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Synthesis and Chemical Properties of 4-Aroyl-3-methyl-4,10-dihydroindeno[1,2-*b*]pyrazolo-[4,3-*e*]pyridin-5-ones

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Abstract—Reactions of 5-amino-3-methylpyrazole with arylglyoxals and indane-1,3-dione afforded 4-aroyl-3-methyl-4,10-dihydroindeno[1,2-*b*]pyrazolo[4,3-*e*]pyridin-5(2*H*)-ones, and their chemical behavior was studied in reactions with alkylating, acylating reagents and hydrazine hydrate. In three-component condensations involving 5-amino-3-methyl-1-phenylpyrazole the intermediate Michael adducts were isolated, 2-[1-(5-amino-3-methyl-1-phenyl-1*H*-pyrazol-4-yl)-2-oxo-2-(aryl)ethyl]-1*H*-indene-1,3(2*H*)-diones that underwent cyclization into 4-aroyl-3-methyl-1-phenylindeno[1,2-*b*]pyrazolo[4,3-*e*]pyridin-5(1*H*)-ones.

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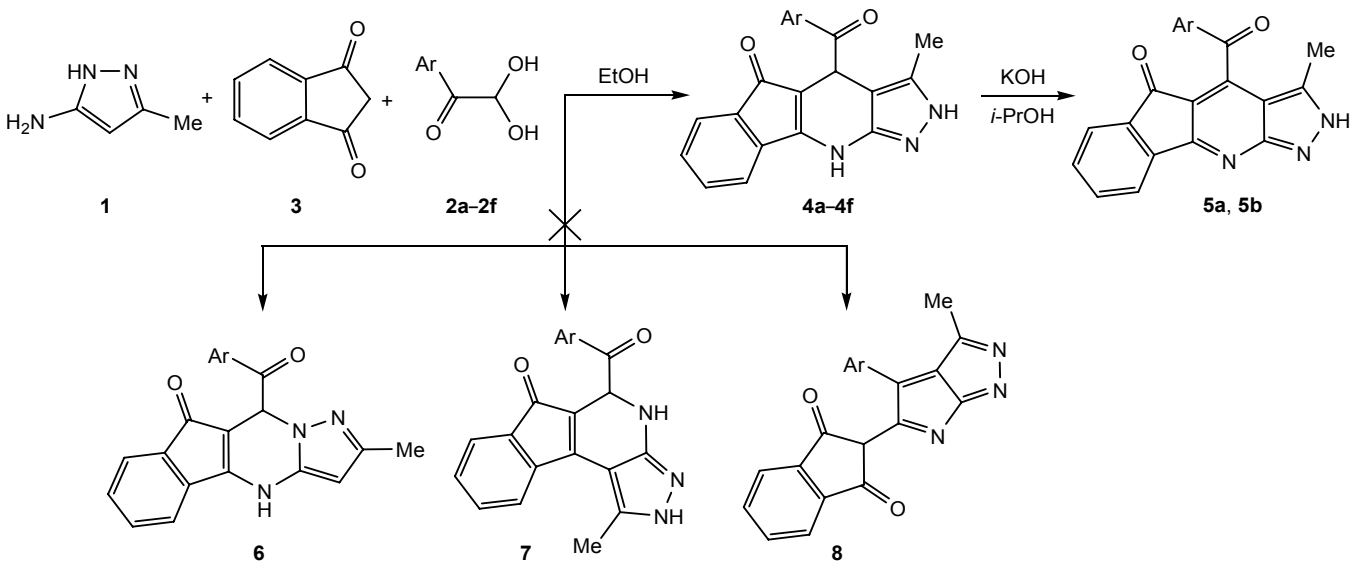
The interest to heterocyclic systems containing an indeno[1,2-*b*]pyridine fragment arose in nineteen seventies due to discovering fungicidal action in a small group of azafluorenone alkaloids, metabolites of a Brazilian plant *Guatteria dielsiana* (of *Annonaceae* family) that contained among others 1-methyl-4-azafluorenone (onychine) [1]. The method of its synthesis was described in [2, 3] even before this alkaloid was isolated from natural sources. Nowadays among the onychine analogs not only substances of anticandidal activity but also modulators of Ca^{2+}-channels [4], antagonists of A2 adenosine receptors, phosphodiesterase inhibitors effective against neurodegenerative disorders and inflammation processes [5, 6], antidepressants [7, 8], and compounds with antibacterial [9], cytotoxic [10] and pronounced antitumor action, inducers of T-lymphocytes apoptosis [11], DNA intercalators, and topoisomerase inhibitors were detected [12, 13].

The methods of preparation of indeno[1,2-*b*]-pyridin-5-ones based on the cyclization of 2-aryl-3-methylpyridines with subsequent oxidation of obtained azafluorenes [2, 3], or on the cyclization under the action of polyphosphonic acid of 2-aryl-substituted nicotinic acid derivatives [14, 15], oxidative rearrangements of 2-indanone oximes O-allyl ethers [8, 14, 16, 17], and Michael addition of α,β-unsaturated ketones to tributyl(inden-3-ylimino)phosphoranes followed by aza-Wittig cyclization [18] are multistage, accompanied with quite a number of side processes, and give low yields. Recently 4-azafluorenone syntheses were described underlain by indanedione condensation with carbonyl compounds and nitrogen-containing 1,3-binucleophiles, among which the most often various 1- and 3-substituted 5-aminopyrazoles were mentioned [11, 19–23]. These reactions proceed as a rule under mild conditions and are characterized by a high regioselectivity in the formation of pyridine ring. The latter criterion along with a high yield of products becomes the main test for the suitability of the procedure for a combinatorial synthesis. In these cascade transformations aromatic or heterocyclic aldehydes are involved as carbonyl components. No published information exists on the application of arylglyoxals in similar domino

Scheme 1.



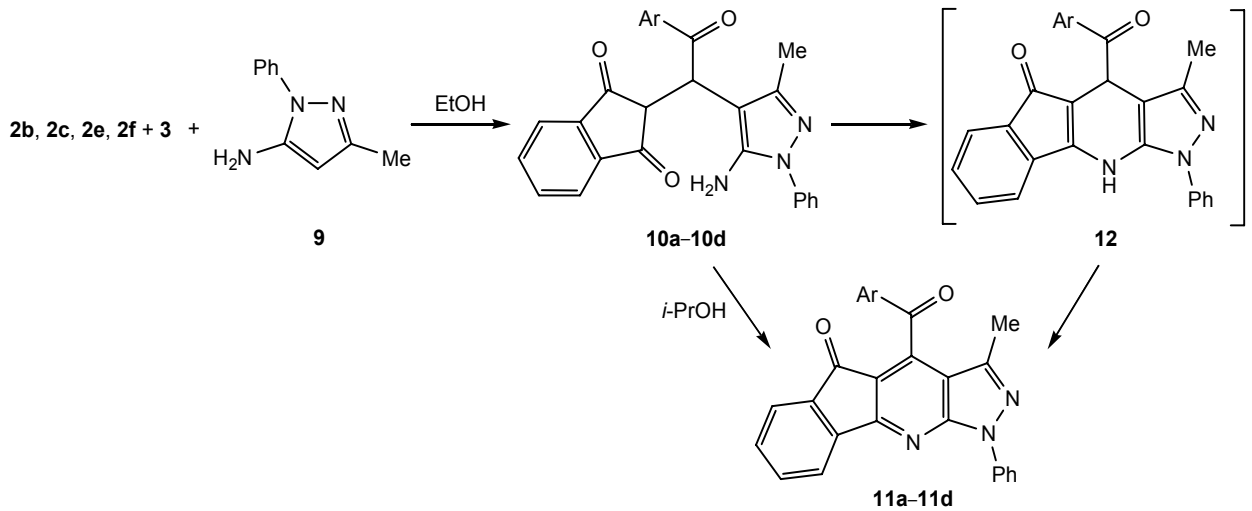
2, **4**, Ar = Ph (**a**), 4-MeC_6H_4 (**b**), 4-$MeOC_6H_4$ (**c**), 4-FC_6H_4 (**d**), 4-ClC_6H_4 (**e**), 4-BrC_6H_4 (**f**); **5**, Ar = 4-MeC_6H_4 (**a**), Ar = 4-$MeOC_6H_4$ (**b**).

reactions. The target of the present study was to establish the direction of the reaction of arylglyoxals hydrates with indanedione, 3-methyl-5-amino-, and 1-phenyl-3-methyl-5-aminopyrazole, and also to investigate the chemical transformations of compounds obtained in the presence of reagents of diverse electronic nature.

At boiling in ethanol of equimolar quantities of 5-amino-3-methylpyrazole **1**, arylglyoxals **2a**–**2f**, and indane-1,3-dione **3** dihydroindeno[1,2-*b*]pyrazolo[4,3-*e*]pyridin-5(2*H*)-ones **4a**–**4f** formed in 55–70% yields (Scheme 1). Their transformation in heteroaromatic derivatives **5** occurred at the treatment with KOH in 2-propanol at room temperature. Compounds of an alternative structure **6**–**8** were not found in any experiment.

The three-component condensations involving N-phenyl-substituted aminopyrazole **9** in ethanol gave Michael adducts **10a**–**10d** (Scheme 2). Their further boiling in 2-propanol (1–3.5 h) led to the formation of heteroaromatic derivatives **11**. Unlike reactions involving aminopyrazole **1** we failed to isolate in any

Scheme 2.

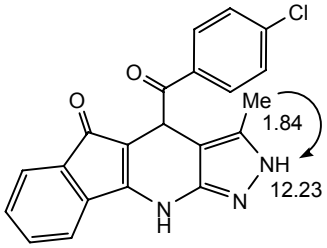


10, **11**, Ar = 4-MeC_6H_4 (**a**), 4-$MeOC_6H_4$ (**b**), 4-ClC_6H_4 (**c**), Ar = 4-BrC_6H_4 (**d**).

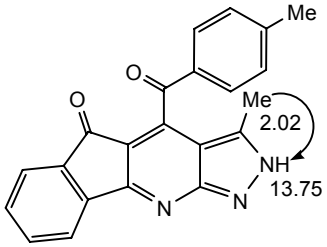
of these experiments dihydroindeno[1,2-*b*]pyrazolo-[4,3-*e*]pyridinones **12**.

The composition and structure of compounds synthesized were established from the data of elemental analysis, mass, IR, and ^{1}H NMR spectra, and also from the X-ray diffraction (XRD) analysis of single crystals of compounds **11a** and **11c**. The mass spectra of indeno[1,2-*b*]pyrazolo[4,3-*e*]pyridin-5-ones **4**, **5**, and **11** contain weak peaks of molecular ions and high intensive peaks of fragment ions arising by elimination of aroyl substituent from the molecular ion.

In the ^{1}H NMR spectra of compounds **4** along with the multiplets of the aryl protons and the singlet of the methyl group of the pyrazole ring the singlets of two NH groups are present in a downfield (δ 11.35–11.40 and 12.18–12.23 ppm) and a singlet of the C^4H proton at 5.40–5.45 ppm showing the formation at the cyclocondensation of a dihydropyridine and not a pyrimidine ring. In the spectra of heteroaromatic derivatives **5** the proton signals of CH and NH of the pyridine ring are absent. The conclusion on the existence of compounds **4** and **5** in the tautomeric N^2H form was done basing on the results of NOE experiments with indeno[1,2-*b*]pyrazolo[4,3-*e*]pyridin-5-ones **4e** and **5b**.

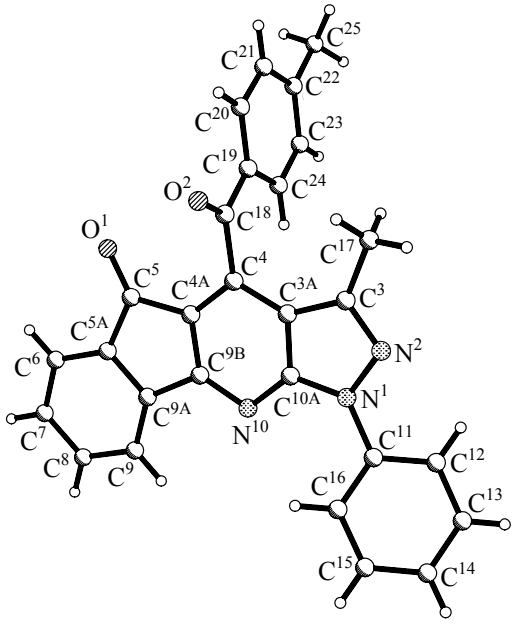


4e

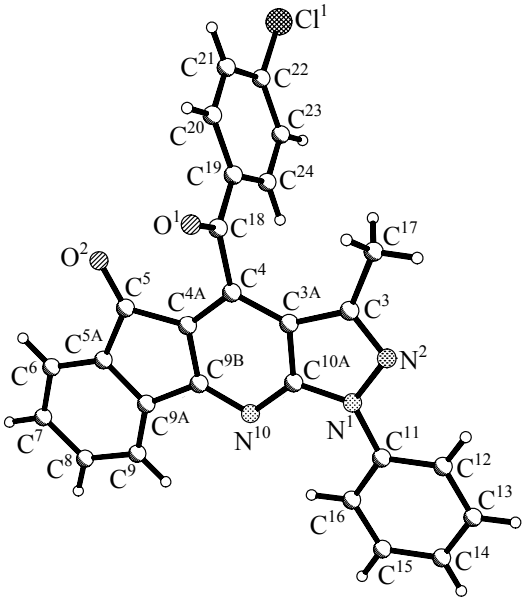


5b

The most characteristic signals in the ^{1}H NMR spectra of adducts **10** are the singlet of the NH_2 group and two doublets of methine protons at 3.78–3.88 and 5.40–5.43 ppm forming an *AB* system. At the deuteroexchange with D_2O in the spectra one doublet of the methine proton disappeared, and the other became a singlet thus indicating the enolization of the aroyl fragment of molecules **10a–10d**. The ^{1}H NMR spectra of heteroaromatic indeno[1,2-*b*]pyrazolo[4,3-*e*]-pyridin-5-ones **11** resemble the spectra of analogous compounds **5** and differ from them only in the resonance region of the aromatic protons. The structure of compounds **11a** and **11c** was completely proved by XRD analysis (see the figure).



11a

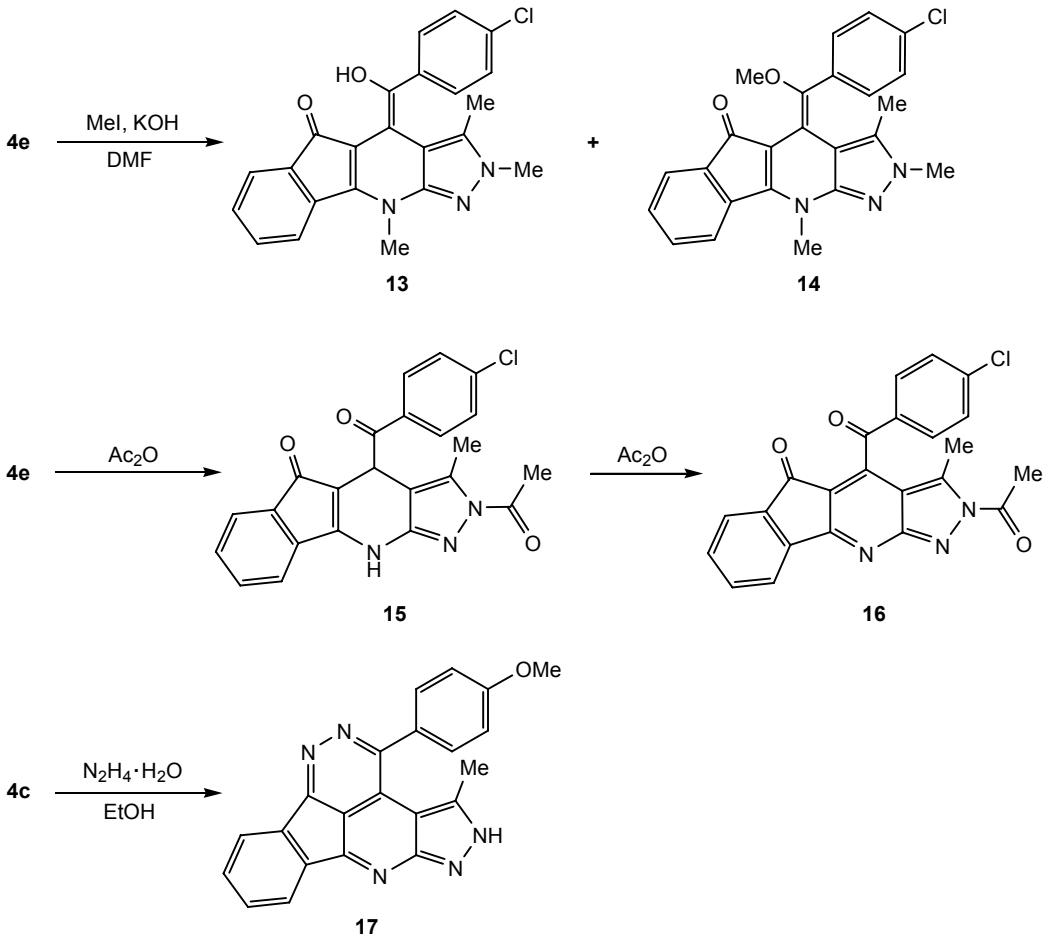


11c

Molecular structure of compounds **11a** and **11c** according to XRD data.

Both molecules have similar geometry, bond lengths and bond angles have close values. Structure **11c** consists of three fragments: chlorobenzoyl $Cl^1O^1C^{18–24}$ (A) planar within 0.009 Å, tetracyclic $N^1N^2N^{10}C^{3–10A}$ (B) planar within 0.022 Å, and phenyl $C^{11–16}$ (C) planar within 0.022 Å. The angles between

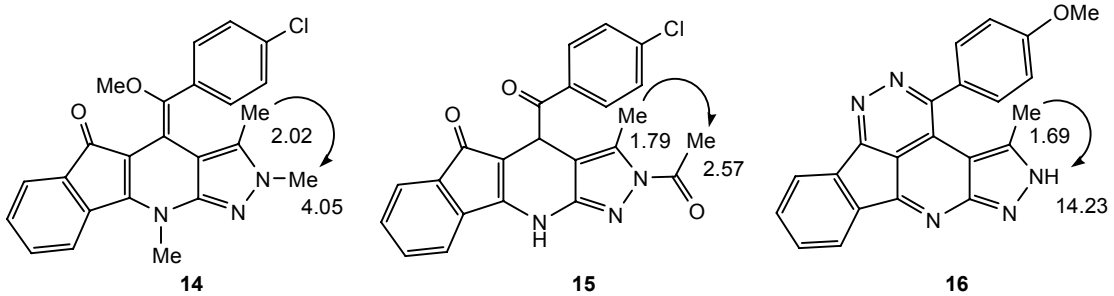
Scheme 3.



the mean square planes of the fragments are as follows: A and B 80.43(8), B and C 1.83(9) deg. In molecule **11a** the position of fragment A takes the methylbenzoyl substituent D ($C^{18–25}$), planar within 0.014 Å; fragments B and C in this molecule are also planar within 0.029 and 0.010 Å respectively. The angle between planes D and B is 83.11(3), between B and C is 30.49(6) deg. The main difference consists in the rotation of the phenyl ring at the atom N^1 in the molecule **11a** with respect to the tetracyclic scaffold by a significantly larger angle than in the molecule **11c**.

Therefore the structure of indeno[1,2-*b*]pyrazolo-[4,3-*e*]pyridin-5(2*H*)-ones **4**, **5**, and **11** corresponds to the interaction of the atom C^4 in the molecules of aminopyrazoles **1** and **9** with the β-carbon atom, and of the exocyclic amino group with the carbonyl group of the enone formed as a result of arylglyoxal condensation with indanedione.

The presence in the composition of compounds **4** of imino groups, aroyl, and indanone fragments makes it possible to subject them to chemical modification. We studied the reactions of dihydro derivatives **4e**



and **4c** with reagents of diverse electronic nature (Scheme 3).

The alkylation of dihydroindeno[1,2-*b*]pyrazolo-[4,3-*e*]pyridin-5-one **4e** with a triple excess of methyl iodide led to the formation of a mixture of tri- (**13**) and tetramethyl (**14**) derivatives in the ratio ~3 : 2, that was easily separated by recrystallization. In the formation of compound **14** besides the atoms N^2 and N^{10} an additional site of the electrophilic attack was the hydroxy group which appeared in compound **4e** due to enolization. At the same time the acylation occurred only at the NH group of the pyrazole ring resulting in compound **15** whose further heating in acetic anhydride gave heteroaromatic derivative **16**. The heteroaromatization of the pyridine ring is confirmed by the absence in the ^{1}H NMR spectrum of compound **14** proton singlets from C^4H and N^{10}H. The position of substituents in compounds **13–16** was established from NOE experiments. The change in the resonance conditions of the C^3Me fragment finds a response from the N^2Me in the spectra of compounds **13** and **14** and of acetyl group in the spectra of derivatives **15** and **16**.

The reaction of compound **4c** with hydrazine hydrate in ethanol results in the formation of a new pentaazacyclopenta[*b*]fluoranthene system **17**. The ^{1}H NMR spectrum of this compound lacks the proton singlets of CH and NH fragments of a pyridine ring, and the singlet of the NH proton of the pyrazole ring appears at 14.23 ppm (it is shifted by ~2 ppm as compared to the spectrum of initial compound **4c**) indicating the heteroaromatic character of the formed fused pentacyclic system **17**. The existence of compound **17** in the tautomeric form N^2H was established from the data of the NOE experiment. The change in the resonance conditions of the C^4Me fragment causes the response of the NH proton of the pyrazole ring.

EXPERIMENTAL

IR spectra were recorded on a spectrometer Perkin Elmer Spectrum One FTIR from pellets with KBr. ^{1}H NMR spectra were registered on a spectrometer Varian Mercury VX-200 (200 MHz) from solutions in DMSO-d_6, internal reference TMS. Mass spectra were obtained on a mass spectrometer Varian 1200 L (EI, 70 eV). Elemental analysis was carried out on analyzer EA-3000 Eurovektor. Melting points were measured on a Koeffler heating block. The reaction progress was monitored and the purity of compounds synthesized was checked by TLC on DC-Fertigfolien ALUGRAM Xtra SIL G/UV_{254} plates, eluents toluene–EtOAc, 2 : 1 and 4 : 1.

4-Benzoyl-3-methyl-4,10-dihydroindeno[1,2-*b*]-pyrazolo[4,3-*e*]pyridin-5(2*H*)-one (4a). A mixture of 0.19 g (2 mmol) of 3-methyl-5-aminopyrazole **1**, 0.30 g (2 mmol) of arylglyoxal **2a**, and 0.29 g (2 mmol) of indane-1,3-dione **3** in 10–12 mL of ethanol was boiled for 1 h. The bright orange precipitate formed on cooling was filtered off and purified by crystallization from ethanol. Yield 0.48 g (70%), mp 272–274°C. IR spectrum, ν, cm^{-1}: 3187 (NH), 1672 (CO). ^{1}H NMR spectrum, δ, ppm: 1.81 s (3H, 3-Me), 5.44 s (1H, C^4H), 7.19 d (1H, C^9H, *J* 6.6 Hz), 7.28–7.67 m (6H, C^6H + C^7H + C^8H + $H^{p,m}_{Ar}$), 7.97 d (2H, H^o_{Ar}, *J* 6.8 Hz), 11.38 br.s (1H, N^{10}H), 12.20 br.s (1H, N^2H). Found, %: C 73.77; H 4.33; N 12.27. $C_{21}H_{15}N_3O_2$. Calculated, %: C 73.89; H 4.43; N 12.31.

Compounds **4b–4f** were synthesized similarly.

3-Methyl-4-(4-methylbenzoyl)-4,10-dihydroindeno[1,2-*b*]pyrazolo[4,3-*e*]pyridin-5(2*H*)-one (4b). Yield 0.39 g (55%), bright orange amorphous powder, mp 270–272°C. IR spectrum, ν, cm^{-1}: 3234 (NH), 1660 (CO). ^{1}H NMR spectrum, δ, ppm: 1.81 s (3H, 3-Me), 2.31 s (3H, Me_{tolyl}), 5.40 s (1H, C^4H), 7.17–7.43 m (5H, C^7H + C^8H + C^9H + H^m_{Ar}), 7.64 d (1H, C^6H, *J* 6.6 Hz), d 7.88 (2H, H^o_{Ar}, *J* 7.8 Hz), 11.37 br.s (1H, N^{10}H), 12.19 br.s (1H, N^2H). Found, %: C 74.30; H 4.88; N 11.91. $C_{22}H_{17}N_3O_2$. Calculated, %: C 74.35; H 4.82; N 11.82.

3-Methyl-4-(4-methoxybenzoyl)-4,10-dihydroindeno[1,2-*b*]pyrazolo[4,3-*e*]pyridin-5(2*H*)-one (4c). Yield 0.51 g (69%), bright orange amorphous powder, mp 235–237°C. IR spectrum, ν, cm^{-1}: 3232 (NH), 1643 (CO). ^{1}H NMR spectrum, δ, ppm: 1.83 s (3H, 3-Me), 3.79 s (3H, OMe), 5.40 s (1H, C^4H), 6.98 d (2H, H^m_{Ar}, *J* 8.6 Hz), 7.17–7.43 m (3H, C^7H + C^8H + C^9H), 7.64 d (1H, C^6H, *J* 6.4 Hz), 7.99 d (2H, H^o_{Ar}, *J* 8.4 Hz), 11.35 br.s (1H, N^{10}H), 12.18 br.s (1H, N^2H). Mass spectrum, *m/z* (I_{rel}, %): 372 (10) $[M+1]^+$, 371 (19) $[M]^+$, 370 (9) $[M-1]^+$, 236 (100), 235 (13), 165 (11), 151 (12), 136 (12), 135 (11), 107 (13), 77 (37). Found, %: C 71.26; H 4.65; N 11.40. $C_{22}H_{17}N_3O_3$. Calculated, %: C 71.15; H 4.61; N 11.31.

3-Methyl-4-(4-fluorobenzoyl)-4,10-dihydroindeno[1,2-*b*]pyrazolo[4,3-*e*]pyridin-5(*2H*)-one (4d). Yield 0.41 g (57%), orange amorphous powder, mp 245–247°C. IR spectrum, ν, cm^{-1}: 3233 (NH), 1669

(CO). ^{1}H NMR spectrum, δ, ppm: 1.82 s (3H, 3-Me), 5.45 s (1H, C^4H), 7.18–7.43 m (5H, $C^7H + C^8H + C^9H + Ar^m$), 7.65 d (1H, C^6H, *J* 6.6 Hz), 7.99–8.10 d.d (2H, Ar^o, *J* 8.6, 5.8 Hz), 11.38 br.s (1H, $N^{10}H$), 12.20 br.s (1H, N^2H). ^{1}H NMR spectrum (DMSO-d_6 + D_2O), δ, ppm: 1.78 s (3H, 3-Me), 5.43 s (1H, C^4H), 7.17–7.42 m (5H, $C^7H + C^8H + C^9H + H^m_{Ar}$), 7.59 d (1H, C^6H, *J* 6.6 Hz), 8.01–8.09 d.d (2H, H^o_{Ar}, *J* 8.6, 5.4 Hz). Mass spectrum, *m/z* (I_{rel}, %): 359 (10) $[M]^+$, 358 (9) $[M-1]^+$, 357 (20) $[M-2]^+$, 328 (12), 236 (100), 123 (24), 91 (19), 76 (10). Found, %: C 70.28; H 3.95; N 11.80. $C_{21}H_{14}FN_3O_2$. Calculated, %: C 70.19; H 3.93; N 11.69.

3-Methyl-4-(4-chlorobenzoyl)-4,10-dihydroindeno[1,2-*b*]pyrazolo[4,3-*e*]pyridin-5(2*H*)-one (4e). Yield 0.49 g (65%), dark orange amorphous powder, mp 262–264°C. IR spectrum, ν, cm^{-1}: 3235 (NH), 1669 (CO). ^{1}H NMR spectrum, δ, ppm: 1.84 s (3H, 3-Me), 5.43 s (1H, C^4H), 7.19 d (1H, C^9H, *J* 6.8 Hz), 7.26–7.44 m (2H, $C^7H + C^8H$), 7.52–7.67 m (3H, $C^6H + H^m_{Ar}$), 7.98 d (2H, H^o_{Ar}, *J* 8.4 Hz), 11.40 br.s (1H, $N^{10}H$), 12.23 br.s (1H, N^2H). Found, %: C 67.20; H 3.69; N 11.22. $C_{21}H_{14}ClN_3O_2$. Calculated, %: C 67.12; H 3.75; N 11.18.

4-(4-Bromobenzoyl)-3-methyl-4,10-dihydroindeno[1,2-*b*]pyrazolo[4,3-*e*]pyridin-5(2*H*)-one (4f). Yield 0.47 g (56%), red amorphous powder, mp 297–299°C. IR spectrum, ν, cm^{-1}: 3244 (NH), 1660 (CO). ^{1}H NMR spectrum, δ, ppm: 1.84 s (3H, 3-Me), 5.42 s (1H, C^4H), 7.18 d (1H, C^9H, *J* 6.8 Hz), 7.29–7.43 m (2H, $C^7H + C^8H$), 7.63–7.71 m (3H, $C^6H + H^m_{Ar}$), 7.90 d (2H, H^o_{Ar}, *J* 8.2 Hz), 11.42 br.s (1H, $N^{10}H$), 12.24 br.s (1H, N^2H). Found, %: C 59.96; H 3.38; N 10.11. $C_{21}H_{14}BrN_3O_2$. Calculated, %: C 60.02; H 3.36; N 10.00.

3-Methyl-4-(4-methylbenzoyl)indeno[1,2-*b*]pyrazolo[4,3-*e*]pyridin-5(2*H*)-one (5a). A mixture of 0.36 g (1 mmol) of compound **4b** and 0.12 g (2 mmol) of potassium hydroxide in 12 mL of 2-propanol was stirred for 5 h. The reaction mixture was diluted with 60 mL of water, neutralized with HCl (1 : 1) water solution till pH ~7. Light yellow precipitate was filtered off, washed twice with water on the filter, and crystallized from ethanol. Yield 0.18 g (52%), light yellow amorphous powder, mp 348–350°C. ^{1}H NMR spectrum, δ, ppm: 2.01 s (3H, 3-Me), 2.36 s (3H, Me_{tolyl}), 7.32 d (2H, H^m_{Ar}, *J* 8.0 Hz), 7.49–7.93 m (6H, $C^6H + C^7H + C^8H + C^9H + H^o_{Ar}$), 13.77 br.s (1H, $N^{10}H$). ^{1}H NMR spectrum (DMSO-d_6 + D_2O), δ, ppm: 2.00 s (3H, 3-Me), 2.35 s (3H, Me_{tolyl}), 7.33 d (2H, H^m_{Ar}, *J* 7.8 Hz), 7.48–7.94 m (6H, $C^6H + C^7H + C^8H + C^9H + H^o_{Ar}$). Mass spectrum, *m/z* (I_{rel}, %): 354 (10) $[M+1]^+$, 353 (23) $[M]^+$, 338 (32), 324 (10), 310 (31), 236 (12), 235 (100), 234 (52), 206 (11), 165 (10), 119 (29), 91 (36), 65 (27). Found, %: C 74.85; H 4.38; N 12.01. $C_{22}H_{15}N_3O_2$. Calculated, %: C 74.78; H 4.28; N 11.89.

Compound **5b** was synthesized similarly.

3-Methyl-4-(4-methoxybenzoyl)indeno[1,2-*b*]pyrazolo[4,3-*e*]pyridin-5(2*H*)-one (5b). Yield 0.25 g (68%), light yellow amorphous powder, mp 336–338°C. ^{1}H NMR spectrum, δ, ppm: 2.02 s (3H, 3-Me), 3.82 s (3H, OMe), 7.02 d (2H, H^m_{Ar}, *J* 8.8 Hz), 7.47–7.92 m (6H, $C^6H + C^7H + C^8H + C^9H + H^o_{Ar}$), 13.75 br.s (1H, $N^{10}H$). ^{1}H NMR spectrum (DMSO-d_6 + D_2O), δ, ppm: 1.99 s (3H, 3-Me), 3.81 s (3H, OMe), 7.02 d (2H, H^m_{Ar}, *J* 8.8 Hz), 7.43–7.91 m (6H, $C^6H + C^7H + C^8H + C^9H + H^o_{Ar}$). Mass spectrum, *m/z* (I_{rel}, %): 369 (24) $[M]^+$, 236 (11), 235 (95), 234 (60), 206 (9), 165 (10), 136 (10), 135 (100), 107 (10), 77 (20). Found, %: C 71.63; H 4.18; N 11.31. $C_{22}H_{15}N_3O_3$. Calculated, %: C 71.54; H 4.09; N 11.38.

2-[1-(5-Amino-3-methyl-1-phenyl-1*H*-pyrazol-4-yl)-2-oxo-2-(*p*-tolyl)ethyl]-1*H*-indene-1,3(2*H*)-dione (10a). A mixture of 0.35 g (2 mmol) of 3-methyl-1-phenylpyrazol-5-amine **9**, 0.33 g (2 mmol) of arylglyoxal **2b**, and 0.29 g (2 mmol) of indane-1,3-dione **3** in 10 mL of ethanol was heated at 60–65°C for 15 min. The formed precipitate was filtered off and twice washed with ethanol on the filter. Yield 0.76 g (85%), white amorphous powder, mp 165–167°C. IR spectrum, ν, cm^{-1}: 3406, 3330 (NH_2), 1706, 1669 (CO). ^{1}H NMR spectrum, δ, ppm: 1.83 s (3H, 3-Me), 2.29 s (3H, Me_{tolyl}), 3.78 d (1H, C<u>H</u>COAr, *J* 4.0 Hz), 5.23 br.s (2H, NH_2), 5.42 d (1H, CH_{indene}, *J* 3.8 Hz), 7.20–7.29 m (3H, $Ph^p + H^m_{Ar}$), 7.39–7.52 m (4H, $H^{m,o}_{Ph}$), 7.72 d (2H, H^o_{Ar}, *J* 7.8 Hz), 7.91–7.97 m (4H, $C^4H + C^5H + C^6H + C^7H$). ^{1}H NMR spectrum (DMSO-d_6 + D_2O), δ, ppm: 1.82 s (3H, 3-Me), 2.23 s (3H, Me_{tolyl}), 5.36 s (1H, CH_{indene}), 7.18–7.52 m (7H, $H_{Ph} + H^m_{Ar}$), 7.68 d (2H, H^o_{Ar}, *J* 7.6 Hz), 7.89–7.96 m (4H, $C^4H + C^5H + C^6H + C^7H$). Found, %: C 74.90; H 5.23; N 9.28. $C_{28}H_{23}N_3O_3$. Calculated, %: C 74.82; H 5.16; N 9.35.

Compounds **10b–10d** were synthesized similarly.

2-[1-(5-Amino-3-methyl-1-phenyl-1*H*-pyrazol-4-yl)-2-(4-methoxy-phenyl)-2-oxoethyl]-1*H*-indene-1,3(2*H*)-dione (10b). Yield 0.59 g (64%), white amorphous powder, mp 150–152°C. ^{1}H NMR spec-

trum, δ, ppm: 1.83 s (3H, 3-Me), 3.73–3.79 m (4H, CHCOAr + OMe), 5.21 br.s (2H, NH_2), 5.40 d (1H, CH_{indene}, *J* 4.2 Hz), 6.94 d (2H, H^{m}_{Ar}, *J* 8.6 Hz), 7.23 t (1H, H^{p}_{Ph}, *J* 6.6 Hz), 7.40–7.51 m (4H, $H^{m,o}_{Ph}$), 7.79 d (2H, H^{o}_{Ar}, *J* 8.4 Hz), 7.90–7.97 m (4H, C^4H + C^5H + C^6H + C^7H). Found, %: C 72.31; H 5.05; N 8.95. $C_{28}H_{23}N_3O_4$. Calculated, %: C 72.24; H 4.98; N 9.03.

2-[1-(5-Amino-3-methyl-1-phenyl-1*H*-pyrazol-4-yl)-2-(4-chlorophenyl)-2-oxoethyl]-1*H*-indene-1,3(2*H*)-dione (10c). Yield 0.50 g (53%), white amorphous powder, mp 164–166°C. IR spectrum, ν, cm^{-1}: 3408, 3328 (NH_2), 1704, 1675 (CO). ^1H NMR spectrum, δ, ppm: 1.86 s (3H, 3-Me), 3.88 d (1H, CHCOAr, *J* 4.4 Hz), 5.24 br.s (2H, NH_2), 5.43 d (1H, CH_{indene}, *J* 4.2 Hz), 7.22–7.58 m (7H, H_{Ph} + H^{m}_{Ar}), 7.80–7.98 m (6H, H^{o}_{Ar} + C^4H + C^5H + C^6H + C^7H). Found, %: C.12; H 4.20; N 8.98. $C_{27}H_{20}ClN_3O_3$. Calculated, %: C 69.01; H 4.29; N 8.94.

2-[1-(5-Amino-3-methyl-1-phenyl-1*H*-pyrazol-4-yl)-2-(4-bromophenyl)-2-oxoethyl]-1*H*-indene-1,3(2*H*)-dione (10d). Yield 0.56 g (55%), white amorphous powder, mp 160–162°C. IR spectrum, ν, cm^{-1}: 3408, 3330 (NH_2), 1704, 1677 (CO). ^1H NMR spectrum, δ, ppm: 1.86 s (3H, 3-Me), 3.88 d (1H, CHCOAr, *J* 4.0 Hz), 5.24 br.s (2H, NH_2), 5.42 d (1H, CH_{indene}, *J* 3.8 Hz), 7.23–7.30 m (1H, Ph^{p}), 7.39–7.51 m (4H, $H^{m,o}_{Ph}$), 7.65 d (2H, H^{m}_{Ar}, *J* 8.2 Hz), 7.77 d (2H, H^{o}_{Ar}, *J* 8.4 Hz), 7.89–8.00 m (4H, C^4H + C^5H + C^6H + C^7H). Found, %: C 63.13; H 4.00; N 8.23. $C_{27}H_{20}BrN_3O_3$. Calculated, %: C 63.05; H 3.92; N 8.17.

3-Methyl-4-(4-methylbenzoyl)-1-phenylindeno[1,2-*b*]pyrazolo[4,3-*e*]pyridin-5(1*H*)-one (11a). A solution of 1 mmol of compound **10a** in 10 mL of 2-propanol was boiled for 2 h. The formed precipitate was filtered off, twice washed with 2-propanol on the filter, and crystallized from ethanol. Yield 0.33 g (78%), light yellow amorphous powder, mp 245–247°C. IR spectrum, ν, cm^{-1}: 1711, 1669 (CO). ^1H NMR spectrum, δ, ppm: 2.10 s (3H, 3-Me), 2.39 s (3H, Me_{tolyl}), 7.32–7.45 m (3H, H^{p}_{Ph} + H^{m}_{Ar}), 7.54–7.65 m (4H, $H^{m,o}_{Ph}$), 7.72–7.87 m (3H, C^7H + C^8H + C^9H), 7.99 d (1H, C^6H, *J* 7.2 Hz), 8.24 d (2H, H^{o}_{Ar}, *J* 7.8 Hz). Found, %: C 78.30; H 4.53; N 9.83. $C_{28}H_{19}N_3O_2$. Calculated, %: C 78.31; H 4.46; N 9.78.

Compounds **11b–11d** were synthesized similarly.

4-(4-Methoxybenzoyl)-3-methyl-1-phenylindeno[1,2-*b*]pyrazolo[4,3-*e*]pyridin-5(1*H*)-one (11b). Yield 0.28 g (62%), light yellow amorphous powder, mp 345–347°C. IR spectrum, ν, cm^{-1}: 1708, 1660 (CO). ^1H NMR spectrum, δ, ppm: 2.11 s (3H, 3-Me), 3.84 s (3H, OMe), 7.05 d (2H, H^{m}_{Ar}, *J* 8.2 Hz), 7.40 t (1H, H^{p}_{Ph}, *J* 6.8 Hz), 7.55–7.65 m (4H, $H^{m,o}_{Ph}$), 7.75 t (1H, C^7H, *J* 6.8 Hz), 7.87–8.00 m (3H, C^6H + C^8H + C^9H), 8.23 d (2H, H^{o}_{Ar}, *J* 8.0 Hz). Found, %: C 75.61; H 4.25; N 9.51. $C_{28}H_{19}N_3O_3$. Calculated, %: C 75.49; H 4.30; N 9.43.

4-(4-Chlorobenzoyl)-3-methyl-1-phenylindeno[1,2-*b*]pyrazolo[4,3-*e*]pyridin-5(1*H*)-one (11c). Yield 0.23 g (51%), light yellow amorphous powder, mp 338–340°C. IR spectrum, δ, cm^{-1}: 1708, 1674 (CO). ^1H NMR spectrum, δ, ppm: 2.14 s (3H, 3-Me), 7.40 t (1H, H^{p}_{Ph}, *J* 7.2 Hz), 7.53–7.67 m (6H, $H^{m,o}_{Ph}$ + H^{m}_{Ar}), 7.75 t (1H, C^7H, *J* 6.2 Hz), 7.92–8.02 m (3H, C^6H + C^8H + C^9H), 8.24 d (2H, H^{o}_{Ar}, *J* 7.6 Hz). Found, %: C 72.16; H 3.65; N 9.42. $C_{27}H_{16}ClN_3O_2$. Calculated, %: C 72.08; H 3.58; N 9.34.

4-(4-Bromobenzoyl)-3-methyl-1-phenylindeno[1,2-*b*]pyrazolo[4,3-*e*]pyridin-5(1*H*)-one (11d). Yield 0.26 g (53%), light yellow amorphous powder, mp 262–264°C. IR spectrum, ν, cm^{-1}: 1717, 1670 (CO). ^1H NMR spectrum, δ, ppm: 2.11 s (3H, 3-Me), 7.39 t (1H, H^{p}_{Ph}, *J* 7.2 Hz), 7.54–7.63 m (4H, $H^{m,o}_{Ph}$), 7.71–7.79 m (3H, H^{m}_{Ar} + C^7H), 7.86–7.98 m (3H, C^6H + C^8H + C^9H), 8.22 d (2H, H^{o}_{Ar}, *J* 7.8 Hz). Mass spectrum, *m/z* (I_{rel}, %): 495/493 (7/7) $[M]^+$, 387/385 (5/5), 310 (5), 185/185 (23/25), 157/155 (24/22), 106 (12), 77 (30), 43 (100). Found, %: C 65.52; H 3.29; N 8.44. $C_{27}H_{16}BrN_3O_2$. Calculated, %: C 65.60; H 3.26; N 8.50.

4-[(4-Chlorophenyl)(hydroxy)methylene]-2,3,10-trimethyl-4,10-dihydroindeno[1,2-*b*]pyrazolo[4,3-*e*]-pyridin-5(2*H*)-one (13) and 4-[(4-chlorophenyl)-(methoxy)methylene]-2,3,10-trimethyl-4,10-dihydroindeno[1,2-*b*]pyrazolo[4,3-*e*]pyridin-5(2*H*)-one (14). A mixture of 0.38 g (1 mmol) of compound **4e**, 0.18 g (3.2 mmol) of potassium hydroxide, and 0.20 mL (3.1 mmol) of methyl iodide in 5 mL of DMF was stirred for 5 h, diluted with 30 mL of water, and neutralized with HCl solution till pH ~7. The orange precipitate was filtered off and washed with ethanol on the filter. The mixture of compounds **13** and **14** was separated by crystallization from ethyl acetate.

Compound 13. Yield 0.18 g (45%), bright orange amorphous powder, mp 330–332°C. ^1H NMR spectrum, δ, ppm: 2.31 s (3H, 3-Me), 4.15 s (3H, N^2Me), 4.65 s (3H, $N^{10}Me$), 7.68 d (2H, H^{m}_{Ar}, *J* 6.6 Hz), 7.87–8.05 m (5H, H^{o}_{Ar} + C^6H + C^7H + C^8H), 8.52 d (2H, C^9H, *J* 7.5 Hz),

the signal of OH group is absent because of intermolecular exchange. Found, %: C 68.32; H 4.39; N 10.47. $C_{23}H_{18}ClN_3O_2$. Calculated, %: C 68.40; H 4.49; N 10.40.

Compound 14. Yield 0.12 g (30%), yellow powder, mp 250–252°C. ^{1}H NMR spectrum, δ, ppm: 2.02 s (3H, 3-Me), 2.91 s (3H, N^{10}Me), 3.95 s (3H, OMe), 4.05 s (3H, N^{2}Me), 7.59 d (2H, H$^m_{Ar}$, *J* 6.8 Hz), 7.76–7.98 m (5H, H$^o_{Ar}$ + C^{6}H + C^{7}H + C^{8}H), 8.17 d (2H, C^{9}H, *J* 8.0 Hz). Found, %: C 70.06; H 4.88; N 10.01. $C_{24}H_{20}ClN_3O_2$. Calculated, %: C 68.98; H 4.82; N 10.06.

2-Acetyl-3-methyl-4-(4-chlorobenzoyl)-4,10-dihydroindeno[1,2-*b*]pyrazolo[4,3-*e*]pyridin-5(2*H*)-one (15). A solution of 0.38 g (1 mmol) of compound **4e** in 5 mL of acetic anhydride was heated for 2 h at 110°C. On cooling the solution the light orange precipitate was filtered off and crystallized from methanol. Yield 0.30 g (73%), mp 232–234°C. IR spectrum, ν, cm^{-1}: 1728, 1675, 1632 (CO). ^{1}H NMR spectrum, δ, ppm: 1.79 s (3H, 3-Me), 2.57 s [1H, C(O)Me], 5.69 s (1H, C^{4}H), 7.19–7.46 m (3H, C^{7}H + C^{8}H + C^{9}H), 7.62 d (2H, H$^m_{Ar}$, *J* 8.0 Hz), 7.89 d (1H, C^{6}H, *J* 7.4 Hz), 8.15 d (2H, H$^o_{Ar}$, *J* 8.2 Hz), 10.51 br.s (1H, N^{10}H). Found, %: C 66.19; H 3.92; N 10.12. $C_{23}H_{16}ClN_3O_3$. Calculated, %: C 66.11; H 3.86; N 10.06.

2-Acetyl-3-methyl-4-(4-chlorobenzoyl)indene-[1,2-*b*]pyrazolo[4,3-*e*]pyridin-5(2*H*)-one (16). A solution of 0.38 g (1 mmol) of compound **4e** in 5 mL of acetic anhydride was heated for 6 h at 110°C. On cooling the solution was diluted with 50 mL of water, the light yellow precipitate was filtered off and crystallized from ethanol. Yield 0.27 g (64%), mp 305–307°C. ^{1}H NMR spectrum, δ, ppm: 2.11 s (3H, 3-Me), 2.85 s [3H, C(O)Me], 7.53–7.65 m (4H, H$^m_{Ar}$ + C^{8}H + C^{9}H), 7.76 t (1H, C^{7}H, *J* 7.4 Hz), 7.89–7.99 m (3H, H$^o_{Ar}$ + C^{6}H). Found, %: C 66.49; H 3.45; N 10.02. $C_{23}H_{14}ClN_3O_3$. Calculated, %: C 66.43; H 3.39; N 10.11.

4-Methyl-1-[3-(4-methoxyphenyl)-5*H*-1,2,5,6,7-pentazacyclopenta[*b*]fluoranthen-5-yl]ethanone (17). To a solution of 0.37 g (1 mmol) of compound **4c** in 8–10 mL of ethanol was added 0.15 mL of hydrazine hydrate, and the mixture was boiled for 8 h. The yellow amorphous precipitate formed on cooling the reaction mixture was filtered off and crystallized from ethanol. Yield 0.19 g (52%), yellow amorphous powder, mp 350–352°C. IR spectrum, ν, cm^{-1}: 3435 (NH), 1609, 1575 (C=N). ^{1}H NMR spectrum, δ, ppm: 1.69 s (3H, 3-Me), 3.86 s (3H, OMe), 7.15 d (2H, H$^m_{Ar}$, *J* 8.8 Hz), 7.59–7.66 m (4H, H$^o_{Ar}$ + C^{9}H + C^{10}H), 8.02–8.14 m (2H, C^{8}H + C^{11}H), 14.23 br.s (1H, NH). Mass spectrum, *m/z* (I_{rel}, %): 366 (25) $[M + 1]^+$, 365 (100) $[M]^+$, 364 (74) $[M - 1]^+$, 334 (30), 294 (11), 264 (10), 169 (10), 135 (31), 92 (18), 76 (12). Found, %: C 72.25; H 4.22; N 19.09. $C_{22}H_{15}N_5O$. Calculated, %: C 72.32; H 4.14; N 19.17.

X-ray diffraction analysis of compounds 11a and 11c. Crystals of compound **11a** ($C_{28}H_{19}N_3O_2$, *M* 429.46) triclinic, at 20°C: *a* 7.7172(8), *b* 11.5490(12), *c* 13.3281(12) Å; β 98.216(8)°, *V* 1072.42(18) Å^3; *Z* 2; space group $P\bar{1}$; d_{calc} 1.330 g/cm^3; μ(MoK_α) 0.085 mm^{-1}; *F*(000) 448. Parameters of the unit cell and intensities of 7492 reflections (4162 independent, R_{int} 0.0322) were measured on a diffractometer Xcalibur-3 (MoK_α radiation, CCD-detector, graphite monochromator).

Crystals of compound **11c** ($C_{27}H_{16}ClN_3O_2$, *M* 449.88) rhombic, at 20°C: *a* 12.310(2), *b* 7.2600(15), *c* 46.356(9) Å; β 93.547(18)°, *V* 4135.0(13) Å^3; *Z* 8; space group *C*2/*c*; d_{calc} 1.445 g/cm^3; μ(MoK_α) 0.217 mm^{-1}; *F*(000) 1856. Parameters of the unit cell and intensities of 9060 reflections (3387 independent, R_{int} 0.128) were measured on a diffractometer Xcalibur-3 (MoK_α radiation, CCD-detector, graphite monochromator).

The structures were solved by the direct method applying software SHELX-97 [25]. The positions of hydrogen atoms were found from the Fourier difference synthesis of the electron density and were refined in the *rider* model with $U_{iso} = nU_{eq}$ of the nonhydrogen atom bound to this hydrogen (n = 1.5 for the methyl groups, n = 1.2 for the other hydrogen atoms). The structures were refined with respect to F^2 by the full-matrix least-squares method in the anisotropic approximation for the nonhydrogen atoms till wR_2 0.0485 for 4162 reflections (R_1 0.0467, *S* 0.986) of compound **11a**; wR_2 0.0874 for 3887 reflections (R_1 0.0563, *S* 0.974) of compound **11c**. Atomic coordinates and complete tables of bond lengths and bond angles are deposited in the Cambridge Crystallographic Data Center [CCDC 1400509 (**11a**), 1400510 (**11c**)] (e-mail: deposit@ccdc.cam.ac.uk).

REFERENCES

1. De Almeida, M.E.I., Braz, F.R., von Bülow, M.V., Gottleib, O.R., and Maia, J.G.S., *Phytochem*., 1976, vol. 15, p. 1186.

2. Prostakov, N.S., Matthew, C.J., and Kurichev, V.A., *Chem. Heterocycl. Compd*., 1967, vol. 3, p. 692.
3. Prostakov, N.S., Soldatenkov, A.T., and Fedorov, V.O., *Chem. Heterocycl. Compd*., 1979, vol. 15, p. 902.
4. Safak, C., Simsek, R., Altas, Y., Boydag, S., and Erol, K., *Bull. Chim. Farm*., 1997, vol. 136, p. 665.
5. Heintzelman, G.R., Averill, K.M., Dodd, J.H., Demarest, K.T., Tang, Y., and Jackson, P.F., WO Patent Appl. no. 2003088963, 2002; *Chem. Abstr*., 2003, vol. 139, no. 350637.
6. Heintzelman, G.R., Averill, K.M., Dodd, J.H., Demarest, K.T., Tang, Y., and Jackson, P.F., US Patent no. 2004082578, 2003; *Chem. Abstr*., 2004, vol. 140, no. 375085.
7. Kunstmann, R. and Fischer, G., *J. Med. Chem*., 1984, vol. 27, p. 1312.
8. Van Emelen, K., De Wit, T., Hoornaert, G.J., and Compernolle, F., *Tetrahedron*, 2002, vol. 58, p. 4225.
9. El-Ossaily, Y.A., *Phosphorus, Sulfur Silicon Relat. Elem*., 2007, vol. 182, p. 1109.
10. Miri, R., Javidnia, K., Hemmateenejad, B., Azarpira, A., and Amirghofran, Z., *Bioorg. Med. Chem*., 2004, vol. 12, p. 2529.
11. Manpadi, M., Uglinskii, P.Y., Rastogi, S.K., Cotter, K.M., Wong, Y-S.C, Anderson, L.A., Ortega, A.J., Van Slambrouck, S., Steelant, W.F.A., Rogelj, S., Tongwa, P., Antipin, M.Yu., Magedov, I.V., and Kornienko, A., *Org. Biomol. Chem*., 2007, vol. 5, p. 3865.
12. Nagarajan, M., Morrell, A., Fort, B.C., Meckely, M.R., Antony, S., Kohlhagen, G., Pommier, Y., and Cushman, M., *J. Med. Chem*., 2004, vol. 47, p. 5651.
13. Magedov, I.V., Manpadi, M., Van Slambrouck, S., Steelant, W.F.A., Rozhkova, E., Przheval'skii, N.M., Rogelj, S., and Kornienko, A., *J. Med. Chem*., 2007, vol. 50, p. 5183.
14. Prostakov, N.S., Soldatenkov, A.T., Radzhan, P.K., Fedorov, V.O., Fomichev, A.A., and Rezakov, V.A., *Chem. Heterocycl. Compd*., 1982, vol. 18, p. 390.
15. Zhang, J., El-Shabrawy, O., El-Shabrawy, M.A., Schiff, P.L. Jr., and Slatkin, D.J., *J. Nat. Prod*., 1987, vol. 50, p. 800.
16. Elmaati, T.M., Said, S.B., Elenein, N.S.A., Khodeir, N.M., and Sofan, M.M., *J. Heterocycl. Chem*., 2003, vol. 40, p. 481.
17. Koyama, J., Okatani, T., and Tagahara, K., *Heterocycles*, 1989, vol. 29, p. 1648.
18. Nitta, M., Ohnuma, M., and Lino, Y., *J. Chem. Soc., Perkin Trans. 1*, 1991, p. 1115.
19. Shi, C.-L., Shi, D.-Q., Kim, S.H., Huang, Z.-B., Ji, Sh.-J., and Ji, M., *Tetrahedron*, 2008, vol. 64, p. 2425.
20. Shi, D.-Q., Yang, F., and Ni, S.-N., *J. Heterocycl. Chem*., 2009, vol. 46, p. 469.
21. Quiroga, J., Cobo, D., Insuasty, B., Abonía, R., Cruz, S., Nogueras, M., and Cobo, J., *J. Heterocycl. Chem*., 2008, vol. 45, p. 155.
22. Shi, F., Zhang, Y., Tu, S.-J., Zhou, D.-X., Li, C.-M., Shao, Q.-Q., and Cao, L.-J., *Chin. J. Chem*., 2008, vol. 26, p. 1262.
23. Ryabukhin, S.V., Plaskon, A.S., Boron, S.Yu., Volochnyuk, D.M., and Tolmachev, A.A., *Mol. Div*., 2011, vol. 15, p. 189.
24. Rana, S., Brown, M., and Mukhopadhyay, C., *RSC Adv*., 2013, vol. 3, p. 3291.
25. Sheldrick, M., *Acta Crystallogr., Sect. A*, 2008, vol. 64, p. 112.