, C_6H_3, *J* 8.9 Hz), 9.40 s (1H, OH), 11.63 s (1H, NH)
XXXVII	1.00 t (3H, CH_3), 1.53 m (2H, CH_2), 1.97 s (3H, CH_3), 2.19 s (3H, CH_3), 2.51 m (2H, CH_2), 5.89 s (1H, C^5H), 7.15 s (1H, CH), 7.33 d (2H, C_6H_4, *J* 9.2 Hz), 7.58 d (2H, C_6H_4, *J* 9.2 Hz), 11.70 s (1H, NH)
XXXVIII	1.02 t (3H, CH_3), 1.61 m (2H, CH_2), 2.04 s (3H, CH_3), 2.23 s (3H, CH_3), 2.62 m (2H, CH_2), 6.02 s (1H, C^5H), 7.29 s (1H, CH), 7.55 m (4H, C_6H_4), 11.68 s (1H, NH)
XXXIX	2.01 s (3H, CH_3), 2.20 s (3H, CH_3), 3.86 s (3H, OCH_3), 6.22 s (1H, C^5H), 7.13 m (5H, CH + arom), 7.43 m (4H, CH + arom), 7.64 m (2H, arom)
XL	1.97 s (3H, CH_3), 2.13 s (3H, CH_3), 3.81 s (3H, OCH_3), 3.83 s (3H, OCH_3), 6.28 s (1H, C^5H), 7.02 m (5H, CH + arom), 7.17 d (2H, arom, *J* 9.0 Hz), 7.47 d (1H, CH, *J* 15.7 Hz), 7.68 d (2H, arom, *J* 9.0 Hz)

EXPERIMENTAL

The NMR spectra were taken on a Bruker DPX-200 (200 MHz) spectrometer in DMSO-d_6 against internal TMS. The melting points were measured on a Boetius apparatus. Aromatic aldehydes purchased from Aldrich and Lancaster were used. THF was purified by refluxing over granulated KOH, distillation, and, finally, refluxing with lithium aluminum hydride.

4,6-Dimethyl-3-(1-oxopentyl)pyridin-2(1*H*)-one (Ic). Magnesium, 12.15 g, was placed in a three-necked flask equipped with a stirrer, a dropping funnel, and a reflux condenser, and containing 300 ml of THF. Butyl bromide, 68.52 g, was added dropwise maintaining the reaction mixture slightly boiling. After the addition had been complete, the mixture was refluxed for 30 min and then 30.0 g of 1,2-dihydro-4,6-dimethyl-2-oxo-3-pyridinecarbonitrile obtained according to the procedure in [13] was added in small portions. The resulting mixture was refluxed for 4 h and then treated dropwise with 15% HCl to pH 2. The precipitate formed was filtered off, washed with water, dried, and crystallized from EtOH. Yield 35.5 g (76%), mp 153–154°C. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 0.83 t (3H, CH_3), 1.26 m (2H, CH_2), 1.50 m (2H, CH_2), 2.01 s (3H, CH_3), 2.13 s (3H, CH_3), 2.78 t (2H, CH_2), 5.90 s (1H, C^5H), 11.90 s (1H, NH). Calculated, %: C 69.60; H 8.20; N 6.75. $C_{12}H_{17}NO_2$. Calculated, %: C 69.54; H 8.27; N 6.76.

Synthesis of chalcones. *Method a*. To a solution of 0.019 mol of KOH in 20 ml of water 0.015 mol of pyridin-2(1*H*)-one was added, and the mixture was

stirred until the latter dissolved completely. Aromatic aldehyde, 0.018 mol, was dissolved in 25 ml of THF, and the solution was added to a solution of pyridin-2(1*H*)-one. The reaction mixture was kept at 30°C for 24–72 h, and then refluxed for 1 h, neutralized with acetic acid to pH 6, and diluted with water. The precipitate formed was filtered off, dried, and crystallized from ethanol or DMF.

Method b. To a solution of 0.021 mol of KOH in 25 ml of water, 0.015 mol of pyridin-2(1*H*)-one was added. The mixture was stirred until complete dissolution of the latter, cooled with ice, and 0.018 mol of aromatic aldehyde was added dropwise. The mixture was stirred for 3 h at 0°C and then left at room temperature for 2 days. After that it was neutralized with acetic acid and diluted with water. The precipitate formed was filtered off, dried, and crystallized from ethanol.

Method c. Compound **I**, 0.010 mol, was added to a solution of sodium methylate prepared from 0.001 g at of sodium and 15 ml of ethanol, and the mixture was stirred until sodium methylate dissolved completely. After that 0.012 mol of aromatic aldehyde was added, and the mixture was kept overnight at 30°C, and then refluxed for 4 h and neutralized with 10% HCl to pH 6. The product was evolved as an oil which gradually crystallized. The crystals formed were thoroughly washed with water, dried, and crystallized from ethanol or 2-propanol.

Method d. Anhydrous THF, 35 ml, was cooled to 0°C, and a solution of 13.0 mmol of $TiCl_4$ in 5 ml of methylene chloride was added dropwise. A solution of 10.0 mmol of ketone and 10.5 mmol of benzaldehyde in 10 ml of anhydrous THF was added dropwise over the course of 30 min to the resulting suspension . The reaction mixture was stirred for 30 min, and, after addition of 50 mmol of triethylamine, stirred for 1 h and then poured into water. The precipitate formed was filtered off and washed with THF. The solvents were evaporated, and the residue was treated with benzene. The organic layer was washed with water and dried over $MgSO_4$. The solvent was evaporated, and the residue was crystallized from ethanol.

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